

ABSTRACTS / RESÚMENES

<u>LUNES 13 DE DICIEMBRE / MONDAY, DECEMBER 13</u> <u>INAUGURAL PLENARY LECTURES / CONFERENCIAS PLENARIAS INAUGURALES</u>	
PL-01	<p>THE CONCURRENT CHALLENGES OF EFFECTIVENESS RESEARCH AND INDIVIDUALIZED THERAPEUTIC STRATEGIES <u>Gianni Tognoni</u></p> <p>South Institute for Pharmacological Research, Santa María Imbaro, Chiety, Italy. email: tognoni@negrisud.it</p> <p>The proposal of focusing the attention on the two apparent extremes of care (on one side the public health relevance and transferability of the paradigm of EBM, on the other side one of the expected clinical yields of genomic-translational research) aims to underline and exemplify the strict complementarity of the two scenarios. Methodologically and operationally, both approaches do propose a very promising future for the development of pharmacological research, with closer links to the highly productive area of outcomes-oriented epidemiology and with the most advanced sector of basic sciences. It seems specifically important that the two areas could be developed in close interaction, possibly within the same department(s), to assure a productive interplay of competences in the collaboration with clinical care, as well as in the training of the new generations of pharmacologists, pharmacists, clinicians.</p>
PL-02	<p>BASIC PERIPHERAL MOLECULAR COMPONENTS OF INFLAMMATORY PAIN <u>H Ferreira</u></p> <p>School of Medicine of Ribeirão Preto. Department of Pharmacology, Campus USP, Ribeirão Preto, SP. Brazil. email: shferrei@fmrp.usp.br</p> <p>When non steroidal anti-inflammatory drugs mechanism of action was discovered, I proposed that their analgesic effect resulted from the prevention of the nociceptor sensitization by prostaglandins. Thus, pain in an inflammatory process results from an action of mechanical, thermal or chemical stimuli upon sensitized nociceptors (hiperalgesia, hypernociception-HPr). A tissue noxious stimulus triggers an array of inflammatory HPr tissue events like the release of bradykinin and C5A complement factor and of a cascade of cytokines. This cascade is initiated by TNF-α and culminates with the release of IL-1 that activates tissue and neuronal cyclo-oxygenases with subsequent release of prostaglandins. Thus, the inhibition of any point of this cascade, causes analgesia by nociceptor sensitization prevention. The molecular mechanism of HPr involves the stimulation of cAMP pathway with subsequent a) activation TTX resistant sodium channel, lowering neuronal threshold and facilitating neuronal membrane conduction and b) an increase in cytosolic K⁺ and Ca⁺⁺ causing a variation of the resting potential which also facilitates nociceptor activation c) activation of “ganglionic retrograde sensitization” which maintains HPr. There are drugs like dipyrone, diclofenac, ketorolac, brexazocine, peripheral opiate analgesics that cause analgesia by opening K⁺ channels ATP sensitive, thus restoring normal resting potential. This effect is dependent of the activation of the arginine/NO/cGMP pathway.</p>
PL-03	<p>CUBAN SCIENTIFIC DEVELOPMENT TODAY: IMPACT OF THE BIOTECHNOLOGY IN THE PHARMACOLOGICAL SCIENCES DEVELOPMENT <u>Luis Herrera Martínez</u></p> <p>Director of the Center for Genetic Engineering and Biotechnology, La Habana, Cuba email: luis.herrera@cigb.edu.cu</p> <p>Cuba is an example of the much a small country with very limited resources can do in the field of sciences. Cuban biotechnology has the special characteristic of being a forerunner, beginning at the precise moment this science was taking its first steps in the United States and the world. Other distinctive features of Cuban biotechnology are the implementation, from the beginning, of the concept that all workplaces involved had to complete the research, technological development, production and commercial cycle, integrating cooperation among them, and achieving results of great impact on the national health care system. <i>Several of the Cuban biotech products are unique, such as the meningitis B vaccine, the Heberprot-P (innovative product indicated to treat diabetic foot ulcers), the PPG anti-cholesterol pill, vaccine against Haemophilus influenzae type b (the first worldwide synthetic vaccine), in addition to monoclonal antibodies and vaccines for the treatment of</i></p>

	<p><i>cancer, together with agro-biotech products.</i> Today, Cuban scientists are working in the development of new projects of therapeutic vaccines, some of which are in very advanced evaluation stages, for instance, therapeutic vaccines against Hepatitis B, Hepatitis C and prostate cancer. Health impact is evident at population level in many fields: <i>Haemophilus influenzae</i> type b epidemics have disappeared; hepatitis-B is about to disappear in the infant population. The Cuban population under 29 years of age is immunized against hepatitis B, whose incidence is the lowest in the world. In Cuba the available production capacities have been able to supply goods for Cuban needs and for export, achieving regulatory standards according to current Good Manufacturing Practices (GMP). For example, the facilities of the Centre for Genetic Engineering and Biotechnology and those of Biocen for the production of Hepatitis-B vaccine have been inspected and received certification of the World Health Organization (WHO), becoming a UN prequalified vaccine to be used by the UN purchasing agencies. The impact of the Cuban biopharmaceutical sector on improving health is undoubtedly larger because there is extensive cooperation between the research institutions and hospitals, when developing the biopharmaceutical products. Certainly, to our knowledge, no scientific, social and economic phenomenon of this nature has occurred in any other developing country.</p>
	<u>MARTES 14 DE DICIEMBRE / TUESDAY, DECEMBER 14.</u>
	<u>PLENARY LECTURES (PL) / CONFERENCIAS PLENARIAS</u>
PL-04	<p>NEW LEGISLATION IMPROVING PHARMACOVIGILANCE IN EUROPE: NEWS ARISING FROM THE RECENT EUROPEAN LEGISLATIVE CHANGES <u>Mariano Madurga</u></p> <p>Jefe del Área de coordinación del SEFV-H. División de Farmacoepidemiología y Farmacovigilancia. Agencia Española de Medicamentos y Productos Sanitarios.</p> <p>The new European legislation in pharmacovigilance aims to streamline and strengthen pharmacovigilance activities and will require joint action the <i>Agencia Española de Medicamentos y Productos Sanitarios (AEMPS)</i> and the Spanish Pharmacovigilance Regional Centers for commissioning, development and implementation. The following are the changes most relevant to the operation of European and Spanish regulation:</p> <p>1. Individual notifications of suspected adverse reaction</p> <ul style="list-style-type: none"> • The SEFV-H will record the suspected adverse reactions arising from any use of medication including, therefore, overdose, mis-administration / misuse, abuse of drugs and medication errors. Computer systems must be prepared for them and identify them once incorporated into the database. • Establish the necessary mechanisms to enable the direct notification of patients and users. In this sense, the more efficient approach would be a web portal to facilitate this notification to citizens who, in turn, must be integrated with database (as FEDRA) to redirect cases to the Regional Centre respective. It is estimated that this could be a 20% increase in the number of ADR reports received today. • It should be made publicly available database of suspected adverse reactions (as the Spanish FEDRA), with different levels of access depending on whether it is a health professional, a patient or pharmaceutical companies. • You must record and process notifications of suspected non-serious adverse reactions received from pharmaceutical companies (so far only sent the cases severe) in prescribed time periods. • It should promote electronic reporting, the health authorities must provide electronic access via websites, for the reporting of suspected ADRs by healthcare professionals and patients and users. <p>2. Moving to a more proactive pharmacovigilance</p> <p>It will need to manage clinical information sources and pharmacological (BIFAP, etc.) that enable epidemiological studies in the new framework of a proactive pharmacovigilance.</p> <p>3. Enhance Transparency</p> <p>It should enhance transparency and disclosure. Programs also should be made to enhance communication of suspected adverse reactions to both health professionals and patients, even for different consumer groups.</p> <p>4. Continuous monitoring of the Benefit / Risk</p> <p>The competent authority shall conduct a continuous monitoring of FEDRA database to identify potential security problems that can lead to changes in the benefit / risk of medicines.</p> <p>5. Audit</p> <p>The Competent authorities on pharmacovigilance will be audited by the European Commission every two years to ensure compliance with these tasks and ensure the quality of the data.</p>

	<p>6. Pharmacovigilance Risk Assessment Committee (PRAC) Currently, the Pharmacovigilance Working Party is a working group of the Committee of Medicinal Products for Human Use (CHMP). New legislation will change it: an assessment committee composed of one member by each Member State, six members of relevant experts (incl. clinical pharmacology, pharmacoepidemiology), one member from healthcare professionals, and one member from patient associations. The mandate of the PRAC shall cover all aspects of the risk management of the use of medicinal products including detection, assessment, minimisation and communication related to the risk having due regard to the therapeutic effect of the medicinal product, the design and evaluation of post-authorisation safety studies and pharmacovigilance audit.</p>
<p>PL-05</p>	<p>PHARMACOVIGILANCE IN AUSTRALIA: FROM PATIENT CARE TO PUBLIC HEALTH Vernon GM,¹ Frauman AG²</p> <p>¹Drug Information, Pharmacy, ²Department of Clinical Pharmacology and Therapeutics; ²Austin Health, Heidelberg, Victoria, Australia. email: graeme.vernon@austin.org.au</p> <p>Introduction: In Australia, reports of adverse drug reactions (ADRs) are collated by the Therapeutic Goods Administration (TGA). TGA can identify early signals and contributes to WHO's pharmacovigilance monitoring. Most reports are from doctors and pharmacists and this is an important public health responsibility. However, reporting is time consuming and details are often insufficient to assess causality. In hospitals, pharmacists work with medical and nursing staff to provide more complete reports and generate alerts to reduce the risk of re-exposure. For clinicians, it is easier to justify this workload by emphasizing its potential for individual patient safety as well as its role in pharmacovigilance. Method: The hospital's ADR reporting program is available to all staff but most reports are by clinical pharmacists. Reports are presented to a committee consisting of pharmacists and clinical pharmacologists. All reports are considered for severity, causality, and whether a clinical alert should be created in the patient's record and an alert card sent to the patient. A summary is provided to the Drug Committee and, if appropriate, the final report is sent to TGA. Results and Discussion: The program has operated for 15 years and has documented more than 2000 reports. Alert cards are created for approximately 65% of reports and 80% are forwarded to TGA. The program allows for detailed assessment and increased patient safety for events which are captured. Electronic discharge summaries and scanned medical records have enhanced our ability to check clinical details and outcomes. A national electronic medical record system is being developed which will provide a more efficient means of warning about future exposure. Conclusion: Collaboration between clinical pharmacists and clinical pharmacologists can enhance pharmacovigilance and patient safety.</p>
<p>PL-06</p>	<p>FARMACOGENETICS IN IBEROAMERICAN POPULATIONS Adrián LLerena, Pedro Dorado, Eva M Peñas-Lledo</p> <p>Clinical Research Centre (CICAB), University of Extremadura Medical School, Hospital Infanta Cristina, 06080 Badajoz, Spain (www.cicab.es). Coordinator RIBEF and Sociedad Iberoamericana de Farmacogenética y Farmacogenómica (SIF). email: allerena@unex.es</p> <p>RIBEF: Iberoamerican Network of Pharmacogenetics and Pharmacogenomics www.ribef.org</p> <p>To study pharmacogenetics in Hispanic populations is one of the main goals of the from Iberoamerican Network of Pharmacogenetics and Pharmacogenomics (www.ribef.org) and the Iberoamerican Society of Pharmacogenetics and Pharmacogenomics (SIF). Hispanics is a large group of world population, including people living in Spanish speaking countries of South and Central America as well as those categorized as Hispanics in the United States Hispanic populations are diverse according to their country of origin or residence, culture, as well as genetic composition resulting from the inter-ethnic crosses between Amerindians, Europeans and Africans. Among the first Europeans (Castilians) arriving America in the XV very many of them were original from the southwestern Spanish region of Extremadura. Among the major determinants of the interindividual and interethnic variability of pharmacokinetics and drug response is the genetic polymorphism of the cytochrome P450-system enzymes (CYP). Population studies have already reported interethnic variability in the frequency of cytochrome P450 genes. Among CYPs, CYP2D6, CYP2C9 and CYP2C9 are the most clinical relevant due to its implication in the metabolism of very important drugs. So far, the most studied cytochrome P450 is CYP2D6, regarding its polymorphisms two phenotypes have been described: subjects who have an inherited decreased capacity to metabolise drugs are classified as "poor metabolizers" (PM), while the rest are "extensive metabolizers" (EM). The existence of very rapid</p>

	<p>hydroxylation due to an inherited amplification of an active gene has also been reported (“Ultrarapid Metabolizers” UM), we showed that 4.93% (95% IC_{2.23-10}) of Spanish subjects from Extremadura carried two CYP2D6 active copies. Phenotypically PMs frequency between Caucasian populations is around 5-7%. The present Project aimed to evaluate the most relevant genetic polymorphism. So far CYP2D6 genetic polymorphism and dextrometorphan or debrisoquine metabolic ratio is analysing in different Ibero-American populations including Spain, South-America (i.e. Argentina, Ecuador, Colombia), Central-America (i.e. Costa Rica, Nicaragua), Caribe and North-America, (i.e México, Cuba). Differences have been found, the frequency of CYP2D6 PMs ranged from 6%-3.9% in Nicaraguans-Cuban-Mestizos. In several Latin American countries, including many Amerindian groups, no information are available on any pharmacogenetic targets. With the purpose of fulfilling this information gap and to promote collaborative pharmacogenetic/genomic research in Spanish- and Portuguese-speaking peoples in the Americas and the Iberian peninsula, a network – the Iberian American Network of Pharmacogenetics and Pharmacogenomics - was created (www.ribef.org). This initiative represents a promising step towards the inclusion of Latin American populations among those who will benefit from the implementation of pharmacogenetic principles and tools in drug therapy.</p> <p><u>Acknowledgments and Financial Support:</u> The study was coordinated in Red Iberoamericana de Farmacogenética y Farmacogenómica RIBEF, www.ribef.org and Agencia Extremeña de Cooperación al Desarrollo AExCID.</p>
<p>PL-07</p>	<p>NATIONAL COORDINATING UNIT OF DRUG SURVEILLANCE. CUBA 10 YEARS OVERVIEW <u>Jiménez G,</u> Alfonso I, Avila J, Calzadilla O, Pérez J</p> <p>Pharmacoepidemiology Development Centre, 44 St No 502 esq 5th Ave, Playa, CP 11300 Havana City, Cuba. email: giset.jimenez@infomed.sld.cu</p> <p><u>Introduction:</u> The Pharmacoepidemiology Development Centre has among its main lines of work: epidemiologic research, teaching, drug information, therapeutic consultation, programme for rational drug use, pharmaco-economic area and pharmacovigilance, this last function with the National Coordinating Unit. The aim of this lecture is to present the main results after 10 years of work with the surveillance system.</p> <p><u>Material and Methods:</u> We based this lecture over a retrospective study to characterize the reports of suspected adverse reactions received by the National Coordinating Unit of Pharmacovigilance, the changes in the system organization, the combination of drug surveillance methods, the risk management activities and risk communication. <u>Results and Discussion:</u> In 10 years of work, the drug surveillance network is well functioning, keeping a reporting rate in more than 600 per million inhabitants, more than 50% of the reports are severe and almost the 37% corresponding to occasional or rare adverse drug effects, also the surveillance count with active plans, for the influenza vaccines, oseltamivir and all products with less than 5 years in the market. The system has courses and training for different health professionals and project of investigations countrywide, also there is an international collaboration and experience share in this important topic. <u>Conclusions:</u> Pharmacovigilance in the world remains a scientific and clinical discipline very dynamic, which is essential to address the problems posed by an arsenal of drugs that is growing in variety and power. The Cuban system still has to much to do.</p>
<p>PL-08</p>	<p>TRENDS IN PHARMACOLOGY OF NATURAL THERAPEUTIC PRODUCTS <u>Evangelina Marrero</u></p> <p>¹National Center for Animal and Plant Health, CENSA, Apdo. #10, San José de las Lajas, La Habana, Cuba. email: eva.marrero@infomed.sld.cu</p> <p><u>Introduction:</u> Natural products (NPs) are the most important source of new commercially viable drug leads because the chemical diversity and novelty associated is higher than that of any other source. Less than 10% of the world’s biodiversity have been tested for biological activity, so still there are many useful lead compounds waiting to be discovered from natural sources. Moreover, NPs that are found to be biologically active in pharmacological assays are generally small molecules with drug-like properties, it means capable of being absorbed and metabolised by the body. Modern pharmacology research is particularly important when searching for lead molecules against newly discovered targets for which there are no known small molecule leads so the challenge is how to access to the great chemical diversity. <u>Material and Methods:</u> Several different strategies emerged in the post genomic era for a better understanding of the molecular mechanism involved in the signalling pathways of different diseases where a good deal of research have been approached oriented to find new promising phytotherapeutic are mentioned. Examples are offered ej. antidiabetic activity of plant samples. <u>Results and Discussion:</u> The <i>in vitro</i> evaluation of natural extracts oriented to obtain new active molecules constitutes a valuable tool for the screening of the biological activity in an appropriate</p>

	<p>therapeutic target battery. The specificity of the mechanism associated to particular pharmacological targets brings the opportunity to investigate the pathogenesis of definite disease at cellular and molecular level and also offers the opportunity to establish the mechanism of action involved in traditional use of medical plant. The bio-guided fractioning will help to find new promising molecules. Conclusions: It is technologically possible to predict and evaluate the biological activity of natural extracts on specific targets of relevant diseases in a reasonable short time in order to develop new phytoterapeutics based on their quality, efficacy and security. References: Harvey, A. Medicines from nature: Are natural products still relevant to drug discovery? Trends. Pharmacol. Sci. 20 1999, 196; Marrero E. Phytopharmaceuticals as therapeutic tools for veterinary and human therapy: Research on natural health products developed at CENSA, Cuba. In: Recent Developments in Medicinal Plant Research, ISBN: 9788130801605 Ed. A Capasso, 2007; B. Patwardhan / Ashok DB. Indian Journal of Experimental Biology. Vol. 48, March 2010, 220-237.</p>
<p>PL-09</p>	<p>3R PROGRESS IN VACCINE LOT RELEASE TESTING: THE EUROPEAN CONTEXT <u>Coenraad FM Hendriksen</u></p> <p>Netherlands Vaccine Institute (NVI), Bilthoven (NL) & Utrecht University, Utrecht. Netherland (NL).</p> <p>Historically, Europe has played a major role in initiating 3R activities in biomedical research and testing. Amongst others this has resulted in the establishment of the European Centre for the Validation of Alternative Methods (ECVAM) and the ban on the use of animals in cosmetic testing. The leading role of Europe will even be more distinct now the revised European Directive 86/609/EEC on animal experimentation has been adopted by the European Parliament, September 2010.</p> <p>This presentation will discuss some of the recent developments that have taken place in Europe in the area of vaccine lot release testing. In terms of animal welfare this area is of particular concern: numbers of animals being used are extensive and routine procedures such as challenge are characterised by high severity levels. Activities range from development of <i>in vitro</i> methods to replace existing animal models such as the cell culture alternatives to histamine sensitisation testing of acellular pertussis vaccine, the international validation of a serological alternative to the Mouse Protection test for potency assessment of whole cell pertussis vaccine, to identifying humane endpoints in challenge tests. Focus in this presentation will be on the current activities with regard to a paradigm shift in vaccine quality control; the consistency approach. The central line in consistency testing is to identify a set of parameters to constitute a product profile (e.g. antigen content, antigen integrity, antigen – adjuvant interaction, etc.) of the vaccine that can replace current release tests. The product profile is established to the satisfaction of the regulators at the time of licensing, and is monitored throughout production under a strict quality system. The product profile ensures that each batch released is similar to a manufacturer-specific vaccine of proven clinical efficacy and safety, with respect to all characteristics agreed upon at licensing between manufacturer and regulator¹. This approach may lead to a reduction in animal use, since a narrow set of animal tests performed on each final batch, with potentially limited power to predict vaccine behaviour in the target populations, may be replaced by a battery of meaningful physicochemical and immunochemical tests with enhanced capacity to measure equivalence with batches of proven safety and efficacy. The concept of consistency testing was adopted by the European Partnership on Alternative approaches to animal testing (EPAA) as a promising strategy to animal reduction. EPAA is a partnership between the European Commission and the European Industry with the aim to replace, reduce and refine the use of laboratory animals. At a recent EPAA workshop on consistency testing (January 2010) it was decided to establish technical working platforms on human and veterinary vaccines in order to identify research needs with regard to consistency testing and to draft a road map for the acceptance and implementation of consistency in routine lot release testing, with the ultimate goal to replace animal use by non-animal test methods. This presentation will provide information about EPAA's activities and the way forward in consistency testing. ¹Definition given in 'The Consistency Approach for Quality Control of Vaccines – A strategy to improve quality control and implement 3Rs' ; a report of EPAA workshop on consistency testing, January 11-12, 2010.</p>
<p>PL-10</p>	<p>IMPLEMENTING THE CUBAN CLINICAL TRIAL REGISTRY AS WORLD HEALTH ORGANIZATION PRIMARY REGISTRY <u>Jiménez Rivero G</u>¹, Pascual López MA¹, Cobas Rodríguez J², Fors López MM¹, Cachimaille Benavides Y¹, Torres Pombert A¹, Rodríguez Álvarez J¹</p> <p>¹National Coordinating Center of Clinical Trials, 200 at 21 Ave, Atabey, Playa, Havana City, Cuba. email: gladys@cencec.sld.cu</p> <p>² Desoft. Investigation, Development and Innovation Technology Division. 198 # 1705 Bt/ 17 and 19, Siboney, Playa, Havana City, Cuba.</p>

	<p>Introduction: Clinical Trial Registries are means to help to maintain transparency in the design and conduct of clinical trials. The World Health Organization (WHO) has claimed that the registration of interventional trials is scientific, ethical and moral responsibility and it implemented the International Clinical Trials Registry Platform (ICTRP). The National Coordinating Center for Clinical Trials developed the Cuban Clinical Trial Registry (RPCEC). From the beginning, the members of RPCEC are working to be a primary registry of WHO. For this it was necessary to develop and to implement a strategy to reach this condition.</p> <p>Material and Methods: A documental review of the requirements of WHO to declare a registry as primary one was performed. The study of WHO standards allowed developing the strategy. Results and Discussion: The strategy included the sending of application forms to the ICTRP, the identification of the requirements, and the development of activities to achieve compliance. As a result of this implementation, RPCEC is free and it has national scope, allows any sponsor worldwide to register a clinical trial without any restriction, it has mechanisms to guarantee data validation and is possible to do electronic search. It has two forms for clinical trial registration (English and Spanish) that contained the WHO data set. The online database is available 24 hours, 7 days. RPCEC has 96 clinical trials registered, 52 of them in English. The difference in those numbers is because until July 2008, the registration was only in Spanish. The Cuban office of Pan American Health Organization translated the trials registered only in Spanish and RPCEC sent this traduction to the sponsors for they complete the English forms. Conclusions: The strategy has allowed fulfilling the WHO standards. The translation into English of all the clinical trials registered will allow to be accepted as a primary registry.</p>
<p>PL-11</p>	<p>IN VITRO BIOEQUIVALENCE. WHY, WHEN AND HOW?: APPLICATIONS OF THE BIOPHARMACEUTIC CLASSIFICATION SYSTEM (BCS) Marival Bermejo. Facultad de Farmacia. Universidad Miguel Hernández de Elche, Alicante. España. email: mbermejo@umh.es</p> <p><i>In vivo</i> bioequivalence (BE) tests are the accepted standard for ensuring the therapeutic performance of drug products following manufacturing changes and for approval of generic drug products. EMA and FDA guidances include now a new standard based on Biopharmaceutics Classification System (BCS). BCS classify drugs according to the fundamental properties governing drug absorption, namely permeability and solubility. A BCS-based <i>Biowaiver</i> is the permission to use dissolution test to demonstrate Bioequivalence as a surrogate of pharmacokinetic data obtained in human volunteers, avoiding unnecessary clinical trials. For this reason this new regulatory approach could have many ethical and economical consequences on medicines development. The recently implemented EMA guideline allows waiver of <i>in vivo</i> BE studies for immediate-release (IR) solid dosage forms of Class 1, (high-solubility, high-permeability drugs) and Class 3 (high solubility-low permeability) drugs in rapidly dissolving drug products. It is important to note that the BCS approach to “biowaivers”, does not waive BE, but waives the <i>in vivo</i> BE test, in lieu of a better, more routinely conducted, and more easily implemented dissolution test. A provisional BCS classification of the drugs contained on the WHO Essential Medicines list suggests that the majority of the drug products contained on the WHO list are candidates for waiver of <i>in vivo</i> bioequivalence testing based on an <i>in vitro</i> dissolution test ‘biowaiver’. The impact of waiver of <i>in vivo</i> bioequivalence (BE) testing and its replacement with rapid and affordable dissolution standards is expected to be of profound significance.</p>
<p>PL-12</p>	<p>THERAPEUTICAL TARGETS OF OZONE OXIDATIVE PRE/POSTCONDITIONING. AN EXPLANATION OF ITS CLINICAL EFFICACY Olga Sonia León Fernández (PhD)</p> <p>Department of Pharmacology, Pharmacy and Food Institute, University of Havana, Cuba</p> <p>Ozonotherapy efficacy in many diseases has been thoroughly evidenced. In 1998-2008 Ozone Oxidative Pre/Postconditioning as ozone’s mechanism of action was demonstrated from experimental and clinical point of view. In this Lecture is shown the efficacy of Oxidative Pre/Postconditioning mediated by ozone in diabetes’ vascular complications, ischemic/reperfusion injury and hernia disk. The starting point has been the analysis of pathological molecular mechanisms in order to identify which redox markers are modified by ozone treatment in relation to clinical improvement. It is demonstrated that Ozone’s therapeutical targets change of particular manner in accordance with the physiological disorder but regulation of SOD activity is a common therapeutical effect of ozonotherapy whatever be the disease.</p>

	<p>SYMPOSIA AND WORKSHOPS / SIMPOSIOS Y TALLERES CONFERENCES AND ORAL COMMUNICATIONS (OC) / CONFERENCIAS Y COMUNICACIONES ORALES</p>
W-1	<p>5TH INTERNATIONAL WORKSHOP ON PHARMACOVIGILANCE IN THE 10TH ANNIVERSARY OF PHARMACOVIGILANCE CUBAN COORDINATING UNIT. / 5^{TO} TALLER NACIONAL DE FARMACOVIGILANCIA EN EL 10^{MO} ANIVERSARIO DE LA UNIDAD COORDINADORA NACIONAL DE FARMACOVIGILANCIA.</p>
OC-01	<p>ASPIRIN USE IN ELDERLY WITH TYPE 2 DIABETES: EFFECTS ON MYOCARDIAL INFARCTION AND GASTRO-INTESTINAL BLEEDING Sirois C^{1,2}, Moisan J^{1,2}, Grégoire J-P^{1,2}</p> <p>¹Faculty of Pharmacy, Université Laval, Québec, Quebec, Canada, G1V 0A6 and ²URESP, Centre de recherche FRSQ du CHA universitaire de Québec, Québec, Quebec, Canada, G1S 4L8.</p> <p>Introduction: Aspirin is recommended for primary prevention of myocardial infarction (MI) in elderly with diabetes. However, the cardiovascular benefit and the gastro-intestinal (GI) bleeding risks of aspirin therapy have not been well established in this population. The objective of this study was to evaluate the association between aspirin use and 1) MI and, 2) GI bleeding among elderly newly treated with oral antidiabetes drugs.</p> <p>Materials and Methods: Using Quebec administrative databases, we conducted two nested case-control analyses within a population-based cohort of 39,680 individuals aged ≥ 66 years, newly treated with an antidiabetes drug, who had not used aspirin, antiplatelet or anticoagulant drugs and had no MI nor GI bleeding in the year before cohort entry. In the first analysis, cases were patients who had a MI, while in the second analysis, cases were those who had GI bleeding. For each case, we selected five controls matched for age, year of cohort entry, sex and cardiovascular disease using incidence density sampling. Exposure to aspirin was defined as current, past or no use. Using paired multivariate conditional logistic regression, we calculated odds ratios (OR) of MI and of GI bleeding. Results and Discussion: There were 1871 cases of MI. Current users of aspirin had no significantly increased risk of MI [OR=1.16 (95% CI: 0.98-1.37)] than did non users, whereas past users had an increased MI risk [1.23 (1.02-1.49)]. There were 614 cases of GI bleeding. Current users of aspirin had higher risks of GI bleeding [1.94 (1.47-2.57)] compared with non users, but the risk was not significantly increased for past users [1.30 (0.90-1.89)]. Conclusions: These results suggest that aspirin does not provide cardiovascular protection to elderly individuals with diabetes while it may expose them to an elevated GI bleeding risk.</p>
OC-02	<p>MONITORING THE TOXICITY OF ANTINEOPLASTIC CHEMOTHERAPY IN CHILDREN WITH CANCER Magyar I¹, Ritli L², Sava C², Miculschi Gabriela², Szilagyi Ariana², Vraci Diana²</p> <p>¹ Department of Pharmacology, Pharmacovigilance Unit, University of Medicine and Pharmacy, P-ta 1 Dec.1918 St. No.10, Oradea, Romania. email: magyar_n@yahoo.com ² Department of Pediatrics Oncology, Clinical "Dr. G.Curteanu" Hospital, C.Coposu St.No.12, Oradea, Romania.</p> <p>Introduction: Although neoplastic diseases are not very frequent in juvenile pathology (8600/year in patients under the age of 14 and 3700/year in patients between the ages of 15 and 18, in the USA), antineoplastic chemotherapy continues to be quite aggressive despite good therapeutic results. Material and Methods: Our study focused on the toxicity of antineoplastic chemotherapy on 42 children between the ages of 3 and 18, with different stages of cancer. The adverse reactions were recorded in special chemotherapy side effects sheets, recommended by World Health Organization, divided into 5 stages (0-4). Results and Discussions: Most patients were diagnosed with acute lymphoblastic leukemia (22; 52.4%). The rest of the patients were diagnosed with Ewing sarcoma (9; 21.4%), Hodgkin lymphoma (7; 16.7%), osteosarcoma (3; 7.1%), and non-Hodgkin lymphoma (1; 2.4%). All patients underwent different antineoplastic chemotherapy treatments according to the type of cancer, its stage and the international protocols on the respective case. Most patients presented hematological toxicity (22, 52.4%) and gastrointestinal toxicity (22, 52.4%). Afterwards come the cutaneous side effects (16, 38.1%) hepatic toxicity (14, 33.3%) and infections (14, 33.3%). Neurological toxicity was present in 5 cases, while renal toxicity was present in 4 cases. As for associated toxicity, most patients, (14 respectively), presented three types: hematological, gastrointestinal, and infectious toxicity.</p>

	<p>Other 8 patients presented 4 associations, 6 patients had 5 associations, while other 6 patients had 6 toxicity associations. The toxicity level, on a scale of 0 to 4, appears very high in the case of leukopenia (level 4, under 1000/mm³) [10; 23.8%], in the case of a haemoglobin decrease (level 4, below 6.5g/dl) [5; 11.9%], and in the case of granulocytopenia (level 4, below 55/mm³) [7; 16.7%]. Conclusions: By strict and standard monitoring of the adverse side effects of antineoplastic chemotherapy, certain correlations can be made regarding a higher or lower toxicity level of certain therapeutic regimens. At the same time, one can select the therapeutic regimens that should accomplish the highest benefit/risk ratio.</p>
OC-03	<p>TRIMETHOPRIM USE DURING PREGNANCY AND THE RISK OF MISCARRIAGE: A REGISTER-BASED NATIONWIDE COHORT STUDY ^{1, 2} Andersen JT, ^{1, 2} Petersen M, ^{1, 2} Solem EJ, ³ Andersen E, ⁴ Andersen NLT, ^{1,2} Broedbaek K, ^{5, 6} Torp-Pedersen C, ³ Keiding N and ^{1,2,6} Poulsen HE</p> <p>¹Laboratory of Clinical Pharmacology, Copenhagen University Hospital Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark. email: jta@rh.dk ²Department of Clinical Pharmacology, Bispebjerg Hospital, Bispebjerg Bakke 23, DK-2400 Copenhagen, Denmark. ³Department of Biostatistics, University of Copenhagen, Øster Farimagsgade 5, DK-1014 Copenhagen K, Denmark. ⁴Psychiatric Center Copenhagen, Bispebjerg Bakke 23, DK-2400 Copenhagen, Denmark . ⁵Department of Cardiology, Gentofte University Hospital, Niels Andersens vej 65, DK-2900 Hellerup, Denmark. ⁶Faculty of Health Sciences, University of Copenhagen, Blegdamsvej 3, DK-2100 Copenhagen, Denmark.</p> <p>Introduction: The antibiotic trimethoprim which is widely used around the world acts as a folate antagonist by inhibiting the dihydrofolate reductase (DHFR). We conducted a nationwide cohort study testing the hypothesis that first trimester use of trimethoprim is associated with a higher frequency of miscarriages in pregnant Danish women. Methods and materials: A nationwide cohort study including all women in Denmark with a known conception in the period of 1997-2005 was conducted. The Danish Fertility Database was used to identify all women giving birth and the Danish Hospital Register was used to identify all women with a record of a miscarriage or induced abortion in the study period. Data on use of trimethoprim was obtained from the National Prescription Register. The primary outcome was the number of miscarriages among users of trimethoprim compared to non-users. Cox proportional hazard regression analysis with exposure to trimethoprim from conception to end of first trimester as time-dependent variable was used to estimate the risk of miscarriage. Results and discussion: We identified 722 519 pregnancies (525 933 live births, 67 137 miscarriages, and 129 449 induced abortions) in the study period. 215 women redeemed a prescription of trimethoprim of whom 26 (12%) experienced a miscarriage. The hazard ratio (HR) of having a miscarriage after exposure to trimethoprim compared to unexposed was 2.03 (CI95% 1.38-3.01); when adjusting for maternal age, income, education, and prior miscarriages this gave a HR=2.09 (CI95% 1.41-3.10). The trophoblasts of the fetus are very sensitive to drugs that interfere with the folic acid cycle and thereby inhibit DNA synthesis. Another DHFR inhibitor, methotrexate, is used as an abortifacient, making the result biologically plausible. Conclusion: These preliminary results show a significant increase in the prevalence of miscarriages in women redeeming a prescription of trimethoprim in the first trimester of pregnancy compared to non-users.</p>
OC-04	<p>FARMARED. INTERNATIONAL COLABORATION FOR THE DEVELOPMENT OF PHARMACOVIGILANCE IN THE CARIBBEAN AREA & LATINAMERICA Everardo Vázquez, México.</p> <p><i>(Resumen no disponible en el momento de la edición del libro.. Abstract non available in the moment of the edition of the book of summarie).</i></p>
S-1	<p>2nd SYMPOSIUM ON THERAPEUTIC UPDATING IN ENDOCRINOLOGY. / 2^{do} SIMPOSIO DE ACTUALIZACION TERAPÉUTICA EN ENDOCRINOLOGÍA</p>
OC-05	<p>INCRETINS: A NEW TERAPEUTICS APPROACHES FOR THE PHARMACOLOGICAL TREATMENT OF DIABETES TYPE- 2 Daniel Abouganem M. Centro de Tratamiento de Diabetes, Hospital Punta Pacífica Afiliado a Johns Hopkins International-Panamá. email: danyel@cwpanama.net</p>

	<p>Every 10 seconds two people are diagnosed with diabetes in the world and equally, every 10 seconds a person dies for diabetes problems. The diabetes is considered by the World Health Organization as an epidemic disease, because one has seen that the incidence has gone increasing quickly. It is calculated that at this time there is in the world 285 million people with diabetes and if one doesn't make something to change this quick growth, for the year 2025 are considered that there will be 380 millions, what is highly alarming. The 60 to people's 70% with diabetes are in the not industrialized countries, what represents bigger costs for the institutions of health. In Latin America 18 million people they have diabetes and the estimates deaths for the 2010 are of 171300 according to the International Federation of Diabetes. It is spoken that in the industrialized countries, among the 11 to 15% of the national budget of health is invested in the diabetes treatment. The epidemic characteristics of the diabetes mellitus (DM) type 2 suppose an important assistance challenge, for the high impact in the use of the sanitary resources required in their treatment, as well as in the prevention and treatment of the associate cardiovascular complications, it causes main of the morbidity-mortality related with the DM, without forgetting their social and personal impact. The physiologic effect that cause the natural incretins (GLP-1 and GIP), hormones of the gastrointestinal tract that act on the regulation of the glycemic increasing the secretion of insulin and reducing that of glucagons, in relation to the ingestion of carbohydrates, it is known for years. Nevertheless, it has only recently been possible the development and the later commercialization of hypoglucemiant drugs based on the increment of the effect of the incretins. At the present time, the therapeutic options are <i>exenatide</i> and <i>liraglutide</i>, mimetics of incretins analogs of GLP-1, administered for via subcutaneous; and, of sitagliptin, vildagliptin and saxagliptin inhibitors of the activity of the enzyme DPP4, administered orally. The hypoglucemiant effect observed with these new drugs on the reduction of the glycosylated hemoglobin (HbA1c) it is of 0.5-1% in most of the studies, offering as potential advantage the absence of hypoglycemia manifestations associated to the treatment and their neuter effect or of weight decrease.</p>
<p>OC-06</p>	<p>INSULIN ANALOGS <u>Manuel Vera</u> National Institute of Endocrinology, Havana, Cuba.</p> <p>Insulin therapy has change prognosis and quality of life of people with diabetes specially in Type 1 DM. First insulin used was regular insulin, therefore patients had to administer insulin before each meal and at 1.00 am. In 1935 intermediate insulin appears and patients diminished the number of insulin shots per day. A study made in 1960 showed that those with more shots had less retinopathies. Treatment for type 1 DM has shown to be the wrong drug, at the wrong time and the wrong dose .Scientific community is aware of this and has been doing efforts to find the best drug .in that sense it has been experienced with several types of insulin such as: Pork, Mono compound, and human insulin. Each one with improved quality in relation with the one before, However up to now insulin treatment has not arrived yet to optimal quality. One of the reasons is that the drug has an HEXAMER composition and it has to spend 30 minutes in order to initiate its action. These clinical limitations motivate the search of more efficient drugs modifying recombinant insulin chains. Since the decade of 90ties It has been developed the Insulin analogs, these new drugs has a different composition (Dimers and Monomers) and its action begins almost immediately after the administration. In this review, we analyze the molecular composition, pharmacokinetics, action, advantages, disadvantages and side effects of all the insulin analogs developed up to now, we compare its action with other insulin.</p>
<p>OC-07</p>	<p>SOMATOSTATIN ANALOGS <u>Arturo Hernández Yero</u> National Institute of Endocrinology, Havana, Cuba.</p> <p>Somatostatin (SST) is a native neurohormonal peptide present in the central nervous system in the neuronal bodies of the preoptical and periventricular areas of the ventral hypothalamus and the system to parvocelular of the nuclei paraventricular and also is synthesized in D cells of the gastrointestinal and pancreatic system, exerting a powerful inhibiting action on pituitary hormones somatotropin(GH) and thyrotropin(TSH). In addition it inhibits the secretions to the digestive system, thus considers the inhibiting peptide for excellence. The native neuropeptide has a short half-life with less than three minutes which has limited its actually therapeutic use and for that reason it's investigated and managed to synthesis in years 70 of last the century an octapeptide analog of the molecule of the SST with a similar biological activity, but with an half-life of 2 hours after its subcutaneous administration and afterwards is managed to synthesis a formulation of deposit with slow liberation and duration in blood of between 4 to 6 weeks from the intramuscular injection. This molecule contain 8 amino-acids and it's known with the name octreotide; later another analog is synthesized</p>

	<p>known like lanreotide, already more recent one has come investigating with a known analog multibinding like pasireotide. As the native SST has an ample range of inhibiting effects on cells of the organism the possibility of telling on analogs with an effect prolonged and greater resistance the enzymatic degradation more has allowed to control different types of diseases. That's why they are used in the treatment of pituitary functioning tumors of GH and TSH; at gastrointestinal level they are from utility in the gastrointestinal bleeding, pancreatic fistula, dumping syndrome gastrointestinal carcinoids, pancreatitis, insulinoma, functional diarras, portal hipertensión, colon, lung and prostate tumors, and others and Grave's ophthalmopathy . The actions of the somatostatin analogs are possibly made through receptors located in the target organs and each receptor has their functional characteristic specificity, according to the cellular groups and their different functions. 5 subtypes of receptors have been identified to SST that they belong to the superfamily of membrane receptors functionally connected to the route of adenilato-ciclase by the mechanism of sensible protein G to the toxin pertussis. The characteristic response of these receptors when they are activated by its link to the native molecule or the somatostatin analogs of the same one would be causing inhibition on adenilato-ciclase, with diminution of the cyclical AMP, which diminishes or inhibits the hormonal secretion, in addition the beta and gamma subunits of protein G would activate specific potassium channels, that they lead towards the outside of the cell the potassium flow, with inhibition of the voltage dependent calcium channels. This inhibition decrease the intracellular calcium and consequently diminishes the hormonal secretion. Effects known the somatostatin analogs:</p> <p>They inhibit the pituitary secretion of GH and TSH; Inhibitor of the intestinal peristalsis and the visceral flow; Antisecretory effect on enteropancreatic hormones (sst2): gastrin, colecistoquinin, secretin, insulin, glucagon, VIP; Antiproliferative effect of tumors (sst2):</p> <ul style="list-style-type: none"> - Inhibition of adenil ciclase activity: Diminution of AMPc. - Activation of phosphotirosin phosphatasa(PTP) and modulation of MAPK - Suppression of the tropin hormone secretion for the tumor: GH, pancreatic peptides. - Inhibition the growth factors : EGF, PDGF, VEGF - Induction of apoptosis (sst3): induction of p53 - It inhibits postranslational processes of conversion of prohormones in hormones (Preproglucagon.glucagon): less active hormones. <p>At level of the normal cells of pituitary gland are the receptors SSTR-1, SSTR-2, SSTR-3 y SSTR-5, whereas in the tumor cells of the producing adenomas of GH predominates ARNm of the receptors SSTR-2 y SSTR-5, therefore the analogs that one to these two receptors are going away to cause one better response in the inhibition of the GH. The drug group identified as somatostatin analogs has represented a remarkable advance in the treatment of the pituitary tumors, with effectiveness demonstrated mainly in the treatment of the pituitary adenomas of GH and TSH. The presurgical preparation of the patients that present these tumors, it is possible that it allows to reach better results in the pituitary surgery and to reach the cure of the patient with remission of the symptoms and the normalization in the levels of GH and IGF-I in the cases of acromegaly, but more studies are needed on the matter. We are expected the presence of more selective analogs and with potentiality of multiple ligands to receptors of SST, that it would allow a medical therapeutic line for the treatment of non-functioning pituitary adenomas and in that direction investigations group and clinical trials will be made in the future. When that is obtained new formulations with possibilities of multiple binding to the subtypes of the SSTR and or null adverse effects can be avisorar that this group of compound could get to become drugs in an important group for pituitary tumors and other neoplastic processes.</p>
<p>OC-08</p>	<p>DIAMEL TREATMENT IN THE METABOLIC SYNDROME Cabrera-Rode E, Orlandi N, Padrón Y, Arranz C, Olano R, González R, Machado M, Hernández-Yero A, Calderín R, Díaz-Horta O</p> <p>National Institute of Endocrinology, Havana, Cuba.</p> <p>Diamel, a natural product derived from lettuce and blueberry extracts has been incorporated in the market. It's a nutritional supplement and also contains vitamins and trace elements acting as biocatalysts and antioxidants. The supplement administration in type 2 diabetic patients has been proved to reduce blood triglycerides, improved metabolic control and beta cell function after 6 months. Accordingly, we believe that Diamel could also be effective in the treatment of persons with insulin resistance. There are no reports of the use of this supplement on MS. Objective: To evaluate the effect of Diamel administration on the clinical and metabolic parameters of metabolic syndrome. Subjects and methods: Inclusion criteria: Diagnosis of MS according to WHO, no present or past treatment for elevated blood glucose concentrations and age between 19-70 years. Diamel intervention trial is a randomized, doubled-blind, placebo-controlled intervention trial undertaken in</p>

	<p>Cuba. Participants were randomly allocated either oral Diamel or Placebo at a dose of two capsules before the three main meals of each day for one year. All subjects were studied for the presence of acanthosis nigricans, as well as for free cholesterol, creatinine and uric acid (UA) concentrations. Insulin resistance (IR) was assessed by estimating of insulin resistance index (HOMA-IR). MS screening was carried out in 267 overweight/obese subjects. 110 individuals fulfilled MS criteria for eligibility being 100 randomized to treatment. Results: Diamel administration improved some parameters of MS and diminished the UA concentrations. No adverse effects were reported. Conclusion: Diamel intervention trial has shown that the use of natural products together with indications for lifestyle improvement aiming at diminishing risk factors for future development of type 2 diabetes or cardiovascular disease is feasible and has high acceptance levels on obese or overweight subjects informed to be “labeled” as persons with MS.</p>
W-2	<p>1ST WORKSHOP ON RESEARCH AND DEVELOPMENT OF GENERIC DRUGS. / 1^{ER} TALLER DE INVESTIGACIÓN-DESARROLLO DE FÁRMACOS GENÉRICOS”</p>
OC-09	<p>GENERIC DEVELOPMENT: THE BIOPHARMACEUTIC CLASSIFICATION SYSTEM AS A DECISION TOOL. APPLICATION TO FLUOROQUINOLONES <u>Bermejo M¹</u>, González-Álvarez M¹, Mangas-Sanjuán V¹, González-Álvarez I¹, Cabrera Pérez MA², Pham The H²</p> <p>¹Department of Engineering, Area of Pharmacy and Pharmaceutical Technology, Miguel Hernández University, 03550 Sant Joan d'Alacant, Alicante, Spain. email: mbermejo@umh.es ²Molecular Simulation & Drug Design Group. Centre of Chemical Bioactive. Central University of Las Villas. Santa Clara, 54830, Villa Clara, Cuba.</p> <p>Introduction: The objective of the work is to establish a provisional classification following the Biopharmaceutic Classification System (BCS) of Ciprofloxacin (CP), Pefloxacin (PF) and Flumequine (FLU) in order to select the requirements for generic formulation development and Bioequivalence of these fluoroquinolones. Materials and Methods: Intestinal permeability of the compounds was determined in rat small intestine and Caco-2 monolayers. Permeability classification in high or low class was done by comparison with metoprolol permeability and confirmed with a previously established correlation between rat/Caco-2 permeability and oral fraction absorbed in rats. Classification was confirmed with the human oral fraction absorbed from literature when the data was available. Solubility was obtained from literature or determined experimentally in house (FLU). Solubility classification was done based on the Dose number calculation (Do) taking into account the usual doses in human. Results and Discussion: Pefloxacin is a high solubility (Do<1) and high permeability (Fa>90%) and belongs to Class 1. Ciprofloxacin is a low permeability (Fa<90%) and high solubility (Do<1) compound, thus it is a class 3 drug. Flumequine is a high permeability (Fa estimated in rat >90%) and low solubility (Do>1) and then a class 2 drug substance. Conclusions: Pefloxacin would be a candidate for <i>Biowaivers</i> in rapidly dissolving formulations (more than 85% dissolved before 30 mins) and bioequivalence could be demonstrated with in vitro dissolution tests (adequately designed). Ciprofloxacin could be also a biowaiver candidate following EMA regulations and WHO recommendations if formulations do not contain excipients altering intestinal permeability or transit time. Flumequine, for which solubility and dissolution are the limiting steps for drug absorption, would be a candidate for in vitro in vivo correlations.</p>
OC-10	<p>“IN SILICO”CONTRIBUTION TO BIOPHARMACEUTICS CLASSIFICATION SYSTEM (BCS): CACO-2 PERMEABILITY PREDICTION <u>Cabrera-Pérez MA¹</u>, Pham The H¹, Bermejo M², González I², Garrigues T³</p> <p>¹Molecular Simulation & Drug Design Group. Centre of Chemical Bioactive. Central University of Las Villas. Santa Clara, 54830, Villa Clara, Cuba. email: macabrera@uclv.edu.cu ²Department of Engineering, Area of Pharmacy and Pharmaceutical Technology, Miguel Hernández University, 03550 Sant Joan d'Alacant, Alicante, Spain. ³Department of Pharmacy and Pharmaceutical Technology, University of Valencia, Burjassot 46100, Valencia, Spain.</p> <p>Introduction: Approximately 90% of all marketed drugs are administered orally and about 30% of them fail in development due to poor pharmacokinetic properties. One important challenge facing an oral drug is their movement across the intestinal epithelial barrier that determines the rate and extent of human absorption and ultimately affects its bioavailability. Caco-2 cell assay is an <i>in vitro</i> method that has been widely used to predict <i>in vivo</i> intestinal absorption and it is recommended by the US FDA for determination of permeability</p>

	<p>of compounds to be classified according to the BCS. Nowadays, as the number of compounds that can be generated has increased dramatically, other alternatives like <i>in silico</i> methods have been employed to predict ADMET properties. Several researchers have explored quantitative structure property relationships (QSPR) involving Caco-2 permeability and reasonable accuracy values were achieved, but their practical use is limited due to the small datasets employed. The main goals of this work were to develop <i>in silico</i> models that discriminate compounds with high permeability ($P_{app} \geq 8 \times 10^{-6}$ cm/s) from those with moderate-poor permeability ($P_{app} < 8 \times 10^{-6}$ cm/s) using a large dataset with Caco-2 permeability values reported. The validation of the model was carried out by a test set and by external data set of 9 compounds which were experimentally determined. Material and Methods: A dataset of 719 organic compounds was collected from more than 250 published articles taking into account the homogeneity of <i>in-vitro</i> protocol. Cluster analysis was performed in training and test set selection. Best subset procedure was fixed as the strategy for variable selection. The principle of maximal parsimony was taken into account as a strategy for classification model selection. The experimental Caco-2 assay followed the standard procedure. Results and Discussion: Twenty one classification models based on indices generated from 20 descriptor families were performed and the best model by family of descriptors were selected considering the percentage of good classifications for training and test sets. The global accuracies of all models were ranking between 78-82%. A general model based on all molecular descriptors was developed and it classified correctly 82.01% and 82.14% for training and test sets. The statistic assumptions and application domain for the final model were verified. An external set of 9 compounds, with different permeability/solubility profiles, were predicted and 78 % (7/9 compounds) good assessed by experimental assay in Caco-2 cells. Conclusions: With the present methodology is possible to obtain models with strong predictive ability and can be used in the design of large libraries of compounds with appropriate values of permeability.</p>
<p>OC-11</p>	<p>A CUBAN EXPERIENCES IN THE RESEARCH AND DEVELOPMENT OF ANTIVIRAL DRUGS Alejandro Saúl Padrón Yaquis¹, Iverlis Díaz¹, Maricela Lara, Nicté González, Antonio Iraizos, et al.</p> <p>¹Drug Research and Development Center (CIDEM), Ave 26 e/ Ave Rancho Boyeros y Puentes Grandes, Plaza, Havana, Cuba.</p> <p>The use of generic drugs has been steadily increasing internationally as a result of economical pressure on drug budgets. Generic drugs provide the opportunity for major saving in healthcare expenditure since they may have substantially lower prices than the innovator brands. The practice of generic substitution is strongly supported by health authorities in many countries. Drug research and development is needed continuously for multiple viruses including HIV, herpes simplex viruses and hepatitis viruses, among others. Novel compounds are also urgently needed to combat HCV infection, as well as for prophylaxis and treatment of influenza in the event of a pandemic. Antiretroviral therapy (ART) has proven to be lifesaving, and can convert AIDS into a chronic but manageable disease. The present paper describes a Cuban experiences in the development of antiviral drugs. During the last years many new antiviral agents have been incorporated to the chemotherapeutics. The most important results of the research (formulation design, stability bioequivalence and other complementary studies) are included. Current research and perspectives are discussed.</p>
<p>OC-12</p>	<p>BIOAVAILABILITY OF ORAL MICROEMULSION OF CYCLOSPORIN A IN RATS Lagarto A, Martínez L, Pereda D, Carrillo C, Zayas F, Castell A, Rodríguez ME</p> <p>Drug Research and Development Center. CIDEM. 17 No. 6208 e/ 62 y 64, Playa, código postal 11300, Ciudad Habana, Cuba. email: alicia@cidem.sld.cu</p> <p>Cyclosporin A is a potent immunosuppressive agent, and is widely used for organ transplantation to overcome graft rejection. Due to low absorption of national oral solution of Cyclosporin A, a new formulation as microemulsion was developing with the aim to obtain higher bioavailability. In the present work the bioavailability of Cyclosporin A microemulsion was compared with Sandimmun Neoral (commercial leader) in rats. Two groups of Wistar rats were given 10 mg/kg of Sandimmun Neoral and Cyclosporin A microemulsion orally. Blood samples were collected from the tail vein at 0, 1, 2, 3, 4, 8 and 24 hours after oral administration. Cyclosporin A levels were determined by radioimmunoassay. Cyclosporin A concentration levels were similar in both treatments as pharmacokinetics parameters of AUC, T_{max} and C_{max}. National formulation of Cyclosporin A microemulsion was bioequivalent to Sandimmun Neoral.</p>
<p>OC-13</p>	<p>DEVELOPMENT AND INTRODUCTION OF A NEW GENERIC DRUG IN TABLET FORM: ATORVASTATINA 20 MG Iverlis Díaz Polanco, Jorge Rodríguez Chanfrau, Viviana Fusté, Addis Bellma Menéndez, Alicia Lagarto Parra, Milennis Arceo Peña, Osiris Blanco, Micaela Couret Trapaga, Angela Alfonso, Ayadamis Martinez,</p>

	<p>Onán Gámez, Jorge Luis Abreu, Efrain Sotolongo, Bárbara Jiménez Drug Research and Development Center (CIDEM), Ave 26 e/ Ave Rancho Boyeros y Puentes Grandes, Plaza, Havana, Cuba.</p> <p>The Atorvastatina is a drug synthetic hipolipemiante of second generation, belonging to the group of the estatinas that reduces the levels of total cholesterol, and triglycerides, in way dependent and sustained dose and it is suitable as helping in the handling of the dislipoproteinemias in patient with primary hypercholesterolemia primary family heterocigota, mixed dislipidemia (type IIa and IIb of Frederickson), family disbetalipoproteinemia and hipertriglyceridemia. Its action mechanism, consists on a potent and effective inhibition of the enzyme HMG-CoA reductasa. This drug is highly marketed at international level by the great demand that it has in the world population, because it reduces the risk of suffering of cardiovascular illnesses, first death cause in Cuba. The present work consisted on the development and industrial introduction of a formulation of Atorvastatina 20 mg tablets. The technological development of the same ones it was satisfactory. The tablets presented appropriate physical-mechanical and technological properties and the same ones were packed in polyethylene high density plastic flasks and Polivinilcloruro/Aluminio blisters. The chemical stability and microbiological of the finished product were studied during 24 months, the results demonstrated the good stability of the same one in both containers. The introduction and production of the product was carried out in NOVATEC pharmaceutical laboratories, Havana City.</p>
<p>OC-14</p>	<p>INTRODUCTION OF OPHTHALMIC GENERIC DRUGS IN THE NATIONAL PHARMACEUTICAL INDUSTRIES Ania González Cortezón, Caridad García Peña, Dunia Casanave Guarnaluce, Tania Márquez Conde, Addis Bellman Menéndez, Alicia Lagarto Parra, Tania Arguelles Bravo, Yanet Montes de Oca, Vivian Martínez, Micaela Couret Trápana, Jesús Domínguez Peña, Martha Botet, Yenilen Troche</p> <p>Drug Research and Development Center (CIDEM), Ave 26 and Boyeros, Plaza, Havana City, Cuba.</p> <p>The development of generic ophthalmic products has constituted an important link at the present for the increase of our therapeutic arsenal, also allowing, adding new medications in the folder of products to be used in the “Miracle Operation”. In this work was executed the whole cycle of investigation-development-introduction of 2 products that are part of the ophthalmic therapy of illnesses of different ophthalmic affections in Cuba: Sodium Diclofenac 0.1% and Betaxolol 0.5%; always including all the in agreement stages to the critical route for the design, registration and industrial introduction of a medication. An study of preformulation was carried out, it included the selection of the components of both formulations, was defined the most viable technological process to introduce in the pharmaceutical industry. An analytic technique was developed by High Performance Liquid Chromatography (HPLC) to study the stability of the proposed formulations and to determine its expiration date, as well as for the quality control, being properly demonstrated the physical, chemical and microbiological stability of each one of these products that at the moment are produced with national technology, fulfilling all the specifications of quality required internationally for pharmaceutical products. The developed products were stable at least for 12 months, fulfilling all the physical, chemical and microbiological parameters, during the period of the stability study. The proposed technologies were introduced in the Pharmaceutical Laboratory “Julio Trigo”, with satisfactory results.</p>
<p>OC-15</p>	<p>MUFER PILLS. NEW IRON SUPPLEMENT FOR WOMEN IN FERTILE AGE Gámez Rodríguez O, García Gallardo R</p> <p>Empresa NOVATEC, Playa, Havana, Cuba</p> <p>Iron is one of the essential micronutrients in the human feeding. Iron contribution in the Cuban population’s diet average diminished in the last years. For such, the present work was guided to design and develop a new product MUFER, pills for the Program of Supplementation with iron to women in fertile age and to contribute to the prevention and control of anemia. In the design and development of this new supplement 185 mg equivalent ferrous fumarate was used, 60 mg of elementary iron, and 0,4 mg of folic acid according to the doses recommended by Institute of Nutrition and Hygiene of Foods (INHAL). With this formulation, the research team, proceeded to carry out 3 pilots lots, which were packed appropriately and subjected to a study of stability that guaranteed the optimal conditions of the products, according to the parameters chemical-physical and technological establishment for this type of pharmaceutical formulation. The pills were stable 24 months after their production. Once approved its sanitary registration in the INHAL was carried out the introduction of the new formulation. The production of the product has overcome the 39 million pills with</p>

	<p>good results, without reprocess, neither reclamation. This innovation allows the satisfaction to the population and improvement the quality of life, therefore it possesses a significant social effect, since the products provides essential micronutrients that contribute to prevent anemia, and to help of diminished the risks of anemia in the pregnancy women. This anti-anemic product is to disposition of our national system of health and it represents a pharmaceutical production of the Novatec laboratory.</p>
<p>OC-16</p>	<p>FORMULATION AND EVALUATION OF DRUG ESTRACIP <u>Martínez E</u>, González J, Santiesteban P, Lugones J, Pared A</p> <p>Empresa Lab. R. Gutiérrez, Ciudad Habana, Cuba.</p> <p><u>Introduction:</u> In our country the pill used with estrogen combination and antiandrogen contains etinilestradiol (50 µg) and acetate of Ciproterona (2 mg). The pill that today is used at international level has changed considerably regarding the product that was marketed in 1960. The original pill of high dose contained up to 150 µg of estrogen, compared with the current of low dose" that contains 35 mcg or less, for example the use of an estrógeno 35 mcg or smaller cocktail with an antiandrogen have gone in growing state with the time due to its effectiveness in the treatment. In the woman: Treatment in serious manifestations of androgenization, for example, very intense hirsutismo (appearance of body hair), alopecia severe androgenetic, often accompanied by squares of acne y/o seborrhea and for the ovary syndrome poliquistico. In the man: Treatment antiandrogenic in inoperable carcinoma of prostate, alopecia androgenic and reduction of the deviated sexual impulse. <u>Materials and Methods:</u> The new formulations with 35 µg etinilestradiol or less dose were designed to reduce the risks and the secondary effects. The pill of low dose that contains much less estrogen, for example, has less effects in the arterial pressure, the sanguine clots, the metabolism of the hydrates of carbon and other relative factors to the cardiovascular illnesses. The lowest doses in estrogen have been related with less nauseas, vomits and headaches. Due to all the previous information and for agreement in the Program for the development of the Pharmaceutical industry in the year 2003 gave ourselves to the task of carrying out a pill combined with these active principles that he/she had the doses that requires the international levels. With the purpose of improvement of this formulation we trace ourselves the following general objective: To achieve a formulation with the estrogen dose (30 µg) of the product Estracip and this way to diminish the undesirable effects of this medication and to achieve a wide use of the same one. <u>Results and Discussion:</u> Was carried out physical, chemical and technological analysis of the granulated ones and the pills, the quick stability and of shelf of the pills, the statistical analysis of the results and economic and social valuation.</p>
<p>OC-17</p>	<p>INTEGRATED PROCESS SYSTEM ENGINEERING IN THE DEVELOPMENT AND PRODUCTION OF GENERICS <u>Jáuregui-Haza U</u></p> <p>Instituto Superior de Tecnologías y Ciencias Aplicadas (InSTEC). Ave. Salvador Allende y Luaces, Plaza de la Revolución, C. Habana, Cuba. ulises@instec.cu</p> <p><u>Introduction:</u> The sales of pharmaceutical industry have increased from 2000 to global values of more than 500 milliards USD, with average increase of 8-12 % per year. In this market, generics take and important place and have become an alternative for developing countries and for a part of the people in developed countries due their less prices if compare with leader pharmaceuticals. In Cuba, where the public health is one of the priorities of the state, the development of national pharmaceutical industry is one of the main columns that has permitted the positive change in the people life. From 1990 the national program for drug development favour the development and production of needed pharmaceutical forms trough the creation of new capacities in research, production and commercialization, with the preparation of human resources. This work presents the role of integrated process system engineering in the strategic development of generic development and production. <u>Results:</u> Among the essential aspects to consider for the development of generics it can be mentioned the health framework and the pharmaceutical epidemiology; the regulatory environment with special attention to good manufacturing, laboratory and clinical practices; the cost, technical and technological issues related to the synthesis of active principles and final formulations; the legal aspects and industrial property and the market situation. The use of integrated process system engineering is an innovative way to guaranty the success of generic production and that help to define the opportunities of pharmaceutical industry not only in our country, not also in the regional and international markets.</p>

<p>OC-18</p>	<p>SITUATION OF THE MULTI-SOURCE MEDICINES LICENSING IN CUBA <u>Suárez Pérez Yamira</u></p> <p>State Control Center for the Quality Control of Medicines (CECMED), Calle 200 No. 1706 e/ 17 y 19, Rpto. Siboney, Playa, Ciudad de La Habana. CUBA. CP 11600, Apdo. Postal 16065. email: yamira@cecmmed.sld.cu</p> <p><u>Introduction:</u> The multi-source medicines are pharmaceutically equivalent products. They are manufactured by different producers worldwide and they are not necessarily equivalent from a therapeutic point of view. Their safety and effectiveness are estimated starting from the demonstration of the bioequivalency regarding the original pharmaceutical product. In Cuba the pharmaceutical products are licensed by CECMED (Cuba National regulatory Authority) and they must demonstrate a high standard in terms of quality, safety and efficacy. Many regulations have been developed for an effective control of generic products. The present work aims to describe the regulatory framework (normative and legal documents) to perform the Licensing of Generic Products in Cuba. <u>Materials and methods:</u> It was used a retrospective method, considering the behavior of the marketed multi - sources products registered since 2007 to 2009 and using as variables the grade of novelty, causes of requesting of complementary information among others. For comparison purposes, we got the information from the Databases of CECMED and consulted normative and procedures from CECMED, WHO, ICH, EMEA and FDA. <u>Results:</u> We found 11 regulations useful for the Licensing of generics products, from them 6 were designed to regulate the therapeutic interchangeability and 5 regulations were created to support administrative, legal and quality aspects of the Licensing. From the 536 products registered in the evaluated period, almost 74 % are generic products, 111 produced in Cuba. The main non conformities detected during the evaluation of these medicines are related with the composition, quality specifications and therapeutic interchangeability, according to the national and international references consulted. <u>Conclusions:</u> The regulatory environment for generic products is changing and improving. All the applications are subjected to proper regulations, which are increasing their standard for the inclusion of relevant aspects such us pharmaceutical development, risk based approach, validation of bioassay and the extent the scope of in vitro guidelines to modified release dosage forms.</p>
<p>S-2</p>	<p>2ND SYMPOSIUM OF PHARMACOLOGY OF NATURAL PRODUCTS. <i>RHOPALURUS JUNCEUS</i> CUBAN VENOM AND OTHERS CUBANS NATURAL PRODUCTS</p>
<p>OC-19</p>	<p><i>Rhopalurus junceus</i> CUBAN VENOM: FROM EMPIRICAL KNOWLEDGE TO SCIENCE / VENENO DEL ESCORPIÓN CUBANO <i>Rhopalurus junceus</i>: DEL CONOCIMIENTO EMPÍRICO A LA CIENCIA</p> <p><u>Alexis Díaz García</u>¹, Luis Morier Díaz², Hermis Rodríguez Sanchez², Juan C. Rodríguez Arreucochea³, Yanelis Riquenes Garlobo¹, Irania Guevara Orellanes¹, Yamira Caballero Lorenzo², Dianeya Mendoza LLanes², Arturo Valdivieso García⁴, Ledys X. López Fuentes², Maika E. Figueredo Bernal², Anamays Govin Chávez², Ana E. Rodríguez Díaz², Regla María Medina Gali¹.</p> <p>¹LABIOFAM, ²IPK, ³INOR, ⁴LIORAD. Cuba email: alediaz@ipk.sld.cu, alexisdg@infomed.sld.cu, labiofam@ceniai.inf.cu</p> <p>Venom of scorpions have provided a wide-reaching branch of pharmacological effects, including inhibition of tumor cells growth. This have created great expectations in the treatment against cancer with natural products. Although <i>Rhopalurus junceus</i> is used in Cuba because of its population, studies are scarce and there's no scientific evidence on its potentialities. This paperwork is aimed at presenting scientific results on experimental studies with pre-clinical models highlighting significant and relative toxicity of venom in epithelial tumors. It includes studies on venom's effect over tumor advance, lung metastasis and survival of lab animals with epithelial tumors. Venom combined with antineoplasia drugs showed synergistic effects, significantly superior than drug simple treatments, which evidences its potentialities against cancer. As a result of the experiment, pre-clinical models presented a group of pharmacological properties which guarantee the use of <i>Rhopalurus junceus</i> venom in clinical trials of patients suffering from cancer; therefore, it is considered a promising natural product against the disease.</p>

<p>OC-20</p>	<p>ANALGESIC AND ANTI INFLAMMATORY PROPERTIES OF <i>RHOPALURUS JUNCEUS</i> VENOM /PROPIEDADES ANALGÉSICAS Y ANTIINFLAMATORIAS DEL VENENO DEL ESCORPIÓN CUBANO <i>Rhopalurus junceus</i> <u>Caridad C. Rodríguez Torres</u>, Irania Guevara Orellanes, María R. Pérez Capote, José A. Fraga Castro.</p> <p>LABIOFAM. Cuba. email: labiofam@ceniai.inf.cu, caridadrt@infomed.sld.cu</p> <p>Pain and swelling are frequent symptoms of several pathologies, including cancer. Scorpion <i>Rhopalurus junceus</i> is endemic from Cuba. Although its venom has been used traditionally by the Cuban population to treat cancer and other affections, its anti proliferating, antitumoral and anti metastasis potentialities have been proved just recently through different experimental models. In order to prove whether this natural product presented analgesic and anti inflammatory activity or not, it was carried out some chemical contortion assays induced by acetic acid and analgesia (hot dish). Anti inflammatory activity was checked using mouse ear inflammation models induced by croton oil and the instauration of cotton in rats. In addition, it was carried out an assay of inflammatory angiogenesis by adjuvant. As a result, there was a significant analgesic activity in mice when administering venom orally and intraperitoneal, in models of contortion induced by acetic acid and analgesia. Anti inflammatory activity was moderate in models using mouse ear inflammation induced by croton oil (oral, external and intraperitoneal administration) and rats with inserted cotton (oral administration). Likewise, there was angiogenic activity in angiogenesis model induced by adjuvant; product inhibited upbringing of new blood vessels. Once potentialities of <i>Rhopalurus junceus</i> venom have been proved; it can be applied in patients suffering from cancer and other inflammatory diseases to improve their life quality.</p>
<p>OC-21</p>	<p>TOXICOLOGICAL SAFETY OF <i>Rhopalurus junceus</i> VENOM AS ANTITUMORAL CANDIDATE. / EVALUACIÓN DE LA SEGURIDAD TOXICOLÓGICA DEL VENENO DEL ESCORPIÓN CUBANO <i>Rhopalurus junceus</i> COMO NUEVO CANDIDATO ANTITUMORAL <u>Irania Guevara Orellanes</u>¹, Caridad C. Rodríguez Torres¹, María R. Pérez Capote¹, Jorge E. González², Antonia C. Remigio³, Alicia Lagarto Parra³, Juan C. Rodríguez Aurrecochea⁴, Yamilé Vega Hurtado³, Janet Piloto Ferrer³, Dalia Álvarez Morejon⁵, Nelson Merino García⁵. ¹LABIOFAM; ²CPHR; ³CIDEM; ⁴INOR; ⁵CEIEB. Cuba. email:labiofam@ceniai.inf.cu, iraidago@infomed.sld.cu</p> <p>The Cuban endemical species <i>Rhopalurus junceus</i> has proved for over a decade its cytotoxic, antitumoral, analgesic, antinflammatory and anti angiogenics activities. The evaluation of this venom has included different assays on toxicology like acute toxicity, irritation of oral mucosa, subchronic and genotoxicological toxicity. Study on oral acute toxicity estimated LD50> 2000 mg/kg and LD50=16.41 mg/kg (15.39 to 17.72) intraperoneal. The oral administration of <i>Rhopalurus junceus</i> (100mg/kg) for 90 days caused no mortality, toxicity signs or significant disorders in hematological and biochemical parameters. There was no irritability of oral mucosa either. <i>Rhopalurus junceus</i> cytotoxicity and genotoxicity, calculated <i>in vivo</i> by inducing micronucleus in bone marrow and <i>in vitro</i> by a Comet assay, were negative. Low toxic potential has proved <i>Rhopalurus junceus</i> is toxicologically safe to be used in humans with a proper dosage and administration.</p>
<p>OC-22</p>	<p>COADJUVANTS THERAPY WITH A COMPLEX OF NATURAL PRODUCTS ORIGINS OF AMINOACIDS AND MINERALS (TROFIN). <u>Aznar García Elisa M</u>¹, González Hernández R²</p> <p>¹Doctor en Ciencias. Investigador Titular. Area de Ensayos Clínicos y Registros Sanitarios . Biocen. ²Lab de Reconstituyentes Trofin Biocen. email : eaznar@biocen.cu y eaznar@infomed.sld.cu</p> <p>Therapeutics alternatives aiming at improving the quality of live reducing adverse effect in disease treatment, for example in cancer therapy, radiations and chemotherapy produced anaemia in these patients. Different diseases demand variety of nutritional supplements. A fundamental point is that when we look at recommended nutrient intakes; in the last 25 years, the levels for some of the micronutrients have been gradually increasing. Studies was purpose to study the effect about natural products origins as coadjuvants to conventional therapies, but the question is whether this comes from better scientific knowledge and understanding of the biochemical role of these products and the nutrients, or whether the criteria for setting the levels of the requirements have changed. Even if the scientific knowledge base has expanded, it appears that the basic criteria for deciding on levels to recommend may be more of the responsibility. The objective of the study was to evaluate the effect of therapy complementary with supplementation with natural product complex of proteins-iron on the quality of life of patients with cancer.All patients received chemotherapy</p>

	<p>treatment and were monitored during six month period. The protocol for the study was approved by the Ethical Committee of the hospital. In the study we evaluate the haematological and clinical-nutrition parameters before the beginning of the treatment and after the supplementation. The results compared before and each month after, showed increased the haemoglobin and immunological indicators. No adverse reaction was observed in the patients studied. Results demonstrated that natural products aminoacids – minerals (Trofin) reduced the anaemia and improvement the quality of life in the patients.</p>
<p>OC-23</p>	<p>CUBAN EXPERIENCE WITH VIMANG, EXTRACT FROM <i>MANGIFERA INDICA</i> L STEM BARK. PHARMACOLOGICALS STUDIES AND THERAPEUTICS POTENTIALITY René Delgado-Hernández¹, B Garrido¹, D García², GL Pardo³, P Hernández⁴, I Rodeiro⁵, I Hernandez⁶, N Merino², MM Guevara⁶, A Alvarez², Y Maragiño³, AJ Nuñez⁷</p> <p>¹Laboratory of Molecular Pharmacology, Drug Research and Development Centre, Plaza, Havana, Cuba. ²Biomolecular Chemistry Center, Havana, Cuba. ³Pharmacy Institute, Havana University, Havana, Cuba. ⁴Molecular Immunology Center, Havana, Cuba. ⁵Center of Marine Bioactive Compounds, Havana, Cuba. ⁶LABIOFAM lab, Cuba, ⁷Science Department. Ministry of Health, Havana, Cuba.</p> <p>The aqueous extract from stem bark of <i>Mangifera indica</i> L (VIMANG) has been used in Cuba for several years in ethnomedical practices for the improvement of the quality of life of patients with different pathologies. A phytochemical characterization of the extract has led to the isolation of nine phenolic constituents, with the glucosylxanthone mangiferin as a major component, and different microelements as zinc, copper, and selenium. The extract has been proven to have, as the main pharmacological property an antioxidant activity. Other studies have shown that the extract also possesses other pharmacological activities, such as: anti-inflammatory, antiallergic, analgesic and as immunomodulator, with very complex and multifactorial mechanisms of action involved. These properties are related to the scavenger capacity of different reactive oxygen species. The interaction of mangiferin and other components of the extract with iron, represents an important antioxidant mechanism recently characterized in our studies. In addition, mangiferin and Vimang have the property of modulating different mediators involved into immune response. In general, the total extract and its xanthone, mangiferin are involved in several immunomodulatory processes, properties that confer an important therapeutic potentiality as adjuvant in the preparation of phytopharmaceutical products for the treatment of pathologies where oxidative stress and immunomodulatory disorders are related with their etiology. Different clinical studies are currently conducted in order to get new knowledge about its therapeutic potentiality. Key words: <i>Mangifera indica</i> L, Vimang, mangiferin, antioxidant, anti-inflammatory, immunomodulation</p>
<p>OC-24</p>	<p>ETHNOPHARMACOLOGICAL VALIDATION OF <i>COSTUS PICTUS</i> D. DON Morón F¹, Victoria MC¹, García AI¹, Cabrera H¹, Morejón Z¹, López M¹, Boucourt E,¹ Robineau L², Fuentes V³, Bacallao Y¹</p> <p>¹ Central Laboratory of Pharmacology (LCF), Faculty of Medical Sciences “Dr. Salvador Allende,” Carvajal s/n entre Agua Dulce y A, Cerro, Havana City, CP 11200, Cuba. email: moron@infomed.sld.cu ² University of Antigua and Guyana, Point a Pitre, Guadeloupe, France. ³ Research Institute on Tropical Fruit Cultivation, Güira de Melena, Havana Province, Cuba.</p> <p>Introduction: Decoction of <i>Costus pictus</i> fresh leaves and stems use to be traditionally administered for kidney lithiasis and renal colic. Our research project demonstrated the diuretic experimental effect of 30% dry leaves decoction (0.2, 0.4, and 0.8 mg/kg PO, single dose) in rats. No previously published studies were found about this species. Materials and Methods: It was collected fresh leaves and stems of the plant and a 30% decoction was made; a phytochemical screening was performed. Pharmacological studies were done in: writhing test induced by acetic acid (0.75%, 0.1 mL/10g IP); tail flick by water (55 °C) immersion (0.5, 1, and 5 g/kg, PO, single dose), both in mice; cotton pellet-induced inflammation (0.5, 1, 5, and 10 g/kg/4 days, PO, single dose) in rats; <i>in vitro</i> isolated ureter in rabbits (200 µL/100 mL); and <i>in vitro</i> antimicrobial activity (50% decoction of fresh leaves + stems 100 µL/well) in <i>S. aureus</i>, <i>B. subtilis</i>, <i>E. coli</i>, <i>P. aeruginosa</i>, <i>K. pneumoniae</i>, <i>E. cloacae</i>, <i>C. albicans</i>. Toxicological study (50% decoction of fresh leaves + stems) was done in acute toxic model (CTA) (maximal volume: 2 mL/100g PO, single dose) and repeated oral doses (1 g/24 h/5 days PO, single dose) in rats. Results and Discussion: It was detected the presence of saponins, phenolic compounds, and tannins, flavonoids, lactonic compounds and coumarins, triterpenes and steroids; protein and aminoacids; and sugars. Decoction (1 and 5 g/kg PO, single dose) inhibited significantly nociceptive response in writhing test and in tail flick model (5 g/kg PO, single dose), as well as the 4 M KCl (0.08 mM/mL)</p>

	<p>induced-ureter contraction. No effect was found in cotton pellet-induced inflammation and no inhibition zone was observed for microbial growth. CTA and 5 days repeated doses did not show death or toxicity sign.Conclusions: The results suggest that the traditional use of fresh leaves and stems decoction for kidney lithiasis and renal colic may be supported too by the experimental analgesic and ureter-relaxant effect and the lack of acute oral toxicity and 5 days repeated-doses.</p>
OC-25	<p>NATIONAL POLICY AND REGULATION OF THE NATURAL PRODUCTS IN CUBA <u>Maritza C. González Ramírez</u> State Center for the Quality Control of Drugs (CECMED), Havana, Cuba.</p> <p>Cuba is one of the WHO member countries from the Region of America that has a national policy regarding Traditional Medicine (TM) which is integrated to the health national system. This policy offers a solid base that defines the TM role which assures the legal base to promote and keep the good practices as well as the safety; the efficacy and the quality of the different therapies are implemented in our country. The State Center for the Quality Control of Drugs (CECMED by its Spanish acronyms), National Regulatory Authority, - related to the therapy with drugs-, has devised the strategies to regulate and control the natural products, establishing new policies and the legal framework about of the regulations which establish the requirements for registration and good manufacturing practice fulfillment, as well as guides, norms, medicinal plants monographs among other technical documents concerning to safety, efficacy and quality, so that the necessary bases are provided to guarantee the access and rational use of these products to the population. The information to be presented is related to the regulatory international situation, the national policies and the legal framework for the regulation and natural products control.</p>
S-3	<p>1ST INTERNATIONAL SYMPOSIUM ON PHARMACOGENETIC / 1^{ER} SIMPOSIO INTERNACIONAL DE FARMACOGENÉTICA</p>
OC-26	<p>PHARMACOGENETICS IN IBEROAMERICAN POPULATIONS: STUDIES IN CUBANS <u>Adrián LLerena</u>, Pedro Dorado, Eva M Peñas-Lledo Clinical Research Centre (CICAB), University of Extremadura Medical School, Hospital Infanta Cristina, 06080 Badajoz, Spain (www.cicab.es). Coordinator RIBEF and Sociedad Iberoamericana de Farmacogenética y Farmacogenómica (SIF). <u>RIBEF</u>: Iberoamerican Network of Pharmacogenetics and Pharmacogenomics www.ribef.org, email: allarena@unex.es</p> <p>To study pharmacogenetics in Hispanic populations is one of the main goals of the from Iberoamerican Network of Pharmacogenetics and Pharmacogenomics (www.ribef.org) and the Iberoamerican Society of Pharmacogenetics and Pharmacogenomics (SIF). Hispanics is a large group of world population, including people living in Spanish speaking countries of South and Central America as well as those categorized as Hispanics in the United States. Hispanic populations are diverse according to their country of origin or residence, culture, as well as genetic composition resulting from the inter-ethnic crosses between Amerindians, Europeans and Africans. Among the first Europeans (Castilians) arriving America in the XV very many of them were original from the southwestern Spanish region of Extremadura. Among the major determinants of the interindividual and interethnic variability of pharmacokinetics and drug response is the genetic polymorphism of the cytochrome P450-system enzymes (CYP). Population studies have already reported interethnic variability in the frequency of cytochrome P450 genes. Among CYPs, CYP2D6, CYP2C9 and CYP2C9 are the most clinical relevant due to its implication in the metabolism of very important drugs. So far, the most studied cytochrome P450 is CYP2D6, regarding its polymorphisms two phenotypes have been described: subjects who have an inherited decreased capacity to metabolise drugs are classified as "poor metabolizers" (PM), while the rest are "extensive metabolizers" (EM). The existence of very rapid hydroxylation due to an inherited amplification of an active gene has also been reported ("Ultrarapid Metabolizers" UM), we showed that 4.93% (95% IC2.23-10) of Spanish subjects from Extremadura carried two CYP2D6 active copies. Phenotypically PMs frequency between Caucasian populations is around 5-7%. The present Project aimed to evaluate the most relevant genetic polymorphism. So far CYP2D6 genetic polymorphism and dextrometorphan or debrisoquine metabolic ratio is analysing in different Ibero-American populations including Spain, South-America (i.e. Argentina, Ecuador, Colombia), Central-America (i.e. Costa Rica, Nicaragua), Caribe and North-America, (i.e México, Cuba). Differences have been found, the frequency of CYP2D6 PMs ranged from 6%-3.9% in Nicaraguans-Cuban-Mestizos. In several Latin American countries, including many Amerindian groups, no information are available on any pharmacogenetic targets. With the purpose of fulfilling this information gap and to promote collaborative pharmacogenetic/genomic research in Spanish- and Portuguese-speaking peoples in the Americas and the Iberian peninsula, a network – the Iberian American Network of Pharmacogenetics and Pharmacogenomics - was created (www.ribef.org).</p>

	<p>This initiative represents a promising step towards the inclusion of Latin American populations among those who will benefit from the implementation of pharmacogenetic principles and tools in drug therapy.</p> <p>Acknowledgments and Financial Support: The study was coordinated in Red Iberoamericana de Farmacogenética y Farmacogenómica RIBEF, www.ribef.org and Agencia Extremeña de Cooperación al Desarrollo AExCID.</p>
OC-27	<p>CYP2D6 POLYMORPHISMS IN PUERTO RICAN PSYCHIATRIC PATIENTS WITH ADVERSE EVENTS González-Tejera G¹, Gaedigk A² and <u>Corey S</u>³</p> <p>¹Univ Puerto Rico Sch Medicine, Dept of Psychiatry, San Juan, PR. email: Gloria.gonzalez1@upr.edu ²Clinical Pharmacology and Therapeutics, Children's Mercy Hospital, Kansas City, MO, 64108 ³Univ Puerto Rico Sch Medicine, Dept of Pharmacology and Toxicology, San Juan, PR,</p> <p>Introduction: The CYP2D6 liver enzyme, which metabolizes 25-30% of common medications, is highly polymorphic. Little is known about the <i>CYP2D6</i> alleles present in Hispanics, and existing studies have focused on Mexicans and Mexican-Americans. The goal of the study was to identify the <i>CYP2D6</i> alleles with reduced or negligible activities present in the Puerto Rican population. Materials and Methods: Research subjects were 40 Puerto Rican psychiatric patients referred because of suspected intolerance of drugs metabolized by CYP2D6, and five subjects without adverse responses to these drugs. All subjects had both parents and all grandparents born in Puerto Rico. Leukocyte DNA was queried for 27 <i>CYP2D6</i> alleles using the Roche AmpliChip P450 test. Results and Discussion: A total of 12 alleles were identified. The most common alleles were <i>CYP2D6</i>*1>*2>*4>*41. The inactive alleles were *5>*31 >*40; reduced activity alleles were *10>*17>*9*=*29; active alleles were *1>*2>*35. Two subjects carried the rare *31 allele. Only one subject carried two non-functional alleles (<i>CYP2D6</i>*5/*40), and was predicted to be a poor metabolizer. No duplicated alleles were identified in this sample. Conclusions: Any conclusions should be interpreted with caution given the small size that was queried for CYP2D6 allelic variants. Nonetheless, the findings strengthen the emerging practice of Personalized Medicine in admixed populations like Puerto Ricans. [This work was supported in part by an RCMI Clinical Research Infrastructure Initiative award, 1P20RR11126, from the National Center for Research Resources, NIH.]</p>
OC-28	<p>LONG-TERM ESTRADIOL TREATMENT INFLUENCES GROWTH HORMONE-REGULATED LIVER TRANSCRIPTOME IN MALE RATS: RELEVANCE TO DRUG METABOLISM <u>L. Fernández-Pérez</u>¹, R. Santana-Farré¹, M. Mirecki de Garrido¹, A. Flores-Morales²</p> <p>¹Department of Clinical Sciences-Pharmacology Unit, Molecular and Translational Endocrinology Group, University of Las Palmas de GC, 35011- Las Palmas, Canary Islands, Spain. email: lfernandez@dcc.ulpgc.es ²Department of Molecular Medicine and Surgery, Karolinska Institute, Sweden. Novo Nordisk Center for Protein Research, University of Copenhagen, Denmark</p> <p>GH is a major regulator of growth and metabolism. Estrogens may modulate GH-regulated endocrine and metabolic functions in liver. To test this hypothesis, we used adult hypothyroid-castrated (TX-OX) male rats to minimize the influence of internal hormones on treatment. TX-OX rats were treated with E2 benzoate (50 □g/kg; sb; 5 days/week) for 20 days before GH replacement (0.3 mg/kg/day; sb; two daily injections) during seven days. Hypothyroidism reduced body weight gain, circulating IGF-I, and mRNA levels of IGF-I and male-specific CYP2C11 gene in liver, which were restored by GH. However, in the presence of E2, GH was not able to restore the changes induced by hypothyroidism. CYP2C12, a female differentiated gene, was induced by E2. To obtain comprehensive information on effects of E2 treatment on GH-regulated gene expression, we performed microarray analysis of liver transcriptome. In the absence of E2, we identified 218 genes that were up-regulated by more than 50% by GH treatment, while 139 were down-regulated to the same extent. In the presence of E2, 172 genes were up-regulated by GH treatment, while 243 were down-regulated. Administration of E2 to hypothyroid rats, provoked drastic changes (up-regulated genes=382; down-regulated genes=290) in liver transcriptome. A set of 84 genes were regulated in common by GH and E2. In the presence of E2, the number of Biological Processes with significant representation in our set of genes that were up-regulated by GH treatment was drastically reduced. This work highlights the influence of estradiol on male liver which has relevance for drug metabolism and several diseases.</p>
OC-29	<p>CLINICAL RELEVANCE OF PHARMACOLOGICAL INTERACTIONS MEDIATED BY THE ABC TRANSPORTERS ABCB1 (MDR1, P-GLYCOPROTEIN): STUDIES IN CUBA <u>Rodeiro I</u>¹, Martínez¹, I. Hernández¹, R. Delgado², JA Herrera³ and J Kirchheiner⁴</p>

	<p>¹Center of Marine Bioproducts (CEBIMAR), Havana, Cuba. ²Drug Research and Development Centre (CIDEM), Havana, Cuba. ³Institute of Materials Science and Technology (IMRE), 10400 Havana University, Havana, Cuba, Havana, Cuba. ⁴Institute of Pharmacology, Toxicology and Natural Products, Ulm University, Germany.</p> <p>P-glycoprotein (P-gp) is a transmembrane active efflux pump for a variety of drugs and the most extensively studied ATP-binding cassette (ABC) coded by MDR1 gene. The importance of P-gp in drug–drug interactions is being identified. Inhibition or induction of P-gp by co-administered drugs and herbal constituents, between others, may result in pharmacokinetic interactions leading to unexpected toxicities or under treatment. Thus, the use of alternative medicine, like herbs has increased significantly. However, for most them, it is unknown whether they affect on drug transporters activity. Results about modulation of different natural Cuban products, like <i>Mangifera indica</i> L extract, mangiferin and <i>Thalassia testudinun</i> extract, on expression and function of P-gp are presented. On the other hands, besides, it is postulated that ABCB1 polymorphisms contribute to variability in P-gp function. Single-nucleotide polymorphisms (SNPs) in MDR1 gene are associated with phenotypic variation in P-gp expression levels of tissue. The wobble C3435T polymorphism at exon 26 has been associated with different expression levels and activity. Differences in allele frequency of the C3435T polymorphism have been demonstrated between ethnic groups. Frequencies of the variant C3435T were evaluated in 140 Cuban unrelated healthy volunteers (73 males and 67 females). Results showed: 65 subjects (46.4%) expressed CC, 58 (41.4%) expressed CT variant and 17 (12.1%) presented the TT variant. Results fit to Cuban population origins. The study of interactions and of genetic factors affecting pharmacokinetics and pharmacodynamics is expected to improve drug safety and will enable individualized drug therapy.</p>
OC-30	<p>FROM PHARMACOGENETICS TO PERSONALIZED MEDICINE: A CUBAN REGULATORY PERSPECTIVE <u>Diadelis Remírez Figueredo</u></p> <p>National Centre for State Quality Control of Drugs, (CECMED). Avenue 17 and 200 , Siboney, Playa, Havana, Cuba. email: diade.remirez@infomed.sld.cu</p> <p>The science of pharmacogenomics has advanced significantly in the last five years, but it is still in infancy and is mostly used on research basis. The Pharmacogenomics helps identify interindividual variabilities in drug response (both toxicity and effectiveness). This information will make it possible to individualize therapy with the intent of maximizing effectiveness and minimizing risk. The aims of this work are to present the bases of pharmacogenetic, the advantage and challenges of this specialty, the main enzymes characterized for the genetic polimorphism and the world and cuban regulatory perspective about this subject. We will show the main biomarkes for pharmacogenetics studies and a general guidance for submission of this type of research. The hope for the future is that through personalized medicine, doctors and patients will be able to make better-informed choices about treatment. This treatment will avoid the adverse drug reaction to the medication and will improve the diagnosis diseases as well as the prevention and treatment of diseases.</p>
W-1	<p>5TH INTERNATIONAL WORKSHOP ON PHARMACOVIGILANCE IN THE 10TH ANNIVERSARY OF PHARMACOVIGILANCE CUBAN COORDINATING UNIT. / 5^{TO} TALLER NACIONAL DE FARMACOVIGILANCIA EN EL 10^{MO} ANIVERSARIO DE LA UNIDAD COORDINADORA NACIONAL DE FARMACOVIGILANCIA</p>
OC-31	<p>HEPATOTOXICITY OF ANTITUBERCULOSIS DRUG TREATMENT: A CASE-CONTROL STUDY <u>Rego J¹</u>, Jiménez G², Yera I², Machado D³, Yera D³, Castellanos A¹, Jiménez R¹, Lizana E¹.</p> <p>¹Salvador Allende Hospital, Calzada del Cerro 1551, Cerro, Havana City, Cuba. email: jose.rego@infomed.sld.cu ²Center for the Development of Pharmacoepidemiology, National Pharamcovigilance Unit, 5^{ta} Ave and 44 St, Miramar, Playa, Havana City, Cuba. ³ Benéfico Jurídico Hospital, Calzada del Cerro 1652, Cerro, Havana City, Cuba.</p> <p>Introduction: Liver toxicity is one of the most well known and worrisome adverse effects of antituberculosis treatment, but epidemiologic evidence regarding this phenomenon is scarce. Material and Methods: A case control observational analytical epidemiologic study was performed. The cases chosen were those patients</p>

	<p>with probable hepatotoxicity. Three controls were selected for each case and were matched according to index day, sex and age. Previous exposure to antituberculosis drugs was identified using structured interviews and clinical case history review. The primary endpoint was hepatotoxicity caused by antituberculosis drugs, which included demographic and clinical variables. Descriptive statistical method and Odds Ratio estimated the risk with a confidence interval of 95% and confounding factors were assessed with logistic regression. Results and Discussion: Hepatotoxicity occurred in 39 patients (37, 8%). The risk of development of hepatotoxicity was estimated at 8.4 (95% CI: 3.7 – 19.3; p= 0,000). In the logistic regression analysis, hepatotoxicity was associated with alcoholism (OR: 12.8, 95% CI 4.12 to 39.81, p = 0.000) and concomitant therapy (OR: 2.9; 95% CI 1.28 to 6.73, p = 0.011). Conclusions: The use of antituberculosis drug at Benéfico Jurídico Hospital increased the risk of hepatotoxicity in patients, which was further associated with alcohol consumption and concomitant therapy.</p>
<p>OC-32</p>	<p>SIGNAL IDENTIFICATION IN LOW FREQUENCY ADVERSE DRUG REACTIONS. CUBA 2004_2008 Santos Muñoz L¹, Jiménez López G², Orta Alfonso I², Marrero Faz E³</p> <p>¹ Provincial Pharmacoepidemiology Centre, Ave San Diego, esq San Juan de Dios. Pueblo Nuevo Matanzas, Cuba. Email: leidys.mtz@infomed.sld.cu ² Center for the Development of Pharmacoepidemiology, National Pharamcovigilance Unit, 5^{ta} Ave and 44 St, Miramar, Playa, Havana City, Cuba. ³ CENSA, San José de las Lajas, Habana, Cuba.</p> <p>Introduction: In the last few years there is been an accelerated growth in medical drugs consumption increasing not only the Health care and personal patients expenses but also the risk of adverse effects. This research has the intention of identifying drugs/signal effects combinations, starting from low frequency Adverse Drug Reaction (ADR), received at the National pharmacovigilance coordinator unit in the last five years. Material and Methods: observational, descriptive, transversal, pharmacovigilance research, to identify the frequency of adverse effects, characterize those of low frequency of appearance, as well as to apply the Cuban algorithm signal system for non-described adverse effects in literature. Results and Discussion: A total of 35624 ADR spontaneous reporting were evaluated, with an annual percentage of 7125 reports, the most ADR reported were the common ones, holding 23434 reports, those of low frequency reached the 34.2%. In low frequency report, adults and female sex were predominating. (8198; 67,2%) y (8032; 65,9%) respectively. The non-opioides pain relievers and rash, were the top reported ones, interaction of adverse effects rated low / severe and moderated: 45.8 / 54.2 and probable reactions were predominant, (66.4%). Considering signals of those combinations which spontaneous reporting of low frequency were over 3, this research rejected the number of 843 (71.8%) , however 332 reports, (28.2%) were not described either in national biography or international references, 56 out of them held 3 reports. Conclusions: The Cuban pharmacovigilance system algorithm was a vital issue in the organization of ideas and work hypothesis creation in matters of medical drugs safeties.</p>
<p>OC-33</p>	<p>GENERATION OF SIGNS IN PHARMACOVIGILANCE REGISTERS: HAVANA CITY 2003 -2009 Midsay B. López Leyte</p> <p>McS. en Farmacoepidemiología. Profesora asistente de Farmacología. Especialista de 1^{er} grado en Farmacología. Center for the Development of Pharmacoepidemiology, Playa, Havana, Cuba.</p> <p>Introduction: The signs in Farmacovigilancia are in company of the rest of the reports of the environment, one lacks a population denominator that allows to estimate risk. The Relative Proportional Risk (PRR) is a statistical quantitative useful technology used for these ends in big databases. Objetive: To describe the adverse reactions of the medicines most brought in 6 years of the basic national picture. Association determines medicament - reaction to generate signs and to design an intervention with educational ends and of procedure of work in generation of signs in farmacovigilancia. Method: an investigation was designed applied to farmacovigilancia, using the axis of classification applicability of results, in Farmacovigilancia's Coordinating Provincial Unit of the Provincial Direction of Health of City of Havana. There selected ten medicaments most brought to the provincial database from 2003 to 2008, at every par medicament - reaction applied to them the statistical quantitative technology PRR. The signs were selected and there was created a Procedure Normalized of Operation (PNO) to generalize the application of the technology to the system. Results: The IECAs, four antimicrobial ones, dipirona and ibuprofeno, as well as the vaccine DPT and the metoclopramida were the most brought medicines. The skin (30.6%), the digestive system (19.2%) and the nervous system (12.3%) were the most affected. In types of reaction the cutaneous eruption turned out to be most brought with 20.3%, followed of the vomit (6.2%) and the cough (6.1 %). Ten signs were obtained.</p>

	<p>Conclusions: The manifestations of hypersensitivity are most associated with the consumption of the most brought medicaments and the principal sign issued on having analyzed the database of City of Havana. The application of quantitative methods to generate signs of farmacovigilancia is a commendable and comfortable method to be applied by the provincial centers of farmacovigilancia.</p>
OC-34	<p>IMPLEMENTATION OF A PROGRAM OF ADVERSE EFFECTS NOTIFICATION FOR PATIENT. GUANTÁNAMO. JUNE 2009 - FEBRUARY 2010 Trabanca Beltrán YA¹, Jiménez G², Alonso I².</p> <p>¹Health Public Direction, Paseo St and Luz Caballero corner. Cuba. email: trabanca@infosol.gtm.sld.cu ² Center for the Development of Pharmacoepidemiology, National Pharmacovigilance Unit, 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba.</p> <p>Introduction: In the last years the drugs have become topic of concern, every time they are more those that are marketed, increase the consumption considerably and as a consequence adverse effects appear, for that becomes necessary the pharmacovigilance to classify and to identify these effects that appear in the habitual clinical practice. In the Cuban system of health we works with the method of spontaneous notification for the sanitary professionals, however the program does not exist where the patients notify their adverse effects in a direct way. Materials and Methods: Observational, descriptive and traverse study, that used the method of pharmacovigilance spontaneous notification of adverse reactions suspicions in the municipal main pharmacies of Guantánamo city to implement a program of notification of adverse effects to drugs for patients. We designed a collection of data schedule that was designed for the patients' disposition in the 10 municipal main pharmacies of the city, in the period among June from 2009 to February 2010. Results and Discussion: The reports of adverse effects were more frequent in patients from 15 to 39 years of old and feminine sex. The pharmacological groups that prevailed were the antimicrobial, AINES and the vaccines, being the most frequent medications the antigripal vaccine, the Cefalexina and the Captopril. The most affected organs systems were the digestive, skin and central nervous system. The light, probable and frequent adverse effects prevailed. Also the reports of adverse effects in their majority were of good quality. Conclusions: The implementation of a program of report of adverse effects for the patients is feasible and it provides important data to the sanitary system.</p>
	<p>THE CHANGING FACE OF MEDICAL EDUCATION IN THE US AND THE NEW EDITION OF GOODMAN & GILMAN Laurence L. Brunton Professor of Pharmacology and Medicine, Department of Pharmacology, UCSD School of Medicine, La Jolla, CA, USA. <i>The editor of Goodman & Gilman's book "The Pharmacological Basis of Therapeutics"</i></p> <p><i>Resumen no disponible en el momento de la edición del libro. Abstract non available in the moment of the edition of the book of summaries.</i></p>
W-3	<p>WORKSHOP: BACTERIAL VACCINES (CURRENT APPROACHES TO PNEUMOCOCCAL, MENINGOCOCCAL AND OTHER BACTERIAL VACCINES) / TALLER VACUNAS BACTERIANAS</p>
	<p>INTRODUCTION OF WORKSHOP Rolando Ochoa. Finlay Institute, Havana, Cuba.</p>
OC-35	<p>SCALE-UP OF PROCESS FOR GMP PRODUCTION OF A SEROGROUP A AND W135 MENINGOCOCCAL OUTER MEMBRANE VESICLE VACCINE FOR AFRICA Luis García¹, Aleida Mandiarote¹, Gunnstein Norheim³, Domingo González¹, Giselle Reyes¹, Gro Tunheim², Bárbara Cedre¹, Humberto González¹, Juan C Martínez¹, Lisbeth Næss², Maritza Hernández¹, René Tejedor¹, Yaremis Hernández¹, José L Pérez¹, Rosa L Solis¹, Paul Arne Kristiansen², Ibis Ontivero¹, Johan Holst², Franklin Sotolongo¹, Dominique A Caugant², Einar Rosenqvist²</p> <p>¹Finlay Institute, Havana, Cuba; ²Norwegian Institute of Public Health, Oslo, Norway; ³University of Oxford, Oxford, UK. email: lgarcia@finlay.edu.cu</p> <p>Epidemics of meningococcal disease in the African meningitis belt are mainly caused by serogroup A and occasionally by serogroup W135 strains. Affordable vaccines providing long-term protection in all age</p>

	<p>groups are highly needed. Antibodies against the non-capsular antigens are able to exert bactericidal activity. Previous vaccines based on serogroup B outer membrane vesicles (OMV) have demonstrated to be safe and efficacious. In order to establish methods for GMP production and formulation of a vaccine based on OMVs from serogroup A and W135 meningococci, two candidate wild-type serogroup A (ST-7) and one W135 (ST-11) strain were cultivated in modified Frantz growth medium. The production process was scaled up to 100 L cultivation volume in a fermentor. OMVs were extracted by use of deoxycholate and purified by ultracentrifugation and gel filtration. At the end of the purification process, OMVs were either precipitated with alcohol, or diafiltrated against sucrose solution. The OMVs from the A and W135 strains were adsorbed to aluminum hydroxide, mixed (1:1) and used for characterization, quality control and immunization of mice. The resulting OMVs contained the major relevant proteins (e.g. PorA, NadA, Opc, FetA). The LOS content and endotoxin level were both within the accepted ranges for OMV vaccines. The vaccine elicited prominent immune responses in mice. The scale-up of the production of the serogroup A+W135 OMV vaccine was successful. These results showed that a combined OMV vaccine could probably be an affordable alternative or supplement to the conjugate approach in countries with mixed A and W135 epidemics.</p>
<p>OC-36</p>	<p>CHARACTERIZATION AND IMMUNOGENICITY EVALUATION OF SEROGROUP A AND W135 OUTER MEMBRANE VESICLES DERIVED FROM GROWTH IN MODIFIED FRANTZ AND CATLIN MEDIUM</p> <p>Giselle Reyes¹, Aleida Mandiarote¹, Gro Tunheim², Domingo González¹, Gunnstein Norheim³, Bárbara Cedré¹, Lisbeth M Næss², Humberto González¹, Juan C Martínez¹, Tania Valmaseda¹, Maritza Hernández¹, René Tejedor¹, Ibis Ontivero¹, Naylet Marrero¹, José L Perez¹, Rosa L Solis¹, Lisa Høyem Kristiansen², Franklin Sotolongo¹, Johan Holst², Dominique A Caugant², Luis García¹, Einar Rosenqvist²</p> <p>¹Finlay Institute, Havana, Cuba; ²Norwegian Institute of Public Health, Norway; ³University of Oxford, Oxford, UK; lgarcia@finlay.edu.cu</p> <p>Serogroup A and W135 meningococcal disease causes a high burden of disease in many African countries. Plain polysaccharide vaccines are available, but they are poorly effective in young children, and polyvalent conjugate vaccines are considered to be too expensive. Outer membrane vesicle (OMV) vaccines from serogroup B meningococci have proven to be safe and efficacious in various epidemic situations. Two “wild-type” A:4/21:P1.20,9 (ST-7) and one W135:2a:P1.5,2 (ST-11) strain from recent epidemics in Africa were cultured in either Frantz or Catlin synthetic media, and the yield, protein expression and immunogenicity of produced OMVs were compared. The OMVs were characterized by SDS-PAGE and by immunoblots with monoclonal antibodies. Balb/C mice were immunized with either two doses of 0.5, 2 or 10 µg of OMV proteins, or with one dose of 50 µg. Immune responses were tested by ELISA and in serum bactericidal assay (SBA). There were no significant differences in the protein profile of OMVs from the two culture media and all relevant proteins were present in the vesicles. One of the two A strains showed higher levels of NadA than the other one, and was preferred. High levels of IgG antibodies against OMVs from all three strains were detected in ELISA. OMVs derived from both serogroup A strains produced in Frantz medium induced similar high SBA titers. Culture medium was not of major importance for protein content or immunogenicity. An A+W-135 OMV combination seems to be a feasible way forward for production of an affordable meningococcal vaccine for Africa .</p>
<p>OC-37</p>	<p><i>BORDETELLA PERTUSSIS</i> DERIVED PROTEOLIPOSOME AS ACELLULAR VACCINE CANDIDATE. PRELIMINARY ANTIGENIC AND BIOLOGICAL CHARACTERIZATION</p> <p>Sonsire Fernández¹, Giselle Reyes¹, María Emilia Gaillard², Matías Fingermann², Daniela Bottero², Yovania Fernández¹, Luis García¹, Rosa L. Solis¹, Daniela Hozbor² and José Luis Pérez¹</p> <p>¹Departamento de Bioquímica. Dirección de Vacunas Bacterianas. Vice-presidencia de Investigaciones. Instituto Finlay. email: sfernandez@finlay.edu.cu</p> <p>²Instituto de Biotecnología y Biología Molecular (IBBM). Facultad de Ciencias Exactas. Universidad de La Plata. Argentina.</p> <p><i>Bordetella pertussis</i> is the causative agent of whooping cough. Although humans of all ages can develop pertussis, the highest morbidity and mortality occurs in children, with over 40 million cases and 350000 deaths each year. In recent years, an increasing number of cases have been reported in more mature age groups, specifically adolescents and adults. These data support the contention that vaccination in infancy does not afford long-term protection and indicate a need for booster immunization in older age groups. There are two variants of vaccines against pertussis at present, inactivated whole cell and acellular vaccines. Both are protective against the disease but the first one is considered to produce undesirable adverse reactions. Our</p>

	<p>group is working on the development of an acellular vaccine candidate based on a proteoliposome derived from <i>Bordetella pertussis</i>. As for all candidates to vaccine, different biological and physical-chemical assays must be performed to evaluate its protective ability and reactogenicity. Protection assays in Balb/C mice using intranasal challenge model against local clinical isolations were done in Argentina. To evaluate the toxicity, pirogenicity and LAL assays were developed. Proteoliposome antigenic composition was preliminarily determined through proteomic analyses and its conformational structure was observed using electronic microscopy. The results indicated that the proteoliposome confers a high protective immune response against all the evaluated clinical strains. Pirogenicity and LAL assays showed that proteoliposome is aprotogenic in the evaluated concentrations, while endotoxin units, measured by LAL, were comparable with the values reported for the constitutive proteoliposome of VA-MENGOG-BC™ vaccine. Proteomic analyses indicated the presence of pertactin and fimbriae, two important antigens that normally are included on commercial acellular vaccines. Electronic microscopy showed spherical particles on the range of 25-70 nm. The results described in this work allow us to consider proteoliposome as a potential acellular vaccine against <i>Bordetella pertussis</i>.</p>
<p>OC-38</p>	<p>PRELIMINARY CHARACTERIZATION OF AN ORAL MULTIVALENT VACCINAL CANDIDATE AGAINST CHOLERA-SHIGELLA-SALMONELLA <u>José Luis Pérez</u>, Adriana Callicó, Sonsire Fernández, Giselle Reyes, Rubén Cabrerías, Michel Acosta, Tania Valmaseda, Yovania Fernández, Yisabel Aranguren, Bárbara Cedré, Maylin Alvarez, Maydelys Alvarez, Isis Montano, Daiyana Díaz, Mildrey Fariñas, Bárbara Yolanda Valdés, Luis Riverón and Luis García.</p> <p>Biochemistry Department. Direction of Bacterial Vaccines. Vice-presidency of Research. Finlay Institute. email: jlperez@finlay.edu.cu</p> <p>Background: Diarrheic diseases remain a health problem and they are an important cause of morbidity and mortality worldwide. A great number of microorganisms are the etiological agents of these diseases, being Rotavirus, Escherichia coli, Shigella, Salmonella and Vibrio cholerae the most relevant. Presently, there are some monovalent vaccinal candidates that have shown short term effectiveness, but no positive results have been obtained yet with multivalent or combined vaccinal candidates. We are working in the development of a proteoliposome (PL) combination-based multivalent formulation, derived from the surface of different bacteria that cause diarrhoeas disease. This multivalent formulation will be orally administered in humans in a microcapsule or cochleates suspension. Methods: Purified PLs were partially characterized by protein determination and LPS, SDS-PAGE and chromatography on Sephacryl S-1000. In addition different formulations were assessed in immunogenicity studies in rats and mice, were measured by IgG serum and IgA saliva ELISAs against each of the different solid-phase antigens. Results: SDS-PAGE showed that PLs contain outer membrane proteins (OMP) with molecular weights ranging 12-96 kDa and that there are protein bands that might be common in the different monovalent preparations. Chromatographic profiles of each case support a successful assembly of OMP with the molecules of the detergent, forming nanoparticulated structures. IgG serum and IgA saliva ELISAs in both rats and mice showed a high and homogeneous response of specific antibodies for each antigen in the evaluated multivalent preparation. Conclusions: These are promising results and they stimulate the development of a PL combination-based multivalent vaccinal candidate to prevent the diarrhea.</p>
<p>W-4</p>	<p>WORKSHOP: 3RS ALTERNATIVES IN PHARMACOLOGY AND TOXICOLOGY / TALLER DE MÉTODOS ALTERNATIVOS EN FARMACOLOGÍA Y TOXICOLOGÍA</p>
<p>OC-39</p>	<p>REGULATORY RISK ASSESSMENT AND THE USE OF ANIMALS <u>Koëter Herman</u></p> <p>Orange House Partnership, Kampendaal 83, 1653 Dworp, Belgium. email: herman.koeter@orangehouse.eu</p> <p>Although our food and drugs have never been safer than today, yet we are finding more contaminants in it than 20 years ago because analytical tools have become much more sophisticated. New technologies include nanotechnology application and the genetic modification of plants, animals and micro-organisms. Although there are currently already more than 20 legislations in the food and feed safety area in the EU alone, animal welfare considerations are hardly mentioned, and no guidance is provided on how to reduce the need for experimental use. At global level discrepancies and contradictory data requirements exist which should give rise to actions to reconsider several regulations currently in use. These discrepancies are not limited to food</p>

	<p>and chemicals risk assessment, they also occur in the area of pharmaceuticals. Harmonization of data requirements is needed to contribute significantly to the reduction of experimental animal use in regulatory safety assessment. Recent new scientific developments in risk assessment justify a rather fundamental reconsideration of current approaches and principles. The use of predictive hazard characterization tools based on existing data, in particular QSARs and TTC (thresholds of toxicological concern) deserve a prominent role in risk assessment. In addition, the newest generation <i>in vitro</i> hazard identification methods have very much matured and the reliability and relevance of test methods aiming at the identification and characterisation of pertubated molecular and cellular metabolic pathways strongly contribute to a better understanding of toxicity. These novel computational and <i>in vitro</i> approaches, complemented with the latest proteomic, metabonomic and carcinogenomic profiling techniques are expected to provide in the near future adequate predictive power to assess the safety (or risk) of substances thus allowing a significant reduction (or abandoning) of the traditional observational animal studies in risk assessment. The presentation will highlight current developments and will point a way forward to embed the novel approaches into regulatory risk assessment requirements.</p>
<p>OC-40</p>	<p>VALIDATION OR SCIENTIFICALLY VALID? <u>Alan M. Goldberg</u></p> <p>Center for Alternatives to Animal Testing, Bloomberg School of Public Health Johns Hopkins University, Baltimore, Maryland 21205 USA. email: goldberg@jhspsh.edu</p> <p>Many groups and individuals have developed criteria to establish whether a method is valid. In the US, the EU and in other countries, validation bodies have been organized to evaluate the validity of methods used in the risk assessment process. These organizations codified a process to determine validity –the validation process. As these organizations developed, in the early stages of the science, they focused on evaluating an <i>in vitro</i> method against an animal-based standard. A major contribution of these organizations was the identification of the criteria necessary for a test to be useful in the risk assessment process. The formal process, however, has limited usefulness as we move forward into the toxicology of the 21st century. The difficulties arise from the observations that this new toxicology will require many different tests to predict risk; that animal-based tests do not necessarily predict human consequences; and that mechanistic assays in development need a completely different approach to validation. The replacement process is actually the process used from the beginning of scientific investigation –scientific publication, reproducibility by others, interpretability of the data, and includes that a test must be developed to a set of identified criteria. This latter process results in what one would call a scientifically valid method. Regulators do not require tests to be validated by a formal process; instead, regulators are responsible that the data they evaluate is produced by scientifically validated methods. As we move from an animal-based toxicology to a human-based toxicology, we must ensure that the access to quality data, the evaluation of scientific validity and the data used in risk assessment are of the highest quality, they must also be transparent and provide predictive capacity to the questions being addressed.</p>
<p>OC-41</p>	<p>TOXICOLOGY IN THE 21ST CENTURY <u>Thomas Hartung</u></p> <p>Johns Hopkins University, School of Public Health, Center for Alternatives to Animal Testing, Doerenkamp-Zbinden Chair for Evidence-based Toxicology, Baltimore, USA</p> <p>A mechanistic toxicology has evolved over the last decades, which is effectively relying to large extent on methodologies which substitute or complement traditional animal tests. The biotechnology and informatics revolution of the last decades has made such technologies broadly available and useful. Regulatory toxicology has only slowly begun to embrace these new approaches. Major validation efforts, however, have delivered the evidence that new approaches do not lower safety standards and can be integrated into regulatory safety assessments. Political pressures especially in the EU, such as the REACH legislation and the 7th amendment to the cosmetic legislation, further prompt the need of new approaches. In the US, especially the NAS vision report for a toxicology in the 21st century and its most recent adaptation by EPA for their toxicity testing strategy have initiated a debate how to create a novel approach based on human cell cultures, lower species, high-throughput testing and modeling. The lecture summarizes the lessons learned from the development, validation and acceptance of alternative methods for the creation of a new approach for regulatory toxicology. Beside the technical development of new approaches such as systems toxicology, a case is made that we need both conceptual steering and an objective assessment of current practices by evidence-based toxicology.</p>

<p>OC-42</p>	<p>ALTERNATIVES FOR POTENCY AND TOXICITY FOR ACELLULAR AND wP VACCINES <u>Coenraad Hendriksen</u> NVI, The Netherlands.</p> <p><i>Resumen no disponible en el momento de la edición del libro. Abstract non available in the moment of the edition of the book of summaries.</i></p>
<p>OC-43</p>	<p>IN VIVO MOLECULAR IMAGING AND NON CLINICAL RESEARCH. <u>Ignacio Hernández</u> Centro de Isótopos, Ave. Monumental y Carretera La Rada, km 3.5, Guanabacoa, Ciudad de la Habana, Cuba. email: ignacio@centis.edu.cu</p> <p>New imaging technologies are increasingly being used in the field of biomedical research. For example, in oncology advances in experimental and clinical imaging should enable doctors not only to locate tumors but also to evaluate <i>in vivo</i> behavior of cancers and molecules designed to treat them. Molecular imaging is a new technology requiring the combination of molecular biology techniques with imaging procedures by different methods. It means that we can see the complexity and diversity of biological process to trace at the same time that we are measuring it. So, successful development and application of molecular imaging requires knowledge from both the life and physical sciences of method available for imaging. There are different imaging systems according with the physical process involved to obtain visual information. To obtain anatomical and physiological information we have now computed tomography (CT), magnetic resonance imaging (MRI) and ultrasound in widespread clinical and preclinical use. Other systems to obtain the necessary molecular information are just emerging, and only some are in clinical and preclinical use, positron-emission tomography (PET) and single-photon-emission CT (SPECT) are the most used because the accumulated experience in clinical practice but other promising techniques based on optical physic are recently introduced. The aim of this review is to provide a background knowledge of molecular imaging from the perspective of pharmacotoxicological research because its importance in the evaluation of new medications and therapeutical approach. Emphasis is made in nuclear medicine application and modalities, especially those one dedicated to animal experimentation.</p>
<p>OC-44</p>	<p>MONOCYTE ACTIVATION TEST (MAT) IS A RELIABLE ASSAY FOR DETECTING PYROGENS IN PARENTERAL FORMULATIONS OF HUMAN SERUM ALBUMIN <u>Zenia Pardo Ruíz</u>, Rolando Perdomo Morales, Ingo Spreitzer, Bettina Loschner, Alicia Lagarto Parra, Thomas Montag</p> <p>Biochemical laboratory. Drug Research and Development Centre (CIDEM). La Habana. Cuba email: zenia.pardo@infomed.sld.cu</p> <p>The screening for pyrogenic contaminations is a crucial step in the quality control of pharmaceuticals. Given the shortcomings in the measurement of pyrogenic contamination of pharmaceuticals by means of the rabbit pyrogen test (RPT) and the Limulus amoebocyte lysate (LAL) test, the Monocyte Activation Test (MAT) have been developed as an alternative method based on the measurement of cytokine production by monocytes. Many blood products, such as Human Serum Albumin (HSA), interfere with the LAL, so still have to be tested with RPT. In the current study HSA was assayed for pyrogens using the RPT, LAL and MAT using fresh-human whole blood (WB-MAT). We found that all batches were contaminated with β-1,3-glucans as assessed by the enhancing response to endotoxin in LAL assay. Interference test in MAT showed an enhancing response to endotoxin likely due to β-1,3-glucans contamination with IL-6 readout, but not with IL-1β. Three batches failed the rabbit test and were also detected with WB-MAT using IL-1 β and IL-6 response. Experiments combining Polymyxin B and MAT demonstrated that all pyrogenic batches were contaminated with endotoxins. However, only one batch was readily detected using endotoxin-specific LAL reagent. Endotoxin equivalent concentration obtained through IL-6 response was usually higher than with IL-1β readout, which is probable produced by direct response of monocytes to β-1,3-glucans. Contaminating β-1,3-glucans do not produced pyrogenic reaction in rabbits. Hence, IL-1β readout resembles better the rabbit pyrogen response than IL-6, although IL-6 can be useful to assess glucan contamination and its immunomodulator potential.</p>

<p>OC-45</p>	<p>DEVELOPMENT OF 3RS ALTERNATIVES FOR DETERMINING POTENCY AND TOXICITY OF VACCINES IN CUBA: CURRENT CHALLENGES AND RESEARCH PROJECTS IN PROGRESS Chovel ML, Mandiarote A, Ontivero I, Herrera L</p> <p>Finlay Institute, Havana, Cuba. email: mlandys@finlay.edu.cu</p> <p>Vaccines have been traditionally released for immunization purposes once controlled a set of relevant quality control parameters. Among them, classical animal Potency and Toxicity tests have played a determinant role. Since a decade, some efforts have been done in Cuba towards the introduction and development of 3Rs alternatives for Potency and Toxicity testing of vaccines. A significant progress has been reached out for some vaccines such as the Potency of Hepatitis B (neutralization ELISA), the toxicity / potency of Diphtheria (guinea-pig serology-Vero cell) and the potency of Tetanus (mouse serology-ELISA). The remarkable reduction in the number of animals used, the refinement of the procedures and the potential for the fully replacement of the challenge Potency tests and some other animal assays have been considered for extending the work on 3Rs alternatives for vaccines. Finlay Institute is the major manufacturer of vaccines in Cuba and it is undoubtedly interested in this field. The purpose of this lecture is to provide an overview of the state of the science and to show the progress we have been having in the introduction / development of 3Rs alternatives for the evaluation of vaccines, as well as the main in-progress or for coming researching projects. As it will be demonstrated, Finlay Institute, along with some other Cuban institutions, it is planning to introduce some of the most updated approaches for classical animal tests for Potency and Toxicity tests of vaccines, including in vitro methods (ELISA, cell culture assays, biochemical and immunological functional tests), serology and consistency approach.</p>
<p>S-4</p>	<p>2ND SYMPOSIUM ON THERAPEUTIC UPDATING IN ASTHMA. / 2^{DO} SIMPOSIO DE ACTUALIZACIÓN TERAPÉUTICA EN ASMA</p>
<p>OC-46</p>	<p>PHARMACOECONOMICS IN THE MANAGEMENT OF CONTROL ASTHMA Gur Levy</p> <p>República Bolivariana de Venezuela.</p> <p>The cost of treating asthma increase if the underlying disease is severe or poorly controlled. Exacerbations, which result from poor control, require costly physician and emergency room visits and hospitalization. The use of appropriate maintenance therapy, although initially increasing drug and physician-based costs, may subsequently reduced direct healthcare costs and indirect costs by improving asthma control. The Asthma Insights and Reality in Latin America (AIRLA) survey at 2005, reveals that daytime asthma symptoms were reported by 56% of the respondents, and 51% reported being awakened by their asthma at night. More than half of those surveyed had been hospitalized, attended a hospital emergency service or made unscheduled emergency visits to other healthcare facilities for asthma during the previous year. Patient perception of asthma control did not match symptom severity, even in patients with severe persistent asthma, 44.7% of whom regarded their disease as being well or completely controlled. Only 2.4% (2.3% adults and 2.6% children) met all criteria for asthma control. Although 37% reported treatment with prescription medications, only 6% were using inhaled corticosteroids and more than 65% use β_2 agonists. Most adults (79%) and children (68%) in this survey reported that asthma symptoms limited their activities. Absence from school and work was reported by 58% of the children and 31% of adults, respectively. Increasing disease severity is associated with an increase in both direct and indirect healthcare costs. In patients with mild-to-moderate disease, the mayor proportion of cost is generally accounted for by drug therapy. With more severe or not well controlled disease, patients required expensive interventions (e.g. emergency room visits and hospitalization) to control exacerbations, and time lost from work significantly increase. The use of unscheduled resource is highest in patients with severe persistent asthma symptoms. However, even patients with mild asthma symptoms incur considerable healthcare costs. Poorly controlled asthma is associated with more than twice the need for unscheduled healthcare resource than well-controlled asthma and assessing patients by their level of control, using the Asthma Control Test (an score <19 is useful for identifying patients with poorly controlled asthma as defined by GINA), offers a simple approach that can lead to reduced healthcare resource use management regimens that aim for and result in well-controlled asthma may reduce the need for unscheduled healthcare and direct cost of the disease. Neffen H, at ALAT congress 2006, demonstrated that not well controlled patients require healthcare resource twice vs. controlled patients. Haahtela T, demonstrate at then years asthma program in Finland, that the number of hospital days has fallen by 54% from 110 000 in</p>

	<p>1993 to 51 000 in 2003, 69% in relation to the number of asthmatics (n = 135 363 and 207 757, respectively), with the trend still downwards. In 1993, 7212 patients of working age (9% of 80 133 asthmatics) received a disability pension from the Social Insurance Institution compared with 1741 in 2003 (1.5% of 116 067 asthmatics). The absolute decreased was 76%, and 83% in relation to the number of asthmatics. The increase in the cost of asthma (compensation for disability, drugs, hospital care, and outpatient doctor visits) ended: in 1993 the costs were J218 million which had fallen to J213.5 million in 2003. Costs per patient per year have decreased 36%. Goal study demonstrated that the majority of patients with uncontrolled asthma across a wide range of severities, comprehensive guideline-defined control can be achieved and maintained. More patients achieved well controlled asthma with combination (inhaled corticosteroid plus a long acting inhaled β_2) more rapidly and at a lower dose of inhaled corticosteroid and control can maintain at least a similar level of control with regular, stable dosing, with little likelihood.</p>
<p>OC-47</p>	<p>ASTHMA: A HEALTH PROBLEM IN CUBA <u>Dania Fabr� Ort�z</u></p> <p>Coordinator of the National Group for Integral Health Care for Asthmatic Children “Juan Manuel M�rquez” Pediatric Hospital, Havana, Cuba. email: Fabre@infomed.sld.cu</p> <p>Introduction: Asthma is one of the most common chronic diseases in the world. It is a health problem in Cuba too, because of its high prevalence, morbidity, social and economic burden.</p> <p>Methods: The following indicators relationship with asthma was analyzed in Cuba, from 1996 to 2009:</p> <ol style="list-style-type: none"> 1. The Prevalence according to the International Study of Asthma and allergies in Childhood (ISAAC). 2. The prevalence rate according to statistics system of Health Ministry. 3. Emergency visits and hospital admissions. 4. Fatality rate of asthma. 5. The global mortality rate, mortality rate in the 5 – 34 year age group and mortality by gender. 6. Asthmatic drugs utilization during this period. <p>Results. The ISAAC, prevalence rate of current wheezing for 6 - 7 year age group was 31% and 17% for 13 - 14 year age group in Playa - Marianao Center. The Cuban prevalence for teenager group was 13%. Prevalence rate date from Health Ministry has increased through recent decades since 59, 7 x 1000 inhabitants, in 1996, to 92, 2 x 1000 inhabitants in 2009. Fatality rate is under 0,1% since 2000. Global mortality has diminished in the last years, with figures fewer than 3 x 100,000 inhabitants, since 1999. In the 5 – 34 year age group, has declined from, 1, 30 x 100,000 inhabitants in 1996 to 0, 24 x 100,000 inhabitants in 2009.</p> <p>Conclusion. Epidemiological situation of asthma has improved, although it continues being a health problem in Cuba.</p>
<p>OC-48</p>	<p>ALLERGEN-BASED THERAPEUTIC VACCINES FOR ASTHMA <u>Alexis Labrada</u></p> <p>Allergens Dept., National Center of Bioproducts (BIOCEN), Havana, Cuba.</p> <p>Allergen immunotherapy (IT) has proven to be effective against respiratory allergy and asthma, particularly, when it is associated to House Dust Mite allergic sensitization. IT is able to alter the allergen-specific immune response, thereby, producing a long-lasting effect and preventing disease progression. Recent advances in this field have allowed better standardization of allergen vaccines, currently available in the market, and Registration of these products according to modern drug standards, thus, improving clinical efficacy and safety. The growing world-wide introduction of the sublingual administration route has the potential to overcome the drawbacks of the traditional injectable route, reducing or eliminating the risk of severe systemic reactions. In Cuba, we have succeeded in the development and Registration of the first three standardized allergen vaccines of relevant mite species: Dermatophagoides pteronyssinus, Dermatophagoides siboney and Blomia tropicalis. Last two species are found only in tropical climates. Its efficacy and safety was assessed in 6 clinical trials of subcutaneous immunotherapy in 235 patients with allergic asthma. Treatment was effective for 76% of patients. Asthma symptoms and medication declined in 60% (CI95%: 51-69) as compared to placebo. Another cluster of 3 Double-Blind Placebo-Controlled clinical trials demonstrated a similar clinical efficacy of these vaccines as administered by sublingual route in drops, using a nearly daily dosing schedule during 1 year. Moreover, safety of this route showed to be clearly superior with no systemic reactions and a low rate (0.4%) of mild local reactions. The sublingual presentation of these products has been introduced in this year country-wide in Cuban allergy services. Thus, the availability of high quality standardized allergen vaccines becomes a valuable tool for expanding the etiological approach for asthma management.</p>

<p>OC-49</p>	<p>EFFECTIVENESS AND SECURITY OF THE <i>XOLAIR</i> IN THE TREATMENT OF ASTHMA <u>Díaz I, Rodríguez E</u></p> <p>Novartis AG, Calle A, Esquina 21, Vedado, Habana, Cuba email: irina2005diazal@yahoo.com, enrique.rod@enet.cu</p> <p>Novartis is a multinational company that is dedicated to the pharmaceutical industry and to the biotechnology. From his creation a priority has turned out to be the development of new medicines; inside the most innovative products of the same one the Xolair (omalizumab) which is an antibody monoclonal humanized, obtained by genetic engineering in cultivation of suspension of cells of mammal (ovary of Chinese hamster, CHO) and whose mechanism of action consists of the selective union to the immunoglobulin A humanizes (IgE). This medicine is indicated for the allergic asthma severe resistant (AA) to corticosteroides. There was carried a program of development of the omalizumab in the paediatric population of 6 to less than 12 years of age (1217 patients), of which 914 received the omalizumab. The majority received the treatment during a minimal period of 24 weeks, which allowed to possess a wide database. Also there was evaluated the use of the long-term omalizumab (3 years of exhibition in 121 patients). Subgroups of the safety populations were examined in order to determine possible differences in the incident of adverse events and in the evaluations of the laboratory parameters. There were effected analyses of the incidents of adverse events in demographic subgroups (age, sex, race, and initial gravity of the disease). During the program of development the profile of adverse events observed in the patients treated with the omalizumab was very similar to that of the placebo, which includes a low incident of adverse serious events. There are no indications of an increase of the risk of cancer, reactions of hypersensitivity induced by the medicament or parasitic infestations in children treated with omalizumab. AA's analyses for subgroups revealed neither risks more frequent nor favorite terms. No patients' subgroup seemed to be exposed to a major risk depending on the age, sex, race or gravity of the disease. There exist sufficient proofs that the Omalizumab possesses an important efficiency from the clinical point of view in the asthmatic population and an innocuousness in the total population who justifies his use, according to the in force directives of the Global Initiative for Asthma, (global Initiative against the asthma).</p>
<p>OC-50</p>	<p>BRONCHIAL ASTHMA: NEW PERSPECTIVES FOR ITS TREATMENT <u>Alfredo Martínez-Aparicio Hernández</u></p> <p>2nd Degree Specialist in Pneumology. ISCMH Assistant Professor, Benéfico Jurídico Pulmonary Teaching Hospital, Havana City, Cuba.</p> <p>Bronchial asthma is one of the most frequent chronic pathologies worldwide. It implies huge medical expenses and indirect economic losses. In one third of the female population this condition can worsen during pregnancy time. Therefore, a wrong treatment of this pathology is associated with the increase of the mother and fetus' morbidity and mortality. Persistent asthma favors the development of irreversible lesions in patients, which causes a permanent bronchial obstruction, a side effect of the inflammatory process affecting the airways. The treatment of this disease is one of the most controversial topics nowadays. Its origin lies mainly in the possible involvement of beta-mimetic bronchodilators in the increase of deaths. The introduction of inhaled glucocorticoids for asthma is, without doubt, the most significant breakthrough of the last years. It has allowed the treatment of asthma with strong anti-inflammatory inhaled drugs, with zero or few systemic side effects. The studies carried out on the effectiveness of budesonide as inhaled corticoid for every type of asthma have shown its therapeutic results in the improvement of the pulmonary function and in the absence of systemic side effects. Likewise, these studies have shown good results in the treatment of asthma during pregnancy, proving the absence of teratogenic effects. Early treatment involving the use of glucocorticoids has proven to be an efficient alternative in the prevention of irreversible damages in asthmatic patients.</p>
<p>OC-51</p>	<p>PROTOCOL TO IMPROVE THE CLINICAL CONDITION OF CHILDREN AND ADOLESCENTS WITH ASTHMA <u>Carlos Dotres Martínez</u></p> <p>Profesor Auxiliar de Pediatría. Máster en Atención Integral al Niño. Especialista de 1er y 2do grado en Pediatría. Jefe del Servicio de Respiratorio del Hospital Pediátrico Docente Juan M. Márquez. Facultad Finlay-Albarrán. Universidad Médica de la Habana.</p>

	<p>Introduction: Asthma is the most common chronic illness in childhood. Inadequate control of asthma in children is one of the problems in our healthcare setting. In this investigation we have presented a protocol for the management of asthma applied together with several current concepts that we have incorporated into the control of asthma in children and adolescents. Objective: Improve the clinical condition of patients suffering from asthma. Methodology: A prospective longitudinal interventional study was performed on 80 children with asthma classified as moderate or severe persistent, all of them discharged from the Respiratory Service of Juan Manuel Marquez Pediatric University Hospital during 2008-2009. A questionnaire was administered before the intervention and between 6 months to a year later to evaluate the course of the disease, the strategy of health education of caregivers and patients, interdisciplinary care and the use of abortive treatment of the attack according to prodromal symptoms. Individualized treatment between attacks was adapted to each patient according to international guidelines. GINA guidelines were used to classify severity of asthma before inclusion in the study and again after the intervention. Results: 80(100%) of the patients had not been classified according to the severity of their disease at the beginning of the study and did not have adequate follow-up to achieve control, 50 (62%) of caregivers lacked basic knowledge about the disease, 55 (69%) of the patients reported an average duration of attack of more than 72 hours before the intervention and 12 (15%) reported this after the intervention. 80 (100%) used rescue medications more than twice a week before the intervention and 26 (32%) used them after the intervention. 37 (46%) reported 15 or more days of school absence before the intervention and 4 (%) after the intervention. 67 of the patients (84%) reported that they always or occasionally experienced fatigue with exercise before the intervention and 28 (53%) experienced fatigue occasionally at follow-up. Before the intervention, hospital costs were estimated to be 62,000 pesos (CUP) and after the intervention 25,000 (CUP). Conclusions: The totality of patients had not been classified according to the severity of their asthma at the time of the first consultation and did not have adequate follow-up of their illness. Three quarters of the caregivers lacked basic knowledge about the management of these patients. Improvement was seen in the control of the patients' illness as well as their quality of life and a reduction was obtained in the hospital costs generated by the care of these patients.</p>
W-5	<p>WORKSHOP: “METHODODOLOGICAL, DESIGN ISSUES ABOUT CLINICAL TRIALS” / “TALLER ASPECTOS METODOLÓGICOS Y DISEÑO DE ENSAYOS CLÍNICOS”</p>
RT-01	<p>PAN AMERICAN NETWORK FOR DRUG REGULATORY HARMONIZATION (PANDRH): GOOD CLINICAL PRACTICE (GCP): WORKING GROUP OVERVIEW, RESULTS, UPDATE, CHALLENGE AND PERSPECTIVE</p> <p><u>Pascual María A</u> MD, Director, National Clinical Trial Coordinator Center of Cuba. Coordinator of GCP Working Group.</p> <p>During early nineties, started an international harmonization process in pharmaceutical regulations. In 1997, the Conference Harmonization (ICH) launched the Good Clinical Practice (GCP) Guidelines, with participation of United State of America, European Union and Japan with Canada and WHO as observers. Regional harmonization initiative started in November 1997 with the I Pan American Conference on Drug Regulatory Harmonization. PANDRH was officially established in Nov 1999 during the II Conference and within the harmonization process, experts groups were conformed and one of them, the GCP Working Group. The goal of this group is to promote the harmonization of Good Clinical Practices in the Americas, its implementation and dissemination of the document “Good Clinical Practices: Document for the Americas” and the development and dissemination of the Educational Program in this region. The major outcomes of the Working Group have been the initial diagnostic study, the elaboration of the document Good Clinical Practices: Document of the Americas and Educational Seminars on Good Clinical Practices. The Good Clinical Practices: Document of the Americas was elaborated following ICH, WHO guidelines and regulations from different countries, considering the peculiarities and realities of the region and the necessity to strength Good Clinical Practice in all countries. The Working Group was reorganized and the results of the last 10 years and perspectives and challenges were discussed very recently. The objective of this paper is to offer a general overview and current state of the performance of the group since its creation and to discuss main results, challenges to face and perspectives.</p> <p>MAIN TENDENCIES IN THE CLINICAL DEVELOPMENT OF NEW PRODUCTS</p> <p><u>Rodríguez J</u> National Center Coordinating of Clinical Trials, 200 at 21 Ave, Atabey, Playa, Havana City, Cuba. email: julian@cencec.sld.cu</p>

	<p>The clinical Trial is the fundamental tool for the clinical evaluation of a new product. The results of these studies allow to demonstrate, or not, their value as preservative, diagnostic and/or therapeutic of the new candidate for the sanitary registration. In the last years it has been increased the number and complexity of these studies notably, as well as novel support technologies have emerged. Reason for which the main sanitary authorities of the world develop projects that allow the upgrade and incorporation of the new tendencies of the science in the systems of current clinical trials. Situation that has come not reflecting alone for the increment in the number of regulations and requirements, but also the specialization of all the documents that govern the clinical investigation with the purpose of accelerating the arrival from the new therapies to the habitual medical practice, guaranteeing the quality, security and effectiveness of the new products.</p> <p>CHALLENGE OF REGULATORY AGENCY <u>S. Deybi Orta</u> Center for the State Control of Drug Quality. CECMED. Havana, Cuba. Email: deybisi@infomed.sld.cu</p> <p>At present, for the Drugs Regulatory Authorities (DRA) there are challenges for new drugs and vaccines, considering the accelerated development of the Pharmaceutical and Biotechnical Industry. For that reason in the clinical evaluation field, the evaluation processes need to be speeded up for such aspects as: introduction of new vaccines that aren't licensed in the country of origin, overlapping of investigation phases, decreasing number of subjects exposed, decreasing global evaluation period, new designs for clinical trials, between others. The DRAs to give answer to this needs the Reinforcement of Sanitary Register System and Reinforcement of Pharmaco-surveillance System. Also, is important the knowledge and application of GCP systematic execution in the involved Institutions in clinical trials, and the responsibilities of the parties (IEC/IRB, Sponsors, Investigators, Monitors, Institutions) should be quantitative and qualitatively evaluated. It allows feedback and to know which aspects to direct the efforts to, in the accomplishment of the GCP implementation in the country, thus forcing to the continuous improvement of the activity. Finally, DRA must ensure clinical studies have been conducted in accordance with acceptable GCP standards. It is necessary to guarantee quality and integrity of study data, and protection of the rights and welfare of subjects under research. The experience and outcomes evaluation of National GCP Inspection Program allowed elaboration of requirements for GCP Certification and implementation of GCP Certification System since 2008. This implies an insurmountable social and ethical value. Besides, this implies a social-economic value given by the fact of performing quality clinical trials just once, involving a smaller number of subjects, and being able to demanding and controlling at the highest levels. Up to the present, we have identified the needs for many guidelines to complete our legal basis. Nowadays, we are still working in the conformation of some of them.</p>
OC-52	<p>CHALLENGES WITH INCLUSION AND RETENTION IN U.S. CLINICAL TRIALS <u>Ellis, G</u></p> <p>Strategies for Well-Being, LLC, 53 Lincoln Avenue, Yeadon, PA, USA</p> <p>Recent concerns about the lack of diverse human subject participation in U.S. clinical trials have sparked considerable interest in how new drugs are discovered, tested, and sold—and in how well those processes serve the interests of U.S. consumers. This presentation presents basic facts about the pharmaceutical industry's challenges with eligibility criteria and retention efforts that ensure minorities can participate in research and development and about the types and numbers of new drugs that result from it. Examination will be made on the social and scientific factors which contribute to the challenges, and how efficacy and successful trials are compromised as a result. The study also analyzes several major barriers to participation related to pharmaceutical R&D.</p>
OC-53	<p>EFFICACY AND SAFETY OF GRANULOCYTE COLONY-STIMULATING FACTOR (IOR®-LEUKOCIM) IN ONCOHEMATOLOGY PATIENTS. PHASE IV <u>Mendoza I</u>¹, García E¹, Wilford M², Menéndez A³, Fernández JD⁴, Vázquez E⁵, Robaina M¹, Piedra P⁶, Sáurez G⁶.</p> <p>¹National Center Coordinating of Clinical Trials (CENCEC), 200 at 21 Ave, Atabey, Playa, Havana City, Cuba. email address: ivismendoza@infomed.sld.cu ²Medical Surgery Research Center (CIMEQ). 13 at 216 Atabey, Playa, Havana City, Cuba. ³Hematology and Immunology Institute (IHI). Havana City, Cuba. ⁴Gustavo Aldereguía Lima Hospital (GAL). Cienfuegos City, Cuba.</p>

	<p>⁵National Oncology and Radiology Institute (INOR), 29 at F. Vedado. Plaza de la Revolución. Havana City, Cuba.</p> <p>⁶CIMAB. Center of Molecular Immunology (CIM), 206 at 21 Ave, Atabey, Playa, Havana City, Cuba.</p> <p>Introduction: Neutropenia does not in itself cause symptoms, but it predisposes patients to infection, especially if the neutrophil count falls below $0.5 \times 10^9/L$ and persists longer than 10 to 14 days. In patients receiving chemotherapy, the administration of G-CSF can lessen the incidence and severity of neutropenia.</p> <p>Purpose: This was a multicenter phase IV study in oncohematology patients under chemotherapy and/or radiotherapy treatment evaluating ior[®] LeukoCIM, a granulocyte colony-stimulating factor. Patients and Methods: Nine hundred three episodes received ior[®] LeukoCIM (300 µg/kg) as primary, secondary prophylaxis or neutropenia treatment, to recovery the neutrophil count ($1.5 \times 10^9/L$) and were assessed for efficacy and safety. Ior[®] LeukoCIM was administered subcutaneous, in prophylaxis beginning 24-72 hours after chemotherapy and/or radiotherapy, and as treatment from neutropenia diagnosis. Results: The 94.6 % (819 episodes) finished treatment with neutrophil count $\geq 1.5 \times 10^9/L$. The 48.2 % of adverse events were evaluated as drug-related adverse events. The most frequently were leucocytosis (14.9 %; 161 episodes), neutrophilia (13.1 %; 142 episodes) and bone pain (10.5 %; 114 episodes). Others adverse events were fever (7.4 %), thrombocytopenia (7.0 %) and headache (5.2 %). Ior[®] LeukoCIM was safe with no serious adverse events. Conclusions: Ior[®] LeukoCIM showed efficacy and safety as primary, secondary prophylaxis or neutropenia treatment in oncohaematology patients under chemotherapy and/or radiotherapy treatment.</p>
OC-54	<p>TREATMENT OF THE HEMORRHOIDAL CRISIS WITH SUPPOSITORIES OF RECOMBINANT STREPTOKINASE. THERESA-3 STUDY</p> <p>Hernández-Bernal F¹, Castellanos G², Valenzuela C¹, Causa JR², Catasús K², Domínguez J², Fernández R², Aguilera A¹, Valle R³, Mendoza Y³, Peláez Y¹, Bermúdez Y¹, Rojas IT², Poch E², Acosta Y², Quintero L², González ME², Martínez O², Ramírez L², Pupo AM², Martínez E¹, Páez R¹, Herrera L¹, López-Saura P¹, on the behalf of the THERESA-2 (<i>Treatment of Hemorrhoid with Recombinant Streptokinase Application</i>) Group, Cuba</p> <p>¹Center for Genetic Engineering and Biotechnology (CIGB), Havana, Cuba. email: hernandez.bernal@cigb.edu.cu</p> <p>²Coloproctology Units, Ministry of Public Health (MINSAP), Cuba. ³National Centre for the Coordination of Clinical Trials, Havana, Cuba.</p> <p>Background/Aims: Hemorrhoids are an important health problem, while being the most frequent proctologic pathology. Its clinical symptoms produce significant discomfort, which include pain, bleeding and pruritus, and it may be associated to complications such as the hemorrhoidal crisis (with the formation of thrombi). It would be very beneficial to have an effective and safe drug that would avoid aggressive procedures. The recombinant streptokinase (SKr) has shown favorable results in animal models of rectal inflammation and in humans. A phase III, open, multicenter, with a positive control and centralized randomization in order to determine the efficacy and safety of the SKr in the treatment of hemorrhoidal crises. Materials and Methods: The 220 patients used were of 16 to 75 years old and gave their consent for their participation in the study. They were distributed into 2 treatment groups: I) SK 200 000 IU (Heber-Biotec, Cuba) and II) Preparation H[®] (Richmond Division of Wyeth, USA). The product under study was administered through the rectal route in the form of a suppository every 6 hours for 48 hours (in the case of SK 200 000 IU) and up to a maximum of 5 days in the case of Preparation H[®]. The patients complied with the treatment in the ambulatory regime and the evaluations were performed at 3, 5 and 10 days after the inclusion. The statistical analyses were made by the intent to treat, and conventional and Bayesian approaches were considered. Results and Discussion: The efficacy of the SK suppository (200 000 IU) was demonstrated in the treatment of hemorrhoidal crises. The success criterion proposed was fulfilled, with a difference of over 20% (42.7 [30.5; 54.2]), favorable to the group receiving SK; the healing rate was significantly higher in the SK group, with an estimated median of 5 days (a median of 10 days for the group treated with Preparation H[®]). The analysis according to the classification (external, internal and combined) and type of hemorrhoids (thrombosis and fluxion) showed efficacy (Total response) of the SK suppository 200 000 IU of above 70% in all cases, without finding any influence of these variables on the response. Conclusions: The Recombinant Streptokinase suppository was effective, safe and tolerable for healing of the haemorrhoidal crisis.</p>
OC-55	<p>NONINFERIORITY CLINICAL TRIALS. WHAT ARE, WHEN AND HOW TO APPLIED THEM</p> <p>Robaina García M¹, Fors López Martha, Rodríguez Julián</p> <p>¹ Centro Coordinador Nacional de Ensayos Clínicos (CENCEC). Calle 200 esquina 21, Atabey. Ciudad de la Habana. Cuba. email. mrobaina@cencec.sld.cu</p>

	<p>Introduction: When investigators are interested to show that the new treatment has an efficacy similar to standard treatment while immediate toxicity, long-term adverse effects or costs may demonstrate to be advantageous for the experimental treatment, they need to design trials called Noninferiority (NI) trials, rather than outright superiority. NI trials have certain number of inherent design and statistical analysis differences compared with superiority trials that frequently are not take in consideration by investigators. How to specify an appropriate NI margin in the design?, what are the differences in statistical analysis approach to analyzed them?, How to report the trials results with quality? Material v methods: A review in these topics and guidelines are presented in this paper. NI designs in Cuban trials publications and approved by regulatory agency were reviewed. Trial design, statistical properties, conduction, data analysis, results, and reporting were examined in NI trials reported from 2000 to 2009. An updating of regulatory issues regarding statistical design and analysis and main features of this designs are presented as well. Results: In Cuba the use of this kind of design is limited, it was found only one published trial, even NI design has been there for years 15-20 years, it is reality that is not been used frequently in our country. Conclusions: Noninferiority trials are necessary in given situations for evaluating the efficacy and comparability of new drugs, for anyone performing such a trial or evaluating its results its important to know issues that make their results more credible.</p>
<p><i>OC-56</i></p>	<p>EFFECTS OF TRANEXAMIC ACID ON DEATH, VASCULAR OCCLUSIVE EVENTS, AND BLOOD TRANSFUSION IN TRAUMA PATIENTS WITH SIGNIFICANT HAEMORRHAGE (CRASH-2): A RANDOMISED, PLACEBO-CONTROLLED TRIAL Marrero-Miragaya MA¹, Avila Albueme Y¹, Navarro Z², Fernández Y², Ballagas Flores C¹, Fors López M¹, Vicente I¹ on the behalf of the CRASH 2 trial collaborators</p> <p>¹National Centre for the Coordination of Clinical Trials, Havana, Cuba. email: acelia@cencec.sld.cu ²Emergency Units Care intensive, Ministry of Public Health (MINSAP), Cuba.</p> <p>Background/Aims: Tranexamic acid can reduce bleeding in patients undergoing elective surgery. We assessed the effects of early administration of a short course of tranexamic acid on death, vascular occlusive events, and the receipt of blood transfusion in trauma patients. Materials and Methods: This randomized controlled trial was undertaken in 274 hospitals in 40 countries. Our country contributes with 575 patients of 10 hospitals. 20 211 adult trauma patients with, or at risk of, significant bleeding were randomly assigned within 8 h of injury to either tranexamic acid (loading dose 1 g over 10 min then infusion of 1 g over 8 h) or matching placebo. Randomization was balanced by centre, with an allocation sequence based on a block size of eight, generated with a computer random number generator. The primary outcome was death in hospital within 4 weeks of injury, and was described with the following categories: bleeding, vascular occlusion (myocardial infarction, stroke and pulmonary embolism), multiorgan failure, head injury, and other. All analyses were by intention to treat. Results and Discussion: 10 096 patients were allocated to tranexamic acid and 10 115 to placebo, of whom 10 060 and 10 067, respectively, were analyzed. All-cause mortality was significantly reduced with tranexamic acid (1463 [14.5%] tranexamic acid group vs 1613 [16.0%] placebo group; relative risk 0.91, 95% CI 0.85–0.97; p=0.0035). The risk of death due to bleeding was significantly reduced (489 [4.9%] vs 574 [5.7%]; relative risk 0.85, 95% CI 0.76–0.96; p=0.0077). Conclusions: Tranexamic acid safely reduced the risk of death in bleeding trauma patients in this study. On the basis of these results, tranexamic acid should be considered for use in bleeding trauma patients.</p>
<p><i>OC-57</i></p>	<p>PHARMACOLOGY MANAGEMENT OF DYSLIPIDEMIA FOR PRIMARY AND SECONDARY PREVENTION IT RELATION WITH THE LARGE-SCALE, PROSPECTIVE, RANDOMIZED CLINICAL TRIALS Hernández A</p> <p>¹ National Coordinating Center of Clinical Trials. 21 Ave and 200 St., Atabey, Playa, Havana City, Cuba. email: alberto@cencec.sld.cu</p> <p>Introduction: Much evidence supports the association between dyslipidemia and an increased risk of coronary heart disease (CHD). Contributing to this evidence are the large-scale, prospective, randomized clinical trials that have shown the strong association between the reductions in plasma low-density lipoprotein cholesterol (LDL-C) achieved with statins (3-hydroxy-3-methylglutaryl coenzyme A-reductase inhibitors) and others hypolipidemic drugs and reduction of CHD. Material and Methods: A restricted literature review of five years of the main databases of clinical trials results was performed using the meta-searcher TRIP Results</p>

	<p>and Discussion. Due to the proven and positive relationship that exists between lipoprotein and CHD, there is a current scientific production of high quality in journals of relevant impact factor that imposes a frequent update of the pharmacological management of dyslipidemia in primary and secondary prevention of CHD, an example of this are articles about the results of trials as ASTEROIDE, 2006; HPS, 2007; ENHANCE, 2008; ASPEN, 2008; ASCOT-LLA, 2008; ALLAHAT, 2008; SEARCH, 2008, JUPITER, 2009 Y ALLHAT-LLT, 2010; much of them are controversial but they offer enough evidence to make the most adequate recommendations to support different clinical questions about the pharmacological management of dyslipidemia. Conclusions. To give updated recommendations about the pharmacological management of this important disease based on most relevant clinical trials in the last five years is of great importance for primary and secondary medical care.</p>
OC-58	<p>EFFECTIVENESS OF A CLINICAL TRIAL EDUCATIONAL PROGRAM FOR CLINICAL RESEARCHER. HAVANA CITY. 2007-2010 Cachimaille-Benavides Yamilé, Rodríguez-Alonso Beatriz, Marrero-Miragaya María Acelia, Hernández-Rodríguez Alberto, Parra-Zabala Jeydy, Uranga-Piña Rolando</p> <p>National Centre for the Coordination of Clinical Trials, Havana, Cuba. Email Address: yamile@cencec.sld.cu</p> <p>Introduction: To improve the quality of clinical trials for the evaluation of biotechnology and medical-pharmaceutical products Cubans, the National Coordinating Center for Clinical Trials has developed an educational strategy directed to the investigators of the National Health System. This study assesses the effectiveness of the program for clinical researchers in Havana in the period 2007-2010. Material and Methods: A quasi-experimental study that included the courses completed between May 2007 and May 2010 it was carried out. The learning needs assessment was conducted based on the analysis of the needs criteria according to the Salas-Perea's classification and the analysis of instruments before and post-training. Data were entered and stored in databases made with the EPI-INFO system, which underwent a quality control. The effectiveness of the program was evaluated by comparing the General Index Knowledge and by topics made before and after the intervention program. We used the nonparametric method for paired samples (Mc Nemar test). Results and Discussion: There were 12 courses involving 410 researchers. After the intervention there was an increase in the level of knowledge in 86.8% of researchers, and 54.6% of them with 80-100 points' assessments. There is marked improvement in all subjects tested, except for elements of basic statistics. No significant differences were found in the evaluations of professionals with experience and previous training. Conclusions: The educational intervention program is effective for human resource development in clinical trials, while significantly improved the level of knowledge regarding the initial investigators.</p>
OC-59	<p>PHASE I CLINICAL TRIAL WITH THE ¹³¹I-LABELED ANTI-CEA CIGB-M3 MULTIVALENT ANTIBODY FRAGMENT IN COLORECTAL CANCER PATIENTS García I¹, Pimentel G², González J², Pérez L³, Velasco M², Calderón C², García FL², García E¹, López R⁴, Ropero R², Ayala M³, López A⁴, López PA¹, Gavilondo JV³, Oliva JP².</p> <p>¹. Center for Genetic Engineering and Biotechnology (CIGB), Clinical Trials Division, Ave 134 e/23 and 25, Cubanacán, Playa, P.O. Box 6332, Havana 10600, Cuba. Telephone: +53 (7) 2087379; 2087465; Fax: +53 (7) 2736008. Email: idrian.garcia@cigb.edu.cu. ² Nuclear Medicine Department, National Institute of Oncology and Radiobiology, 29 and F, Vedado, Havana 10400, Cuba. ³. Recombinant Antibody Group, Cancer Research Department, CIGB, Ave 31 e/158 and 190, Cubanacán, Playa, P.O Box 6162, Havana 10600, Cuba. ⁴. Nuclear Medicine Department, "Hermanos Ameijeiras" Hospital, San Lázaro No. 701 e/ Belascoaín and Marquez González, Havana 10300, Cuba.</p> <p>Introduction: CIGB-M3 is a multivalent recombinant single-chain Fv antibody fragment specific for carcinoembryonic antigen (CEA). Studies with radiolabelled CIGB-M3 have shown that the antibody fragment accumulates in human colon tumor xenografts growing in nude mice. Material and Methods: An open label, Phase I clinical trial was carried out to determine safety, biodistribution and pharmacokinetics of the radiolabelled CIGB-M3 multivalent antibody fragment in two groups of patients with CEA+ colorectal cancers. Group I (10 patients) received a single intravenous injection of 0.3 mg of ¹³¹I-CIGB-M3. Group II (7 patients) received 1 mg. In both groups, the total amount of radioactivity was similar (185-259 MBq). Results and Discussion: No adverse events related with the injected product were recorded, and no HAMA response was detected up to 6 months after the injection. ¹³¹I-CIGB-M3 was stable in serum in the form of immune complexes with CEA or free antibody fragment for up to 24 hrs post-administration. Tumors were detected by</p>

	<p>gammagraphy in 15 of the 17 studied cases, and specific radioactivity recovered in 5 tumor surgical samples obtained 7-9 days after administration of the product. All patients showed radioactivity in kidneys, 47% in stomach and 23.5% in thyroid. Bone marrow absorption was very low. The pharmacokinetic profile was better fixed to a bicompartamental model, with beta half times of 14.1 and 6.3 hours for Groups I and II, respectively. Seventy two hours after the administration of the product 85% of the total injected dose was detected in urine in the form of free ¹³¹I. Conclusions: The administration of ¹³¹I-radiolabelled CIGB-M3 is safe in patients with colorectal cancer. Radiolabelled CIGB-M3 accumulated in a high percentage of the tumors. Overall, safety, biodistribution and pharmacokinetic data suggest that the product can be further tested for molecular radiotherapy of CEA+ tumors.</p>
OC-60	<p>ACTIVE SPECIFIC IMMUNOTHERAPY WITH 1E10/ALUMINUM ANTIIDIOTYPE (RACOTUMOMAB) VACCINE IN THE TREATMENT OF PATIENTS WITH METASTATIC BREAST CANCER: CLINICAL AND SAFETY REPORT Pérez L¹, Pascau LJ¹, Lorenzo-Luaces P¹, Viada C¹, Toledo D¹, Santiesteban E², González D³, Mendoza I³, Vázquez AM¹, Macías A¹. ¹ Center of Molecular Immunology. Havana. Cuba ² Oncology Unit, José Ramón López Tabranes Hospital. Matanzas. Cuba ³ National Clinical Trial Coordinator Center. Havana. Cuba Center of Molecular Immunology (CIM) calle 216 esq. 15, Atabey, Playa. Ciudad Habana, Cuba. CP email: leslie@cim.sld.cu & liesel@jagua.cfg.sld.cu</p> <p>Introduction: The obtained results with Racotumomab vaccine in patients with melanoma, advanced breast cancer and small cell lung carcinoma evidenced that the vaccine was well tolerated with a good level of immunogenicity, capable of generating specific antibodies against the 1E10 monoclonal antibody and against the NeuGCGM3 ganglioside. These results showed that Racotumomab has behaved as an “internal image” anti-idiotype. Materials and Methods: A phase II, randomized, controlled, double blind clinical trial of 80 patients with metastatic breast cancer (MBC) diagnosis was carried out. Arm I: Treated with Racotumomab and best supportive care (BSC), Arm II: Treated with placebo and BSC after achieving control disease (CR+PR+SD) with the standard first line onco-specific therapy established in the Oncology Therapeutic Guidelines (NCCN v3.2009). Primary endpoint was the overall survival (OS). The vaccination schedule was: 15 doses of Racotumomab 1 mg by intradermal route. The first 5 doses were administered every 14 days (induction period) and the rest every 28 days (maintenance period) during one year. Results: There was not statistical significance (Log Rank test p= 0.545) between OS in the patients treated with more than 5 immunization doses with a pursuit in the study of at least 24 months (28 patients, OS mean: 23.06 months; OS median: 25.66 months) and the control group (25 patients, OS mean: 21.30 months; OS median: 16.00 months). However, the survival rate at 18 months and 24 months between the two arms: at 18 months: vaccine 45%, placebo 32%, at 24 months: vaccine 43% placebo 27%, showed a trend of benefit towards the vaccinated arm. The vaccination was safe, just local adverse events grade I/II and not serious adverse events were observed (CTC-NCI Criteria v4.02). Conclusions: The clinical results and the safety data obtained in this study suggest that the Racotumomab has a clinical benefit in MBC patients.</p>
	MIERCOLES / WEDNESDAY DICIEMBRE / DECEMBER 15
	PLENARY LECTURES / CONFERENCIAS PLENARIAS
PL-14	<p>GLOBALIZATION AND DRUG USE. Julián Pérez Peña MD, MSC, Director, Pharmacoepidemiology Delopment Center, Havana, Cuba.</p> <p>The author analyzes the impact of the globalization on the rational use of drugs (RUD). The paper recognize and discuss the consequences of the impact of the globalization on different subjects as drug regulations, drug information and medicine knowledge, clinical use of pharmaceuticals and drug innovation. At last the author draws up a proposal of actions to face this challenge.</p>
PL-15	<p>CLINICAL DEVELOPMENT OF DRUGS AND MEDICATION ERRORS Eduardo L. Mariño Full Professor of Pharmacy and Pharmaceutical Technology, Head of the Clinical Pharmacy and Pharmacotherapy Unit Department of Pharmacy and Pharmaceutical Technology Faculty of Pharmacy. University of Barcelona.</p>

	<p>At present and since some time ago, the discovery and production of medicines have gone to become "as art" to be "as science", getting to be one of the main tools of the health system of any country. Industrialization allowed the reach the production in a repetitive, constant and uniform form and in large quantities of all drugs, ensuring their stability and dose uniformity in manufacturing. In the course of this time, at the stage of development, clinical trials are the gold standard for ensuring the effectiveness and safety, the latter as far as possible, which certainly involve the greatest cost in obtaining the drug. The increase in life expectancy at birth, the increase in the geriatric population that is susceptible to use a greater number of drugs and raising the cost of achieving a new drug, are a clear indication of the probable growing drugs bill, which constitutes a clear concern and an important field of action for any health system. Methodological, legal and ethical improvements, especially in clinical trials, have indisputably contributed also to the improvement of drug safety, although unable to prevent the occurrence of adverse reactions, whose unpredictable does not completely confirm the security before marketing. In contrast, the predictability of what we know as "Medication Errors" make this a very attractive topic to improve the use not only cost-effective of medicines, but also and especially to get the levels of safety for all desired.</p>
<p>PL-16</p>	<p>BETTER MEDICINES USE: IMPLEMENTING A NATIONAL PROGRAM THROUGH LOCAL DELIVERY TO PRIMARY HEALTHCARE PROFESSIONALS ACROSS AUSTRALIA. Higgins G, Azam R</p> <p>National Prescribing Service, PO Box 1147 Strawberry Hills NSW 2012 Australia. email: ghiggins@nps.org.au</p> <p>Introduction: Quality use of medicines (QUM) is one of the four core elements of Australia's National Medicines Policy: it is defined as medicine use that is judicious, appropriate, safe and effective. The National Prescribing Service (NPS) was formed in 1998 to implement a QUM service as part of this policy. Materials and Methods: Educational visiting, outreach or academic detailing has consistently been shown to improve prescribing internationally. It is one of many services in multi-faceted interventions used by NPS to improve QUM. Educational visits are funded and delivered to general practitioners across Australia by 90 locally based NPS facilitators. These facilitators are trained:</p> <ul style="list-style-type: none"> • generally in providing one-to-one communication focusing on delivery of therapeutic key messages • specifically in the clinical therapeutics and evidence for each therapeutic topic. <p>The visits, usually 20-30 minutes in duration, are provided free of charge at a time and location suitable for the GP.</p> <p>Results and Discussion With each therapeutic topic, resources are developed to:</p> <ul style="list-style-type: none"> • support delivery of key messages for to health professionals • assist consumer understanding of QUM and enhance their interactions with their health professionals e.g. pain diary for assessing response to analgesics. <p>Therapeutic topics targeting drug use areas such as antibiotics, analgesics and type 2 diabetes may be repeated after 3-4 years, using some similar and some new key messages.</p> <p>The proportion of GPs (N=14,509 full-time equivalents) participating in local programs had grown from 20% in 1999 to 79% in 2009. When time and circumstances permit, NPS facilitators also provide visits to pharmacists, nurses and other health professionals.</p> <p>Conclusions Educational visiting is a widely accepted strategy for improving prescribing in Australia. NPS will continue to evaluate its benefits, to promote sustainability of prescribing changes and to harness opportunities for further improvements in QUM across all audiences. Acknowledgements: NPS team who develop materials and provide support for NPS facilitators to deliver educational visits, past and present over the period 1999 - 2010. See www.nps.org.au</p>
<p>PL-17</p>	<p>ECONOMIC EVALUATION OF TECHNOLOGIES AND SANITARY PROGRAMS APPLIED TO THE TAKING OF DECISIONS. THE INTERNATIONAL EXPERIENCE Joan Rovira Forns. University of Barcelona. Spain.</p> <p><i>Resumen no disponible en el momento de la edición del libro. Abstract non available in the moment of the edition of the book of summaries.</i></p>
<p>PL-18</p>	<p>VASCULAR SIGNALLING IN HUMAN DIABETES. TRANSLATIONAL RESEARCH Teresa Tejerina¹, Santiago Redondo¹, Jorge Navarro-Dorado¹, Marta Ramajo¹, Karen Au Yeung², Cornelis van Breemen², Elena Okon², Emilio Ruiz¹</p>

	<p>¹Department of Pharmacology, School of Medicine, Universidad Complutense, 28040 Madrid, Spain. ²Department of Pharmacology and Therapeutics, The University of British Columbia, Vancouver, BC, Canadá.</p> <p>Background: An emerging body of evidence suggests that vascular remodeling in diabetic patients involves a perturbation of the balance between cell proliferation and cell death. Aim: was to study whether arteries and vascular smooth muscle cells (VSMC) isolated from diabetic patients exhibit resistance to apoptosis induced by several stimuli. Methods: Internal mammary arteries were obtained from patients who had undergone coronary artery bypass graft surgery. Results: Arteries from diabetic patients showed increased levels of Bcl-2 expression in the media layer measured by immunofluorescence and by Western blotting. Human internal mammary artery VSMC from diabetic patients showed resistance to apoptosis, measured as DNA fragmentation and caspase-3 activation, induced by C-reactive protein and other stimuli, such as Hydrogen peroxide and 7β-hydroxycholesterol. The diabetic cells also exhibited over expression of Bcl-2. Consistent with the above we found that pretreatment of non diabetic VSMC with high glucose abolished the degradation of Bcl-2 induced by C-reactive protein . In addition, cell proliferation was increased in diabetic cells compared to non diabetic. Yet again, this differential effect was potentiated by glucose. Conclusion: We have presented new data which enhance our understanding of the mechanisms which underlie vascular remodeling in diabetic patients and form the basis for discovering promising targets for new drugs to prevent the vascular complications in type 2 Diabetes. This work was funded by Fondo de Investigaciones Sanitarias FISS PI080920 and RECAVA RD06/0014/1007 (Health Research Fund from the Spanish Ministry of Health). We thank the Cardiac Surgery Service (Hospital Clínico San Carlos, Madrid) for providing us with the IMS.</p>
<p>PL-19</p>	<p>THE APPLICATION OF NOVEL PHARMACOLOGICAL NEUROIMAGING METHODS IN THE INVESTIGATION OF DRUG ACTION IN HEATH AND DISEASE Hall SD¹, Stanford IM¹, Furlong PL¹</p> <p>¹ Neurophysiology and Clinical Neuroimaging Research Group, School of Life and Health Sciences, Aston University, Birmingham, UK. Email: Hallsd@aston.ac.uk</p> <p>Introduction: Investigations into the neurophysiological effects of neuroactive substrates are predominantly conducted using animal models. This is, in part, a consequence of the potential hazards associated with novel drug exploration, but is equally a reflection of the inadequacies of human neuropharmacological methods. Specifically, human neuroimaging methods have been able to achieve either high spatial-resolution or high temporal-resolution, but not both; however, recent developments in magnetoencephalography (MEG) methods have made this possible. Here we discuss pharmaco-MEG, a novel method for characterizing whole cortex pharmacodynamics during drug uptake, and its application for investigation of drug action in healthy and disease states. Material and Methods: Pharmaco-MEG is a specific implementation of the synthetic aperture magnetometry (SAM) beamforming method, which determines the whole-cortex profile of neuronal network oscillatory change, between drug-passive and drug-active states. Furthermore, the use of MRI co-registration and a focal method called a 'virtual electrode' (VE) affords the anatomically discrete reconstruction of cortical activity over the period of drug uptake (Hall et al., 2010a). Results and Discussion: Pharmaco-MEG can be used alongside functional localization to determine the effects of drugs on functionally specific brain regions. Furthermore, this approach can be extended to investigate the mechanisms of therapeutically effective substances on specific neuropathologies. Initial implementation of this method has revealed that drugs effective in the treatment of Stroke and Parkinson's disease work by desynchronizing 'pathological oscillations' in these conditions (Hall et al., 2010b). Conclusions: Current pharmaco-MEG methods have proven effective in investigating various neuropathologies and have the potential for application to a wider range of neurological disorders. Moreover, the use of a combined investigation of multiple effective therapeutics has the potential to identify specific therapeutic targets for drug development. References: Hall et al., (2010a). <i>Human Brain Mapping</i>. 31(4):581-94; Hall et al., (2010b). <i>Clinical Neurophysiology</i>. 121(4):549-55.</p>
<p>PL-20</p>	<p>VASCULAR EFFECT OF FOCAL CEREBRAL ISCHEMIA: BENEFICIAL EFFECTS OF ANTIOXIDANTS Vila E</p> <p>Department of Pharmacology. Therapeutics and Toxicology, Faculty of Medicine, Autonomous University of Barcelona, 08193 Bellaterra, Spain. email: elisabet.vila@uab.cat</p>

	<p>Introduction: Cerebral blood vessel properties determine blood flow in the brain, and blood flow in the cerebral blood vessels is directly related to ischemic infarct size. Cerebral ischemia alters brain arteries properties in rats¹. We studied the participation of oxidative stress on structural, mechanical and myogenic alterations in rat middle cerebral artery (MCA) induced by ischemia-reperfusion. We also tested the beneficial effects of CR-6, a structurally simple derivative of Vitamin E with capacity to scavenge oxygen and nitrogen reactive species². Material and Methods: Male SD rats were subjected to MCA occlusion (90 min) followed by reperfusion (24 h). Animals were treated with CR-6 (100 mg/kg in 1 mL of olive oil) or vehicle (1 mL of olive oil) at 2 h and 8 h after the onset of ischemia. Structural, mechanical and myogenic alterations of MCA were investigated by pressure myography. Anion superoxide (O₂⁻) production and nitrotyrosine expression were evaluated in MCA rings by ethidium fluorescence and immunofluorescence respectively. Results: Infarct size was prevented ($P<0.05$) by CR-6. In MCA the increase ($P<0.05$) in wall thickness, cross sectional area and wall:lumen as well as the decrease ($P<0.05$) in wall stress induced by ischemia-reperfusion was prevented by CR-6. However, impaired myogenic response after ischemia-reperfusion was unchanged by CR-6. Furthermore, CR-6 treatment inhibited the O₂⁻ production and partially prevented the enhanced protein tyrosine nitrosylation that occurred in response to ischemia-reperfusion. Recent studies showed that the <i>Mangifera indica L extract</i> (Vimang) and its main component mangiferin prevented the <i>in vitro</i> O₂⁻ formation in mesenteric arteries. Conclusions: Our findings suggest that oxidative stress is involved in the alterations of MCA properties after ischemia-reperfusion. Treatment with CR-6 provides an experimental basis for the benefits of antioxidant therapy during stroke. References: 1. Jiménez-Altayó F, Martín A, Rojas S, Justicia C, Briones AM, Giraldo J, Planas AM, Vila E. <i>Am J Physiol Heart Circ Physiol</i> 2007; 293: 628-35; 2. Miranda M, Muriach M, Almansa I, Arnal E, Messeguer A, Díaz-Llopis M, Romero FJ, Bosch-Morell F. <i>Free Radic Biol Med</i> 2007; 43: 1494-8</p>
PL-21	<p>THE ROLE OF CANCER IMMUNOTHERAPY IN THE CONTROL OF THE ADVANCED DISEASE: AN EMERGENT PARADIGM Rolando Pérez Rodríguez</p> <p>Centro de Inmunología Molecular, Ciudad de La Habana, Cuba. email: rolando@cim.sld.cu</p> <p>Cancer immunotherapy has not fulfilled the expectations so far. However, cancer immunotherapy continues to be an intense area of research and development worldwide. Nowadays there is a renewed interest in tumor immunology trying to understand the interaction between the immune system and malignant tumors. The immune system can prevent but also promote tumor development. Chronic inflammation is a promoter of carcinogenesis, therefore we hypothesize that tumor progression is an immune pathological process. In particular, we postulate that both EGFR (Epidermal Growth Factor Receptor) and NeuGcGM3 ganglioside, are molecular targets associated to chronic inflammation in the tumor microenvironment. Experimental and clinical data suggest that antibody-based specific immunotherapy against those targets induces an enhancement of anti-tumor cellular immunity, most likely by reverting the immune suppressive tumor microenvironment but also increasing tumor-antigen presentation. The phenomenon of time-delayed separation of survival curves observed in controlled clinical trials with the above mentioned targeted-therapies could be related to the induction period of a protective immunity in cancer patients. It is becoming evident that cancer immunotherapy requires a new clinical evaluation paradigm, which comprises novel statistical designs, chronic use, treatment beyond early progression and combination therapy. Cancer immunotherapy should have an increasing impact in the long-term control of the advanced disease.</p>
	<p>SYMPOSIA AND WORKSHOPS / SIMPOSIOS Y TALLERES CONFERENCES AND ORAL COMMUNICATIONS / CONFERENCIAS Y COMUNICACIONES ORALES</p>
W-6	<p>5TH INTERNATIONAL WORKSHOP ON PHARMACOEPIDEMIOLOGY / 5^{TO} TALLER INTERNACIONAL DE FARMACOEPIDEMIOLOGÍA</p>
OC-61	<p>INCREASING USE OF ANTIDEPRESSANTS AMONG PREGNANT WOMEN BETWEEN 1995 AND 2008 IN DENMARK Solem EJ¹, Andersen JT¹, Broedbaek K¹, Afzal S¹, Petersen M¹, Jørgensen NH¹, Rasmussen MH² and Poulsen HE¹</p>

	<p>¹Department of Clinical Pharmacology, Bispebjerg Hospital, Tagensvej 20, 2200 Copenhagen, Denmark. email: solem@rh.dk</p> <p>²Department of General Medicine, Bispebjerg Hospital, Bispebjerg Bakke 23, 2400 Copenhagen, Denmark.</p> <p>Introduction: Antidepressants are one of the most commonly used medications among pregnant women. Use of antidepressants during pregnancy, has been associated with malformations and negative birth outcomes. We therefore set out to quantify the rate of exposure to antidepressants in a cohort of pregnant Danish women.</p> <p>Materials and methods: Retrospective cohort study of 869 407 pregnancies. We performed a nationwide cohort study using the Danish Fertility Database to identify every pregnant woman in Denmark giving birth between 1995 and 2008. The National Prescription Register was used to identify women redeeming an antidepressant-prescription during pregnancy. Results: We identified 11 510 women exposed to antidepressants in the study period. The rate of exposure increased from 0.3% in 1995 to 3.6% in 2008 (p<0.001). This 12-fold increase is mostly due to the use of SSRI's, which increased from 0.2% to 3.1% (p<0.001) during the same period. Maternal age over 35 was one of the significant predictors of exposure to antidepressants (Odds ratio=1.48 (95% CI: 1.41-1.57)). Conclusion: This substantial increase in antidepressant use during pregnancy, between 1995 and 2008, underlines the need for further studies elucidating the risks of antidepressant exposure during pregnancy. This change in prescription rates might be due to health care increased knowledge of risks associated with antidepressant use during pregnancy, and better tools for diagnosing depression. To our knowledge, this is the largest study performed to date examining this issue.</p>
OC-62	<p>THERAPEUTIC DRUG INFORMATION IN HOSPITAL PRACTICE Vernon GM</p> <p>Drug Information, Pharmacy, Austin Health, Heidelberg, Victoria, Australia email: graeme.vernon@austin.org.au</p> <p>Introduction: Hospital pharmacists have a long history of providing therapeutic advice on the safe and effective use of drugs for both hospital and community practitioners. However, the justification for drug information centres is being challenged by increased access to electronic sources of information and decision support software within computerised prescribing programs. Method: The scope and activities of the drug information service at Austin Health will be described. The service provides clinical advice to health professionals within the hospital and contributed to a national drug information service for community practitioners funded by the National Prescribing Service (NPS). A drug information service integrates a range of information resources with clinical experience and training in data interpretation. The focus is on patient safety and optimum patient care. The nature and quality of approved product information is not sufficient to support optimum use of a drug. It needs to be interpreted, supplemented with recently published information, and patient-related factors must also be considered. Results and Discussion: Over 75% of enquiries relate to a specific patient and in many cases the advice required exceeds the scope of the approved product information in terms of indication, dose, age, route of administration or comorbidities of the patient. Hospital-related questions provide support for the implementation of therapeutic strategies and the service works closely with the clinical pharmacists who provide direct patient care. The adverse drug reaction reporting process helps to protect patients from future exposure to hazardous drugs as well as creating pharmacovigilance data. Conclusion: Access to electronic drug information resources is not sufficient to ensure patient care. It is necessary to select the best information resources and implement this in clinical practice. Drug information pharmacists combine data analysis with clinical imperatives to help practitioners deliver better health outcomes.</p>
OC-63	<p>ASSESSMENT OF PHARMACOTHERAPEUTIC COMMITTEE IN POLYCLINICS. HAVANA, CUBA, 2009 Broche Villarreal L¹, Furonos Mourelle JA¹, Cruz Barrios MA¹</p> <p>¹Center for the Development of Pharmacoepidemiology, 5ta and 44 St, Miramar, Playa, Havana City, Cuba. email: lourdes.broche@infomed.sld.cu</p> <p>Introduction: Inappropriate use of medicines wastes resources and seriously undermines the quality of patient care. A pharmacotherapeutic committee can significantly improve drug use and reduce costs in health care facilities. It is suspected that there are weaknesses in the work of pharmacotherapeutic committee in the polyclinics of Havana, so it was a descriptive observational study to assess its work and determine the level of knowledge about the methodology of work of the committee from pharmacotherapy committee chairmen</p>

	<p>Methods: 62 polyclinics from Havana were selected, with a simple random sampling. The pharmacoepidemiologist of the municipality applied a survey to the director of the polyclinic to verify the existence and structure of the committee, and they got information too about work of the committee from record of the meetings did in 2009, the level of knowledge was obtained through a questionnaire, it was applied to 57 presidents of pharmacotherapeutic committee, who participated in a workshop in Havana, in last December. Results and discussion: The committee was formed in 98.4% polyclinics, 53.2% of them were presided by the director, the secretary of the committee was represented in 29% polyclinics by medicines' responsible, the members less involved were ginecoobstetricia and pediatric specialists, 61.3% and 58.1% each one, the composition of the committees was valued as not appropriate at 43.5% of them. The activities less analyzed at the committee were pharmacovigilance (34.4%), promoting the rational use (80.3%), dispensing (65.8%) and training (65.5%), 89.4% of presidents did not possess sufficient knowledge about the methodology of the work. Conclusions. The poor observed functioning committees suggests that it is not taken into account the importance of this activity to ensure the quality of health care provided.</p>
OC-64	<p>ANTIBIOTICS: CHARACTERISTICS OF THEIR USE AND PHYSICIANS'S OPINION. POLYCLINIC GRIMAU, ARROYO NARANJO, CITY OF HAVANA, 2009 López Aguilera AF¹, Furones Mourelle JA², Cruz Barrios MA²</p> <p>¹ Faculty of Medicine Julio Trigo, Medic University of Havana. St Bejucal km 7 1/2, Havana City, Cuba. email: alopez@fcmjtrigo.sld.cu ² Center for the Development of Pharmacoepidemiology, 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba.</p> <p>Introduction: The uses of antibiotics have a bad use in primary health care in the world, we suspect it happened in the polyclinic Grimau, in municipality of Arroyo Naranjo, Havana; that why there was described how the physicians did prescribe the antibiotics and their opinion about this subject. Method: A descriptive, transversal and observational research was done, it was classified as a drug utilization research. Data on antibiotic utilization were collected prospectively from medical prescriptions from January 2009 to March 2009 and by a questionnaire applied to the doctors, the studied variables were age, sex, diagnosis, type of antibiotic, dose and duration of treatment and the prescription pattern was assessed using the best national recommendations. Also there was developed a focus discussion group as qualitative research, with the participation of doctors from the polyclinic. Results and discussion: A total of 287 prescriptions of antibiotics were analyzed; the 52% of prescriptions were doing in patients over 65 years old and in women 62%, the diagnoses more frequents were pharyngoamigdalitis (23%), urinary tract infections (16%) and acute diarrhea disease (15%), the most prescribed medications were amoxicillin (21%), azithromycin (18%) and cotrimoxazole (13%) and they were indicated for 3 to 6 days (41%); 61% of schemes were correct and the antibiotic selection was adequate in 56% of prescriptions. The physicians commented insecurity of diagnosis, availability of antibiotics and ignorance of antimicrobial treatment policies and protocols as cause of probably bad use of antibiotics. Conclusions: the study showed that the prescription of antibiotics at the polyclinic Grimau was not so good, it is necessary do interventional programs on rational antibiotic prescription aimed at minimizing the future emergence of bacterial resistance.</p>
OC-65	<p>ASSESSMENT OF SOME PROCESSES OF THE MEDICATIONS SUPPLY MANAGEMENT CYCLE. VILLA CLARA, JANUARY-DECEMBER 2009 Gómez LA¹, Lorenzo G², Lara Bastanzuri MC³</p> <p>¹Villa Clara Drugstore. Email : lalberto@vcl.quimefa.cu, ²Molecular Immunology Center. email: cim@capiro.vcl.sld.cu ³Pharmacoepidemiology Development Center. Email: cristina.lara@infomed.sld.cu</p> <p>Introduction: The medications supply management cycle is organized in processes that characterize the medication chain in the country. These processes are neither evaluated nor controlled in an overall and periodical form as there are neither integrated parameters identified by general consent nor identified strengths and areas that need improvements in their implementation. Objectives: To identify and assess the relevant parameters that characterize the quantification, acquisition and distribution processes as well as defining the strengths or areas that need to be improved in Villa Clara province, during 2009. Method: In order to identify the parameters, the criteria expressed by national and provincial experts that work with a nominal group dynamics were used. The "Kendall Coefficient of Concordance" was added to these criteria to determine their reliability. In order to assess quantification and acquisition processes the "Differential measurement method" and the "Client</p>

	<p>satisfaction index” were applied. Also, to prioritize the areas that require improvements within medication distribution the “Matrix of attributes” was used. Results: The quantification and acquisition were assessed as non adequate, when comparing the results of the quality simple indexes in the province with the national average basic indexes. Also, the distribution process was assessed as “good” by the clients. Conclusions: The quantification and acquisition processes in this province were implemented with less quality in comparison with the national average. Distribution assessment behaved differently, which yielded good results, and the clients identified “medication availability” as the main dissatisfaction in relation with this process.</p>
<p>OC-66</p>	<p>CRITERIA OF PRIMARY CARE PROFESSIONALS ON THE BULLETIN OF INFORMATION IN THERAPEUTICS APS. CUBA. 2009 Alonso Liuba¹, Calvo Dulce², García Ana J³, Yero Isis B⁴, Lopez Pedro⁵</p> <p>¹Esp II Degree in Pharmacology, Master in health promotion. Assistant Professor. ²ESP II Degree in Pharmacology. Assistant Professor. ³ESP II Degree in Pharmacology, Master in Health Economics. Researcher and assistant professor. ⁴Esp II Degree in Biostatistics, Master in Health Economics. Assistant Professor. ⁵Esp II Degree in General Medicine, Masters in Primary Health Care. Assistant Professor. National School of Public Health. (ENSAP).</p> <p>Centro for the Development of Pharmacoepidemiology. Calle 44 esq 5ta ave. No.502. Playa, Ciudad de La Habana. email:liuba@mcds.sld.cu</p> <p>Abstract: Background: Many issues directly related to therapeutic newsletters must be subject to investigation and assessment, in that sense this research is done in order to characterize the acceptability of these professionals with the BIT published by the CDF to make this research. Method: A total of nine provinces, of which 25% were selected from areas of health, through simple random sampling. The sample consisted of 605 prescribers. The questionnaire was developed by specialists of the CDF and included questions related to: receive frequency, size, size, font, theme selection, ease of reading and usefulness of the newsletter. The same was implemented by the municipality pharmacoepidemiological. Results: Over 80% of respondents have ever received said, most of them noted that the frequency with which the recipient is an annual (31.9%), while a quarterly basis, only 15.2% receive it. With regard to typography for more than 90%, found between adequate and very adequate, and 7.3% classified it as inappropriate. Of those surveyed 96% felt that the topics covered are very interesting or interesting in general, and only 15 (2.5%) classifies it as uninteresting. Conclusions: The results obtained confirm the acceptance by prescribers at primary health care Therapeutic Information Bulletin APS (BIT) published by the CDF in terms of its design and content. The BIT is useful to its users primarily for training, consultation and therapeutic update.</p>
<p>OC-67</p>	<p>INFORMATION NEEDS ON THERAPEUTIC HEALTH PROFESSIONALS. CUBAN MEDICAL MISSION. CARONI MUNICIPALITY. BOLIVAR STATE. 2009 Linares IM¹, Calvo BD², Debesa GF²</p> <p>¹Cuban Medical Mission in Venezuela. ²Center for the Development of Pharmacoepidemiology, National Pharmacovigilance Unit, 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba. dulce@mcds.sld.cu</p> <p>Introduction: In Bolivar state found problems with the use of information technology in the search for scientific information by health professionals and therapeutic errors identified by performance indicators, health insurance area, the causes are unknown these deficiencies. Objectives: To identify sources of information on treatment and determine the relevance in the case of electronic and information needs therapy. Designing an educational strategy to meet those needs. Method: We conducted an observational, descriptive and cross-sectional Caroni municipality, Bolivar State, Venezuela Bolivarian Republic in the months from May to July 2009. Operationalized the variables are given output targets. A structured questionnaire was drawn up to apply for health professionals. A questionnaire was developed to evaluate the relevance of websites visited by the respondents. Results: 52% of respondents mentioned not having access to scientific information in the network. The most visited sites were Infomed, Medline, Lilac, while found to be most relevant Cochrane Library, Medline, Pubmed, Infomed and Finisterre. Books and print journals are preferred by professionals. The issues they care most about are drugs (27.7%) and therapy (23.4%). As for the drug groups, the greatest demand are: antimicrobials (20%), antihypertensives (19.6%) and antidiabetics (16.7%). Health problems that matter most are diabetes mellitus, hypertension and asthma. Conclusions: Health professionals from Caroni municipality does not have sufficient and timely information on therapeutics, as most mentioned not having access to search sites of scientific information. The preferred sources of</p>

	information were sometimes outdated, in addition, the sites visited did not always match those that were considered most relevant.
OC-68	<p>ECONOMIC AND HEALTH IMPACT OF THERAPEUTIC INTERVENTIONS IN ELDERLY HOMES IN SANCTI SPIRITUS MUNICIPALITY León O, Labrada A, Ruíz H, Ramos L, García R</p> <p>Elderly home . Sancti Spiritus Municipality. SSpíritus, Cuba. E- mail: oleon_1958@dmss.ssp.sld.cu</p> <p>Introduction: It is imprescindible to improve old men and women Therapeutics Care for it is a risk group where phisiopatological and habitual polipharmacy expose them to risks and avoidable conditions. It was intended to identify difficulties in individual treatments to correct them and make a rational use of medications to benefit the facility economy. Material and Methods: A prospective study was carried out with timely interventions. This included the in-patients admitted as a universe in Sancti Spiritu municipality elderly home in a period from January 2009 to April 2010 analyzing each treatment individually, detecting non imprescindible drugs, interacting ones, over dose ones, and other therapeutic deficiencies, correcting and valueing their economic impact. Minded health patients, nurses and nurses assistants were interviewed. Clinical records were reviewed. Graphs and tables were made. A percentual data analysis was made. Results and Discussion: Around 40 % of the patients had therapeutic mistakes: excess of drugs, high doses according to age and phisiopathological conditions, bad pharmacological combinations, uneffective drugs or with low safety margin, renal failure notdiagnosed, etc, with multiple interaction risks, toxicities and complications, many of them serious or potencially fatals. Some therapeutic arrangements were made to minimize health risks of patients at the time the pharmaceutical expenses of the facility were reduced. Conclusions: Detection and conection of therapeutic mistakes in these old people benefit a more rational use of the drugs which save health complications and unnecessary expenses for the facility economy.</p>
OC-69	<p>CONSUMPTION OF DRUGS IN THE ADULT POPULATION OF CUBA. 2007 TO 2010. García Ana J¹, Alonso Liuba², Lopez Pedro³</p> <p>¹Esp II Degree in Pharmacology, Master in Health Economics. Researcher and assistant professor. Center for the Development of Pharmacoepidemiology. Calle 44 esq 5ta ave. No.502. Playa, Ciudad de La Habana. anaj@mcdf.sld.cu</p> <p>²Esp II Degree in Pharmacology. Assistant Professor. Center for the Development of Pharmacoepidemiology. Calle 44 esq 5ta ave. No. 502. Playa, Ciudad de La Habana.</p> <p>³1^{er} Espec Degree in General Medicine, Masters in Primary Health Care. Assistant Professor. National School of Public Health.</p> <p>Introduction: In Cuba, works with a view to raising standards of health of the population through various strategies, one of them is pharmacoepidemiology, whose main objective is to make appropriate use of medicines. Numerous studies have described several factors that influence the use of them, highlighting those working in production, prescription, dispensing and consumption. Objective: To characterize the pattern of drug consumption in the adult population in Cuba. Method: Study, an observational descriptive cross-sectional, in the period 2007-2010. The collection of information is achieved with the implementation of a survey by face to face interview. Results: Over half of respondents taking medications, the average consumer drug was 2.16. The most used drug groups are the antihypertensives and NSAIDs. 7.3% of subjects including nonprescription drugs consumed. The 86.8% of the population receive drug information referred to in different ways dominate television and physicians. 22.6% reported having experienced an adverse event, being more common in females and in those over 40 years of age. The drugs most responsible for producing reported as adverse events were penicillins and acetylsalicylic acid. The skin was the organ most affected by adverse events, evaluated mostly mild. Compliance with antihypertensive therapy in the adult population is 77.9%, with male sex and increasing age, the most responsible for the breaches. Forgetting and the occurrence of adverse reactions were reported more cases of abandonment of therapy. Conclusions: The pattern of drug consumption is the basis for the establishment of health policies that mitigate the effects of inappropriate use of medicines in the adult population of Cuba.</p>
OC-70	<p>ULCER THERAPY COMPLIANCE. “CARLOS M. DE CÉSPEDES” UNIVERSITY HOSPITAL. 2009 Ramos K, Ortíz Y , Martínez H, Álvarez R</p> <p>¹Bayamo Medical School. Medical University of Granma Province. Cuba. email: keniaramos.grm@infomed.sld.cu</p>

	<p>Introduction: Dyspepsia is classified as organic (duodenal and gastric ulcers) and functional. A peptic ulcer is a depression that extends through the mucous membrane to the muscle layer of the esophagus, the stomach or the duodenum; it has an annual incidence of 2,9 per 1000 inhabitants and a prevalence of 1,68 % in the general population. The prevalence of infection by <i>Helicobacter pylori</i> is high although it is variable, among 30% and 80% of the adult population is infected. Treatment can be pharmacological or non-pharmacological. Pharmacological treatment has different regimens that consist in the combination of antimicrobial, antisecreting and cytoprotective agents, for a period of time that ranges from 4 to 8 weeks; however, patients do not get cured due to lack of treatment compliance. Material and method: A descriptive study was carried out in 40 patients admitted at “Carlos Manuel de Céspedes” University Hospital of Bayamo with a diagnosis of peptic ulcer during the period from January to April, 2010. A structured interview was used to explore aspects such as treatment compliance, drugs used, doctor’s performance, and patient’s behavior. Results: It was found that 57,1% of the patients complied with the treatment while 42,8% showed non-compliance. Among the drugs used for treatment were cimetidine, metronidazol and tetracycline. Conclusion: Inpatients showed an adequate compliance with pharmacological treatment for ulcer.</p>
<p>OC-71</p>	<p>CONTROL BY PHARMACEUTICAL PROFILE IN A HOSPITAL SERVICE. CHALLENGES AND IMPACT Romero K</p> <p>Hospital General Docente “Dr. Agostinho Neto”. Carretera El Salvador K1¹/₂. Guantánamo. Cuba. Correo electrónico: email:katherine@infosol.gtm.sld.cu</p> <p>As everybody knows that thank to the setting in march of the pharmaceutical attention has been possible to forge the one on the way to the health and the patients well-being. The practice by the way of the pharmaceutical of get knowledge with it therapeutic, independently of the problems which has to be suffered, has allow besides a diminishing the cost by medical spending because in our country health attention is free, this point out and important cost for the country and patient himself. It was done a prospective study to evaluate the quality of the prescription in the Internal Medicine at the General Teaching Hospital “Dr. Agostinho Neto” at Guantanamo city from january to may 2010 with the aim to detect the Problem Induced with the Drugs (PID) and give solution in a less possible time. It will follow by pharmaceutical profile a total of 112 patients and it were detected 64 PID included the risks. The more frequent PID were the PID 5 (43.75%), PID 1 (26.56%), PID 4 (15.63%), the remaining 14.06%, which more frequent main causes the health problems not attended sufficiently and the dosage, standard or inadequate treatment time. Thank to pharmaceutical intervention it was fulfilled a diminishing of therapy cost by concept of used drugs to solve adverse effects, non-adequate interaction and long-hospital stay because the patient did not improve his health state.</p>
<p>OC-72</p>	<p>PHARMACOTHERAPEUTICAL EDUCATION STRATEGY IN PREGNANT AND NURSING WOMEN Marrero R, Bermúdez A, E Barreto, JM Medina, Martín Y, San Gabino Y</p> <p>Centre for Studies, Documentation and Information of Drugs. Medical Sciences University. Acueduct rd. and Circunvalation rd. Santa Clara. Villa Clara. Cuba. email: rayza76@ucm.vcl.sld.cu</p> <p>Introduction: Among the main problems facing the health team in the community is the misuse of drugs is more sensitive in the case of special populations such as children, the elderly and pregnant and breastfeeding. The solution of this problem must be directed not only to the proper control of pharmacotherapy, but also an intense and educational effort. Materials and Methods: an investigation in Systems and Services of Health typified as a transversal, observational and descriptive type, with a systemic approach and forwarded to the characterization of the pharmacotherapeutical education in pregnant and nursing women and to the valuation of a strategy of intervention for the pharmacotherapeutical education in them, was carried out. The spatial context was the health area of the Docent Polyclinic “Chiqui Gómez Lubián” in Santa Clara city, from March to October, 2009, using strategic planning as methodological guide. The sample consisted of women during these stages of a core working group, professionals from two of them and medium level managers. Results and Discussion: the characterization of the pharmacotherapeutical education status showed a non adequate structure since the documentation and material resources were insufficient and human resources were not available. The process was considered as non adequate because the activity was not correctly executed evidenced when directives and basic working group were contacted. The identification of learning needs was medially adequate and the 100% of professionals expressed high knowledge needs so the results, as the last</p>

	<p>element of the system, showed that the majority of women in both groups had medium information needs, non adequate conducts and problems related to medication. To solve these problems and taking into account the results, it was elaborated a strategy of intervention for the pharmacotherapeutical education in these periods which was valuated as very adequate by the experts.</p>
S-5	SYMPOSIUM “PHARMACOLOGY OF PAIN” / SIMPOSIO “FARMACOLOGÍA DEL DOLOR”
OC-73	<p>PARTICIPATION OF NITRIC OXIDE (NO) IN THE MECHANISM OF PERIPHERAL ANALGESICS <u>SH Ferreira</u></p> <p>School of Medicine of Ribeirão Preto, Department of Pharmacology, Campus USP, Ribeirão Preto, SP, Brazil.</p> <p>About thirty years ago we proposed that the mechanism of analgesic effect of aspirin- like drugs could be explained by the blockade of prostaglandin’s (PGs) inflammatory nociceptor sensitisation (hypernociception). This suggestion was incorporated in Vane’s proposal of the anti-pyretic and anti-inflammatory effect of non-steroidal anti-inflammatory drugs: inhibition of prostaglandin’s synthesis. Late, we discovered the peripheral analgesic action of opiates by demonstrating their direct antagonistic effect upon ongoing PGs induced hypernociception. Thus, their analgesic effect was peripheral but independent of cyclooxygenase inhibition. Other agents, in particular the analgesic dipyron, had a similar mechanism of action. Inflammatory hypernociception is the result of the lowering nociceptor threshold and the induction of <i>functional</i> “sodium channels tetrodotoxin resistant”, characteristic of C fibers. In the last decade, it was demonstrated by ours and other laboratories that the antinociceptive effect of “direct anti- hypernociceptive drugs” (DAHD) resulted from the stimulation of the arginine-NO-cGMP-PKG” pathway, leading to the opening of the ATP dependent K⁺ channels of the primary nociceptive neuron. The lowering of the neuronal K⁺ promotes the restoration of the normal high nociceptor threshold. Thus, instead of preventing (like the COX inhibitors) the DAHD directly block ongoing acute or persistent hypernociception. In addition to morphine, the kappa opioids like bremazocine, U 50488H and ICI 204448 and a factor present in the venom of <i>Crotalus durissus terrificus</i> possesses such mechanism of analgesic action. Pure DAHD has no gastric side effects as shown by drugs like keterolac or diclofenac that also inhibit COX-1. Thus, the development of new DAHD that does not cross the blood brain barrier or devoid of intestinal side effects (kappa agonists or dipyron like) is a promising target for substitution of COX-2 inhibitors in long term therapies.</p>
OC-74	<p>ANTINOCICEPTIVE EFFECT OF <i>Thalassia testudinum</i> EXTRACT (BM-21) IS MEDIATED BY INHIBITION OF THE ASIC CURRENT BY PHENOLIC COMPOUND THALASSIOLIN B <u>Garateix A¹</u>, Salceda E², Menéndez R¹, Regalado EL¹, López O², García T¹, Morales RA.¹, Palmero A¹, Laguna A¹, Thomas OP.³ y Soto E²</p> <p>¹Centro de Bioproductos Marinos, Agencia de Medio Ambiente, Ministerio de Ciencia, Tecnología y Medio Ambiente, La Habana, Cuba. email: cebimar@infomed.sld.cu ²Instituto de Fisiología, Benemérita Universidad Autónoma de Puebla, México. ³Université de Nice-Sophia Antipolis, Laboratoire de Chimie des Molécules Bioactives et des Arômes, UMR. 6001 CNRS, Institut de Chimie de Nice, Faculté des Science, Parc Valrose, Nice, France.</p> <p>Acid-sensing ion channels (ASICs) have a significant role in pain perception and constitute an important target for the search of new antinociceptive drugs. In this work we studied the antinociceptive properties of BM-21 extract, obtained from the sea grass <i>Thalassia testudinum</i> in chemical and thermal models of nociception in mice. Single oral administration of BM-21 (40, 400 and 1000 mg.kg⁻¹) produced significant inhibition on chemical nociception induced by acetic acid and formalin (specifically in the second phase of this test) and increased the reaction time on the hot plate test. It was also found that BM-21 and the major phenolic component isolated from this extract, a sulphated flavones glycoside flavonoids named thalassiolin B, selectively inhibited the fast desensitizing ($\tau < 400$ ms) ASIC currents in dorsal root ganglion (DRG) neurons obtained from Wistar rats, with a non-significant action on ASIC currents with slow desensitizing time course. The high concentration of thalassiolin B in the extract may account for the antinociceptive action of BM-21. To our knowledge, this is the first report of an ASIC current inhibitor in a marine plant extract, and in a compound of phenolic nature. The fact that the active components of the extract are able to cross the brain blood barrier gives it an additional advantage for future applications as tools to study pain mechanisms with a potential therapeutic application.</p>

<p>OC-75</p>	<p>INTRODUCTION OF <i>MANGIFERA INDICA</i> L. EXTRACT (VIMANG) IN NEUROPATHIC PAIN SYNDROMES. PRECLINICAL AND CLINICAL RESULTS Garrido BB^{1,2}, Bosch B², Rabí MC², Porro J², García ME¹, Delgado R¹</p> <p>¹Laboratory of Molecular Pharmacology, Center of Research and Drug Development, Ave 26, No. 1605 Boyeros y Puentes Grandes. CP 10600, Plaza de la Revolucion, Habana City, Cuba. ²Pain Clinic of 10 de Octubre Hospital. Calzada de 10 # 130 entre Alejandro Ramírez y Agua Dulce, CP 10300 Cerro, La Habana, Cuba.</p> <p>Introduction: Neuroimmune activation has been proposed as a source of new targets for therapeutic intervention in neuropathic pain. Vimang® is the brand name of an aqueous extract of <i>Mangifera indica</i> L. with inhibitory effect on transcription nuclear factor κB (NFκB). Here we determined the effects of oral acute and chronic administration of a mango stem bark extract (MSBE) in animal models of persistent pain and its formulations (Vimang's tablets and cream 1,2 %) in patients with Complex Regional Pain Syndrome (CRPS), that received a daily dose of 1800 mg of extract for 120 days, sympathetic blocks once for weeks and physiotherapy since 30 days. Material and Methods: The chronic post-ischemia pain (CPIP) a model of CRPS type I in rats was reproduced and the mechanical antihyperalgesic effect of MSBE was evaluated using a modification of the pin prick method. In formalin test at 5%, two quantifiable behaviors indicative of pain (lincking/biting and flinching) were identified in the early (I) and late phase (II) (acute phases). In addition, was evaluated the secondary chronic mechanical antihyperalgesic effect of MSBE in the third phase at 3 and 7 days after subcutaneous formalin injection. An open uncontrolled clinical trial in 15 patients with CRPS was conducted. The change in average daily pain score (ADPS) through a Likert scale, the area and rate of mechanical dynamic allodynia, rate of cold allodynia, deep somatic allodynia and burning spontaneous pain frequency were evaluated. Results and Discussion: MSBE (250mg/Kg) decreased mechano-hyperalgesia with respect control CPIP group ($p<0.001$) from 24 to 72 h after reperfusion. NFκB are involved in CPIP model and potentially of human CRPS-I, it is pivotal in microglial activation. Formalin at 5% produces spinal glutamate release and glial activation, in special in the third phase. Chronic administration of MSBE (125-500 mg/Kg) once for 4 days decreased dose-dependended lincking/biting only in phase II, but decreased flinching in the both phases. The combination of oral MSBE (500 mg/Kg) with sub-effective dose of ascorbic acid (1mg/Kg) i.p. produces a significant reinforcement of these effects in the two phases, increased the latency period about 20-25 min for both behaviors and decreased mechano-hyperalgesia ($p<0,001$) at 3 and 7 days. Likeness with preclinical results, the pain score and sensory abnormalities showed a significant improvement ($p<0,001$), from week 2-3 in CRPS patients treated with Vimang formulations. Conclusions: MSBE could modulate some molecular targets implicated in central sensitization mediated by spinal and supra-spinal mechanisms. The significant reinforcement of the MSBE-ascorbic acid combination suggests that this extract could reduce the phosphorylation of N-methyl-D-aspartate receptor (NMDA) subunit 1 (pNR1) in the spinal cord, depending of its potent antioxidant effect. References: 1-<u>Manning DC</u>. The role of Neuroimmune Activation in Chronic Neuropathic Pain and New Targets for Therapeutic Intervention. In: Campbell JN, Basbaum AI, Dray A, Dubner R, Dworkin RH, Sang ChN. Editors. Emerging strategies for the treatment of neuropathic pain. Seattle: IASP Press; 2006.pp.161-192. 2- <u>Garrido G</u>, et al. Analgesic and anti-inflammatory effects of <i>Mangifera indica</i> L. extract (Vimang). <i>Phytother Res</i> 2001; 15:18-21. 3- <u>Coderre TJ</u>, et al. Chronic post-ischemic pain (CPIP), a novel animal model of complex regional pain syndrome type I (CRPS-I; reflex sympathetic dystrophy) produced by prolonged hindpaw ischemia and reperfusion in the rat. <i>Pain</i> 2004;112:94-105. 4- <u>Kim HK</u>, et al. Analgesic effect of vitamin E is mediated by reducing central sensitization in neuropathic pain. <i>Pain</i> 2006; 122:53-62. 5- <u>Gao X</u>, et al. Reactive oxygen species (ROS) are involved in enhancement of NMDA-receptor phosphorylation in animal models of pain. <i>Pain</i> 2007; 131:262-271. 6- <u>Hacimuftuoglu A</u>, et al. Antioxidants attenuate multiple phases of formalin-induced nociceptive response in mice. <i>Behavioural Brain Res</i> 2006; 173:211-216. 7- <u>Li K</u> et al., Peripheral Formalin injury induces two stages of microglial activation in the spinal cord, <i>J. Pain</i> (2010) doi: 10.1016/j.pain.2010.01.268.</p>
<p>OC-76</p>	<p>THE SST4 SOMATOSTATIN RECEPTOR AS A PROMISING TARGET OF NOVEL ANTI-INFLAMMATORY AND ANALGESIC DRUGS Pinter E¹, Sandor K¹, Elekes K¹, Kemeny A¹, Szolcsanyi J¹, Emson PC², Markovics A¹, Pozsgai G¹, Helyes Zs¹</p> <p>¹Department of Pharmacology and Pharmacotherapy, Faculty of Medicine, University of Pécs, H-7624 Pécs, Szigeti u. 12., Hungary. email: erika.pinter@aok.pte.hu ²Laboratory of Molecular Neuroscience, The Babraham Institute, Babraham Research Campus, Babraham, Cambridge, CB22 3AT, UK.</p>

	<p>Introduction: We previously established that somatostatin released from sensory nerves exerts anti-inflammatory and anti-nociceptive effects. Data obtained with receptor-selective agonists suggested the involvement of somatostatin receptor subtype 4 (SST₄) in these inhibitory actions. In order to provide direct evidence for the roles of these receptors in inflammation and pain, the first aim of our studies was examining SST₄ gene-deleted (SST₄^{-/-}) mice in a variety of related disease models. Secondly, the effects of orally active non-peptide sst₄ agonists were also investigated. Material and Methods: Experiments were performed on SST₄^{-/-} and SST₄^{+/+} mice. Acute paw edema and mechanical hyperalgesia was induced by intraplantar carrageenin. Chronic arthritis was evoked by intraplantar complete Freund's adjuvant. Oxazolone was used for inducing allergic contact dermatitis and mustard oil for eliciting neurogenic inflammation on the mouse ear. Airway inflammation and bronchial hyperreactivity was evoked by intranasal lipopolysaccharide administration. Sst⁴ agonists were applied orally. Results and Discussion: Acute carrageenan-induced paw edema, mechanical hyperalgesia and inflammatory pain in the early phase of adjuvant-evoked chronic arthritis, as well as oxazolone-induced delayed-type hypersensitivity reaction in the skin were much greater in sst₄^{-/-} mice. Sst₄ agonists significantly inhibited mustard oil-induced ear oedema induced by mustard oil in wild-type mice, but it was ineffective in SST₄^{-/-} animals. Airway inflammation and consequent bronchial hyperreactivity elicited by intranasal lipopolysaccharide administration were also markedly enhanced in sst₄ knockouts including increased perivascular/peribronchial edema, neutrophil/macrophage infiltration, mucus-producing goblet cell hyperplasia, myeloperoxidase activity, interleukin-1β, necrosis factor-α and interferon-γ expression in the inflamed lung. Conclusions: It is concluded that during these inflammatory conditions the released somatostatin has pronounced counter-regulatory effects through SST₄ receptor activation. On the basis of the present study we conclude that SST₄ receptor agonists could be effective in different acute and chronic inflammation and pain models and also inhibit the neurogenic components of inflammation.</p>
OC-77	<p>MOLECULAR MODELING IN THE DISCOVERY NEW ANALGESIC CANDIDATES FROM MOLECULAR STRUCTURES López-Sacerio A¹, Casañola Martín G², Marrero-Ponce Y¹</p> <p>¹Pharmacy Department. Chemistry- Pharmacy Faculty. Central University of Las Villas. Carretera a Camajuani km 5.5, CUBA. email: arelysls@uclv.edu.cu ²Bioplant Center. Ciego de Avila, CUBA</p> <p>Introduction: Treating pain is a great medical challenge and it is estimated that as many as half of all patients receive inadequate pain treatment. More effective and better tolerated treatments are needed. Main goal of this work is to identify new compounds with analgesic activity by means of <i>in silico</i> tests. Materials and Methods: To this end, firstly a database was compiled using compounds reported in the literature with analgesic activity to obtain a reliable analysis and modulation of the data. Using TOMOCOMD-CARDD descriptors, quantitative structure-activity relationships (QSAR) models was obtained that allowed virtual screening processes to be carried out, using a database of 1190 compounds and the lineal stochastic and non-stochastic atomic indices as molecular descriptors. Through the multivariate selection method descriptors were identified that allow the separation of the data into two classes (analgesic and non-analgesic compounds). Results: The results of the analyses indicate that the total and local TOMOCOMD-CARDD descriptors, provide an excellent separation of the data (> 88%) in the training and prediction series. Finally, the obtained models were applied to virtual screening of chemical compounds which allowed the <i>in-silico</i> activity estimation of compounds with other pharmacological uses as well as new molecular entities. Several drugs currently used in therapy and new series heads were identified as possible analgesics although the activity of the compounds selected as analgesic has to be corroborated experimentally. Conclusion: The TOMOCOMD-CARDD method is promising in the development of QSAR models that permit biosilic discovery of new drugs with analgesic activity.</p>
OC-78	<p>TRANSDERMIC SYSTEM IN THE HANDLING OF PAIN / SISTEMAS TRANSDÉRMICOS EN EL MANEJO DEL DOLOR Enrique Granizo</p> <p>Universidad Central del Ecuador, Presidente de la Asociación Latinoamericana de Farmacología, Ecuador.</p> <p><i>Resumen no disponible en el momento de la edición del libro. Abstract non available in the moment of the edition of the book of summaries.</i></p>

S-6	SYMPOSIUM PRECLINIC AND CLINIC EXPERIMENTAL PHARMACOLOGY / SIMPOSIO FARMACOLOGÍA EXPERIMENTAL PRECLÍNICA Y CLÍNICA
OC-79	<p>THE SPECIFIC DIFERENTIAL BIOLOGY AND HISTOLOGY OF THE LABORATORY RATS AND MICE AS SUMMONS OF THE PRE CLINICAL STUDIES IN PHARMACOLOGY AND TOXICOLOGY <u>Nelson de J. Merino García</u></p> <p>Institute of Pharmacy and Foods. Havana University Ave. 23 No. 21425 e/ 214 y 222. La Coronela, La Lisa. Ciudad Habana. email: nmerino@infomed.sld.cu</p> <p>The laboratory rats and mice are still very important in the pre clinical Pharmacology and Toxicology, in spite of the actual relevance of the alternative techniques in Toxicology to reduce or substitute the use of animals. It may happen that novel scientifics begin to work with laboratory animals without to have the complete knowledge of the diferencial biology and histology of these animals. The aim of this conference is to show and explain some important topics of the biology and histology that make the diference in comparison with other laboratory animals. In summary, the exposition will deal with the pulmonary veins, the extramedulary heamatopoyesis, the sexual dimorfhism of rats and mice, the Pancreas, the hair follicles, the vibrisas and the skin of mouse tail, the Adrenal gland of the mouse, the Zimbal gland, the vomeronasal organ, the brown adipose tissue, the poliploidia of the hepatocytes, tha Mast cells of the rat, the Harder gland, the Mammary gland and other.</p>
OC-80	<p>ROLE OF CAPSAICIN-SENSITIVE SENSORY NERVES AND TRPV1 RECEPTORS IN IODOACETATE-INDUCED OSTEOARTHRITIS IN MICE. <u>Markovics A.</u> Nagy P, Perkecz A, Sándor K, Pintér E, Szolcsányi J, Helyes Zs</p> <p><i>Department of Pharmacology and Pharmacotherapy, University of Pécs, Szigeti str. 12, Pécs, Hungary</i> email: adri.markovics@yahoo.de</p> <p>Introduction: Interactions between sensory neuropeptides and cellular inflammatory mediators (cytokines, proteases, lipid mediators) play an important role in joint diseases and related pain. In the present study we investigated the role of capsaicin-sensitive afferents and Transient Receptor Potencial Vanilloid 1 (TRPV1) ion channels in a chronic osteoarthritis model. Material and Methods: Monosodium-iodoacetate (MIA; 20 □l, 25 mg/ml), which inhibits chondrocyte metabolism was injected into the right tibiotarsal joint of C57Bl/6 wildtype and TRPV1 receptor-deficient mice. For selective destruction of the capsaicin-sensitive fibres, high dose resiniferatoxin (RTX) pretreatment was performed in CD1 mice. Joint diameter was measured with a digital micrometer, the mechanonociceptive threshold with a dynamic plantar aesthesiometer, and spontaneous weight distribution with an incapacitance tester throughout a 14-day experimental period. Semiquantitative scoring of the inflammatory and degenerative histopathological parameters was also performed. Results: MIA injection induced a 15-20% joint swelling, a 30-35% mechanical hyperalgesia, impaired ipsilateral weight bearing, as well as synovial hyperplasia and desruption/necrosis of the cartilage layer. In RTX-pretreated mice swelling and cartilage erosion/destruction were significantly greater, but there was no difference in the nociceptive tests. The lack of TRPV1 receptors did not alter any of the examined parameters. Conclusion: In this osteoarthritis model activation of the capsaicin-sensitive fibres inhibits joint swelling and some histopathological parameters, but not through the stimulation of the TRPV1 channel. However, neither these nerves nor TRPV1 receptors remarkably influence the nociceptive parameters. This might be explained by distinct roles and functional significances of the released pro- and anti-nociceptive sensory neuropeptides in the pathological mechanism.</p>
OC-81	<p>ROLE OF PITUITARY ADENYLATE-CYCLASE ACTIVATING POLYPEPTIDE (PACAP) IN ENDOTOXIN-INDUCED AIRWAY INFLAMMATION IN MICE <u>Elekes K</u>¹, Sándor K¹, Móricz A¹, Kereskai L², Kemény Á¹, Szöke É¹, Pintér E¹, Perkecz A¹, Szolcsányi J¹, Reglődi D³, Hashimoto H⁴, Helyes Zs¹</p> <p>Departments of ¹Pharmacology and Pharmacotherapy, ²Pathology, and ³Anatomy, University of Pécs, Hungary; ⁴Graduate School of Pharmaceutical Sciences, Osaka University, Japan email: krisztian.elekes@aok.pte.hu</p>

	<p>Introduction: The presence of pituitary adenylate-cyclase activating polypeptide (PACAP) and its in capsaicin-sensitive peptidergic sensory nerves, inflammatory and immune cells suggests its involvement in inflammation. However, data on its role in different inflammatory processes is contradictory and there is little known about its function in the airways. Therefore, our aim was to examine endotoxin-induced airway inflammation in PACAP gene-deficient (PACAP^{-/-}) mice. Material and Methods: Subacute pneumonitis was evoked by intranasal E. coli endotoxin (lipopolysaccharide: LPS) in PACAP^{-/-} and PACAP^{+/+} mice. Airway responsiveness to inhaled carbachol was determined in unrestrained mice with whole body plethysmography 6 and 24 h after LPS. Interleukin-1α (IL-1α) concentration was measured with ELISA, myeloperoxidase (MPO) activity referring to the number of accumulated neutrophils/macrophages with spectrophotometry from the lung homogenates. Histological evaluation and semiquantitative scoring were also performed. Results and Discussion: Bronchial responsiveness, as well as IL-1α concentration and MPO activity markedly increased at both timepoints. Perivascular oedema dominated at 6 h, while remarkable peribronchial granulocyte accumulation, macrophage infiltration and goblet cell hyperplasia were seen at 24 h. Airway hyperreactivity was significantly higher and inflammatory histopathological changes were more severe at both timepoints, MPO was almost double at 6 h in PACAP^{-/-} mice compared to the wildtypes. In contrast, there was no difference between the IL-1α concentrations. Conclusions: These results provide evidence for a protective role for PACAP in endotoxin-induced airway inflammation and hyperreactivity.</p>
OC-82	<p>PITUITARY ADENYLATE-CYCLASE ACTIVATING POLYPEPTIDE MEDIATES NITROGLYCEROL-INDUCED TRIGEMINOVASCULAR ACTIVATION: IN VIVO STUDY WITH GENE-DELETED MICE Helves ZS¹, Markovics A¹, Lashgarara A¹, Szöke É., Sándor K., Tuka B³, Kormos V¹, Szolcsányi J¹, Gaszner B², Reglódi D², Hashimoto H⁴, Tajti J³</p> <p>¹Department of Pharmacology and Pharmacotherapy, University of Pécs, Szigeti u. 12. H-7624, Pécs, Hungary. Email: zsuzsanna.helvey@aok.pte.hu ²Department of Anatomy, University of Pécs, University of Pécs, Szigeti u. 12. H-7624, Pécs, Hungary. ³Department of Neurology, University of Szeged, Semmelweis u. 6. H-6725, Szeged, Hungary. ⁴Graduate School of Pharmaceutical Sciences, Osaka University, 1-6, Yamadaoka, Suita-shi, 565-0871, Osaka, Japan.</p> <p>Introduction: Pituitary Adenylate-Cyclase Activating Polypeptide (PACAP) is present in sensory neurones and vascular smooth muscle cells. We have shown its central pro-nociceptive function in a variety of pain models. PACAP and its receptor are localized in meningeal vessels, and its infusion triggers long-lasting migraine-like headache in humans. Therefore, our aim was to investigate the role of PACAP in nitroglycerol (NG)-induced pathophysiological changes using PACAP gene-deleted (PACAP^{-/-}) and wildtype mice (PACAP^{+/+}). Materials and Methods: Migraine-like alterations were induced by 10 mg/kg i.p. NG. Mice were individually observed in a light-dark box to evaluate photophobia as a characteristic sign of migraine-like behaviour. Meningeal microcirculation was measured by laser Doppler imaging, and systemic blood pressure was determined through the carotid artery under urethane anaesthesia. Expression of the c-Fos protein as an early marker of neural activation was examined in the trigeminal nucleus caudalis (TNC) with immunohistochemistry. Results: Significantly reduced light aversive behaviour was detected in PACAP^{-/-} mice both in the early (0-30 min) and late phases (90-120 min) due to acute vasodilation and sensitization of the trigeminal system, respectively. NG produced significant (30-35%) biphasic increase of meningeal blood flow with a second peak starting 170 minutes after its injection. In contrast, in PACAP^{-/-} mice NG did not alter microcirculation in the first 2 h-period and exerted only a minor increase in the later phase. Mean arterial blood pressure decreased by 20-25% in both groups, so it does not explain these differences. Exogenous PACAP (300 microg/kg i.p.) produced a 30% increase in meningeal flow. C-Fos expression in the TNC 2 h after NG injection was significantly smaller in PACAP^{-/-} mice. Conclusions: PACAP has both direct and indirect vasodilating effects on the brain surface and activates the trigeminovascular system. Exploration of its precise mechanism and targets might open future perspectives in novel anti-migraine therapy.</p>
OC-83	<p>DIFFERENT EFFECTS OF NICARDIPINE AND VERAPAMIL ON THE CIRCULAR AND LONGITUDINAL MUSCLE OF THE ISOLATED RAT UTERUS Milovanovic RS, Trbojevic S¹, Oreščanin-Dušić Z², Blagojević D², Spasić M²</p> <p>¹Department of Pharmacology, Faculty of Medicine Foča, University of East Sarajevo, Republic of Srpska. e-mail: milarados@ptt.rs ²Department of Physiology, Institute for Biological Research “Siniša Stanković”, Belgrade, Serbia</p>

	<p>Influence of calcium antagonists (nicardipine and verapamil) on the various types of activation (spontaneous rhythmic activities and contractions provoked by electrical field stimulation or by calcium) of the circular and longitudinal muscle was studied on the isolated rat uterus taken from the non-pregnant Wistar rat (180-250g) in oestrus. Uterus, was incubated in an organ bath in De Jalon solution at 30 and 37°C and was gassed with 95% oxygen and 5% carbon dioxide. In order to register the isometric contractions of the circular muscle the isolated uterus of the rat, one horn of the isolated uterus was cut into two segments 1 - 1.5 cm in length. Through the lumen of the segment of the isolated uterus which was set horizontally there were pulled two steel wires, 0.5 mm in diameter, in the form of a triangle 1.5 cm in size. Then the segment of the isolated uterus was horizontally suspended in a bath for isolated organs so that the top of the lower triangle was fixed to the bath bottom, and the top of the upper triangle was tied by ordinary thread to the isometric Ugo Basile transducer. On the basis of our results it can be concluded that the longitudinal muscle is more sensitive to nicardipine and verapamil, than the circular muscle of the isolated rat uterus, i.e. that for the inhibition of the same types of activation in the circular muscle there are necessary considerably higher concentrations of both calcium antagonists. These findings are also an indirect proof of the probable existence of various types (or subtypes) of voltage and receptory calcium channels in the longitudinal and circular muscles of the isolated rat uterus.</p>
<p>OC-84</p>	<p>PHARMACOKINETICS AND DOSAGE REGIMEN OF CIPROFLOXACIN FOLLOWING SINGLE INTRAMUSCULAR ADMINISTRATION IN <i>TEDDY</i> GOATS Iqbal Z¹, Javed I², Basit A³, Jan IU⁴, Khan AA⁵ ¹Department of Pharmacology, Isra University, Hyderabad, Pakistan. Email: zahid_dr@ymail.com ² Department of Physiology and Pharmacology, University of Agriculture, Faisalabad, Pakistan. ³ Faculty of Veterinary Sciences, Bahauddin Zakaria University, Multan, Pakistan. ⁴ Department of Animal Health, NWFP Agricultural University, Peshawar, Pakistan. ⁵ Department of Pathology, Nishtar Medical College, Multan, Pakistan.</p> <p>Introduction: Ciprofloxacin is one of the very important fluoroquinolone antimicrobial agents and is being used to treat various infectious diseases in animals and human. Because there is wide spread clinical use of ciprofloxacin in local animals, but little information is available regarding its disposition, the present study was undertaken with the objective to determine the pharmacokinetics and optimal dosage regimen of this drug in <i>Teddy</i> goats. Materials and Methods: Ciprofloxacin was administered intramuscularly at 5 mg/kg body weight in each of eight animals. Following drug administration, blood samples were collected at different time intervals and analyzed for ciprofloxacin using HPLC. Pharmacokinetic parameters were calculated using two compartment open model. Results and Discussion: Peak plasma concentration (C_{max}) of ciprofloxacin, 1.77 ± 0.20 µg/mL was achieved at 0.90 ± 0.04 hours (T_{max}). Values for half life of absorption (t_{1/2} abs), distribution (t_{1/2} α) and elimination (t_{1/2} β) were 0.52 ± 0.04, 0.52 ± 0.04 and 2.62 ± 0.39 hours, respectively. The value for apparent volume of distribution (V_d) was 3.76 ± 0.92 L/kg, area under the curve (AUC) was 5.89 ± 0.91 µg.hr/mL and total body clearance (CL) was 1.09 ± 0.11 L/hr/kg. Based on these parameters, an optimal intramuscular dosage of ciprofloxacin in adult <i>Teddy</i> goats was calculated as 15.57 mg/kg, to be repeated after 24 hours interval. These results show that ciprofloxacin in these goats has the general pharmacokinetic characteristics of a typical fluoroquinolone antimicrobial agent. That is, it has distribution, clearance and half life that are similar to other studies. Conclusions: Based on these results, it was concluded that calculated dose was higher than the dose recommended by the manufacturer and this higher dose should be used to treat susceptible bacteria in <i>Teddy</i> goats.</p>
<p>OC-85</p>	<p>EFFECTS OF OZONE OXIDATIVE PRECONDITIONING ON DIFFERENT HEPATIC BIOMARKERS OF OXIDATIVE STRESS IN ENDOTOXIC SHOCK IN MICE Zamora ZR¹, Guancho DG¹, González RÁ¹, Martinez YL¹, Alonso Y¹ and Schulz S².</p> <p>¹ Laboratory of Biological Assays, Department of Biomedical Research, Ozone Research Center. P. O. Box 6414, Havana, Cuba. email: zullyt.zamora@cnic.edu.cu ² Veterinary Services and Laboratory Animal Medicine, Philipps-University of Marburg, Marburg 35033, Germany.</p> <p>Introduction: Endotoxin induces lipid peroxidation (LPO), which plays an important role in the pathogenesis of multiorgan injury during endotoxemia. Reactive oxygen intermediates including singlet oxygen, hydrogen peroxide and radicals such as superoxide anion and hydroxyl radical are important mediators of cellular injury and play a potential role in oxidative stress associated with endotoxin. In addition, oxidative stress is associated with the alterations of superoxide dismutase (SOD) and glutathione peroxidase (GPx). In the endotoxic shock it is known that it occur variations in different biochemical parameters and the liver is a</p>

	<p>specially affected organ which is due to its important role in the metabolic activity. This research look for the effect ozone oxidative preconditioning (OOP) on different biomarkers of oxidative stress in hepatic tissue of mice treated with lipopolysaccharide (LPS). Material and methods: LPS doses of 30 mg/kg were administered intraperitoneally (i.p) and pretreatment with ozone/oxygen mixture (OOM) was applied i.p at 0.2, 0.4 and 1.2 mg/kg once daily during five days before LPS injection. The mice were euthanized under ether atmosphere at different times, 1h and 24 h after LPS injection. Hepatic tissue was taken from all animals for biochemical determinations of oxidative stress such as thiobarbituric acid reactive substances content (TBARS) and activity of antioxidant enzymes superoxide dismutase (SOD), glutathione peroxidase (GPx) and glutathione transferase (GST). Results and discussion: Our results demonstrated that OOP reduces levels of TBARS content and increases the activity of GPx in hepatic tissue. Conclusions: In conclusion, OOP was able to recover the redox balance and in this way to protect the animals against the oxidative damage induced by endotoxemia.</p>
<p>OC-86</p>	<p>ALTERED OXIDATIVE STRESS INDEXES RELATED TO DISEASE PROGRESSION MARKER IN HUMAN IMMUNODEFICIENCY VIRUS INFECTED PATIENTS WITH ANTIRETROVIRAL THERAPY</p> <p>Gil L¹, Tarinas A¹, Hernández D¹, Vega B¹, Pérez D¹, Tápanes R¹, Pérez J¹ ¹Institute of Tropical Medicine “Pedro Kourí” (IPK), P.O. Box 601, Marianao 13, Ciudad de La Habana (Cuba). email: lgil@ipk.sld.cu</p> <p>Introduction: It is generally accepted that oxidative stress (OS) is implicated in immunological and metabolic abnormalities during HIV infection. The acting mechanism used by Highly Active Antiretroviral Therapy (HAART) comes to add metabolic alterations. Material and Method: This is an observational study assessing the effect of two HAART national generic combinations on redox indicators and on progression markers of disease. A cohort of 84 healthy and 84 HIV+ subjects were followed for 6 months. Fifty six HIV+ subjects were distributed in group I (AZT, 3TC, IND) and group II (D4T, 3TC, NEV) according to drug combination. Peroxidation potential (PP), glutathione (GSH), malondialdehyde (MDA), total hydroperoxides (HPO), superoxide dismutase (SOD), catalase (CAT), advanced oxidation protein products (AOPP), percent of DNA fragmentation (% FDNA), CD4+, CD38+, CD95+ T lymphocytes subsets, viral load and body mass index (BMI) were measured at baseline and 6 months after beginning HAART. Results and Discussion: After HAART started CAT values for both groups receiving treatment did not show significant difference. For group II all other OS indexes were significantly higher than those for group I and the HIV+ not treated group (p<0.05) except for GSH values in group II (p<0.05) which was lower than in group I values. These data suggest poor prognosis for group II. Not significant differences were found between treatment groups respect CD4+, CD8+, CD38+, CD95+ T cell subset count, viral load and BMI. Conclusions: The findings suggest that increased OS occurs additionally to persistent redox imbalance associated to HIV infection during apparently successful HAART. This does not only underline HAART associated toxicity but it may be also methodologically important for the follow-up of further clinical studies.</p> <p>References</p> <ol style="list-style-type: none"> Pasupthi P, Ramachandran T, Sindhu PJ, Saravanan G, Bakthavathsalam G. Enhanced oxidative stress markers and antioxidant imbalance in HIV infection and aids patients. <i>J Sci Res</i> 2009; 1:370-80. Ngondi JL, Oben J, Forkah DM, Etame LH, Mbanya D. The effect of different combination therapies on oxidative stress markers in HIV infected patients in Cameroon. <i>AIDS Res Ther</i> 2006; 3:19.
<p>OC-87</p>	<p>ANTIOXIDANTS AND LIPID PEROXIDATION IN TUNISIAN TYPE 2 DIABETIC PATIENTS WITH AND WITHOUT CARDIOVASCULAR COMPLICATIONS</p> <p>Belkhiria MN¹, Maatouk F², Jebali MA¹, Kacem M³, Achour A⁴, Ben Hamda K²</p> <p>¹Laboratoire de Pharmacologie, Faculté de Médecine, 5019 Monastir, Tunisie. Noura.Belkhiria@fmm.rnu.tn ²Service de Cardiologie, CHU Fattouma Bourguiba, Monastir, Tunisie. ³Service d'Endocrinologie, CHU Farhat Hached, Sousse, Tunisie. ⁴Service de Néphrologie, CHU Sahloul, Sousse, Tunisie.</p> <p>Introduction: We investigated lipid peroxidation and antioxydants status in Tunisian patients with type 2 diabetes mellitus. Material and Methods: One group included 34 type 2 diabetic patients without cardiovascular complications (CVC) and the other consisted of 32 type 2 diabetic patients with CVC. Thirty five healthy subjects served as controls. Superoxide dismutase (SOD), Erythrocyte glutathione peroxydase (GPx) and Thiobarbituric acid reactive substance levels (TBARS) were estimated. Results and Discussion: GPx activity was decreased in diabetic patients compared to controls, but no significant change in Superoxide</p>

	<p>dismutase (SOD) activity was observed in diabetic patients (GPx: 32.4 ± 8.1 U/g Hb vs 40.9 ± 6.9 U/g Hb, $P < 0.001$; SOD: 1.13 ± 0.21 U/mg Hb vs 1.20 ± 0.18 U/mg Hb, $P = NS$). In comparison with the diabetic group without CVC, the diabetic group with CVC had decrease GPx and SOD activities (GPx: 29.7 ± 8.0 U/g Hb vs 34.9 ± 7.5 U/g Hb, $P < 0.01$; SOD: 1.05 ± 0.21 U/mg Hb vs 1.20 ± 0.17 U/mg Hb, $P < 0.01$). TBARS concentrations were significantly increased in the group with CVC compared to the group without CVC (TBARS: 3.82 ± 1.28 $\mu\text{mol/l}$ vs 3.11 ± 0.84 $\mu\text{mol/l}$, $P < 0.01$). Conclusion: The increase in TBARS and the decrease GPx and SOD activities in diabetics with CVC in this study indicate that these factors may contribute to the occurrence of CVC in diabetic patients.</p>
<p>OC-88</p>	<p>ANDROGENIC AND ANABOLIC EVALUATION AND EFFECT ON SPERMATOGENESIS OF DI-31, A SEMISYNTHETIC PHYTOHORMONE ANALOGUE González Blanco I¹, García Simón G², Santos Estrada M², Coll García Y³, Merino García N⁴, Díaz Llera S</p> <ol style="list-style-type: none"> 1. Departamento de Farmacología y Toxicología, Instituto de Farmacia y Alimentos, Universidad de la Habana, Ciudad de La Habana, Cuba. email: sdllera@infomed.sld.cu; gisel@infomed.sld.cu 2. Laboratorio de Liofilizados, Hormonas y Anestésicos Dentales, Cuba. 3. Laboratorio de Productos Naturales. Facultad de Química, Universidad de la Habana, Cuba. 4. Centro de Evaluaciones e Investigaciones Biológicas, Instituto de Farmacia y Alimentos, Universidad de la Habana, Ciudad de la Habana, Cuba <p>Introduction: DI-31 is a phytohormone analogue regulating plant growth with effects on cell division which has been employed to increase crop yield and crop quality. This polyoxygenated steroid has certain chemical similarities with animal steroidal hormones. Considering the above and knowing that it is a product applied by man, the possible anabolic and androgenic activity and the effect on spermatogenesis were evaluated in <i>in vivo</i> models. Materials and Methods: In the evaluation of hormonal activity young castrated male Wistar rats were treated with 5 and 10 mg/kg of DI-31 and testosterone propionate (as reference) to determine the relative weight increase of seminal vesicles, prostate and levator ani muscle (MEDA). Additionally, a morphometric analytic study of MEDA was performed. Sperm morphology assay was also done using OF1 mice, 7-8 weeks of age treated with 0,05; 0,25; 0,5 and 1 g/kg of DI-31 for 5 days. Cyclophosphamide (50 mg/kg) was used as positive control. Animals were sacrificed at day 35 and epididima were processed. Results and Discussion: DI-31 dose increment did not induce a significant increase in the relative weight of the anatomical structures studied. The biological potency values obtained led us to conclude that DI-31 has not anabolic or androgenic activity in this animal model at the tested doses. For the sperm morphology assay, DI-31 was found cytotoxic at the highest doses for the spermatocyte phase. Conclusion: These results confirm the low toxicity of this phytohormone analogue.</p>
<p>OC-89</p>	<p>RATIONAL DISCOVERY OF NEW ANTI-INFLAMMATORY COMPOUNDS BY FUSION “IN SILICO” AND “IN VIVO” METHODS Silverio-Mota D¹, Herrera-Pis Y¹, Casañola-Martín GM¹, Marrero-Ponce Y¹, Crawford A², de Witte P², Giner RM³, Recio MC³, Galvez-Llompert M⁴</p> <ol style="list-style-type: none"> 1 Unit of Computer-Aided Molecular “Biosilico” Discovery and Bioinformatic Research (CAMD-BIR Unit), Faculty of Chemistry-Pharmacy, Central University of Las Villas, Santa Clara, 54830 Villa Clara, Cuba. email danys@uclv.edu.cu 2 Department of Pharmaceutical Sciences, Katholieke Universiteit Leuven, Leuven, Belgium. 3 Department of Pharmacology. Faculty of Pharmacy. University of Valencia, Spain. 4 Department of Physical Chemistry. Faculty of Pharmacy. University of Valencia, Spain. <p>Introduction: Nonsteroidal and steroidal anti-inflammatory drugs had been widely used for the treatment of inflammatory diseases. However, the clinical use of these drugs has been limited by unfavourable side effects such as gastrointestinal and renal damage and so on. Nowadays, the search of new anti-inflammatory molecules, which can be available in future as new anti-inflammatory drugs, is very necessary. In this sense, the drug's discovery assisted by computer offer vantages in order to decrease time and money respect other research's methods. Furthermore, the main purpose of this study is to develop simple linear discriminant-based quantitative structure-activity relationship (QSAR) models for the prediction of anti-inflammatory activity using some of the TOMOCOMD-CARDD fingerprints, so as to enable computational screening from virtual combinatorial datasets. Materials and Methods: In this sense, a database of 1213 organic chemicals having great structural variability, 587 of them anti-inflammatory agents and 626 compounds having other clinical uses, was analyzed. Afterward, linear classification functions were derived in order to discriminate</p>

	<p>between anti-inflammatory and non anti-inflammatory compounds. The developed models were then used in a virtual screening of databases of organic compounds. The experimental corroboration of theory prediction was carried out using three “<i>in vivo</i>” models the sequential form. Results and Discussion The mathematic models correctly classify more than 85% of the compound set, in both training and external prediction datasets demonstrating the robustness and predictive power of them. During screening, 32 compounds were identified with potential anti-inflammatory activity by QSAR models. The biological evaluation of these chemicals, using zebrafish as biologic material, was performed. Seven compounds were tested, also, in rodent’s models showing similar results to indometacine (reference). Conclusions. The approach described here seems to be a promising QSAR tool for the molecular discovery of novel anti-inflammatory drugs.</p>
S-2	<p>2nd SYMPOSIUM OF PHARMACOLOGY OF NATURAL PRODUCTS. / 2^{DO} SIMPOSIO DE FARMACOLOGÍA DE PRODUCTOS NATURALES</p>
OC-90	<p>PRELIMINARY PHYTOCHEMICAL AND ANTIMICROBIAL EFFECT <i>IN VITRO</i> OF <i>HAMELIA PATENS</i> JAQ., AGAINST <i>STAPHYLOCOCCUS AUREUS</i>, <i>STAPHYLOCOCCUS EPIDERMIDIS</i> AND <i>STREPTOCOCCUS PYOGENES</i> Bautista Santiago A¹, Montejano Rodríguez JR¹, Almaguer Vargas G¹, Olvera Hernández EG¹, Bautista Mogica FI¹, Gayosso de Lucio JA¹, Pérez Monroy VA¹</p> <p>¹Autonomous University of Hidalgo State, Institute of Health Sciences. Pharmacy Academic Area, Highway Conception ex hacienda s / n, Tlucuatla, Hidalgo, Mexico. email: georginaalmaguervargas@yahoo.com.mx</p> <p>Introduction: Medicinal plants constitute a form of self-care for a significant proportion of poor people in the world, in Mexico to treat skin infection have been reported medicinal plants 589. In the state of Hidalgo, specifically in the Huasteca people used the <i>Hamelia patens</i> Jaq. (maduro platano) to wash his wound. Material and Methods: In this study used ethanol and aqueous extracts for preliminary phytochemical and antimicrobial effect. The antimicrobial effect was evaluated by the Kirby-Bauer method. The concentrations used were 25, 30, 100, 1000 µg/10µL. For antimicrobial screening, the following micro-organism were used: Staphylococcus epidermidis, S. aureus and Streptococcus pyogenes. The results were classified as resistant (R), intermediate (I), moderately sensitive (MS) and sensitive (S), depending on the diameter of inhibition zone. Results and Discussion: Results of the phytochemical screening indicate that ethanol and aqueous extracts of <i>Hamelia patens</i> Jaq. (maduro platano) leaves contained alkaloids, flavonoids, triterpenes and steroids, coumarins, sugars reducers, phenols and tannins, free amino acids and amines in general, saponins, cardiac glycosides, bitter or astringent principles. Using the Kirby Bauer Disk Diffusion Method, it is shows that aqueous extracts of maduro platano has not activity for any of the tested strains. While the ethanol extract presented activity against S. aureus at concentrations of 100 and 1000 mg considered as moderate activity. Conclusions: In this study in the identification of secondary metabolites were found alkaloids, flavonoids, triterpenes and steroids, coumarins, sugars reducers, phenols and tannins, free amino acids and amines in general, saponins, cardiac glycosides, bitter or astringent principles. <i>Hamelia patens</i> Jaq ethanol extract possesses an antimicrobial activity against Staphylococcus aureus.</p>
OC-91	<p>EFFECT OF GLYCYRRHIZA-DERIVED LIQUIRITIGENIN AND ISO-LIQUIRITIGENIN IN A MENOPAUSAL DEPRESSIVE-LIKE STATE IN FEMALE MICE Lyttle KA, Yoshimura H</p> <p>Behavioral Pharmacology Laboratory, Ehime University Graduate School of Medicine, Shitsukawa, Toon City, Ehime, Japan 791-0295</p> <p>Introduction: Mood disorders and emotional lability are a common experience of the menopause. Hormone replacement therapy is known to manifest significant adverse effects, and therefore the development of alternative therapy has received great interest. It was recently demonstrated that the <i>Glycyrrhiza</i> radix, which is used for the treatment of menopausal syndrome in traditional Chinese medicine, has an estrogenic component: liquiritigenin, a highly selective beta-estrogen receptor agonist in vitro. Bilateral ovariectomy in female mice produces a menopausal depressive-like state, therefore we investigated whether liquiritigenin alleviates the menopausal depressive-like state in female mice comparing with isoliquiritigenin. Material and Methods: 9 week old female ICR mice were ovariectomized and chronic liquiritigenin and isoliquiritigenin administered orally at four dose levels (0, 2.5, 5.0, 7.5 mg/kg/day) for 14 days. Intact animals received the same drug treatment. We determined both the immobility time in the forced swimming test and the general</p>

	<p>motor activity in a neutral cage. Results and Discussion: Liquiritigenin dose-dependently reduced the ovariectomy-induced prolongation of immobility time ($p < 0.001$) with no effect on motor activity. Contrast to this liquiritigenin did not affect the immobility time in intact female mice. Isoliquiritigenin, isomer of liquiritigenin, had no significant effect on immobility time or motor activity. Conclusion: These results suggest that liquiritigenin has an antidepressant effect on the menopausal depressive-like state in female mice.</p>
<p>OC-92</p>	<p>ANTIMICROBIAL ACTIVITIES OF ISOLATED ENDOPHYTES FROM SOME IRANIAN NATIVE MEDICINAL PLANTS Ebrahimi A, Asgharian S ¹Department of Pathobiology, School of Veterinary Science, Shahrekord University, P. O. Box: 115, Postal Code, 88186/34141, Shahrekord, Iran. email: A_kahrizsangi@yahoo.com</p> <p>Introduction: A variety of microorganisms, mainly bacteria and fungi, inhabit plants and are, therefore, known as endophytic. Nowadays scientific communities have become interested in bioprospecting these microorganisms due to their potentially important secondary metabolite production for applications particularly in the pharmaceutical and food industries. Thus in this study, we focus on the isolation of endophytes from some native medicinal plants of Chaharmahal province in west center of Iran and screening them for antimicrobial activities. Materials and Methods: Random samples from asymptomatic leaves and branches of five native medicinal plants: <i>Stachys lavandulifolia</i>, <i>Rumex pulcher</i>, <i>Hypericum scabrum</i>, <i>Starja bacteriarica</i> and <i>Achillea kellalensis</i> were collected from Chaharmahal province of Iran and examined for the presence of endophytic bacteria and fungi with biological activity. Results and Discussion: From 8 isolated endophytic fungi, all displayed considerable activity against at least one indicator fungi. Fungal isolates from <i>R. pulcher</i> leaves and branches showed activity against <i>Aspergillus niger</i>, <i>Penicillium</i> spp, <i>Alternaria</i> spp and <i>S. aureus</i>. From five <i>Bacillus</i> spp strains isolated from <i>R. pulcher</i> leaves and branches, four (80%) showed activity against <i>S. aureus</i>, and two strains were active against all indicator fungi. <i>Bacillus</i> spp strain isolated from leaves of <i>H. scabrum</i> was active against <i>S. aureus</i> and all 3 indicator fungi. None of the isolated endophytes showed antibacterial activity against <i>E. coli</i>. Conclusions: Further investigations in order to exploit the potential of the substances produced to inhibit pathogenic microorganisms is suggested.</p>
<p>OC-93</p>	<p>EFFECT OF COMBINATION OF NIGELLA SATIVA AND TRIGONELLA FOENUM-GRAECUM SEEDS WITH GLIBENCLAMIDE ON BLOOD SUGAR LEVELS IN TYPE-2 DIABETES MELLITUS PATIENTS Memon A¹, Memon AR¹, Shah SS², Khand F³, Shaikh IA⁴, Khushk IA⁵</p> <p>¹Department of Pharmacology, Isra University, Hyderabad Sindh-Pakistan. ²Department of Pharmacology Liaquat University of Medical & Health Sciences, Jamshoro, Sindh-Pakistan, ³Department of Biochemistry Isra University, Hyderabad Sindh-Pakistan. ⁴Department of Pharmacology Liaquat University of Medical & Health Sciences, Jamshoro, Sindh-Pakistan. ⁵Department of Community Medicine Isra University, Hyderabad Sindh-Pakistan email: dr_ashfaque@hotmail.com.</p> <p>Introduction: Diabetes Mellitus Type-2 accounts for 90-95% of diabetic cases. The beneficial effects of oral Anti-diabetic drugs on glycemic levels are well documented but preventing activity of these drugs against progressive nature of diabetes and its complications is not very clear and these drugs have many side effects. In view of above problems, the popularity of complementary medicine has increased. More than 1200 different plants have been described as traditional treatment for diabetes. This study was carried out to evaluate the effect of combination of <i>Nigella sativa</i> and <i>Trigonella foenum-graecum</i> seeds with Glibenclamide on blood sugar levels in type-2 diabetes mellitus patients. Materials and Methods: Type-2 diabetic mellitus patients on Glibenclamide, were randomly divided into two groups. Group "A" (Control Group) patients remained on routine dose of Glibenclamide, while Group "B" (Intervention Group) were kept on a capsule containing equal amount combined powder of <i>N-sativa</i> & <i>T. foenum-graecum</i> seeds powder, in addition to their routine dose of Glibenclamide. Patients in both the groups were evaluated for a period of 3 months for fasting and random sugar levels. Results and Discussion: It was found that the blood sugar level fasting (p-value=0.003) and random (p-value<0.001) significantly decreased in intervention group compared to control group. Pharmacological and clinical evaluations had indicated that herbal drugs have a mild, but significant, blood glucose lowering effect and that the long-term use of these may be advantageous over oral Anti-diabetic drugs in alleviating some of the complications caused by diabetes. Additionally, the use of these natural agents in conjunction with oral Anti-diabetic drugs permits the use of lower doses of the oral Anti-diabetic drugs drug, which decreases the most commonly observed side effects. Conclusion: This study</p>

	indicates that combination therapy of <i>N. sativa</i> and <i>T. foenum-graecum</i> seeds with Glibenclamide has significant effect in controlling hyperglycemia.
OC-94	<p>ANTIPARASITIC ACTIVITY OF THE EXTRACT AND ESSENTIAL OIL OF <i>SIPARUNA GUIANENSIS</i> AUBL BASED ON THE TIME OF HARVEST Saavedra G¹, Poka D¹, Ruiz G²</p> <p>¹Centro de Tecnología Agroindustrial, UMSS, Cochabamba-Bolivia email: gloriasa7@yahoo.es. ²Instituto de Investigaciones Fármaco–Bioquímicas, UMSA. La Paz-Bolivia</p> <p>Introduction: Bolivia is characterized by high plant diversity, which includes little known and/or exploited vegetal species, carriers of active compounds that may be potential sources of raw materials for the useful natural products preparation for the humanity. Biological activity of plant species belonging to the Siparunaceae family was studied in previous research, demonstrating that the <i>Siparuna guianensis</i> is potentially exploitable.</p> <p>Material and Methods: Random samples were collected from the aerial part of plants in their reproductive stage: full flowering (October) and fruition (December), the taxonomic identification was made in the Herbario Nacional “Martin Cárdenas”. Essential oils were obtained from fresh material by the water steam extraction method (Hidrodiffusion), the identification of their components was made by GC and GC-MS. Crude extracts were prepared by ethanol maceration of dry vegetal material at room temperature, filtration and evaporation. Both, essential oils and extracts, were evaluated “in Vitro” to determine their antiparasitic activity in Chagas (<i>Tripanosoma cruzi</i>), Malaria (<i>Plasmodium falciparum</i>) and Leishmaniasis (<i>Leishmania amazonensis</i>, <i>brasiliensis</i> and <i>donovani</i>). Results and Discussion: The chromatographic profiles of the essences obtained in both months are similar, being basically represented by terpenics hydrocarbons and oxygenated terpenes, with quantitative variations in some majority components. Essential oil obtained at the time of flowering stage presents activity before the 3 studied parasites, exhibiting greater activity in front of the parasites that cause Leishmaniasis and Chagas, whereas the single extract front to the Malaria parasite.</p> <p>Conclusions: The variation in the percentage value of some components of the <i>Siparuna guianensis</i> according the time of collection defines the parasite activity involving oil and extract; this plant specie must be harvested at flowering stage.</p>
OC-95	<p>EPIGENETIC MODULATION OF GENE EXPRESSION AND THE INFLUENCE OF NATURAL PRODUCTS Díaz Llera S</p> <p>Departamento de Farmacología y Toxicología, Instituto de Farmacia y Alimentos, Universidad de la Habana, Ciudad de La Habana, Cuba. email: sdllera@infomed.sld.cu</p> <p>Epigenetics is described as the study of changes in gene expression that occur not by changing the DNA sequence, but by modifications of the DNA methylation and chromatin structure patterns. The recent progress have remarked the key role of epigenetic mechanisms in the maintenance of the proper control of biologic processes such as genomic imprinting, inactivation of X chromosome or establishment of cell identity. The gene expression regulation is a complex process. Many eucariotic genes are packed within chromatin structures which lead to high gene condensations that require of dinamic chromatin remodelation to facilitate transcription. DNA methylations and histone modifications represent two of the main processes of modulation of gene expression. A wide variety of common diseases, behaviors, and other health conditions could have at least a partial epigenetic ethiology, including cancer, respiratory, cardiovascular, reproductive and autoimmune diseases as well as neurologic disorders such as Parkinson, Alzheimer, and other degenerative diseases. The epigenome is dinamic and respond to environmental signals, not only during development but also through life; there is increasing evidence that chemical substances could cause changes in gene expression which persist long after the exposure has ceased. The efectors of epigenetic changes include many xenobiotic and biologic agents, radioactivity, diet and social environment. The pharmaceuticals commonly used can cause persistent epigenetic changes. Epigenetics will be essential to many biological fenomenons of current interest as stem cells, nuclear transference (cloning), cell reprogramming, aging, evelution and speciation, agriculture and, besides, for the design of new pharmaceuticals. Within agents inducing epigenetic effects natural products are highlighted.</p>
OC-96	<p>NEUROPHARMACOLOGICAL PROFILE OF <i>Thalassia testudinum</i> EXTRACT (BM 21) IN MICE Garateix A¹, Menéndez R¹, Regalado AI¹, García T¹, Morales RA¹, Palmero A¹, Fernández I³, Juarez Díaz I², Flores G², Sánchez D², Regalado EL¹, Laguna A¹</p>

	<p>¹Centro de Bioproductos Marinos, Agencia de Medio Ambiente, Ministerio de Ciencia, Tecnología y Medio Ambiente, La Habana, Cuba. E.mail: cebimar@infomed.sld.cu; ²Instituto de Fisiología, Benemérita Universidad Autónoma de Puebla, México; ³Centro de Investigación y Regeneración del Tejido Nervioso (CIREN), MINSAP, La Habana, Cuba.</p> <p>Recent studies on the action of BM-21 revealed many relevant properties such as anti-inflammatory activity, antinociceptive action, antioxidant effects and hepatoprotective action. Also, oral administration of BM-21 showed peripheral and central neuroprotective action. This indicates that active components are able to cross the blood–brain barrier acting at the level of CNS. Fitochemical studies have shown that BM-21 is complex mixtures containing several constituents such as flavonoids, terpenes, saponins, steroids, catechins, proanthocyanidins, etc. Evidence supports that many of these constituents possess several pharmacological action in mammals. Thus, the present study was designed to investigate the putative central nervous system properties of BM-21 in several behavioral models in OF1-mice. Acute and prolonged administration (10 days, p.o) of BM-21 (40, 400 and 1000 mg.kg⁻¹) had no significant effects on exploratory activity, elevated plus maze test, marble burying test, electroshock induced convulsions and thiopental-induced sleeping time. Additionally, elevated plus-maze, passive avoidance paradigm and Morris water maze were employed to test BM-21 effects on learning and memory (administration for 4 weeks at 400 mg.kg⁻¹ p.o). The extract exerted a positive effect on memory retention 24 hours after training as compared to control group indicating significant improvement of learning and memory. BM-21 had no effect one week after training in both elevated plus-maze and passive avoidance paradigm. Moreover, a significant increase in the latency to reach the hide platform in the Morris water maze test was also observed followed prolonged BM-21 administration. In conclusion the present work has shown that acute and prolonged BM-21 administration did not produce any undesirable side effects in the studied models. Conversely, it has been found that BM-21 positively modulated learning and memory. This opens new perspectives of BM-21 use as a memory enhancer. The combination of anti-inflammatory, antioxidant and neuroprotective properties of BM-21 could all be leading to the observed memory-enhancing effect, however further studies are required to determine the mechanisms that support this effect.</p>
S-7	<p>2ND SYMPOSIUM PHARMACOTHERAPEUTIC UPDATING IN CANCER / 2^{DO} SIMPOSIO DE ACTUALIZACIÓN FARMACOTERAPÉUTICA IN CÁNCER.</p>
OC-97	<p>CHANGING THE PARADIGM OF CANCER CONTROL IN CUBA. <u>Teresa Romero.</u> Jefa de la Unidad Nacional del Control del Cáncer, MINSAP, Cuba.</p> <p><i>Resumen no disponible en el momento de la edición del libro. Abstract non available in the moment of the edition of the book of summaries.</i></p>
OC-98	<p>HOLISTIC VISION OF THERAPEUTIC IN CANCER <u>Jorge Soriano García.</u> Jefe del Servicio de Oncología Clínica. Hospital Hermanos Amejeiras. Havana, Cuba.</p> <p><i>Resumen no disponible en el momento de la edición del libro. Abstract non available in the moment of the edition of the book of summaries.</i></p>
RT-02	<p>UPDATING OF CANCER THERAPY IN THE MAIN LOCATIONS</p> <p><i>Resúmenes no disponibles en el momento de la edición del libro. Abstracts non available in the moment of the edition of the book of summaries.</i></p> <p>CANCER OF BREAST <u>Jorge Soriano García</u> Hospital Hermanos Amejeiras. Havana, Cuba.</p> <p>CÁNCER OF RECTUM AND COLON <u>Maité Lima Perez.</u> Hospital Hermanos Amejeiras. Havana, Cuba.</p>
	<p>CANCER OF PROSTATE <u>Elías Gracia Medina</u> Instituto Nacional de Oncología y Radiobiología. Havana, Cuba.</p>

CLINICAL COURSE OF PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER TREATED WITH CIMAVAX-EGF: A NOVEL THERAPEUTIC VACCINE

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Introduction: In patients with advanced non-small cell lung cancer the EGFR is overexpressed in tissues during development and progression. The magnitude of EGFR expression has been reported as a predictive factor of response to biological therapy in non-small-cell lung cancer patients. We undertook this study to describe the relationship between EGF-based cancer vaccine treatment and survival in this highly frequent and lethal disease. **Methods:** A review of four of the principal trials that describes the relationship between immunogenicity and survival was conducted: pilot clinical trials 3, 4 and 5 and a Phase II trial. Pilot 3 study included 20 patients with advanced nscLC who were randomly immunized with EGF/P64/Al and EGF/P64/Montanide ISA 51, Pilot 4 evaluated two doses levels of the EGF vaccine in 40 patients; Pilot 5 combined our vaccine with chemotherapy in 20 patients. Phase II was a control trial with the enrolment of 80 patients to evaluate the survival benefit of Cimavax EGF after first line chemotherapy. **Results:** the analysis of the Pilot 3 showed a survival advantage for patients with higher immune response (GAR) median 9,1 months vs 4,5 months in poor Ab response (PAR). In Pilot 4 trial survival in GAR patients significantly exceeded the historical control (median 8 months vs 4,1 months). Pilot trial 5 founded a median survival for all patients of 12,8 months while the subgroup of patients who achieved objective response or disease stabilization after chemotherapy showed a median survival of 16,2 months. First 2 trial showed that median survival for patients with high Ab titers was 11,7 months vs 3,7 months in patients with poor antibody response and 5,33 months in the control arm. Longer survival was observed in all vaccinated patients. **Conclusion:** Our data highlight the need for further evaluation of different combination regimens in longer and randomized series.

OC-99

THE EFFECT OF PACLITAXEL TREATMENT ON THE OCCURENCE OF LYMPHEDEMA OF THE ARM IN UNILATERAL BREAST CANCER PATIENTS WITH AXILLARY LYMPH NODE DISSECTION: A PROSPECTIVE STUDY.

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Background Secondary lymphoedema of the ipsilateral arm (LE_{arm}) is the most important chronic complication after dissection of the axillary lymph nodes (AD). Incidence rates for LE_{arm} range from 5% to 56% within two years after surgery. (Lacomba et al., 2010)

Compared to other formulated risk factors, the influence of chemotherapy on the development of LE_{arm} has not yet been studied.

Objective To define the possible causal relationship between paclitaxel treatment and the occurrence of LE_{arm} in breast cancer (BC) patients (pts) after unilateral breast surgery with AD. **Design** A prospective observational population based study. **Setting** University hospital in Jette, Brussels, Belgium. **Participants** 52 early, unilateral, lymph node positive female BC pts, treated with breast surgery and AD. **Intervention** The intervention group was treated with post operative adjuvant concomitant irradiation and anthracyclines, 4*FEC(500/75/600mg/m²), followed by paclitaxel, 12*weekly (80mg/m²). The control group received the adjuvant concomitant irradiation and anthracyclines, 4*FEC(500/75/600mg/m²), only. **Main outcome measure** Incidence of clinically significant LE_{arm} (> 1,5 cm increase in arm circumference measured at two adjacent points compared with the non-affected arm). Measurements were conducted via tape measure during a follow up of two years post diagnosis. **Results** 40% of the 52 pts developed an LE_{arm}, of which 80% was developed early during the adjuvant therapy with paclitaxel (intervention group). An incidence of 13% LE_{arm} was found retrospectively in the control arm. **Conclusion** This study suggests the potential causal relationship between the previous concomitant chemo-irradiation and LE_{arm}, through capillary leakage. This is the first prospective analysis of the incidence of LE_{arm} in early BC pts treated with concomitant postoperative irradiation and anthracyclines followed by taxanes. The same research group is now further investigating whether and how the onset of LE_{arm} during this treatment can be monitored, prevented and treated.

OC-100	<p>CENTER OF MOLECULAR IMMUNOLOGY. CANCER IMMUNOTHERAPY PIPELINE AND CLINICAL IMPACT <u>Pedro Camilo Rodríguez</u>, Center of Molecular Immunology, Havana, Cuba.</p> <p><i>Resumen no disponible en el momento de la edición del libro. Abstract non available in the moment of the edition of the book of summaries.</i></p>
W-7	<p>1ST INTERNATIONAL WORKSHOP ON IPV (INACTIVATED POLIO VACCINES) / 1^{ER} TALLER INTERNACIONAL SOBRE VACUNAS DE POLIO INACTIVADAS</p>
	SESSION 1. IPV WORLD STRATEGY
OC-101	<p>POLIO ERADICATION: GLOBAL STATUS AND WORLD IMMUNIZATION STRATEGY <u>Jackie Fournier</u>, WHO, Switzerland</p> <p><i>To help Cuba in the decision making process on how to introduce IPV in the national immunization program as a replacement of OPV, the author is offered the opportunity to give three talks related to the global status of polio eradication, the WHO recommendations for the production of IPV and an update of clinical studies on vaccine efficacy.</i></p> <p>When the World Health Assembly launched the Global Polio Eradication Initiative in 1988, over 125 countries were considered to be endemic for the disease, with an estimated 350,000 children paralysed each year. Application of the eradication strategy developed in the Americas had by 2004 resulted in the eradication of one of the three serotypes of wild polio viruses, type 2 last isolated in 1999, a 99% drop in the annual incidence of the disease globally, and the elimination of the remaining indigenous virus serotypes from all but six countries in the world. Despite the development, licensure and widespread application of new monovalent and bivalent oral poliovirus vaccines since 2005 to enhance the impact of supplementary immunization activities in key remaining reservoirs, and the intensification of the global eradication effort in 2007, indigenous wild poliovirus type 1 and 3 transmission has continued in geographically limited areas of four countries: Nigeria, India, Pakistan and Afghanistan. The challenge of interrupting the residual wild polio viruses transmission in these areas has been compounded by the recurrent exportation of wild polio viruses from northern Nigeria and northern India into previously polio-free areas within and outside their borders. The presentation intends to provide an update on the global status of the polio eradication as of December 2010 and to present the current and future immunization strategies implemented world wide.</p>
OC-102	<p>IPV POLICY AND IPV TENDER IN THE AMERICAN REGION <u>Mauricio Landaverde</u>, PAHO, USA.</p> <p><i>Resumen no disponible en el momento de la edición del libro.. Abstract non available in the moment of the edition of the book of summaries.</i></p>
OC-103	<p>POLIO IMMUNISATION IN CUBA. HISTORY AND FUTURE PLANS <u>Miguel A. Galindo Sardiñas</u>, MINSAP, Cuba</p> <p><i>Resumen no disponible en el momento de la edición del libros. Abstract non available in the moment of the edition of the book of summaries.</i></p>
	Session 2. IPV Production
OC-104	<p>WHO RECOMMENDATIONS FOR THE PRODUCTION OF IPV <u>Jackie Fournier</u>, WHO, Switzerland.</p> <p>Recommendations published by WHO are intended to be scientific and advisory and constitute guidance for national control authorities and for the manufacturers of biological products. In the current IPV Recommendations (TRS 910 annex 2) that have been issued in 2002, the general provisions for the production of inactivated poliomyelitis vaccine (IPV) is described as well as national control requirements. The presentation intends to provide a summary of the recommendations that can be adopted by the country to regulate the production and control of IPV, to present the bio-containment requirements that should be applied to all IPV in a post OPV cessation era and define what need to be revised in the current IPV TRS.</p>
OC-105	<p>PRODUCTION OF IPV BASED ON SABIN STRAINS IN JAPAN <u>Yoshio Tano</u>, Kengo Wakabayashi, Yasumitsu Ouchi, Yoshihiro Ohta, Toshiyuki Adachi, Shinobu Abe and Shudo Yamazaki</p> <p>Japan Poliomyelitis Research Institute, 5-34-4 Kumegawa-cho Higashimurayama-shi Tokyo, Japan. email: tano@jpri.or.jp</p>

	<p>During the final stages of global polio eradication, the risk of paralytic polio outbreaks due to vaccine-derived polioviruses (VDPVs) cannot be ruled out as long as the use of oral poliomyelitis vaccine (OPV) continues. To minimize the potential risk of polio outbreaks associated with VDPV strains, the introduction of inactivated poliovirus vaccine (IPV) use in countries where OPV has been used, is urgently needed particularly for the post eradication era. We have developed a formalin-inactivated poliovirus vaccine (sIPV) using the attenuated Sabin strains as alternative and safer seed viruses than currently used wild-type viruses. To speed up production of sIPV, our facilities meeting GMP requirements have recently been renovated, and the production procedures and quality control testing methods are routinely validated to ensure a manufacturing consistency of all batches of sIPV. We have reported that antigenic modifications on Sabin 1, 2 and 3 antigens occurred during the process of formalin inactivation in sIPV production, which was revealed by using ELISA assays and type- and site-specific panels of monoclonal antibodies. Furthermore, type 1 sIPV showed higher immunogenicity than type 1 IPV derived from the wild type poliovirus (wIPV), whereas type 2 sIPV induced lower level of immunogenicity than type 2 wIPV, and type 3 sIPV induced equal or lower level of immunogenicity than type 3 wIPV. “Study group on quality assurance of the combined vaccine, DTaP-sIPV” organized by National Institute of Infectious Diseases (NIID) of Japan suggests that the predicted optimal antigen contents of sIPV for human use would be each 3-100-100 Du/dose for type 1, type 2 and type3 respectively. However, final optimal Du contents/dose of our sIPV should be determined on the results from clinical efficacy trials of the combined vaccine, DTaP-sIPV, which are being conducted in collaboration with some domestic DTaP manufacturers in Japan.</p>
<p>OC-106</p>	<p>INACTIVATED POLIO VACCINE (IPV) PRODUCTION BASED ON ATTENUATED SABIN STRAINS : CURRENT STATUS IN SABIN-IPV DEVELOPMENT <u>Wilfried AM Bakker</u>, Yvonne E. Thomassen, Aart G. van 't Oever, Janny Westdijk, Monique G.C.T. van Oijen, Peter van 't Veld, Lars Sundermann, Gideon F.A. Kersten, Johan van der Gun, Ahd Hamidi, Nico van den Heuvel, Leo A. van der Pol</p> <p>Netherlands Vaccine Institute, P.O. Box 457, 3720 AL Bilthoven, The Netherlands. email: wilfried.bakker@nvi-vaccin.nl</p> <p>The Netherlands Vaccine Institute (NVI) is developing a production process for Sabin-inactivated polio vaccine (Sabin-IPV) based on the current large-scale Salk-IPV production technology. This activity plays an important role in the WHO polio eradication strategy. The use of attenuated Sabin instead of wild-type Salk polio strains will provide additional safety during vaccine production. Further, it opens the opportunity to implement process improvements. For that, a scale-down – scale-up strategy was followed initially using historical manufacturing data. Such data can potentially harbour a wealth of information for process optimization and enhancement of efficiency and robustness. Therefore, at first multivariate data analysis (MVDA) was applied on data from current IPV production (more than 50 Vero cell culture based runs) to extract relevant information, like operating ranges. Subsequently, based on the MVDA analysis, a 3-L scale-down model of the current twin 750-L bioreactors has been setup. Currently, in this lab-scale process, both USP (cell and virus culture) and DSP unit-operations approximate the large-scale and process improvement studies are in progress. For USP this includes the application of increased cell densities, animal-component free media, and DOE optimization in multiple parallel bioreactors. Using this lab-scale (3-L bioreactor volume) model, the process was developed up to production-scale (i.e. approximately 2 × 350-L bioreactor working volume) and used to generate Master- and Working virus seedlots and inactivated trivalent polio vaccine for clinical trial purposes. Phase I clinical trials are scheduled early 2011. Sabin-IPV was made following cGMP-guidelines and meets the current European release criteria for Salk-IPV, and follows WHO guidelines, where appropriate. In parallel to the above, a research program was initiated to further modernize and optimize the process, and reduce the cost per dose. Finally, technology transfer to vaccine manufacturers in low and middle-income countries is foreseen.</p>
<p>OC-107</p>	<p>DEVELOPMENT OF sIPV <u>Iin Susanti</u></p> <p>BIO FARMA – INDONESIA</p> <p>Polio immunization has been the biggest effort in supporting WHO polio eradication program to interrupt Polio transmission worldwide. There are two different types of Polio vaccines in the market, namely, Oral Polio Vaccine (OPV) and Inactivated Polio Vaccines (IPV). OPV is used mainly in developing countries. Ultimately when wild poliovirus (WPV) transmission is interrupted worldwide and Polio eradication has been</p>

	<p>achieved, global routine use of OPV would need to be terminated to prevent vaccine associated paralytic poliomyelitis and outbreaks associated with circulating vaccine-derived polioviruses. Consequently in the near future, we have to be ready with IPV. In developing IPV, several challenges lie ahead particularly by developing countries, such as technology, investment of the facilities in relation with WHO Global Action Plan (GAP III) which require high containment together with GAP III risk management to minimize poliovirus circulation which are hardly achieved by developing countries. Bio Farma as a sole vaccine manufacture in Indonesia has been proactively develop IPV. In this regards, sabin IPV is chosen in alignment with WHO's strategy in reducing the use of wild poliovirus. Bio Farma is currently acquiring technology transfer from Japan Poliomyelitis Research Institute (JPRI). Experimental lot has been produced and it is anticipated that full production can be implemented by 2015.</p>
<p>OC-108</p>	<p>CLINICAL STUDIES ON VACCINE EFFICACY. WORLD EXPERIENCE Jackie Fournier, WHO, Switzerland.</p> <p>Since the first clinical trial conducted in the USA in 1954, many other studies have clearly demonstrated the efficacy of IPV in different settings. In addition, the importance of the interval between the 2nd and 3rd doses in persistence of the immunity was demonstrated by comparing several immunization schedules. More recently, additional clinical data has been generated with the use of combined vaccines that may include six different components such as DTaP-IPV-Hib-HepB. To get more affordable IPV, several projects have been launched over the last decade and promising clinical data have been collected with IPV given intradermally or Sabin IPV produced from Sabin OPV strains. The presentations intend to give an overview of the world experience with the use of IPV and an update of the current research and development activities at WHO.</p>
<p>OC-109</p>	<p>CLINICAL STUDIES ON VACCINE EFFICACY. CUBAN EXPERIENCE Sonia Resik</p> <p>Director Polio National Reference Lab. IPK, Cuba.</p> <p>In 1988, the World Health Assembly passed a resolution calling for the eradication of poliomyelitis by the year 2000. Because of the progress with implementation of the eradication strategies, the planning and preparations for the era after eradication of poliomyelitis began more than 10 years ago. The most important decision—to discontinue the routine use of oral poliovirus vaccine (OPV), because it contains live attenuated poliovirus—was suggested in 1997 and was formally endorsed in 2004 by the Advisory Committee on Poliomyelitis Eradication and in 2008 by the Scientific Advisory Group of Experts. The OPV cessation prerequisites have been published, the vaccination options have been identified, and the risks for paralytic disease following OPV cessation are being assessed in a series of studies conducted in developing countries. Because data on the immunogenicity of IPV in tropical developing countries are limited, Cuba conducted a randomized, controlled trial of IPV. Vaccination with two or three doses of IPV resulted in a rate of seroconversion of at least 90%, except for seroconversion against type 2. The viral titer of OPV shed in the stool after OPV challenge was reduced in both groups receiving IPV. Another issue to be in account is the necessity of an “affordable inactivated poliovirus vaccine (IPV)” appropriated for use in developing countries. It was added to the list of prerequisites in 2007 by the Advisory Committee on Poliomyelitis Eradication. IPV dose reduction through intradermal delivery to both stretch available supplies and reduce cost, with a potential for rapid implementation, appears a feasible approach. To permit an unbiased evaluation of fractional-dose IPV, a clinical study design was selected that enrolled newborns and infants that were vaccinated at 6, 10, and 14 weeks of age with either fractional-dose IPV or full-dose IPV, before these infants had an opportunity to be exposed to poliovirus secondarily through trivalent oral poliovirus vaccine [tOPV] use. Cuba provided an ideal trial site because it administers tOPV only twice a year in national campaigns (usually February and April), and several studies have demonstrated that 6–8 weeks after the last campaign, no poliovirus can be found in sewage or in stool samples from children. Findings demonstrated that fractional-dose IPV given intradermally by needle-free device results in significantly lower seroconversion rates than does full-dose IPV given intramuscularly for all poliovirus serotypes. In addition, after each dose of IPV, the rate of seroconversion in the fractional-dose IPV arm was significantly or substantially lower than the rate in the full-dose IPV arm. Both routes of administration were well tolerated, and only minor adverse events were reported. The immunogenicity of IPV is affected by levels of maternally derived antibody. Given that the half-life of maternally derived antibody decay is ~1 month, a delay in administration of IPV usually results in much higher seroconversion rates. Because the well-characterized interference of maternally derived antibody with IPV immunogenicity, fractional dose IPV is being evaluated in Cuba using a schedule that administers the first dose at 4 months of age and subsequent doses at 8 months.</p>

<p>OC-110</p>	<p><u>THE LICENSING OF VACCINES IN CUBA AND WHO PRECALIFICATION PROCESS</u> <u>Rolando Domínguez Morales</u></p> <p>State Control Center for the Quality of Drugs. (CECMED), 200 at 17 Ave, No. 1708, Siboney, Playa, Havana City, Cuba.</p> <p>The aim of the presentation is to give an overview of the licensing system of vaccines in Cuba. It will address the basic regulatory functions in the control of vaccines in a country like Cuba, which both outsource and produce the vaccines used in the National Immunization Program (NIP). An overview of the current and future regulatory issues for the licensing and authorization of vaccines in Cuba will be presented. Based on a data gathered through more than 30 years of experience, a general overview of the achievements of the National Immunization Program (NIP) is also provided. Since Cuba has currently two vaccines assessed and approved by World Health Organization (WHO), the presentation of Mr. Dominguez Morales will also address some current aspects of the evaluation system that local manufacturers should take into considerations when preparing a Product Summary File (PSF) for vaccines intended to be subject of the precalification process in order to be eligible for supplying them through United Nations agencies like UNICEF.</p>
<p>S-8</p>	<p><u>SYMPOSIUM OF VASCULAR PHARMACOLOGY / SIMPOSIO DE FARMACOLOGIA VASCULAR</u></p>
<p>OC-111</p>	<p><u>OXIDATIVE STRESS IS INCREASING IN PATIENTS UNDER CORONARY ARTERY BYPASS GRAFTING SURGERY AND PREDICTS A HIGHER CORONARY RISK.</u> <u>José Antonio González Correa</u>¹, Manuel Carnero², Javier Muñoz-Marin¹, José Pedro de la Cruz¹, Jorge Navarro-Dorado³, Marta Ramajo³, Santiago Redondo³, <u>Teresa Tejerina</u>³</p> <p>¹Department of Pharmacology, School of Medicine, Universidad de Málaga. ²Service of Cardiac Surgery, Hospital Clínico San Carlos, Madrid, ³Department of Pharmacology, School of Medicine, Universidad Complutense de Madrid, Spain</p> <p><u>Introduction:</u> Oxireduction enzymatic mechanisms in human beings can be physiologically altered due to inflammatory or infectious stimuli to the organism, also, several reports have demonstrated the important role of oxidative stress in the biomolecular pathways of atherogenesis. Most of these reports are based in animal or in vitro models. Inflammatory response to heart surgery has been widely studied, but, up to date, little is known about its possible influence over oxidative stress, and its implication in atherogenesis or its possible influence on the coronary risk in human beings. We studied the variations of multiple oxidative stress related products and enzymes in a cohort of patients who underwent a coronary artery bypass grafting surgery (CABG). <u>Materials:</u> We measured 2 hours before and 24 after CABG the concentration of malondialdehydic acid (MDA), nitrates, and peroxy-nitrites (all of them considered to be prooxidative markers); and reduced glutation and mitochondrial superoxide dismutase (SOD-Mn) (antioxidative markers) in a cohort of patients with coronary disease in a single center. <u>Results:</u> 119 patients were included in the present study. Statistically significant differences were detected in the mean plasmatic MDA concentration before (0.148 mmol/L (SD 0.12)) and after (0.283 mmol/L /SD 0.16) surgery (p<0.001). Higher concentrations of peroxy-nitrates (p=0.443) and nitrates (p=0.078) were also detected, though differences did not reach statistical significance. On the other hand, lower levels of reduced glutation and SOD-Mn were detected after surgery (p=0.94 and p=0.070), though differences were not significant. Hematite MDA and nitrite levels were independent predictors of greater Framingham/ATP III scale punctuations (B=32.146 points / mmol/mL (IC 95% 24.132- 40.16); B=0.326 points / μmol/g (IC 95% 0.049- 0.604). On the other hand, GSH levels were inversely related to Framinghn/ATP III punctuation (B= -0.175 points/ μmol/g (IC 95%=-0.344- -0.005)). No significant relationship was detected between SOD-Mn (p=0.559) or peroxy-nitrites (p=0.721) and Framingham/ATPIII risk. <u>Conclusions:</u> CABG surgery worsens the oxidative stress in patients with coronary disease higher oxidation activity and greater concentrations of its products and a lower antioxidant activity. MDA and nitrite levels predict greater Framinghn/ATP III scale punctuations. On the contrary, GSH levels are related to lower Framingham predicted coronary risk.</p> <p>This work was funded by Fondo de Investigaciones Sanitarias FISS PI080920 and RECAVA RD06/0014/1007 (Health Research Fund from the Spanish Ministry of Health). We thank the Cardiac Surgery Service (Hospital Clínico San Carlos, Madrid) for providing us with the IMS.</p>

<p>OC-112</p>	<p>COENZYME Q10 AS AN ADJUVANT THERAPY IN HEART FAILURE (HF) <u>Adarsh Kumar</u></p> <p>Govt Medical College/ GND Hospital , Amritsar, INDIA. email: adarshkumar_27@yahoo.com</p> <p>Congestive heart failure has become a global epidemic and its prevalence is increasing with the increasing longevity of life and improvement in management of acute coronary syndrome, hypertension and diabetes mellitus. It is the number one cardiac cause of hospitalizations in patients above 60 years and has prognosis worse than most of malignancies. None of the conventional and latest treatments of HF have made any significant improvement in mortality and morbidity. CoQ10 levels have been found to be consistently low in HF in most of reported studies. Coenzyme Q10 by improving oxidative phosphorylation at mitochondrial levels improves cellular bioenergetics of cardiac muscle cells and also by its antioxidant, vasodilatory and membrane stabilising effects produces symptomatic improvement when added to the conventional treatment. In our own study, the addition of CoQ10 (100-200mg/day) to conventional decongestant therapy lead to significant improvement in Quality Of Life and 6 Minutes Walk Test with reduced number of hospitalizations and reduction in development of refractory stage thereby decreasing the requirement for Assisted cardiac devices and cardiac transplantations although there was no significant improvement in the mortality pattern. So it can recommended as an important adjuvant therapy in HF at least to improve the quality of life in such cases.</p>
<p>OC-113</p>	<p>HOW TO VALIDATE BLOOD PLATELET RESPONSE TO ASPIRIN (ASA) IN PATIENTS WITH CORONARY HEART DISEASE (CHD) AND TYPE 2 DIABETIC (T2DM) PATIENTS – A NEW DATA ANALYSIS APPROACH Jozef Drzewoski¹ and <u>Cezary Watala</u>²</p> <p>¹Department of Internal Disease, Diabetology and Clinical Pharmacology, Medical University of Lodz, email:jdrzew@poczta.onet.pl and ²Department of Haemostatic Disorders, Medical University of Lodz, Poland. email: cwatala@csk.umed.lodz.pl</p> <p>Introduction: A common problem in monitoring of incomplete inhibition of platelet function by ASA (“aspirin-resistance”) is the lack of simple, standardized methodology, best suited to reflect platelet reduced sensitivity to ASA. In this study we aimed at reliable discrimination between good and poor responders among coronary heart disease patients (CHD) with or without type 2 diabetes mellitus (T2DM), using various platelet function tests. Material and Methods: One hundred twenty six patients with stable CHD (26 with T2DM), all receiving ASA in secondary prevention, were enrolled (40 women, 57.9 ± 6.9 yr, and 86 men, 56.2 ± 6.3 yr) to determine whether increasing ASA dose from 75 mg to 150 mg daily may improve antiplatelet effect upon four-week treatment. Raw data of collagen (coll)- or arachidonic acid (AA)-induced whole blood platelet aggregation (WBEA), and thromboxane (Tx) generation, were Box-Cox transformed and analyzed using paired inference tests. Results: The differences between the observed values of Tx generation or WBEA in patients and the reference threshold values in the ASA-treated (75 mg/d, 10d) reference group of healthy individuals (AA: 18.6Ω, collagen: 76.2Ω, Tx: 14.3 ng/ml) were standardized and used to calculate the comprehensive scores (CS) of three-parametric refractoriness to ASA (the higher CS means the higher insensitivity to ASA)¹. While the reductions in individual platelet function parameters were significantly greater for 150 mg/d vs. 75 mg/d ASA (collagen: 12±3%, AA: 10±3%, Tx: 20±9%) (<i>p</i>< 0.02), the three-parametric CS was even more discriminative between two ASA doses (3.0; ±95%CI: 2.7-3.3 vs. 2.4; ±95%CI: 2.2-2.6 for 75 or 150 mg/d ASA, resp., <i>p</i>< 0.0001). Conclusions: To enable more reliable discrimination between two low ASA doses, the use of multi-parametric measure of platelet refractoriness may be considered. This approach validated our conclusion that the dose > 75 mg may overcome reduced platelet sensitivity to ASA.</p> <p>¹ Watala <i>et al. Thromb Res</i> 113 (2004): 101-13</p>
<p>OC-114</p>	<p>ARRHYTHMOGENIC EFFECTS OF SEROTONIN IN TRANSGENIC MICE <u>Neumann J</u>, Keller N, Gergs U</p> <p>Department of Pharmacology and Toxicology, Medical Faculty, University Halle, Germany. email: Joachim.neumann@medizin.uni-halle.de</p>

	<p>Introduction: Supraventricular arrhythmias lead to genesis of thrombi in the left atrium. It is thought that these thrombi release serotonin (5HT) from thrombocytes and this is worsening arrhythmias. However, the underlying mechanism(s) of 5HT-induced arrhythmias are not fully understood. Material and Methods: We generated transgenic mice overexpressing human 5HT₄-receptors in the heart (transgenic mice, TG). We studied surface ECG and isolated electrically driven left atria (LA) or spontaneously beating right atria (RA) from TG and littermate wild type mice (WT). Results and Discussion: Only in TG but not in WT intraperitoneal injection of 5HT (100 µl of 1µM 5HT) led to a positive chronotropic effect, measuring R-R intervals on surface ECG (increase from 520 ± 20 to 734 ± 24 beats per minute, n=3 each). On the other hand the positive chronotropic effects of injection of isoprenaline in the ECG were similar in TG and WT (n=3). This indicates that the receptor is active in vivo. In RA and LA from TG significantly more spontaneous arrhythmias (no drug addition) than in WT were noted. The arrhythmias in from TG could be suppressed by addition of the 5HT₄ antagonist GR 113808 (10 µM) in RA. Moreover, the incidence of arrhythmias in RA was significantly reduced by the H89 (10 µM, an inhibitor of the cAMP dependent protein kinase) and by W7 (10 µM), an inhibitor of the Ca²⁺-calmodulin dependent protein kinase. Conclusion: the overexpressed receptor is able to act in vivo. At least in vitro tissue shows arrhythmias. Their genesis involves 5HT₄-receptors, actions of cAMP and Ca²⁺. This signal cascade might be amenable to drug therapy in patients with supraventricular arrhythmias.</p>
OC-115	<p>ANGIOTENSIN II DIFFERENTIALLY AFFECTS INTERLEUKIN-1beta INDUCED CYCLOOXYGENASE-2, MICROSONAL PROSTAGLANDIN E₂ SYNTHASE-1 AND PROSTACYCLIN SYNTHASE EXPRESSION IN ADVENTITIAL FIBROBLASTS</p> <p>¹M Galan, ¹M Miguel, ¹A Beltrán, ²C Rodríguez, ¹AB García-Redondo, ¹MJ Alonso, ²J Martínez-González, ¹M Salaiques</p> <p>¹Dpt. de Farmacología, Facultad de Medicina, Universidad Autónoma de Madrid, Instituto de Investigación Hospital Universitario La Paz (IdiPAZ), ²Centro de Investigación Cardiovascular, (CSIC-ICCC), Hospital de la Santa Creu i Sant Pau, Barcelona, Spain. email: mercedes.salaiques@uam.es</p> <p>Introduction: Adventitial layer plays a critical role in the regulation of vascular function and structure. Angiotensin II (Ang II) is involved in hypertension-induced inflammation. Cyclooxygenase-2 (COX-2) and prostaglandin E synthase-1 (mPGES-1) are induced by several proinflammatory agents like cytokines. Our aim was to assess the ability of Ang II to modulate key enzymes of the COX-2/prostanoid pathway, including prostaglandin E synthase-1 (mPGES-1) and prostacyclin synthase (PGIS), in cultures of rat aortic adventitial fibroblasts in the presence or absence of an inflammatory stimulus (interleukin-1β [IL-1β]). Results and Discussion: IL-1β (10 ng/ml, 24h) up-regulated COX-2 and mPGES-1 (protein and mRNA) and increased PGI₂ and PGE₂ release, without altering PGIS protein expression. By contrast, Ang II (0.1 µM, 24 h) did modify neither COX-2 and mPGES-1 expression nor prostanoid levels, but it induced PGIS expression. Interestingly, Ang II further enhanced IL-1β-induced COX-2 expression and PGI₂ release and concomitantly reduced IL-1β-induced mPGES-1 expression. IL-1β activated p38 MAPK and ERK1/2 pathways, and coinubation with Ang II resulted in a higher and more sustained phosphorylation of both MAP kinases. Inhibition of either p38 MAPK (SB203580) or ERK1/2 (PD98059) reduced COX-2 and mPGES-1 expression in cells treated with IL-1β or with IL-1β plus Ang II. The synergistic effects elicited by Ang II were prevented by the Ang II receptor type I (AT1) antagonist losartan. Ang II did not modify COX-2 transcriptional activity but increased COX-2 mRNA stability in IL-1β treated cells; by contrast, it increased PGIS mRNA levels through a transcriptional mechanism. Conclusions: These results suggest that Ang II could enhance the response of perivascular fibroblasts to inflammatory stimulation by the synergistic induction with inflammatory cytokines of COX-2 expression whereas an increase in PGI₂ production and reduction of mPGES-1 expression would compensate such effect. This effect of angiotensin II is caused by signalling pathways in which p38 and ERK 1/2 MAP kinases are involved. Supported by Ministerio de Ciencia e Innovación (SAF 2009-07201 and Red RECAVA, RD06/0014/0011/RD06/0014/0027)</p>

<p>OC-116</p>	<p>REGULATION OF NO PRODUCTION AND COLLAGEN PRODUCTION BY CARDIAC FIBROBLASTS <u>Laurence L Brunton</u></p> <p>Professor of Pharmacology and Medicine, Department of Pharmacology, UCSD School of Medicine, La Jolla, CA, USA.</p> <p><i>The editor of Goodman & Gilman's book "The Pharmacological Basis of Therapeutics"</i></p>
<p>W-8</p>	<p>WORKSHOP OF BIODRUG DELIVERY / TALLER LIBERACIÓN CONTROLADA DE PRODUCTOS BIOLÓGICOS</p>
<p>OC-117</p>	<p>POLYMER WITH A HIGH DEGREE OF BRANCHING ENHANCES STABILITY OF MONOPEGYLATED PROTEINS <u>Páez R¹</u>, Ramón JA¹, Castro FR¹, Saez V¹, Torres D¹, Hidalgo Y¹, López M¹, Báez R¹, Amarante O¹, Muñoz L¹, Fernández E², Magalhaes AC³, Pereira AM³</p> <p>¹ Formulation Development Department, Center for Genetic Engineering and Biotechnology, Havana, Cuba. email: rolando.paez@cigb.edu.cu; ² Institute of Food and Pharmacy, University of Havana, Havana, Cuba. ³ Immunobiological Technology Institute, Bio-Manguinhos, Oswaldo Cruz Foundation (Fiocruz), Rio de Janeiro, Brazil.</p> <p>Many new peptides and proteins are now available for potential application as new drugs. The clinical utility for protein-based drugs, however, has been limited by its relatively restricted bioavailability. Other problems that may also restrict the successful use of these drugs in therapy are: susceptibility to degradation by proteases, immunogenicity and antigenicity. Over the last years, PEGylation technology has been used to develop long-acting forms of proteins and peptides that help avoid most of these problems. Linear and two-branch PEG has been used to modify proteins. Two-branch PEGs turns out to be a very exciting protein PEGylation reagent because of its unique characteristics when compared to linear PEGs. For example, PEG2 attached to proteins 'acts' much larger than a corresponding linear mPEG of the same Mw. In this work, we described the synthesis of a four-branch PEG. The binding of this dendrimer-like polyethylene glycol to therapeutic proteins improves their <i>in vitro</i> and <i>in vivo</i> stability in a greater degree than two-branch with similar Mw. In this study we explored the conjugation of IFN-α2b to a four- branched, high molecular weight (48 000), polyethylene glycol (PEG_{4,48K}). The purified PEG_{4,48K}-NHS-conjugated IFN-α2b showed more <i>in vitro</i> and <i>in vivo</i> stability than the native cytokine and the purified PEG_{2,40K}-NHS-conjugated IFN-α2b.</p>
<p>OC-118</p>	<p>PRESENT AND FUTURE OF PEPTIDE AND PROTEIN PEGYLATION: LABORATORY AND CLINICAL EXPERIENCES <u>Francesco M. Veronese</u></p> <p>Department of Pharmaceutical Sciences, Padua University, 35128 Padua-Italy email: francesco.veronese@unipd.it</p> <p>Up to now PEGylation (the covalent binding of poly(ethylene glycol) to protein surface) is the most successful approach used to improve the therapeutic properties of proteins that present intrinsic limitations such as immunogenicity, instability, rapid clearance or low solubility (1). This technique already brought to the market several conjugated proteins of therapeutic value and furthermore it was also studied for oligonucleotide modification, this yielding the approval of a PEG-aptamer conjugate. The thirty years history of PEGylation has been marked with developments in the conjugation chemistry in order to improve yield, product homogeneity, batch to batch reproducibility and to respond to the FDA or EMEA requirements for approval. Now these needs are more pressing and they are stimulating more precise chemistries to get site directed conjugation, but also enzymatic procedure for protein conjugation as well as the use of releasable PEGs. However, the results obtained over the years revealed that PEGylation might presents sometimes certain unclear behaviours, such as kidney cell vacuolization, the presence or the elicitation of neutralizing antibodies in sensitive individuals or the possibility of complement activation. These problems together with the constraints by the huge number of patents in the field, is stimulating alternative strategies to PEGylation;</p>

	<p>polysialylation, genetic engineering approaches to obtain fusion proteins, hydrophobic tails linkage, or the use of structurally different polymers as PVP, hydroxyethyl starch or POZ (polyoxazoline).</p> <p>1. 'PEGylated Protein Drugs: Basic Science and Clinical Applications' (Milestones in Drug Therapy), Francesco M. Veronese Ed. (Birkhauser Verlag, SW).</p>
OC-119	<p>RECENT ADVANCES IN NOVEL DRUG DELIVERY SYSTEMS FOR TREATMENT OF LUNG INFECTION IN CYSTIC FIBROSIS PATIENTS <u>Abdelwahab Omri</u></p> <p>The Novel Drug and Vaccine Delivery Systems Facility, Department of Chemistry and Biochemistry, Laurentian University, Sudbury, Ontario, Canada, P3E 2C6 email: aomri@laurentian.ca</p> <p>Cystic fibrosis is a lethal genetic recessive illness with a prevalence of 1:2,000 individuals among Caucasians. This illness is caused by mutations in a single gene situated on the long arm of chromosome 7, which encodes the cystic fibrosis transmembrane regulator gene. These mutations lead to series of cellular dysfunctions and resulting in a generalized dysfunction of exocrine glands. Although many organs such as the liver, pancreas and intestines are affected in cystic fibrosis patients, pulmonary disease is the major cause of morbidity and virtually all mortality due to bacterial infection with <i>Pseudomonas (P) aeruginosa</i>. This bacterium exhibits a number of resistant mechanisms including enzymatic inactivation of antibiotics, alterations of the target sites of antimicrobial agents, antibiotic efflux systems, and reductions in cell wall membrane permeability. Reductions in outer-membrane permeability, however, are the main contributing factor to antibiotic resistance in <i>P. aeruginosa</i>. The development and characterization of liposomal antibiotics in an effort to improve antibacterial activities of encapsulated drugs against resistant strains of <i>P. aeruginosa</i> isolated from cystic fibrosis patients will be discussed.</p>
OC-120	<p>A NEW FORMULATION OF CLOBETASOL PROPIONATE LOADED LIPOSOMES FOR TOPICAL APPLICATION <u>Xiomara Pérez Gutiérrez</u>, Nilia de la Paz Martín-Viaña, Natalia Diduk, Ladyth de la Caridad García León, Ania González Cortezón, Juana Inés Tillán Capó, Aymeé Roche Gonzáles, Laura Ester Hernández Fernández, Ignacio Hernández González</p> <p>Center for Drugs Research and Development (CIDEM). Ave. 26 No. 1605, Nuevo Vedado, Plaza, CP 10400. Havana, Cuba. email: xiomarapg@infomed.sld.cu</p> <p>Clobetasol propionate is a potent corticosteroid especially useful for short treatment of recalcitrant dermatoses. However, their systemic side-effects, particularly inhibition of the hypothalamic-pituitary-adrenal axis, limit its use as maximum up to 14 days. In the present study Clobetasol propionate was encapsulated into liposomes for improving its dermal action. Liposomes composed of soy Phosphatidylcoline, Cholesterol, Butylated hydroxytoluene and Clobetasol Propionate (CP) were prepared using polyol dilution method and a factorial design approach was used. Amount of Cholesterol (Chol), homogenization speed and homogenization time were taken as variables at two different levels. Liposomes were characterized for vesicles size and encapsulation efficiency. Gel containing liposome dispersion (batch with higher liposome size) was prepared in Carbopol® 940 NF and was characterized for gel viscosity. Drug percutaneous absorption from liposomal gel and conventional formulations was evaluated <i>in vitro</i> through excised human skin using Franz diffusion cells and liquid scintillation to measure the drug content in samples. <i>In vivo</i> anti-inflammatory effect was tested on mice and rats. Polyol dilution method was found to produce multilamellar and homogeneous population of liposomes. Results of regression analysis revealed that vesicle size was dependant on the cholesterol concentration (positive correlation) and the homogenization speed (negative correlation) during preparation. Incorporation of liposomal suspension to 1% Carbopol gel base at 1:3 ratio gave a suitable viscosity for apply to the skin. Percutaneous absorption study showed both better accumulation of CP into skin and lesser levels in receptor fluid than conventional formulations. From these results one may expect a lower diffusion of the CP incorporated in liposomes towards the systemic circulation after <i>in vivo</i> application. <i>In vivo</i> experiments demonstrated the same anti-inflammatory effect of CP liposomal formulation as the marketed cream and ointment, even when CP concentration in liposomal gel is a half of the commercial products. A suitably developed liposomal formulation of Clobetasol propionate can be of actual value for enhancing its localization into the skin, thus improving its dermal action in topical therapy.</p>
OC-121	<p>SUSTAINED RELEASE OF BIOLOGICALLY ACTIVE EPIDERMAL GROWTH FACTOR FROM POLYMERIC MICROSPHERES PROMOTES WOUND HEALING <u>Saez V</u>¹, Caballero L¹, Berlanga J², Aldana R¹, Ramón J³, Cruz E¹, Peniche C³, Paez R¹</p>

	<p>¹ Formulation Development Department, Center for Genetic Engineering and Biotechnology (CIGB), PO Box 6162, Havana, Cuba, e-mail: vivian.saez@cigb.edu.cu ² Pharmaceutical Division, Biomedical Research (CIGB) ³ Macromolecular Chemistry Department, Biomaterials Center BIOMAT, University of Havana (UH), P.O. Box 6130, Havana, Cuba.</p> <p>Introduction: Epidermal Growth Factor (EGF) is a therapeutic peptide used in wound healing and more recently for preventing the amputation of lower limbs in diabetic patients having chronic ulcers. A novel delivery system based on microspheres containing EGF could offer some advantages over an immediate release formulation. This work was aimed to obtain polymeric microspheres of biologically active EGF having a potential healing effect. Materials and Methods: EGF-loaded microspheres were prepared by the double emulsion-solvent evaporation method using copolymers of lactic and glycolic acid as polymeric matrices. Results and Discussion: Spherical particles with a smooth surface having randomly distributed pores were obtained. A 3² factorial design allowed knowing that an increase in the EGF concentration and the volume of the inner aqueous phase generates an increase in protein loading, while the encapsulation efficiency decreased. A quantitative extraction procedure was designed for evaluating the properties of encapsulated EGF. Several experimental samples were analyzed using such procedure and in all of them the extracted EGF exhibited their initial properties. The release profile of encapsulated EGF showed a two-stage pattern with a burst release of about 30% followed by a slow release stage. A study performed <i>in vivo</i> in a model of full-thickness wounds in rats showed evidences (capillarogenesis and maturation of collagen fibers) of the potential healing effect of EGF released from polymeric microspheres. Conclusion: The results presented here support the idea that these microspheres could be a good approach for designing novel EGF delivery systems with potential applicability to the treatment of diabetic foot ulcers.</p>
OC-122	<p>PREFORMULATION APPROACHES USING PREDICTIVE METHODS AND ACCELERATED STABILITY STUDIES Sophie Richert Head, Preformulation Unit, Merck Serono, Switzerland</p> <p>This presentation will introduce the different preformulation approaches used at Merck Serono. In order to discuss about them, the main topics discussed will be:</p> <ul style="list-style-type: none"> - Predictive methods and accelerated stability studies in order to enhance biologics storage efficiency. - Some cases studies will be presented to support this strategy with data from Differential Scanning Calorimetry and Self Interaction Chromatography experiments. - Exploration of agitation and freeze/thaw studies will also be shown to understand the propensity of proteins to aggregate and approaches to protect them from aggregation caused by external stresses.
OC-123	<p>CHITOSAN BASED MATRICES FOR DRUG DELIVERY Carlos Peniche</p> <p>Macromolecular Chemistry Department, Biomaterials Center BIOMAT, University of Havana (UH), P.O. Box 6130, Havana, Cuba. email: peniche@reduniv.edu.cu</p> <p>Microencapsulation with polymer matrices has received increasingly growing attention in the last decades, resulting in a great number of applications in industry, agriculture, medicine, pharmacy, and biotechnology. In medicine and pharmacy it has been used for masking unpleasant tastes and odours, the controlled release of drugs, the protection of drugs from aggressive body fluids, such as gastric fluids, the immunoisolation of cells, and in immunoassays. Chitosan is a cationic linear polysaccharide composed essentially of $\beta(1\rightarrow4)$ linked glucosamine units together with some proportion of N-acetylglucosamine units. Chitosan occurs rarely in nature. It is generally obtained by extensive deacetylation of chitin, a homopolymer of $\beta(1\rightarrow4)$ linked N-acetyl-D-glucosamine, present in the shells of crustaceans, molluscs, the cell walls of fungi, and the cuticle of insects. From a biomedical point of view, chitosan and chitosan derivatives are very attractive compounds because of their biocompatibility, immunostimulating activity, anticoagulant properties, antibacterial and antifungal action, and also because of their promotion of wound healing in surgery. In the field of drug delivery, chitosan and chitosan derivatives have been proposed as matrices in numerous pharmaceutical formulations, in the form of gels, films, emulsions, transmucosal devices, microspheres, and so on, for the prolonged release of drugs, delivery of vaccines, DNA, insulin, and anticancer agents such as 5-fluoracil, among others. The great potentialities of chitosan for multiple applications in medicine and pharmacy is</p>

	evidenced by the increasing number of patents conferred worldwide and scientific articles published annually involving this biopolymer. In this presentation the results of our group in the preparation chitosan based matrices (films, hydrogels, microspheres, nanoparticles, liposomes) for the design of drug delivery systems will be described.
W-9	1ST INTERNATIONAL WORKSHOP ON MEDICATION ERRORS / 1^{ER} TALLER INTERNACIONAL SOBRE ERRORES DE MEDICACIÓN
OC-124	<p>MEDICATION ERRORS AND SAFE MEDICATION USE <u>Eduardo L. Mariño</u></p> <p>Full Professor of Pharmacy and Pharmaceutical Technology. Head of the Clinical Pharmacy and Pharmacotherapy Unit, Department of Pharmacy and Pharmaceutical Technology, Faculty of Pharmacy. University of Barcelona. Spain.</p> <p>From the edition in 1999 of the book <i>To Err is Human: Building a Safer Health System</i> by the <i>Institute of Medicine's Committee on Quality of Health Care in America</i> (IOM) and in 2001 of <i>Building a safer NHS for Patients: improving medication safety</i>, by the <i>National Health Service UK</i> (NHS), there have been numerous publications on the importance of the identification, prevention and reduction of medication errors (ME) to improve the safe use of medicines by the patient. One of the most internationally accepted definitions of what is a ME is the proposal by the <i>U.S. National Coordinating Council for Medication Error Reporting and Prevention</i>, (NCCMERP), which indicates that a ME is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use. From a social point of view, various publications estimate that ME are responsible for about 7,000 deaths each year in the U.S., between 4.5 and 17% of hospital admissions and between 10 and 15 % of emergency room visits and that about 1 ME per patient is produced each day, among other figures. However, the actual incidence of ME is unknown in many cases because ME detected before they reach the patient or without damage are not usually provided by different causes.</p>
OC-125	<p>ANTIMICROBIAL PRESCRIPTION ERRORS IN EMERGENCY SERVICES PEDIATRIC HOSPITAL OF CAPITAL <u>López R,</u> Echavarría M</p> <p>Foods and Pharmacy Institute, Havana University. 23 Ave. No. 21425. Coronela, Lisa. Havana City. Email: farmexp@infomed.sld.cu</p> <p>The rational use of antimicrobials and antibiotics policy in the medical service is vital to keep track of the proper use of them and avoid all negative consequences of medication errors resulting from poor and indiscriminate use of this group drugs, especially in vulnerable groups such as pediatric patients. Taking into account these elements and other current reports on the use of these drugs, it was decided to conduct this study pharmacoepidemiology, classified into studies of drug use as Indication-Prescription The research was conducted in the emergency services of 3 pediatric hospitals in Havana. Was used as a working tool for the interview and it was made to family physicians and patients. The sample sizes was 550 patients and of these 277 were males and 273 females, the age group most represented was the 0-5. The most common infections were respiratory and groups most frequently prescribed antibacterial penicillins and cephalosporins. In most patients do not use additional means for presumptive diagnosis. The prescription was incorrect in more than 50% of cases, we found some potential drug interactions, patient oriented care was adequate in only 33.3% of cases, and adherence to treatment was satisfactory, while the response to it was not a high percent positive, something that is largely correlated with prescribing errors found.</p>
OC-126	<p>IDENTIFICATION OF DRUG-RELATED PROBLEMS IN THE ELDERLY WITH POLYPHARMACY IN THE CALIXTO GARCÍA HOSPITAL. 2009 vs 2006 <u>Hydes E</u> García O, Alfonso I.</p> <p>CITED. 27 y G. Plaza de la Revolución. Havana City, Cuba. email: editha@infomed.sld.cu</p> <p>Introduction: A Drug-Related Problems (PRM) is any health's problems in relations with a patient's treatment. The polimedication is one important cause of these problems. Materials and Methods: It is a</p>

	<p>descriptive, transversal and retrospective study in the elderly with polypharmacy at Calixto García Hospital in 2009, with the objective of determines presence of PRM. The results were compared with other similar study in 2006. Results and Discussion: A research with 165 patients was done, and 148 PRM were found. This result was light better in comparison with the before research, but still alarm because the high percentage of this problems. The most frequency problems found were: security, and particular medicament potential interactions and adverse reactions by medicine, and therefore is imperative necessary to analyse the treatment of each patient in order to minimize the risk of these problems represents. Conclusions: This study demonstrate the very high importance of Developer of Clinic Pharmacist activities for identify and specially to prevent PRM, especially in this populations.</p>
OC-127	<p>LOGISTICS DRUGS INFLUENCE IN THE APPEARANCE OF MEDICATION ERRORS Ferrer Y. López R, Miranda M Foods and Pharmacy Institute, Havana University. 23 Ave. No. 21425. Coronela, Lisa. Havana City. email: farmexp@infomed.sld.cu</p> <p>The drug delivery system or drug logistics, is the key link in the functioning of health institutions, as for the provision of services such as raison d'être of these institutions requires an adequate supply of necessary and monitor them, if this is not true can appear real and the known potential medication errors. In this paper we conducted a study on drug supply in five municipalities in Havana and assessed the influence of the same in the occurrence of medication errors. Through surveys of pharmacy managers found that only 37.6% of pharmacies surveyed in the studied areas have pharmacist. A high percentage of pharmacists (66.1%) who expressed interest in conducting research work and 16.1% who said they had no time, however, 35.7% reported having no interaction with physicians, this being most unfavorable situation in the municipality of La Lisa, where 80% of the pharmacists raised the ratio of regular to zero. It was also noted deficiencies in the pharmacist-patient interaction; it is generally passive and not fully met dispensing activities. Drug selection is done primarily through the method of historical consumption. From these results it was found possible occurrence of medication errors in prescribing, dispensing and administering medications in the population of the municipalities.</p>
OC-128	<p>DETECTION OF ERRORS IN MEDICATION. 10 YEARS OF EXPERIENCE Arbesú MA, Ropero RJ, Proveyer S, Fente BA.</p> <p>Institute of Oncology and Radiobiology. Calle F y 29, Plaza de la Revolución. Havana City. Email: marbesu@infomed.sld.cu</p> <p>Introduction: Error is one of the principal causes that increase the expenses in public health around the world. Knowing the mistakes and taking actions in order to eradicating them, in the Institute of Oncology, was a challenge. Material and methods: During the last 10 years, cause of the work routine and the requirements made by the Pharmacotherapeutic Committee, all prescriptions of parental and cytostatic antimicrobials, which were issued by surgery, medical oncology, pediatrics and outpatient chemotherapy, were reviewed and validated through pharmaceutical intervention. Results: The pharmaceutical validation avoided 1,269 errors in the prescription of antimicrobials for a period of 10 years; also it avoided 2,501 errors in cytostatic prescription in 5 years. Overall, 4,769 pharmaceutical interventions were made. A quarterly newsletter was edited (12 copies); conferences, talks and trainings (9 in total) about the main causes of the errors were offered to the involved personnel; and 6 scientific articles were published a propos of results. The common found errors were related to omissions (weight, height, diagnosis) and transcriptions (by residents in the most of the cases). The number of errors has decreased a 50% due to implemented measurements. Conclusions: A package of actions have been identified and applied in order to detecting and avoiding medication errors.</p>
OC-129	<p>BIOETHIC AND MEDICATION ERRORS ON THE HEALTH CARE Sedeño C¹, Valdés R²</p> <p>¹ Foods and Pharmacy Institute, Havana University. 23 Ave. No. 21425. Coronela, Lisa. Havana City. email: caridad.sedeno@infomed.sld.cu ² Instituto Superior de Ciencias Médicas Manuel Fajardo.</p> <p>The prevention and detection of potential medication errors that may be present in common clinical practice are functions that the health care team has to work with in order to prevent them from reaching the patient and cause iatrogenic events. Teamwork is essential to provide quality health care. In the exercise of this one, doctors, pharmacists, nurses and patients have a hegemonic role; however, given the scientific and technical development achieved over the past four decades in the sciences health, other professionals have become</p>

	<p>members of the team, which requires a multidisciplinary integration work that achieves the health strategies assumed. However, to prevent, detect and avoid potential medication errors, the teamwork and the strong scientific and technical training of its members are not enough. It is important to recognize that human error is an inherent attribute of the social being, coded from the perspective of bioethics with the incorporation of principles and moral values in professional relationships in order to minimize them. Only by applying this new approach we will be able to ensure the professional bridge to the future in clinical practice, in which we should combine the scientific knowledge focused on the biological part and the humanistic knowledge oriented to the human values.</p>
OC-130	<p>PHARMACEUTICAL INFORMATION CENTER: INCIDENCE AS A PROVIDER OF SPECIALIZED INFORMATION RESOURCES <u>Ricardo Castro Armas</u>, Ambar Suárez Fajardo, Maray Pons Blanco, Sandra Rodríguez Pérez, Yamilet Rodríguez Más, Regla de las Cuevas de las Cuevas.</p> <p>Drug Research and Development Center (CIDEM). Ave 26 No. 1605 e/ Boyeros y Puentes Grandes. Plaza. Ciudad de La Habana. CUBA. email: ricardo.castro@cidem.sld.cu / cinfa@infomed.sld.cu</p> <p>The Pharmaceutical Information Center (CINFA) organizes the information of the Drug Research and Development Center (CIDEM) and the Cuban pharmaceutical sector. Its mission is oriented to supply information for the research and development of medicine all over the country as well as to provide support for the training of new pharmacists or other professionals in related sciences nationwide. Institutions and users mainly interact with CINFA by accessing The Pharmaceutical Portal and the Virtual Library, which take into account the generalization of the use of new information and communication technologies, the quantity and quality of the information resources available and their immediate access and use. CINFA has reaffirmed its position as a provider of information services and products and it has had a direct influence on the development and consolidation of the pharmaceutical industry. This work presents details of the pharmaceutical virtual library which has been the result of a systematic process. In this process different information sources have been identified, selected and acquired so that they can be managed in an efficient and decentralized way. The Data Bases, currently part of the virtual library, as well as the perspective of designing and developing new and updated resources to serve the users of the pharmaceutical sector are described and characterized. We focus on the possibilities available for students, teachers, and others to use CINFA's facilities to access relevant and updated information to help them work in their professional fields.</p>
	JUEVES / THURSDAY DICIEMBRE / DECEMBER 16
S-9	2ND NATIONAL SYMPOSIUM ON TEACHING OF PHARMACOLOGY / 2^{DO} SIMPOSIO INTERNACIONAL SOBRE ENSEÑANZA DE LA FARMACOLOGÍA
OC-131	<p>COMPARISON OF THE CORE CURRICULUM FOR MEDICAL STUDENTS IN CLINICAL PHARMACOLOGY WITH INTERNATIONAL STANDARDS <u>Groning E</u> Facultad "Dr. Miguel Enriquez". Medical University of Havana. Ave. Ramón Pinto # 202. C. Habana. email:groning@infomed.sld.cu</p> <p>There is a general concern that the prescribing ability of students will suffer because of the relative lack of factual knowledge about drugs. In order to improve the situation, there has been much attention paid to the concept of a core curriculum in clinical pharmacology for medical students. The concept of core includes the essential, central principles of clinical pharmacology that every medical student should master before becoming a physician. Core material includes information, skills, and attitudes. The objective of this work is to establish a comparison of the core curriculum in clinical pharmacology in the Medical University of Havana with international standards. The comparison revealed some differences in core information and skills related to clinical pharmacokinetics, therapeutic drug monitoring, pharmacogenetics, writing prescriptions, communication skills and poisoning. In core attitudes, we observed differences associated to the prescription as an experiment and the importance of the therapeutic contract. We conclude that the comparison of the core curriculum for medical students in clinical pharmacology with international standards is a valuable tool in the improvement of the discipline pharmacology.</p>
OC-132	<p>EDUCATIVE STRATEGIES IN PHARMACOEPIDEMIOLOGY <u>Furones Mourelle JA</u>, Cruz Barrios MA Center for the Development of Pharmacoepidemiology. 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba. email: furones@infomed.sld.cu</p>

	<p>Taking into consideration that there are thousands of drugs registered in the World (a great proportion of them have not demonstrated to be useful in therapeutics and in some of them its efficacy and safety is doubtful) the importance of teaching pharmacology and therapeutics in medical universities is significative related to drug prescription, and the qualitative and quantitative decisions that go into the prescription for each health disorder become appropriate. The main objective of pharmacoepidemiology is to collect information about efficacy and safety of drugs to protect the population. Since the opening in 1996, the Center for the Development of Pharmacoepidemiology and its network has taken important steps to improve prescription habits of health professionals. Some of them are showed like the Guide to Good Prescribing- a step by step guide to select drugs according to efficacy, safety, convenience and cost-; the education of thousands of health professionals through postgraduate courses and diplomate -among them there were teachers of family medicine of medical university-; use of information and communication technologies in learning and software to create Web-based courses.</p>
OC-133	<p>A METHODOLOGY FOR SEMINARS IN CLINICAL PHARMACOLOGY ACCORDING TO THE GUIDE TO GOOD PRESCRIBING <u>Cruz Barrios MA</u>, Furones Mourelle JA</p> <p>Center for the Development of Pharmacoepidemiology, 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba. email: maria.cruz@infomed.sld.cu</p> <p>The traditional method of teaching pharmacology is supported by lectures, usually accompanied by seminars and other teaching events. The subject Pharmacology II for medical students is delivered in the sixth semester. It is based on the pharmacological basis or therapeutics and recommends the use of the Guide of Good Prescription, but the methodological guidelines on how to apply it, are neither clear nor uniform in all the topics of the program. A strategy to be accomplished in the seminars, based on the Guide of Good Prescription will be easy to apply and would allow certain uniformity with the use of this method in Cuban Medical Universities. We propose precise methodological guidelines, according to the resources available. Considering that students should be accustomed to proceeding through a logical sequence of deliberate steps as they consider instituting any pharmacotherapeutic process, this methodology becomes necessary to develop the ability of the student to accurately assess and estimate the potential risks and benefits of using a drug in a specific patient and to contribute to rational use of drugs.</p>
OC-134	<p>QUALITY OF THE SPECIALIZATION IN PHARMACOLOGY AT HAVANA MEDICAL UNIVERSITY <u>Martínez Torres MC</u></p> <p>Facultad “Dr. Salvador Allende”. Havana Medical University.Havana, Cuba. email: maricarmen@infomed.sld.cu</p> <p>The management of quality as a process (in Cuban Higher Education) is organized in different steps: self evaluation, adjustment and improvement, external evaluation, accreditation and acknowledgement. The current curriculum of the specialization in pharmacology has been transformed since its introduction, but neither research has ever been done to support the changes nor has the quality been evaluated. It remains only as an authorized curriculum. A research was carried out to determine the quality in the specialization of pharmacology at Havana Medical University and to propose actions to improve it. The Guide for Evaluation of Specializations of the Ministry of Higher Education was used as a pattern. A questionnaire was designed and applied in order to measure the degree of satisfaction of residents. An interview was applied to employers that agreed to participate. The analysis of different variables gave 80 points (from 120) to the specialization according to the Guide for Evaluation. Main difficulties were: material and administrative support to the syllabus (11 points from 30) and to the curriculum (6 points from 15). Main causes of dissatisfaction among residents were: prevalence of theoretical activities; excess of basic courses and little access to updated bibliography. Employers agreed with insufficient practical training and expressed the need to include other topics, increase the clinical approach and social contribution. The specialization was evaluated with the minimal category of “ratified curriculum”. A plan for improvement is proposed to apply for a higher category.</p>
OC-135	<p>NEUROBIOLOGY AND THERAPEUTICS OF DRUG ABUSE. EDUCATIVE SOFTWARE <u>Nuvia Pérez Cruz</u></p> <p>M.D. Associate Professor of Pharmacology. “Dr. Salvador Allende” Faculty of Medicine. Medical University of Havana. email: antares@infomed.sld.cu</p>

	<p>Introduction:The traditional method of teaching could and should be enriched by the possibilities that offer the New Technologies of Informatics and Communications, especially with innovators alternatives which respond to demands of a preponderant visual society. Pharmacology and drug abuse topic (and the rest of the subjects of medical sciences) would be beneficiary from these options. The educational software in it's multimedia variant with the attached of pedagogic metaphor in a graphic type, constitute an attractive teaching tool in times where instruction acquires the challenge of help students to discover information inside them, showing a different perspective of the phenomenon. Objective: To expose the design and the basis of the educational software "Neurobiology and Therapeutics of drug abuse". Methods: An updated bibliography about drug abuse, the impact of the New Technologies of Informatics and Communications and the use of pedagogic metaphor were consulted, establishing criteria for the selection of the contents, multimedia elements and the design of the platform. Results: Educational software based in HTML language, illustrate the contents using a metaphoric audiovisual language with quotidian references helped by rhetoric and humorous elements. Conclusions: Multimedia based in pedagogic metaphor constitute a new way to present pharmacological information and contribute to a natural and long term creation of new knowledge in students.</p>
<p>OC-136</p>	<p>PEDAGOGICAL LEARNING NEEDS IN PHARMACOLOGY PROFESSORS <u>Vilches Juanes T</u></p> <p>Facultad de Ciencias Médicas "Victoria de Girón." Havana Medical University. Calle 146 esquina 31.C.Habana. email: tvj@infomed.sld.cu</p> <p>The identification of the pedagogical learning needs is an alternative that could be advantageous for creation of professional competences in Medical Sciences during postgraduate. To identify the basic learning needs on pedagogical aspects in pharmacology professors of Health Technology career was the main objective of this research. Theoretical and empirical methods were used. Information was collected through the application of a questionnaire on pedagogical opinions. A selected sample of 17 professors was surveyed. statistical procedures for the analysis of results and design of tables were also used. Based on the identification of learning needs of the surveyed professors, a more comprehensive analysis was made to assess collected data, which allowed characterizing those professors under study .A proposal of pedagogical professional upgrading for licentiates working as professors in middle level and higher medical education is necessary in order to increase their knowledge and abilities, as well as their professional competence and performance. The results obtained lead us to conclude that learning needs in pharmacology professors were detected in connection with:- self-training and -the ignorance about some pedagogical topics, such as: teaching organization forms, teaching methods and evaluation.</p>
<p>OC-137</p>	<p>METHODOLOGY OF CLINICAL TRIAL. ITS APLICATION IN EXPERIMENTAL PEDAGOGICAL INVESTIGATION <u>Hernández A, Robaina M</u></p> <p>¹ National Coordinating Center of Clinical Trials. 21 Ave and 200 St., Atabey, Playa, Havana City, Cuba. email: alberto@cencec.sld.cu</p> <p>Introduction. One of the problems that are frequently found in published and unpublished pedagogical experimental investigations, where a new learning method is proposed, is that the investigational method chosen is inappropriate to achieve reliable results. Clinical trial methodology is the gold rule to perform clinical studies, but can be used in other fields; adaptations can be implemented and be employed in other experimental investigations like pedagogical studies. To demonstrate the applicability of this kind of methodology was the purpose of this work. Materials and Methods: Methodological key elements of clinical trials were reviewed and it was chosen the three most important of them, objectivity of the observation, concurrent comparison and randomization to be applied to the design of pedagogical experimental investigations. Results and discussion: Two master theses were designed taking into account the features of an experimental study, prospective, controlled, and randomized and with statistical analysis in a blinded manner. It was explained how to use these methodological elements of clinical trials in the design of pedagogical studies. Conclusions: Experimental pedagogical investigations can be designed using methodological aspects of clinical trials, which give scientific and methodological strengths to guarantee reliable results of this kind of study.</p>

OC-138	<p>LEARNING BASIC AND CLINICAL PHARMACOLOGY IN PBL-TUTORIAL GROUPS. THE WALTER SISULU UNIVERSITY-FACULTY OF HEALTH SCIENCES EXPERIENCES. <u>J. Aguirre</u> Department of Pharmacology .Walter Sisulu University.Faculty of Health Sciences. Mthatha05117.SouthAfrica. email:jah3748@yahoo.com</p> <p>The Walter Sisulu University (WSU,) previously known as University of Transkei (UNITRA), was established in Mthatha 1977. The Faculty of Medicine was inaugurated in 1985 and later on its name was changed to Faculty of Health Sciences. The WSU Faculty of Health Sciences (FHS), which is a pioneer medical school in South Africa for Community Based Education (CBE) and Problem Based Learning (PBL), has reduced formal lecturing to a minimum and has introduced tutorial groups. Some of the students orientated goals identified for the training program will be discussed as well as the instructional processes. The learning process is integrated and not discipline –based. The contents of basic and clinical pharmacology are covered in 3rd year together with those of Anatomical Pathology, Clinical Pathology, Microbiology and Community Medicine. Important attention will be given to the tutorial group dynamic (as a core of students activity) and also to the clinical cases (as motivation and starting point of the learning process). The development of learning issues (particularly in pharmacology) and the acquisition of clinical skill will be analysed. Finally the evaluation process and the assesment tools used will be shown. All of the above in relation to the acquisition of knowledges in basic and clinical pharmacology.</p>
OC-139	<p>TRAINING FOR DELIVERY OF KEY THERAPEUTICS MESSAGES TO HEALTH PROFESSIONALS ACROSS AUSTRALIA <u>Higgins G</u></p> <p>NPS, PO Box 1147 Strawberry Hills NSW 2012 Australia.e mail:ghiggins@nps.org.au</p> <p>More than 90 NPS trained Facilitators currently deliver key therapeutic messages to health professionals in the 112 primary care networks around Australia. One of the major enablers to the strong performance by NPS Facilitators is their initial skills based training. The 3-day <i>Best Practice in Educational Visiting</i> training for 1:1 interactions with GPs uses a combination of techniques such as role plays, demonstrations and discussion groups. Participants are systematically led through the structure of an educational visit, being provided the chance to practise each component of the visit as well as delivery of an educational visit to a GP. 1-day Therapeutic briefings are provided twice annually for each new topic: a specialist provides the evidence behind the program key messages; a GP insight into how they will hear the call to action of the messages; and facilitators discuss the barriers and enablers to their delivery of the messages to GPs, pharmacists and nurses. Ongoing support, networking and further training ensure facilitators achieve and sustain high levels of activity and make an impact on better use of medicines. Support and networking is provided via regular teleconferences and a facilitator specific website: these are used to discuss issues, to provide feedback to NPS, and to share highlights and challenges. Further training offered includes: Small Group Facilitation Skills: a 2-day workshop in which facilitators learn about behavioural styles and practice the skills for conducting a case based discussion meetings Building on Skills and Enhancing Facilitator Skills: 1-day workshops designed to strengthen the skills of NPS Facilitators who have been in their role for at least 1 and 3 years respectively Short 1.5 hour skills based workshops at biennial Facilitator Forums NPS investment in facilitator training and support is high: continuation of this model is supported by their strong performance, their high levels of local activity and their passion and commitment with more than half being in their role for more than 5 years.</p> <p>Acknowledgements: NPS staff, consultant trainers and experienced facilitators who provide support and training for NPS facilitators. See www.nps.org.au</p>
S-10	<p>SYMPOSIUM OF ANTIMICROBIAL THERAPY AND BACTERIAL RESISTANCE. APUA, CUBA./ SIMPOSIO TERAPIA ANTIMICROBIANA Y RESISTENCIA BACTERIANA. APUA, CUBA.</p>
OC-140	<p>THE EMERGENCE AND DEVELOPMENT OF THE ALLIANCE FOR THE PRUDENT USE OF ANTIBIOTICS (APUA) <u>Moisés García Morejón</u></p> <p>President of APUA-Cuba</p>

	<p>The Alliance for the Prudent Use of Antibiotics (APUA) was created in 1981, organized by Dr. Stuart Levy, professor at Tufts University, Boston, USA., Who has been his manager and promoter constant in his capacity as chairman of this organization. As its name implies, APUA is an organization aimed at promoting rational and appropriate use of antimicrobial agents recognizing that resistance to these compounds is one of the larger problems facing the twenty-first century in relation to infectious diseases. APUA is an international organization composed of more than 60 national chapters across five continents and individual members from more than 100 countries. Maintains close contacts with scientific institutions dedicated to the preservation of health, such as the World Health Organization (WHO), Pan American Health Organization (PAHO), the Center for Disease Control and Communicable Diseases (CDC), the Food and Drug Administration (FDA) and the ministries of health of several countries. The Alliance was founded in Cuba in 1996 but it was not until 2007 that a change of line of work, from 7 members manages to grow and spread throughout the island, counting today more than 450 members of 44 medical specialties throughout the country, with centers in Matanzas, Santiago de Cuba and Isla de la Juventud. The Alliance has done multiple events (conferences, symposia, workshops, courses) in the capital and other provinces on issues update on infectious diseases, promoting the appropriate use of antimicrobials.</p>
OC-141	<p>REALITY MICROBIOLOGY OF A MODERN HOSPITAL, <u>Fidel Espinosa Rivera</u> Hospital “Hnos Ameijeiras”, Ciudad de la Habana, Cuba.</p> <p><i>Resumen no disponible en el momento de la edición del libros. Abstract non available in the moment of the edition of the book of summaries.</i></p>
OC-142	<p>POLITICS OF ANTIBIOTICS IN A HOSPITAL OF HIGH COMPLEXITY. <u>René Zamora Marín</u> Presidente del Comité de Antibióticos. Hospital “Hnos Ameijeiras”, Ciudad de La Habana, Cuba.</p> <p><i>Resumen no disponible en el momento de la edición del libros. Abstract non available in the moment of the edition of the book of summaries.</i></p>
OC-143	<p><i>SOME CONSIDERATIONS ABOUT THE USE OF STRATEGIC’S ANTIBIOTICS</i> <u>Zuleica del C. Galí Navarro</u></p> <p>Esp. II grade in Intensive Medicine and Emergency . “Hermanos Ameijeiras” Hospital</p> <p>A revision of antibiotics that can be considered strategic in the treatment of infection in the community or nosocomial, it is another alternative in the treatment of sepsis caused by multiresistant germs. The family of antibiotics, quinolonas, has a great importance in the management of many community and nosocomial illnesses. Since 1962 that quinolona was created, until now, have been introduced new quinolonas generations to the market, arriving until the fourth generation. The new quinolonas have antineumococic activity and it has demonstrated to be effective in several clinical studies carried out in patient with community pneumonia. The teicoplanina is a glycopeptides antibiotic that offers great help in the sepsis treatment for aerobic and some anaerobic gram-positive germs. The teicoplanina was 4 times more active than vancomycin against Staphylococcus meticillin resistant, and it was from 2 to 8 times more active than vancomycin against the Streptococcus and Enterococcus. It has a good synergism with the rifampicina.</p>
OC-144	<p>LAST STEP OF ANTIMICROBIAL THERAPY <u>Moisés Morejón García</u></p> <p>Clinical-infectious. University Hospital Comandante Manuel Fajardo. Havana City. email:moisesm@infomed.sld.cu</p> <p>From the very emergence of antimicrobial scientists identified strains of bacteria resistant to them, an example was the description by Edward Penley Abraham strains of staphylococci resistant to penicillin before the start of their clinical use in 1941. This phenomenon has been a worrying rise, reaching an extension that includes all the types of bacteria present, involving even the newest antimicrobial creation. This situation together with the small appearance in the market of new drugs has created some uncertainty in the medical world, because there is now a significant number of multiresistant bacteria against which antibiotics have no effect. However, in the last 10 years have seen a series of powerful antimicrobials have given us some hope in the future outlook. Families as streptogramins, oxazolidinones, lipopeptides, glycyclines new ketolides and</p>

	glycopeptides and beta-lactams are among them. This conference will address the pharmacokinetic and pharmacodynamic aspects of new compounds as they are, Linezolid, Synercid, Daptomycin, telavancin, tigecycline, Telithromycin; Ceftobiprole and others.
S-11	1ST INTERNATIONAL SYMPOSIUM OF NURSING NETWORK ON CHILDHOOD HEALTH. “NURSING CARES AND PHARMACOTHERAPEUTIC ON CHILDHOOD HEALTH” / PRIMER SIMPOSIO INTERNACIONAL DE LA RED DE ENFERMERÍA EN SALUD INFANTIL ENSI- CUBA. “CUIDADOS DE ENFERMERÍA Y FARMACOTERAPÉUTICA EN LA SALUD INFANTIL”
OC-145	NURSING CARE OF CHILDHOOD PAIN <u>María José Aguilar Cordero</u> Presidenta de la Asociación Iberoamericana del Dolor en la Infancia. Universidad de Granada. España. <i>Resumen no disponible en el momento de la edición del libro. Abstract non available in the moment of the edition of the book of summaries.</i>
OC-146	THE PAIN IN THE CHILDHOOD AND THE NURSING CARES. SITUATION IN CUBA. <u>Norma Mur Villar</u> Coordinadora Nacional de la Especialidad de Enfermería Materno Infantil. Hospital “Gustavo Aldereguía” Cienfuegos. Cuba / Atención de enfermería ante el dolor en la infancia. La situación de Cuba. <i>Resumen no disponible en el momento de la edición del libro de resúmenes. Abstract non available in the moment of the edition of the book of summaries.</i>
OC-147	CARING AND HANDLING PAIN IN THE CRITICAL NEWBORN: SOME DIFFICULTIES AND PARADOXES <u>Vázquez A</u>¹, Blanco F², Díaz ML³, Sellán C⁴, Santamaría JM⁵, Amezcua M⁶ ¹ Hospital Universitario La Paz, Pº Castellana 261, Madrid, España. email: avazsel@yahoo.es ² Facultad de Psicología Universidad Autónoma, Ciudad Universitaria de Cantoblanco, Madrid, España. email: florentino.blanco@uam.es ³ Escuela Universitaria de Enfermería La Paz, Universidad Autónoma de Madrid, Pº Castellana 261, Madrid, España. email: mluisa.diaz@uam.es ⁴ Escuela Universitaria de Enfermería La Paz, Universidad Autónoma de Madrid, Pº Castellana 261, Madrid, España. email: c.sellan@uam.es ⁵ Fundación para el Desarrollo de la Enfermería, C, Veneras 9, Madrid, España. email: chesantgar@hotmail.com; Escuela Universitaria de Enfermería La Paz, Universidad Autónoma de Madrid, Departamento de Enfermería Universidad de Alcalá de Henares (Madrid) ⁶ Fundación para el Desarrollo de la Enfermería, C, Veneras 9, Madrid, España. email: directora@fuden.es Introduction: Pain always has been one of the main problems nurses have been to cope, this problem grows in newborn cases because they can't put in words her pain experience. An additional problem has to do with the fact that there are different ways to express pain according to gestational age. First, this paper tries to identify the more frequent difficulties nurses have to cope with in order to palliate pain of newborn in intensive care units (NICU). Second, we will point out some of the measures nurse can carry out to manage newborn's pain. Materials and method: This paper is based both in a critical bibliographical review and an analysis of the authors' clinical and formative experience. Results and discussion: Nurse has at her disposal a wide range of measures to prevent and/or to reduce pain in newborn. First, we can find general measures of comfort, which exist to prevent improve comfort. In order eliminate newborn's pain nurse has also at her hand a group of useful measures such as the administration of sucrose and/or the induction of no nutritional suction, to promote the use of kangaroo's method (contact skin with skin) or the use of caressing during or immediately after of a painful procedure. This is a group of simple but effective measures to limit pain in newborn which nurse must include in her daily practice. Conclusions: As we have pointed out, nurse has a variety of measures that can and must be carried out to handle newborn's pain in NICU. In our opinion, some of the strategies of professional improvement would include: (1) a increased awareness among health professionals to the pain suffered by newborn in the NICU CU and (2) the strengthening of autonomous nursing activities in relation to the pain.

<p>OC-148</p>	<p>THE MANAGEMENT OF PAIN IN NEWBORN INTENSIVE CARE UNITS AND THE DEBATE ON THE HUMAN BOUNDARIES: PRACTICAL AND PHILOSOPHICAL CONSIDERATIONS Blanco F¹, Vázquez A², Sellán C⁴, Díaz ML³, Santamaría JM⁵, Arribas A⁶</p> <p>¹ Facultad de Psicología Universidad Autónoma, Ciudad Universitaria de Cantoblanco, Madrid, España. email: florentino.blanco@uam.es ² Hospital Universitario La Paz, Pº Castellana 261, Madrid, España. Email: avazsel@yahoo.es ³ Escuela Universitaria de Enfermería La Paz, Universidad Autónoma de Madrid, Pº Castellana 261, Madrid, España. email: mluisa.diaz@uam.es ⁴ Escuela Universitaria de Enfermería La Paz, Universidad Autónoma de Madrid, Pº Castellana 261, Madrid, España. email: c.sellan@uam.es ⁵ Fundación para el Desarrollo de la Enfermería, C, Veneras 9, Madrid, España. email: chesantgar@hotmail.com; Escuela Universitaria de Enfermería La Paz, Universidad Autónoma de Madrid, Departamento de Enfermería Universidad de Alcalá de Henares (Madrid) ⁶ Fundación para el Desarrollo de la Enfermería, C, Veneras 9, Madrid, España. email: antonioarribas@hotmail.com</p> <p>Introduction: The symbolical nature of pain may be confirmed not only in the variety of cultural and personal ways of experiencing and expressing it (see Le Breton, 1999) but also in the way we socially organize ourselves to face pain and its consequences. This paper focuses in this second pathway. Reflexive consciousness of pain uses to be considered a feature of humanity. So the management of pain in NICUs is often conditioned by the ambiguity of the phenomenological experience of pain in newborns. If pain is only to be experienced from the first person perspective and then translated by symbolic means to the perspective of the other, the lack of symbolic competence in newborns exacerbates the ambiguity of pain. This ambiguity is often increased by the more radical ambiguity of the very idea of life along these scenarios. Materials and procedures: This paper attempts to analyze the discourse of nurses around the politics of analgesic management in NICUs as a way of reflect on the ubiquity and instability of such notions as humanity, artificiality, life or death in the dynamics of care. A focal group debate has been used in order to elicit conflicts which allowed the emergence of arguments on these topics. Ten cards presenting dilemmatic stories on pain in NICUs were used to center the debate. Four nurses working in NICUs participated in the debate. Results: Our provisional results show the pervasive instability of the criteria used by nurses in their decisions on the management of pain. One of the most frequent sources of instability and ambiguity has to do with the relative lack of professional autonomy and support when analgesic procedures have to be used. Conclusions: Our results points out the philosophical and cultural ground of the politics of pain in the extreme scenario of NICUs, where the boundaries between life and death are always to be questioned.</p>
<p>OC-149</p>	<p>THE PAIN NURSING DIAGNOSES (ACUTE AND CHRONIC): A REALITY WHICH LIMITS THE POPULATION CARE Santamaría JM¹, Arribas A², Sellán C³, Vázquez A⁴, Díaz ML⁵, Amezcua M⁶</p> <p>¹Fundación para el Desarrollo de la Enfermería, C, Veneras 9, Madrid, España. email: chesantgar@hotmail.com; Escuela Universitaria de Enfermería La Paz, Universidad Autónoma de Madrid, Departamento de Enfermería Universidad de Alcalá de Henares (Madrid) ²Fundación para el Desarrollo de la Enfermería, C, Veneras 9, Madrid, España. email: antonioarribas@hotmail.com ³Escuela Universitaria de Enfermería La Paz, Universidad Autónoma de Madrid, Pº Castellana 261, Madrid, España. email: mluisa.diaz@uam.es ⁴Hospital Universitario La Paz, Pº Castellana 261, Madrid, España. email: avazsel@yahoo.es ⁵Escuela Universitaria de Enfermería La Paz, Universidad Autónoma de Madrid, Pº Castellana 261, Madrid, España. email: c.sellan@uam.es ⁶Fundación para el Desarrollo de la Enfermería, C, Veneras 9, Madrid, España. email: directora@fuden.es</p> <p>Introduction: Diagnosis of care related with the Pain, formulated by NANDA (North American Association of Nursing Diagnosis), refer to it as Chronic Pain and Acute Pain. This fact limits in the time the case mix of care problems and it moves away from the conceptual models posed by human care problems as limitations of not compensated action by the person or their carers. The CENES project (<i>Conocimiento Enfermero Estandarizado</i>, Standardized Nursing Knowledge) extends this categorization for implementation in computer systems. Materials and method: This paper shows a study of knowledge acquisition through a strategy of</p>

	<p>extraction and deduction (which has involved more than 600 nurses). This paper shows a study of knowledge acquisition through a extraction and deduction strategy (which has involved more than 600 nurses). Results and discussion: This study has allowed to standardize the entire "journey methodological" normalizing all variables described in the bibliography. Many variables of pain diagnoses in the field of Nurse have been shown as inter-diagnostic variables, both of symptomatic and etiological. Conclusions: New diagnostic labels should be developed to diagnose problems related care Pain Management. New diagnostic labels should be developed to diagnose problems related care Pain Management. Imported languages of associations must be completed effectively and efficiently through real case studies and comprehensively with the new trends in care worldwide. This study has achieved a double objective, to standardize the language proposed by NANDA, a fact that the association itself had not yet achieved, and to generate knowledge that can be used by other health Disciplines.</p>
<p>OC-150</p>	<p>CONSTRUCTION OF THE PAIN'S MEANING Fernández, L</p> <p>Facultad de Enfermería. Universidad de la República. Jaime Cibils 2810.Tel.: 6130036. Fax: 9248727. Montevideo. Uruguay email: liaofer@hotmail.com</p> <p>Introduction: Certain competitions are needed to handle the pain in pediatrics, due to the fact that small children communicate their painful experiences of diverse nonverbal forms. For a long time one supported that for his biological immaturity - the children did not perceive the pain in the same way and intensity as the adult, that the pain was less perceptible, more tolerable, that was leaving scanty or void records in the memory. According to the evolutionary development, in the fetus there have been demonstrated that from 7^a week of age gestational sensory cutaneous recipients appeared in region perioral. The newborn child has the anatomical and functional components for the perception of the pain. The evidence holds that the painful procedures can have prolonged effects in his neurological and psychosocial development. The considered interventions of routine on the part of the equipment of health can turn out to be a stressful experience for the children, which are translated in dramatic changes in the vital parameters. Material and methods: There was realized a study of qualitative cut, applying Weiss's methodology, to identify the construction of the meaning of the pain in the personnel of health in pediatric services and how they act in consequence. The above mentioned study was realized in the major pediatric hospital center of the country, throw out interviews in depth and non-participant observations, for 1 year. Results and discussion: The elaborated categories and his components reveal that they handle conceptions of forefront on the pain and his treatment, but this does not accompany on the practice. Conclusions: a gap Exists between the speech on the importance of treating the pain and to the personnel's work. The weight of the personal experiences during the infancy of the personnel plays a preponderant role the moment to value and treat the pain of the pediatric patients.</p>
<p>OC-151</p>	<p>NURSING INTERVENTIONS FOR THE MANAGEMENT OF PAIN IN PEDIATRIC PATIENTS. Sellán MC¹, Díaz ML², Vázquez A³, Amézcuca M⁴, Santamaría JM⁵, Blanco F⁶</p> <p>¹ Escuela Universitaria de Enfermería La Paz, Universidad Autónoma de Madrid, Pº Castellana 261, Madrid, España. email: c.sellan@uam.es ² Escuela Universitaria de Enfermería La Paz, Universidad Autónoma de Madrid, Pº Castellana 261, Madrid, España. email: mluisa.diaz@uam.es ³ Hospital Universitario La Paz, Pº Castellana 261, Madrid, España. email: avazsel@yahoo.es ⁴ Fundación para el Desarrollo de la Enfermería, C, Veneras 9, Madrid, España. email: directora@fuden.es ⁵ Fundación para el Desarrollo de la Enfermería, C, Veneras 9, Madrid, España; Escuela Universitaria de Enfermería La Paz, Universidad Autónoma de Madrid; Departamento de Enfermería Universidad de Alcalá (Madrid). email: chesantgar@hotmail.com ⁶ Facultad de Psicología Universidad Autónoma, Ciudad Universitaria de Cantoblanco, Madrid, España. email: florentino.blanco@uam.es</p> <p>Introduction: Pain is a reality, it is a subjective experience which is culturally constructed and socio-historically determined since the earliest childhood. The importance that each person gives to a painful experience will vary according to its features: type of pain, duration, intensity, impact on daily life and on life projects. Approaches for the treatment of pain have changed and improved as our knowledge about the neurophysiology and biochemistry of pain increased, and the different treatment pathways became more effective; therefore, we can take advantage of both pharmacological and non-pharmacological therapeutic</p>

	<p>interventions. Nursing professionals have capabilities to act in situations of pain and suffering at different stages of human development. The goal of our study was to assess the degree of knowledge about therapeutic interventions not dealing with drug administration in nursing, as well as their degree of implementation in the professional practice with pediatric patients. Material and methods: It has been carried out a interpretative-transversal study and information has been obtained through a specifically designed questionnaire. The selected population was consisted of nurses which work in different units of children's Hospital. Results and discussion: Some of the results show an incomplete evaluation of pain and poor use of analgesic techniques in the common procedures within the hospital context. The drug treatment is commonly used as the first option to decrease pain, whereas non-pharmacological treatments are used less frequently. Conclusions: In our opinion continuous training is necessary in order to strengthen those autonomous activities that nurses can carry out in relation to pain, the awareness of health workers towards pain-suffering pediatric patients should be increased, the difficulty of using this type of intervention by the lack of staff in the hospital units and also the need to develop postgraduate studies in Pediatric Nursing.</p>
OC-152	<p>FARMACOTERAPEUTIC AND OTHERS THERAPEUTIC ALTERNATIVES IN CHILDREN WITH MENTAL DISORDERS. NURSING CARES EXPERIENCE <u>Marta Otero Ceballos</u></p> <p>Professional Nurse. Auxiliary professor. Master Degree. National School of Public Health. 100 Ave and Perla st. Boyeros. Havana City. Cuba.</p> <p>Introduction: Since 1978 at Alma Ata declaration was evident the necessity of changes in Health Services including those directly involve with the attention of peoples affected by mental disorders. Multiples therapeutic experiences in order to humanize the attention of children and teenagers with mental disorder have been develop. They are “specials group” so in their treatment is frequently necessary the combination of therapeutics’ method and psycho pedagogic techniques in order to improve their live quality. Nurses as member of the multidisciplinary care team have an important role in the development of these therapeutic alternatives. Materials and Methods: A descriptive study in order to describe Cuban nurse’s experience using the combination of therapeutics’ method and psycho pedagogic techniques and also describe their advantage was made. Conclusions: Cuban’s nurses experiences using the combination of therapeutics’ method and psycho pedagogic techniques during the handling and care of children with mental disorders was evident and allowed to design a proposal of academic formation that include this specific experience.</p>
OC-153	<p>EDUCATIVE INTERVENTION TO INCREASE NURSE’S KNOWLEDGE ABOUT TECHNICAL RULES DURING VACCINATION <u>Noemí Reyes Quijala</u></p> <p>Professional Nurse. Instructor professor. Infectious diseases Master Degree. Pediatric Hospital “Juan de la Cruz Martínez Maceira” in Santiago de Cuba.</p> <p>Introduction: Vaccines are immunobiological substances which prevent diseases thought the acquired immunity with a minimal of unexpected reactions. Vaccination is an important activity carried out by nurses and the quality of this activity is very linked to the knowledge of the professional involved in this procedure. Materials and Methods: An educative intervention in order to increase nurse’s knowledge about technical rules of vaccination was done. The study was done during june 2008- june 2009 at the Pediatric Hospital “Juan de la Cruz Martínez Maceira” in Santiago de Cuba province. The universe of the study was 25 nurses involved in the vaccination process of patient at the institution. Some of the variables included were: technical qualification, ward of work. Conclusions: The development of the educative intervention is able to increase nurse’s knowledge in vaccination rules and the quality of nurse’s attention.</p>
OC-154	<p>RESEARCH IN SYSTEM AND HEALTH SERVICES BY NURSING IN THE ATTENTION OF PHARMACOTHERAPEUTIC COST <u>Nelcy Martínez Trujillo</u></p> <p>Professional Nurse. Assistant professor. Public Health Master Degree. National School of Public Health. 100 Ave and Perla st. Boyeros. Havana City, Cuba.</p> <p>Introduction: Health policy and systems research (HPSR) has been defined as the production and application of knowledge to improve how societies organize themselves in order to achieve health goals. It encompasses how societies plan, manage and finance health services as well as investigation of the role and interests of different actors in the health system. HPSR include the cost evaluation of technology like drugs and medicine</p>

	<p>in order to manage their rational use. Nurses are directly involved with farmacoterapeutic because they are responsible of drugs administration so the development of HPRS is an important element in order to economize their use. Materials and Methods: A transversal study was made. A bibliometric revision of 123 articles published during the period January 2000- December 2009 in 13 Nursing Reviews was made in order to describe nurse's development of HPSR in the specific field of drugs cost evaluation. The reviews selection's criteria were: Review for nurses; Internet access; Spanish, English, and French as language. Results and Discussion: Only a few numbers of articles describe this kind of research. There are different between the design and objectives of them. Conclusions: Although nurses are directly involve with drugs administration they don't use to develop this kind of research in order to economize their use.</p>
OC-155	<p>NURSES ACTIONS AND THERAPEUTIC ANSWER IN NEWBORN WITH MENINGOENCEPHALITIS DIAGNOSTIC. "WILLIAM SOLER" HOSPITAL. 2010 <u>Juana Mirtha Porra Casals</u></p> <p>Professional Nurse. Public Health Master Degree. Paediatric Hospital "William Soler", Havana, Cuba.</p> <p>Introduction: Meningitis can be a sequela of newborn sepsis. The incidence of neonatal sepsis is reported by some studies to be 1 to 8.1 in 1000 live births. The incidence of meningitis associated with new born sepsis is thought to be approximately 25 percent of those presenting with sepsis. Those infants often required long term antibiotic therapy, and often venous access is a problem. Nurse's actions are decisive in this kind of patient. Materials and Methods: A descriptive, prospective study during the period of January - July 2010 was done in order to evaluate the therapeutic answer of newborns meningoencephalitis diagnostic. Also nurse actions were analyzed in order to evaluate to what extend they contributed to improve patient answer. Some of the variables included were: Classification, sex, complications, therapeutics answer and nurses managements. Conclusions: Neonatal nurse's role during the management of newborns with meningoencephalitis diagnostic is crucial in order to obtain an adequate therapeutic answer and to avoid complications develop.</p>
OC-156	<p>NURSES ROL IN THE PHARMACOLOGICAL TREATMENT IN THE EXTRAVASATIONS WITH ONCOLOGICAL CHEMOTHERAPY <u>María Antonieta Arbezu</u></p> <p>Instituto Nacional de Oncología (INOR), Havana, Cuba.</p> <p>Introduction: Extravasation is the most common complication that arises when using nursing techniques, in patients with cancer that are been treated with cytostatic chemotherapy. The extravasation can get to the tissue inducing necrosis and it can appear far from injection point around 4 to 12 weeks after administering the injection. The proper procedure to treat these patients is critical. In order to update the work procedures in the Institute of Oncology and Radiobiology (INOR), a verification check was made to corroborate the grade of information that the nursing personnel had. Material and methods: A questionnaire was applied to nurses who had two or more years of work in the institution with at least one year experience treating patients with cytostatic administration to ambulatory patients as well as those hospitalize. Questions were asked directly, face to face, and they were focused on: the identification of an extravasation; primary, physical and pharmacological treatments; and practical advices for cytostatic administration. The answers were discussed with accuracy rates. Results: The question related with the identification of an extravasation, was answered correctly by the 25 selected nurses; the question about previous and physical treatments was answered accurately by the 95% and 92%, respectively. The 97% of nurses agreed on advices on how to avoid issues when administrating drugs. The grade of information about pharmacological treatment in the extravasation was poor (45%). Conclusions: Overall, nurses had correct information about primary and physic treatments, as well as identifying extravasations; while they had poor knowledge with reference to specific pharmacologic treatment. Actions have been taken in order to solve the problems that were found.</p>
W-10	<p>1ST INTERNATIONAL WORKSHOP ON PHARMACOECONOMY / 1ER TALLER INTERNACIONAL SOBRE FARMACOECONOMÍA</p>
OC-157	<p>IMPACT OF THE INTELLECTUAL PROPERTY RIGHTS ON THE PRICES AND ACCESS TO THE DRUGS <u>Joan Rovira</u>, Universidad de Barcelona. España.</p> <p><i>Resumen no disponible en el momento de la edición del libro. Abstract non available in the moment of the edition of the book of summaries.</i></p>

<p>OC-158</p>	<p>WHO GLOBAL STRATEGY AND PLAN OF ACTION ON PUBLIC HEALTH, INNOVATION AND INTELLECTUAL PROPERTY. AN ANALYSIS FROM A CUBAN POINT OF VIEW <u>Lisette Pérez Ojeda</u>, Rafael Pérez Cristiá</p> <p>Center for the State Control of Drug Quality (CECMED). Havana, Cuba</p> <p>The international debate on Intellectual Property Rights and the way those directly affect scientific health research and drugs access has reached a surprising level last years. An Intergovernmental Working Group was called to analyze this subject in the Pan-American Health Organization context, which concluded its work during 2008 adopting the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA). This strategy should provide a sustainable framework for research and development activities on those diseases which disproportionately affect developing countries. That implies that all of WHO country members, including Cuba, may adopt national measures to guarantee this strategy implementation. Firstly it has to be analyzed the elements defined by this strategy from a national point of view. The objectives of the investigation presented are to analyze the elements of the Global Strategy and Plan of Action and Cuba situation regarding its implementation, as well as to identify the priority actions according to WHO recommendations. For this; it was made an observation, exploratory and, retrospective study by a documentary analysis method using the Global Strategy and Plan of Action as basic document. The elements set out in this document were analyzed and besides national situation regarding this subject. There were also consulted WHO and PAHO documentation available as well as experts and no governmental organizations publications linked with IGWG process. Apart from that, it was also analyzed national information related to patent legislations, the work performed by the National Working Group created for that purpose and the reports of Cuba participation in the Intergovernmental Working Group. This analysis reached as conclusion that Cuba's strengths constitute advantages for the EGPA implementation. These advantages are: Cuban State political will; the scientific policies are established as state policies, a solid human resources training program emphasizing on health professional formation; the integration of primary health care to secondary and tertiary health care services; having institutions devoted to biomedical research with acknowledged international prestige and directly linked to the national health programs, moreover the strength of its biopharmaceutical industry and national regulatory authorities. It was also identified the subjects are needed to start working immediately such as: the need of approving a new Government Decree on patents, the implementation of mechanisms to strengthen the link between the intellectual Property National Office and competent Health Authorities to vigil the public health interest in the patents granting process and finally to study the position to be adopted by the country regarding the creation of an open code systems and drugs chimiolibrary proposed by GSPA.</p>
<p>OC-159</p>	<p>MEASURING THE PRICES OF MEDICINES FOR NATIONAL SYSTEM OF HEALTH IN CUBA <u>De la Cruz Pérez B.</u>, Jacobo Casanuevas OL, Pérez Cristiá R</p> <p>Center for the State Control of Drug Quality (CECMED). Havana, Cuba</p> <p>Introduction: Every day, there are more drugs that are available on the world market; however, in many countries there is no adequate access due to the high cost of these. When we talk about access to essential drugs means that there is equitable and affordable availability with a demonstration of its quality, safety and efficacy. It is very important to include in the health regulation the monitoring of the price of medicines. The absence of a standard model to evaluate the price is an obstacle to ensure access for medicines, that's why the State must devise strategies toward resources optimization, and in this way, to take advantageous procurement, therefore, the objective of this research is to design a system for the measuring of the medicine prices which are imported for National System of Cuban Health (SNS). Material and Methods: Two criteria are used to define the range of price proposed and as variables: Name of active ingredient, strength, pharmaceutical form, description in the medicines basic list (CBM), presentation, category of the medicinal product, referenced prices in other markets, WHO, and local historical price. Results and Discussion: Due to this system implementation, have been evaluated 67 medicines, with a minimum and maximum price proposal. From this list (67), the 88% is included in the CBM and belong to the category II. The 61% is found in a suitable pricing range, the rest, is out of the proposed range, so the importing company is advised to analyze the price offer by the supplier. The pharmaceutical form more frequently was solution for injection. Conclusions: The system allows monitoring of medicinal products which are imported to the SNS, price proposed by suppliers, ensuring timely access of medicinal products with quality, safety and efficiency at the lowest possible price.</p>

<p>OC-160</p>	<p>COST-EFFECTIVENESS EVIDENCE-BASED TREATMENT OF PARKINSON'S DISEASE <u>Álvarez M¹</u>, García M², Álvarez L³, Pedroso I⁴, Padrón A⁵, Díaz de la Fe A⁶</p> <p>International Center of Neurological Restoration (CIREN), Ave 25 No 15805, Reparto Siboney, Playa, Havana City . Cuba</p> <p>Introduction: Parkinson's disease (PD) is a progressive neurodegenerative condition. Estimated to affect 100–180 per 100,000 of the population and has an annual incidence of 4–20 per 100,000. There is a rising prevalence with age and a higher prevalence and incidence of PD in males. The goals of treatment differ depending on the patient's condition, in initial PD keep the patient's autonomy and independence as long as possible by controlling symptoms and in advanced PD manage complications arising from the use of drugs in this disease, such as dyskinesias, motor fluctuations and psychiatric complications. At the same time has a large and growing therapeutic arsenal. Some drug groups have been developed exclusively for this condition. These options should be analyzed to select the most effective, economical and safe. Material and Methods: Reviewed 333 articles, 308 scientific references in support and 25 introductions or comments. Select the investigations were related to the clinical question, preferably with a high scientific evidence. Reject the non-indexed journals or articles in the form of electronic advance. The basic steps in the process of producing a guideline are: developing clinical questions, systematically searching for the evidence, critically appraising the evidence, incorporating health economics advice, distilling and synthesising the evidence and writing recommendations, grading the evidence statements and recommendations, agreeing the recommendations, structuring and writing the guideline. Results and Discussion: We developed guidelines of clinical practice to unify criteria on various aspects of care for patients with Parkinson disease than taking aim at improving their quality of life.</p>
<p>OC-161</p>	<p>IMPACT OF DRUG BENEFIT POLICY ON CHRONIC DRUG THERAPY <u>Hsu J^{1,2}</u>, Price M^{1,2}, Fung V².</p> <p>¹Mongan Institute for Health Policy, Massachusetts General Hospital, Boston MA Harvard Medical School, Boston MA ²Center for Health Policy Studies, Kaiser Permanente Division of Research, Oakland CA email: Jhsu7@partners.org</p> <p>Introduction: There is limited information on how drug benefit policy affects chronic drug therapy. Methods: We examined the proportion of days covered (PDC) with drug supply in three therapeutic drug classes (cholesterol, antidepressants, and anticonvulsants). We compared the PDC for subjects who faced the standard Medicare Part D coverage gap with those who had generic-only coverage during the gap, using random-effects models adjusted for age, gender, and risk scores. There were 427,346 cholesterol drug users, 230,089 antidepressant drug users, and 88,095 anticonvulsant drug users (28%, 37%, and 41% with generic gap coverage, respectively). Results: Both brand and generic drug users with generic-only gap coverage had a higher PDC in each drug class, compared with generic drug users with no gap coverage (e.g., increase=3.3,95%CI:3.0-3.5 and increase=6.9,95%CI:6.6-7.1 for cholesterol drugs among brand and generic users, respectively). Among subjects with no gap coverage, brand drug users had a lower PDC in each drug class compared with generic users (e.g., decrease=4.0,95%CI:3.9-4.2 for cholesterol drugs). Entering the gap was associated with significant reductions in drug supply; however, the reduction was greater among subjects with no gap coverage and among subjects who were receiving a brand drug, compared to those receiving generic drugs prior to gap entry. Discussion: Generic-only gap coverage was associated with increased drug use among both generic and brand drug users in all three therapeutic drug classes. While patients with generic-only drug gap coverage had higher levels of drug use on average compared with patients with no gap coverage, brand and generic users in both groups faced significant reductions in drug use after reaching the gap. Conclusion: Drug benefit policies create strong incentives for patients, albeit not always in accordance with clinical goals. In particular, gaps in drug coverage are associated with poor adherence, particularly for patients taking brand drugs.</p>
<p>RT-04</p>	<p>"PHARMACOECONOMIC IN CUBA: PREPARATIONS TO ASSUME THE CHALLENGE"</p>

Currently, resources that may be spent in pharmacoeconomics expenditure are limited so it is necessary to rationalize their consumption and prioritize in the allocation of these resources to the options with higher economic advantages. Pharmacoeconomic studies will permit us to know what the efficiency of different therapeutic alternatives is so they will help to determine the therapeutic options that we should use in routine medical practice. The information of pharmacoeconomic studies will be important when negotiating price and reimbursement of new drugs as well as if we want that in both Primary Health Care and Hospital Care settings the therapeutic alternatives with the best cost/effectiveness relationship will be used routinely. Although the evaluation and uses of published pharmacoeconomic it dates it plows discussed, there are not doubts that the pharmacoeconomic literature is to vast and powerful source of information for pharmacists and others who must make decisions about services and products. The economic evaluation is consolidating in many countries like a tool for the analysis of the technologies and sanitary programs. However, the systematic, explicit and transparent use of the economic evaluation for the taking of decisions and the assignment of resources on the part of the directive of the sanitary system is only given in a relatively reduced number of countries, among those that the United Kingdom, Australia and United States highlight. In Cuba efforts are made to qualify professionals and leaders of the sector health and to motivate the investigations that include the economic analysis. To identify where and as applying the pharmacoeconomic in the country and if our professionals are prepared to make it, they are brought to debate in this intervention.

RESEARCH AND TEACHING ON PHARMACOECONOMY IN CUBA TODAY

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The health sector assumes the challenge of reaching the excellence of its services. It is imposed, therefore, the goal of making an efficient use of the resources and perfecting their control mechanisms. Because of this, there is a need to enlarge its knowledge about economy and its relationship with the health. This discipline, of relatively recent appearance, approaches very varied topics. Among them, the pharmacoeconomic evaluation like instrument for the taking decisions in the area of medications has a great importance. In Cuba, the formation of human resources and the pharmacoeconomic investigation comes developing for some years ago. Numerous professionals of different disciplines have been graduated in different courses. Along every year there are numerous scientific forums, national and international ones, that have taken place in the country, where a wide debate has settled down on the topic. The National School of Public Health (ENSAP), the Area of Economy of the Cuban Health Ministry (MINSAP), the Pharmacoepidemiology Development Centre (CDF) and the Institute of Tropical Medicine "Pedro Kourí", are some of the institutions that have prioritized the investigation and teaching in these topics, with tangible results. However, challenges still exist in this sense. A long road begins with a single step, this "to start to walk" in the context of the Cuban public health it should be each worker's concern to eliminate the unnecessary costs and to maximize the results, in narrow relationship with the quality of the offered service. The current situation of the Pharmacoeconomic in the country is a prelude that he/she announces the strong growth that will experience this science that already constitutes an interesting field of professional specialization in the future. Their value will be evaluated in the measure in that we have contributed to an improvement in the taking of decisions directed to improve the use of the medications and consequently the population's health.

OC-162

QUALITY ASSESSMENT OF ECONOMIC EVALUATIONS IN CUBAN MEDICAL JOURNALS. THE LAST TEN YEARS (1999-2009)

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Introduction: Economic evaluation is one of the tools that the manager has to promote the efficiency in the process of incorporating new health technologies. The objective of this paper was to assess the quality of original economic evaluations articles published in Cuban medical journals between 1999 and 2009, in order to identify areas of strength and weakness. **Material and Methods:** In each journal was made a research using the keywords: economic evaluation, cost-effectiveness, cost-benefit, cost-utility and cost-minimization. Accepted articles were categorized by study type, by journal and by year of publication. Previously was developed a checklist based on the Cuban guidelines for economic evaluations. 17 articles were identified for analysis. **Results and Discussion:** 2003 was the year with the highest number of papers (17.6%). The Cuban Journal of Pharmacy and the Cuban Journal of Public Health accumulated around the 40% of the articles

	<p>published on this decade. The items 'definition of a problem', 'definition of study aim' and 'identify alternatives' were considered as strengths. On the half of the papers were not clearly defined the horizontal time and the perspective. In the most of the papers the sensibility analysis was inexistent. Conclusions: The authors and referees should pay more attention to the methodological issues of the economic evaluations in order to improve the quality of such studies.</p>
W-11	<p>1ST INTERNATIONAL WORKSHOP ON EXPERIMENTAL AND MOLECULAR NEUROPHARMACOLOGY / 1^{ER} TALLER INTERNACIONAL DE NEUROFARMACOLOGÍA EXPERIMENTAL Y MOLECULAR.</p>
OC-163	<p>EVALUATION OF NEW MOLECULAR ENTITIES BELONGING TO TRIPLE REUPTAKE INHIBITORS IN ANIMAL MODELS OF DEPRESSION <u>SK Kulkarni and Ashish Dhir</u></p> <p>University Institute of Pharmaceutical Sciences, Panjab University , Chandigarh-160014, India.</p> <p>Major depression is a severe neuro- and psychological disorder that is associated with high degree of social stigma. The agents that increase the availability of the so-called classic neurotransmitters, serotonin, norepinephrine, and dopamine, have been the mainstay in the treatment of depression. In spite of the large number of antidepressants available at the present time, they are far from ideal and all or most of them are shown to have a similar slow, and frequently, incomplete response. One approach that may extend the therapeutic action of monoamine-based antidepressants is the use of compounds which exert a simultaneous action on more than one, two or more of the neurotransmitters. The discovery of venlafaxine (dual reuptake inhibitor of serotonin and norepinephrine) has encouraged medicinal chemists and pharmacologists to synthesize and test compounds having multiple targets (reuptake sites) for the antidepressant action. In recent years dopamine is gaining as one of the important modulators in behavioral disorders like mental depression. In the present study, we have evaluated some of the new molecular entities hypothesized to block the reuptake of norepinephrine, serotonin and dopamine known as triple reuptake inhibitors using animal behavioural paradigms like the mouse forced swim and tail-suspension tests. Substitution of methoxyl or dimethoxyl group at phenyl ring of phenylethylamine moiety enhanced the antidepressant-like activity of these compounds. Further, neurochemical analysis revealed that the compounds with methoxyl derivative at the phenyl ring increased the levels of norepinephrine, serotonin and dopamine. In conclusion, these triple reuptake inhibitors could be potential drugs for the treatment of patients who are suffering from pharmacoresistance depression and still left untreated.</p>
OC-164	<p>DOPAMINE/ADENOSINE INTERACTIONS RELATED TO MOTOR CONTROL AND MOTIVATION: A2A ANTAGONISTS AS PHARMACOTHERAPIES IN NEUROLOGY AND PSYCHIATRY <u>Salamone JD¹</u>, Correa M², Nunes EJ¹, Collins LE¹, Randall PA¹, Santerre JL¹, Pardo M²</p> <p>¹Dept. of Psychology, University of Connecticut, Storrs, CT, USA 06269-1020. Email: john.salamone@uconn.edu ² Area de Psicobiol., Dept. Psicol., Universitat Jaume I, 12071, Castello, Spain.</p> <p>Introduction: Forebrain dopamine (DA) is a critical component of the brain circuitry regulating aspects of motivation and motor control. Adenosine A_{2A} receptors are co-localized with D₂ receptors on striatal medium spiny neurons. The present work was undertaken to determine if adenosine antagonists with different patterns of receptor selectivity (A_{2A} antagonists, non-selective adenosine antagonists, A₁ antagonists) could reverse the motivational and motor effects of DA antagonism in rats and mice, and to determine if these effects depended upon whether D₁ or D₂ receptors were being antagonized. Material and Methods: DA antagonists (ecopipam, eticlopride, haloperidol) were administered to produce alterations in behavioural activation and effort-related decision making. Rats with impaired DA transmission are less active, and they also reallocate their motivated behavior away from food-reinforced tasks with high response requirements, instead selecting less effortful food-seeking behaviors. For these studies, behavioral tasks included locomotor activity, operant conditioning, and performance in a T-maze barrier task. Additional experiments studied the ability of adenosine antagonists to reverse the oral tremor induced by the DA antagonist pimozone; this procedure is used as a rodent model of parkinsonian tremor. Various adenosine antagonists (nonselective adenosine antagonists: caffeine and theophylline; A_{2A} antagonists: MSX-3 and istradefylline; A₁ antagonists: DPCPX and CPT) were tested for their ability to reverse the effects of DA antagonism. Results and Discussion: The effects of DA antagonism on behavioral activation, effort-related decision making and oral tremor were reversed by co-administration of adenosine A_{2A} antagonists and nonselective adenosine antagonists, but not by A₁ antagonists. Generally,</p>

	<p>adenosine A_{2A} antagonists could more easily reverse the effects of D2 antagonists than those of D1 antagonists. These observations are consistent with the co-localization of A_{2A} and D₂ receptors. It is possible that adenosine A_{2A} antagonists could be used to treat effort-related symptoms of depression as well as idiopathic and drug-induced parkinsonism.</p>
<p>OC-165</p>	<p>MARKERS OF CARDIOVASCULAR RISK IN DEPRESSION: EFFECTS OF TREATMENT <u>Halaris A</u></p> <p>Loyola University Stritch School of Medicine, 2160 South First Avenue, Maywood, Illinois, USA. email: ahalaris@lumc.edu</p> <p><u>Introduction:</u> Morbidity and mortality of cardiovascular disease (CVD) is exceedingly high worldwide. Depressive illness afflicts a significant portion of the population in all countries and a high co-morbidity exists between these two conditions. Mechanisms accountable for this co-morbidity include sympathoadrenal activation, homeostatic imbalance between the sympathetic and the parasympathetic systems with diminished vagal tone and loss of heart rate variability (HRV) in depression; hypothalamic-pituitary-adrenal axis activation resulting in hypercortisolemia; platelet activation and hypercoaguability; and, a persistent low-grade pro-inflammatory status. <u>Material and Methods:</u> We have studied 35 patients with Major Depressive Disorder (MDD) and 20 healthy control subjects. All study participants were medically healthy and showed no clinical or laboratory signs of cardiovascular disease. We used platelet aggregation and flow cytometry to assess platelet activation status. We used Randox methodology to assess pro-inflammatory cytokines. We used the SphygmoCor software (AtCor Medical Inc.) to measure arterial stiffness and HRV and its time and frequency domain components. Patients received escitalopram for 12 weeks. All procedures were obtained at baseline and at the end of treatment. Appropriate rating instruments were used at specified intervals to assess response to treatment. <u>Results and Discussion:</u> Compared to the healthy subjects, MDD subjects showed platelet activation and significant elevations in pro-inflammatory cytokines. Similarly, they showed diminished HRV and evidence of arterial stiffness that was most pronounced amongst postmenopausal females. Escitaloram produced symptom remission in most patients. However, there were variable effects on the biomarkers studied with some showing a trend toward normalization while others did not. <u>Conclusions:</u> We confirmed and expanded previously reported findings in the literature. MDD is a disorder that poses significant cardiovascular risk that must be assessed by means of specialized tests and treated vigorously. <u>References:</u> A. Halaris. Co-morbidity between depression and cardiovascular disease. <i>International Angiology</i> 28 (2), 92-99 (2009).</p>
<p>OC-166</p>	<p>ACTIVATION OF THE LIGAND-OPERATED CHAPERONE SIGMA-1 PROTEIN IS PROTECTIVE AGAINST NEURODEGENERATIVE PROCESSES. THE THERAPEUTIC POTENTIALS OF SIGMA-1 RECEPTORS LIGANDS AS NEUROPROTECTANTS IN PRECLINICAL ALZHEIMER'S DISEASE MODELS <u>Tangui Maurice</u> (1)</p> <p>¹, Johann Meunier², Fanny Malhaire-Ferreux¹, Emeline Keller¹, Susanna Malmström¹, Vanessa Villard, Alexandre Vamvakides (2)</p> <p>Insertm U . 710, University of Montpellier 2, 34095 Montpellier, France Anavex Life Sciences, 15351 Pallini, Greece¹</p> <p>²<i>Cellular Pathobiology Section, Cellular Neurobiology Research Branch, Intramural Research Program, NIDA, NIH, DHHS, Baltimore, MD 21224, USA.</i></p> <p>The sigma-1 receptor (S1R) has been historically identified as a subtype of opiate receptors, 30 years ago. After the 90's, considerable progresses have been made on the comprehension of its exact nature and cellular function. It appears to be an intracellular protein highly expressed in the brain, in neurons and glial cells, and localized on endoplasmic reticulum (ER), mitochondria and plasma membranes. The S1R acts as an ER chaperone protein by modulating ER protein activation and inositol trisphosphate receptor (IP3R)-dependent calcium release. The S1R also, contributes to lipid rafts formation and plasticity of the plasma membrane and was identified as a ligand-operated molecular chaperone targeting the mitochondrion-associated ER membrane (Hayashi & Su, <i>Cell</i> 131, 596, 2007). Drugs selectively activating S1R show anti-amnesic, antidepressant and neuroprotective properties in rodents. In particular, S1R agonists protect cortical neurons cultures from the toxicity induced by application of amyloid beta₂₅₋₃₅ peptide (Ab) (Marrazzo et al., <i>Neuroreport</i> 16, 1223, 2005). We analyzed their in vivo protective activity against Alzheimer's disease (AD)-related neurotoxicity. Central administration injection of aggregated oligomeric preparation of amyloid</p>

	<p>peptides (Aβ) into the rodent brain is has been validated as a pathomimetic validated non transgenic model of AD. Aβ induces, after one week, ER stress, oxidative stress, neuroinflammation, mitochondrial damage, then lead to cell loss, and learning and memory deficits, highly reminiscent of AD. We Using this model, we examined demonstrated the neuroprotective activity of S1R ligands acting either selectively, like (PRE-084,) or nonselectively, as , like the acetylcholinesterase ChE inhibitor and S1R ligand (donepezil) or as the muscarinic and S1R ligands (ANAVEX1-41, or ANAVEX2-73) (Meunier et al., Brit J Pharmacol Br J Pharmacol 149, 998, 2006; Villard et al., Neuropsychopharmacol Neuropsychopharmacology 34, 1552, 2009 ; J Psychopharmacol 2010). . The compounds prevented the hippocampal cell loss, the induction of astrocytic reaction in the hippocampus and cortex, the induction of oxidative stress or proapoptotic caspases and the resulting learning and memory deficits. One of prior effect was identified as protection against Aβ-induced ER stress, in coherence with the chaperone role of the S1R. A molecular analysis in the hippocampus extracts of the changes in expression of IP3R subtypes and sarcoendoplasmic reticulum Ca²⁺-ATPase pump type-3 (SERCa3), using semi-quantitative RT-PCR, showed that showed thatSERCa3 expression is upregulated by Ab toxicity and the neuroprotective activity of S1R ligands, acting at IP3R, involves an upregulation of IP3RR type1 and SerCa pumps expression and release of ER-dependent caspases, suggesting a direct role on ER calcium homeostasis. Finally, mixed compounds showed a clear synergistic efficacy between their cholinergic and S1R agonist activities, with significant efficacy at 10-100 μg/kg systemic doses. These data identify a new mechanism for neuroprotective agents targeting ER chaperones in neurodegenerative AD, and point out the interest in speeding up selective or non selective S1R drugs at the clinical level, which are able to target ER stress, one of first hallmark in Alzheimer's disease.</p> <p>Disclosure : JM was recipient of a PhD grant from <i>Fondation pour la Recherche Médical</i> (Paris, France).</p>
<p>OC-167</p>	<p>EFFECTS OF METHYL AND METHOXY DERIVATIVES OF PHENCYCLIDINE ON FOOD AND WATER INTAKE IN MALE WISTAR RATS Salari AA¹, Solati J², Ahmadi A³, Saeedi N², Zavarmand S², Amir-kamali S² ¹<i>Young Researchers Club, Islamic Azad University, Karaj branch, Karaj, Iran</i> email: aa.salari@yahoo.com ²<i>Department of Biology, Faculty of Sciences, Islamic Azad University, Karaj branch, Karaj, Iran</i> ³<i>Department of Chemistry, Faculty of Sciences, Islamic Azad University, Karaj branch, Karaj, Iran</i></p> <p>Introduction: Drinking and feeding behavior is known to be modulated by various neurotransmitters and receptors. Different structures which are involved in regulation of ingestive behavior. There is direct and circumstantial evidence to indicate that some circuits involved with ingestive behavior include glutamatergic elements. Phencyclidine (1-(1-phenylcyclohexyl) piperidine, CAS 956-90-1, PCP, I) and its derivatives as a NMDA glutamatergic receptor antagonist, have shown many pharmacological and behavioral effects. The present study examined whether administration of PCP and its methyl and methoxy derivatives affect food and water intake under deprivation. Materials and Methods: In this research PCP and its Methyl and methoxy derivatives synthesized and their effects on ingestive behaviours have been investigated. Animals were deprived for 24 h before tested for food and water intake. PCP and its derivatives were injected intraperitoneally and treated groups measured 1-12 h for food and 30-180 mins. for water intake post-injection. Results and Discussion: The results showed that, both of derivatives, can increase food and water intake in comparison to the PCP and saline groups. Conclusions: Methyl and methoxy derivatives of Phencyclidine may affect central systems that are involved in feeding behavior.</p>
<p>OC-168</p>	<p>CURRENT TRENDS AND PRECLINICAL RESULTS IN NEUROPROTECTION IN STROKE. García Rodríguez JC¹, Rodríguez Cruz Y, ² Mengana Támos Y¹, Sosa Testé I¹</p> <p>¹National Center for Laboratory Animals Breeding. Cuba. email: neurotox@cenpalab.inf.cu ²Institute of Medical Sciences of Havana. Faculty Playa "Victoria de Girón". Cuba.</p> <p>Introduction: Stroke can be devastating, but the complete restoration of the brain is possible. Therapeutic action quickly, safely and effectively is the key to minimize brain injury. Thrombolytic and neuroprotective properties are the fundamental objective of the current preclinical research and clinical trials for the treatment of acute stroke. A brief summary of this preclinical and clinical research will be presented and discussed. Objective: To discuss the current trend of neuroprotection in stroke, illustrating the main preclinical and clinical results achieved to date. Methods: A critical review of the literature (2005-2010) in stroke [1]. Preclinical studies and clinical trials and recent preclinical results of the authors [2]. Results: The factor plasminogen activator and risk their generalization. Neuroprotection in acute stroke treatment highlights albumin, magnesium, citicoline, hypothermia and hyperbaric oxygen therapy. As anti-inflammatory eicosanoids. The growth factors erythropoietin (EPO) and colony-stimulating factor granulocyte (G-CSF)</p>

	<p>have shown encouraging results in clinical trials. We discuss the key preclinical results obtained in our country with two molecules produced by Cuban biotechnology. It discusses the advantages of applying variants of erythropoietin with erythropoietic neuroprotective action but not as Asialo EPO, carbamylated EPO and EPO Neuro-which has potential benefits to other variants developed [2]. Conclusions: Cuba has satisfactory evidence of preclinical and molecules produced by Cuban biotechnology that may be assessed as a neuroprotective in the acute phase of stroke.</p> <ol style="list-style-type: none"> 1. Kidd, P.M. (2009) Integrated Brain Restoration after Ischemic Stroke – Medical Management, Risk Factors, Nutrients, and other Interventions for Managing Inflammation and Enhancing Brain plasticity. <i>Alternative Medicine Review</i> 14, 14-35. 2. Rodríguez, J.C.G., and Teste, I.S. (2009) The Nasal Route as a Potential Pathway for Delivery of Erythropoietin in the Treatment of Acute Ischemic Stroke in Humans. <i>TheScientificWorldJOURNAL</i> 9, 970-981.
OC-169	<p>C-PHYCOCYANIN AMELIORATES EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS AND INDUCES REGULATORY T CELLS Nielsen Lagumersindez-Denis¹, Giselle Pentón-Rol², Gregorio Martínez-Sánchez¹, Majel Cervantes-Llanos², Emilio Felino Acosta-Medina¹, Viviana Falcón-Cama², Ruby Alonso-Ramírez³, Carmen Valenzuela-Silva², Efraín Rodríguez-Jiménez², Alexey Llópez-Arzuaga², Javier Marín-Prida¹, Pedro Antonio López-Saura², Gerardo Emilio Guillén-Nieto², Eduardo Pentón-Arias^{2,3}.</p> <p>¹ Center for Genetic Engineering and Biotechnology (CIGB), PO Box 6162, Havana. Cuba ² Center for Research and Biological Evaluations, Institute of Pharmacy and Food Sciences, University of Havana, PO. Box: 430. Cuba. ³ Center of Molecular Immunology, PO. Box 16040. Cuba.</p> <p>For decades Experimental Autoimmune Encephalitis (EAE) has remained as an unsurpassed multiple sclerosis (MS) animal model. C-Phycocyanin (C-Pc) has been reported to exhibit pharmacological properties that may be expected to symptomatically improve EAE and MS. However, in this study we reveal a basic underlying mechanism that may provide a new approach to the rationale of the overall beneficial effect of this natural antioxidant. We demonstrate that C-Pc is able to trigger mechanisms preventing or downgrading EAE expression and induces a regulatory T cell (Treg) response, in peripheral blood mononuclear cells (PBMC) from MS patients. These results agree with reports suggesting that Treg limit acute MS attacks and that C-Pc may act as a neuroprotector and thereby reverts the organic and functional damage in neurodegenerative disorders of the central nervous system (CNS). Moreover, evidence is provided on the antioxidant activity of C-Pc within the CNS, intended to improve the myelin and axonal damage of EAE induced Lewis rats. Our results indicate that specific Treg activation may represent a central and essential mechanism in supporting the therapeutic potential of C-Pc for MS and may lead to new and more effective therapies; this property would then complement and enhance other proven active principles such as interferons (IFN), giving rise to combined therapies.</p>
OC-170	<p>NEUROPROTECTIVE EFFECTS OF BM-21, AN EXTRACT FROM <i>Thalassia testudinum</i>, ON GLOBAL CEREBRAL ISCHAEMIA IN GERBILS R. Menéndez, T García, A Garateix, G Marrero, RA Morales, EL Regalado , A Laguna, A Palmero</p> <p>Departamento de Farmacología, Centro de Bioproductos Marinos. Agencia de Medio Ambiente. CITMA. La Habana, Cuba. email:roberto.menendez@infomed.sld.cu</p> <p>Previous studies have demonstrated the neuroprotective effect of BM-21(40 and 400 mg.kg⁻¹) against acrylamide-induced neurotoxicity. Oral administration of BM-21 increased antioxidant status in sciatic nerve and in brain, suggesting that this citoprotective effect is at least in part the result of its antioxidant properties. Also, the fact that the extract produced beneficial effects against oxidative stress in brain, suggests that the antioxidant compounds of BM-21 are able to readily cross blood brain barrier. A great deal of evidence suggests that oxidative stress is one of the primary factors in triggering and maintaining the neuronal damage in ischemia. Thus, we tested BM-21 in two model of global ischemia in Mongolian Gerbil. Permanent unilateral occlusion of the right common carotid artery (CCA) resulted in a severe neurological deficit and a high mortality. However, oral administration of BM-21 at 200 and 400 mg.kg⁻¹ once-a-day for 8 days prior to occlusion significantly decreased mortality (35,2 and 51,4 %; respectively), neurological signs (50.0 and 51.6%, respectively) and significantly attenuated locomotor hyperactivity. Furthermore, in the ischemia /reperfusion model, oral administration of the extract (400 mg.kg⁻¹) using the same dosage schedule, prevent mortally and brain infarction volume after 15 min-ischemia and 72 h-reperfusion induced by the bilateral</p>

	<p>occlusion of the CCA. Also, BM-21 significantly reduced ($p < 0.05$) the stroke index 12 hours following release of bilateral carotid arterial occlusion. Additionally, oral administration of BM-21 to normal gerbils at the same dose significantly decreased basal MDA concentrations in brain tissue and the susceptibility of brain homogenates to “in vitro” metal-induced lipid peroxidation. In conclusion, data of present work showing a neuroprotection in animals pretreated with BM-21 against ischemia-induced brain injury that could be mediated at last partially, through reduction in oxidative stress in brain. However the central neuroprotective effects of BM-21 observed in the present study need to be substantiated in other animal models more closely related to clinical ischemic events.</p>
<p>OC-171</p>	<p>MANGIFERIN: A NEUROACTIVE POLYPHENOL Pokorski M¹, Delgado Hernández R², and Rekawek A¹</p> <p>¹Medical Research Center, Polish Academy of Science, 5 Pawinski St., 02-929 Warsaw, Poland. email: m_pokorski@hotmail.com ²Drug Research and Development Center, Drug Research and Development Center (CIDEM). Ave 26, No. 1605 Boyeros y Puentes Grandes, CP 10600, Plaza de la Revolucion, Ciudad Habana, Cuba.</p> <p>Introduction: Mangiferin is a polyphenol present in Mango trees, having a spate of purported beneficial health effects, including nervous disorders. Respiration is essential for the maintenance of biological health. In the present study we set out to determine the influence of mangiferin on the hypoxic ventilatory reflex (HVR), generated by carotid body chemoreceptors. The rationale for the study design was based on the following premises: 1/ mangiferin is a scavenger of free radicals and an iron chelator; 2/ hypoxia increases the formation of reactive oxygen species (ROS) in carotid chemoreceptors, and both ROS and iron chelation stabilize hypoxia inducible factor-1α (HIF-1α), a key step in the hypoxia-sensing process. We hypothesized that mangiferin is well suited to down-regulate HVR through either depleting ROS or prior chelation-induced HIF-1α stabilization. Since respiration is controlled at both peripheral and central levels, we started off with assessing the ability of mangiferin to penetrate into the brain. Materials and Methods: Wistar rats were used for the study. Mangiferin was injected in a single dose of 300mg/kg, i.p. The study consisted of the biochemical and functional parts. In the former, thin-layered chromatography and UV/VIS spectrophotometry were used to trace the recovery of mangiferin in brain homogenates after its i.p. administration. In the latter, the ventilatory responses to 8% O₂ in N₂ were taken before and 40min after mangiferin in spontaneously breathing unsedated rats in a whole body plethysmograph. Results: We demonstrate that mangiferin did not cross the blood-brain barrier after systemic injection, as its presence could not be substantiated in brain extracts. We did not observe any signal alike the mangiferin standard; neither on TLC plates nor in UV/VIS spectra. At the functional level, we found, however, that mangiferin significantly depressed the profile of HVR over the 3-min test. Peak hypoxic ventilation decreased by 733\pm145(SE)ml/min/kg ($P < 0.02$). To distinguish between the scavenging and chelating mechanisms of mangiferin we examined its effects on HVR after chronic antecedent iron chelation with ciclopirox olamine (20mg/kg daily for 1wk). The dampening effect on HVR of mangiferin was preserved in pre-chelated rats, which points to the preponderance of the antioxidant/scavenging over chelating properties of mangiferin in its ventilatory effects. Conclusions: Although the exact determinants of mangiferin action in ventilatory control remain unclear, we believe we have shown that mangiferin interacts with peripheral neural chemosensory pathways which are central to the generation and processing of hypoxic hyperventilation. The study underlines a novel modulatory role of oxidative signaling in hypoxia-sensing, which broadens the possible therapeutic application of mangiferin toward the regulation of ventilation in pulmonary pathologies.</p>
<p>OC-172</p>	<p>FROM THE IDENTIFICATION OF PHARMACOLOGICAL TARGET TO THE SYNTHESIS OF NEW NEUROPROTECTORS COMPOUND. PRELIMINARY RESULTS AND FUTURE PERSPECTIVES René Delgado Hernández¹, Yanier Nuñez Figueredo¹, Laura García Pupo¹, Beatriz Garrido Suárez¹, Jeney Ramírez Sánchez¹, Estael Ochoa Rodríguez², Yamila Verdecia Reyes², Juan Enrique Tacoronte Morales³.</p> <p>¹Drug Research and Development Centre (CIDEM), Plaza, Havana, Cuba. ²Chemical Faculty, Havana University, Havana, Cuba. ³CIQ, Havana, Cuba.</p> <p>The neurological disorders are a serious problem of health in the world. The search of new neuroactive compounds more effectives and safe, represents today a challenge for the researchers that are investigating in this field. The Molecular Pharmacology laboratory of the Drug Research and Development Center (CIDEM), has as one of their biggest priorities, the evaluation of molecules obtained from different sources using <i>in vitro</i> and <i>in vivo</i> models of experimental neuropharmacology such as excitotoxicity, neuroinflammation,</p>

	<p>oxidative stress, anxiety, depression, epilepsy, cerebral ischaemia and neuropathic pain, among others. Also, our group works together with chemical-synthetic researchers from Havana University in the design of new molecules potentially active on Central Nervous System. In this moment the laboratory develops the evaluation of prenylated benzofenones and flavonoids obtained from natural sources; benzodiazepines, dihidropiridines and coumarins obtained by chemical synthesis and also, some proteins from recombinant technologies. The present work shows the main results obtained from the preliminaries studies and their perspectives for the development of new drugs neuroprotectives.</p>
<p>OC-173</p>	<p>AN INTEGRATIVE CHARACTERIZATION OF SCA2 IN CUBA: EPIDEMIOLOGICAL, GENETIC NEUROCHEMICAL AND ELECTROPHYSIOLOGICAL FINDINGS IN 7 926 CUBAN CARRIERS Velázquez-Pérez Luis, Sánchez-Cruz Gilberto, Galicia-Polo Lourdes, Herrera-Paneque Milena, García-Rodríguez Julio, Rodríguez-Labrada Roberto Laffita-Mesa Jose M, Almaguer-Mederos Luis, Aguilera Raul, González-Consuelo, Canales-Ochoa Nalia</p> <p>¹Centro para la Investigación y Rehabilitación de las Ataxias Hereditarias (CIRAH), Holguín, Cuba.</p> <p>Objective: To evaluate the clinical epidemiology, electrophysiological, molecular and neurochemical biomarkers of SCA2. Background: Spinocerebellar ataxia type 2 is the second most frequent dominant ataxia worldwide. In Holguin, the stable prevalence of SCA2 along time, despite the existence of genetic anticipation is likely the result of the high frequency of large normal alleles with pure CAG, which represent reservoirs of mutated alleles, driving to the continuous raising of new SCA2 cases. Methods: Availability of a high number of SCA2 carriers enables us to assess Clinical epidemiology, molecular, neurochemical and neurophysiological studies were done in all Cuban SCA2 families. Results: The highest frequency of SCA2 mutation was observed in Holguín province, where the prevalence rate is 163.18 per 100 000 inhabitants, but there are regions within where the prevalence reaches up to 700 per 100 000 people. The genetic anticipation was observed in the 80% of transmissions and the expansions were presented in 89.02%. The neurochemical analyses demonstrated a significant decrease of serum and CSF levels of Zn, Cu and Fe in patients. The neurophysiological studies showed the involvement of nervous structures since presymptomatic stages, specially the sensitive amplitudes and N20 and P40 components of the SSEPs. The progression of these abnormalities was correlated with disease duration, polyglutamine expansion size and ataxia score. The polysomnographic recording showed the severe REM pathology with insufficient muscle atonia and periodic legs movements (PLMs) occurs in several cases. The electronystagmographical studies showed a significant reduction of maximal saccade velocity (MSV) in patients and presymptomatic. MSV was negatively correlated with the polyglutamine expansion in both groups. Conclusions: Hereditary ataxias in Cuba make up the highest prevalence in the world. Electrophysiological abnormalities of peripheral nerves and somatosensory pathways reflect an early and progressive axonal damage. REM pathology can be associated with the pons, nigrostriatal and thalamic degeneration and PLMs may be related with a dysfunction of dopaminergic pathways. MSV is the most important electrophysiological biomarker for genetic researches of SCA2. Neurochemical results indicate an impairment of the microelements homeostasis in SCA2. These evidences support the application of new strategies for treating this disease.</p>
<p>OC-174</p>	<p>ASTROCYTE- INDUCED SYNCHRONIZATION AS A RELEVANT MECHANISM FOR EPILEPSY Martínez-Cancino R^{1,2}, Sotero RC¹</p> <p>¹National Bioinformatics Center (BIOINFO). InSTEC. Havana. Cuba. ²Cuban Neuroscience Center. Havana. Cuba.</p> <p>Introduction: Astrocyte in the brain has been increasingly recognized as having a critical role in normal brain function and neurological disorders, including epilepsy. However, whether exuberant neuronastrocyte-neuron transmitter-mediated signaling promotes abnormal neuronal synchronization in epilepsy still remains as an open question. The goal of this research is to elucidate this mechanism and identify a possible pharmacological target by using biophysical modeling tools. Materials and Methods: A model of interacting neurons and astrocytes described by N coupled tripartite synapses is proposed. Each tripartite synapse consists of presynaptic and postsynaptic terminals, as well as the synaptically associated astrocytic microdomain, and is described by a system of 13 stochastic differential equations. Then, by applying a dynamical mean field approximation, the system of 13N equations is reduced to 13(13+2) = 195 deterministic differential equations for the means and the second order moments of local and global variables. Results and Discussion: The experimentally observed phenomenon of spontaneous activity in astrocytes was replicated on the neural-glia mass. The model predicts that astrocytes can have a strong and activity-dependent influence on synaptic</p>

	<p>transmission. Finally, simulations show that the dynamics of astrocytes influences the synchronization ratio between neurons, predicting a peak in the synchronization for specific values of the astrocytes' parameters.</p> <p>Conclusions: According to the model proposed here, astrocyte-induced synchronization could be a relevant underlying mechanism for synchronization-related pathologies in the brain such as epilepsy. Therefore, each element of the identified mechanism should be studied as a possible pharmacological target.</p>
W-7	<p>1ST INTERNATIONAL WORKSHOP ON IPV (INACTIVATED POLIO VACCINES). CONTINUATION. DAY 2</p>
	<p>Session 4. IPV laboratory assays. IPV Research and Development.</p>
OC-175	<p>LABORATORY TESTS, NORMS AND STANDARDS FOR THE QUALITY CONTROL OF IPV Javier Martín, Gillian Cooper, Laura Stephens, Jackie O'Brien and Philip Minor</p> <p>Division of Virology, NIBSC (HPA), Potters Bar, Hertfordshire, United Kingdom</p> <p>The batch release of IPV products requires the use of <i>in vitro</i> assays to measure the amount of protein antigen and <i>in vivo</i> tests to assess the immune response in animals. The use of International Standards in these analyses is essential to allow comparison of different IPV products across laboratories. International Standards are established in collaborative studies involving manufacturers and control laboratories. There are important differences in method formats and reagents used by different laboratories. However, attempts to establish common methods have failed since results were found to be more variable when using standard methods than in-house tests. The antigen content and relative vaccine potency can also change when different poliovirus strains are used for vaccine production. A new <i>in vivo</i> test using transgenic mice that express the human poliovirus receptor is described. The test evaluates the protection of mice immunised with different vaccine formulations against paralyzing doses of wild-type poliovirus.</p>
OC-176	<p>ANTIGENIC FINGERPRINTING AND STANDARDIZATION OF SABIN BASED INACTIVATED POLIO VACCINE. PROPOSAL FOR A NEW ANTIGEN UNIT FOR INACTIVATED POLIO VACCINES Janny Westdijk^{1,3}, Debbie Brugmans¹, Javier Martin², Aart van 't Oever¹, Wilfried Bakker¹, Lonneke Levels¹, Gideon Kersten¹</p> <p>¹ Netherlands Vaccine Institute, Antonie van Leeuwenhoeklaan 9-11, 3720 AL Bilthoven, the Netherlands ² National Institute for Biological Standards and Control, Blanche lane, South Mimms, Potters Bar, Hertfordshire, UK ³ Presenting author</p> <p>Inactivated polio vaccine based on attenuated Sabin strains is a candidate vaccine to replace current Inactivated Polio Vaccine (IPV) made from virulent Salk strains. Safer polio vaccines are part of the (post) eradication strategy of the WHO. Clinical GMP-batches of Sabin-IPV were characterized for their antigenic and immunogenic properties. Antigenicity was determined with a panel of monoclonal antibodies in two assay formats: ELISA and biosensor analysis. Immunogenicity was measured in rats. Readout was <i>in vitro</i> virus neutralization. A Sabin product profile consisting of the intrinsic antigenic and immunogenic properties is a powerful tool to monitor and prove production consistency. Antigenic fingerprints of Sabin-IPV reveal that the current unit of antigen content (D-antigen unit) is not a fixed amount of antigen. Instead of the D-antigen unit we propose standardisation of IPV based on protein amount for dose and D-antigenicity for quality of the vaccine. A biosensor based calibration free concentration analysis (CFCA) combines the two methods for quantity and quality in one assay for both Sabin and Salk polio vaccines without the need for a reference vaccine.</p>
OC-177	<p>RESEARCH AND DEVELOPMENT ON NEW IPV SEEDS. Javier Martín, Lindsay Forrest, Thomas Wilton, Gillian Cooper, Andrew Macadam and Philip Minor</p> <p>Division of Virology, NIBSC (HPA), Potters Bar, Hertfordshire, United Kingdom</p> <p>The use of Sabin live attenuated poliovirus strains for the production of inactivated polio vaccine (IPV) is viewed by WHO as an advantage in terms of reduced containment requirements with respect to using wild</p>

	<p>poliovirus strains as for current IPV. This advantage would be highly relevant for the post-eradication era. However, we and others have found that type 2 Sabin IPV candidates are poorly immunogenic which means that this vaccine might be commercially unviable. We have analyzed several Sabin IPV preparations using standard procedures required for the batch release of IPV and other laboratory assays. The results confirmed previous findings showing poor immunogenicity of Sabin 2 IPV which was however significantly increased in the presence of adjuvant. Differences between Sabin IPV preparations could be attributed to variation in the actual D-Ag content of some of these Sabin IPV candidates since significant between-laboratory variability was found in the D-Ag values determined for a Sabin IPV reference standard in a recent collaborative study involving manufacturers and control laboratories. Experiments are also underway to try to understand the molecular basis of Sabin 2 IPV's low immunogenicity. We conclude that improvements in vaccine formulation and standardization as well as exploring the use of other chemicals for virus inactivation might be required before Sabin IPV is considered a suitable vaccine for use in humans. The development of novel strains with increased attenuation and their use as alternative vaccine seeds for IPV production will also be discussed.</p>
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	<p>CLOSING CONFERENCES / CONFERENCIAS DE CLAUSURA</p>
<p>PL-22</p>	<p>RATIONAL USE OF DRUGS AND DEVELOPMENT OF THE SYSTEMS OF HEALTH IN THE AMERICAS <u>José L. Castro</u> PAHO, Washington, USA / OPS-OMS <i>Resumen no disponible en el momento de la edición del libros. Abstract non available in the moment of the edition of the book of summaries.</i></p>
<p>PL-23</p>	<p>DRUG'S RESEARCH AND DEVELOPMENT IN CUBA. IMPACT IN THE NATIONAL SYSTEM OF HEALTH <u>Marlene Porto Verdecia</u> Directora, Centro de Investigación y Desarrollo de Medicamentos (CIDEM), Ciudad de La Habana, Cuba. email: cidem@infomed.sld.cu & direccion@cidem.sld.cu</p> <p>The arsenal and readiness of drugs constitute an important part of the Cuban National System of Health, contributing to improve the patterns of health and quality of our population's life. It has been established that, besides the saving in foreign currencies for the drugs purchases, it has contributed decisively in the favorable indicators of Health for Cuba and for the countries with those that we collaborate.</p> <p>The development of the pharmaceutical industry has been established as premises of the current situation in spite of the economic limitations imposed by the North American blockade. The creation of different programs for development of drugs; first, the program for the development of generic drugs and, second; the one dedicated to natural products, represent two important pillars of the Cuban public health today.</p> <p>Undoubtedly, drug's I & D programs, and an adequate and quick introduction to the Cuban Pharmaceutical Industry, have been decisive factors in order to achieve excelent levels in drug access by the population quality of production and low prices. In general, it is shown, the results of a sustainable pharmaceutical production of the essential drugs with a significant impact in the main health programs.</p> <p>At the present time, 85% of the products of the National Basic Square (essential drugs) have been developed by our professionals of the health with an economic translation for concept of substitution of imports.</p> <p>Also, the presentation will analyze the work that we implement in the investigation and development of natural products, as another contribution from the pharmaceutical laboratories and research institutions to the National System of Health.</p>
<p>PL-24</p>	<p>PHARMACOLOGY IN CUBA TODAY: 15 YEARS OF WORKS AND SCIENTIFIC ACTIVITY OF THE CUBAN SOCIETY OF PHARMACOLOGY <u>René Delgado Hernandez (PhD)</u></p> <p>Head of Molecular Pharmacology Department. Drug Research and Development Center, Ave 26 and Boyeros, Plaza de la Revolución, Havana, Cuba. Email: rdelgado@infomed.sld.cu President of National Council, Cuban Society of Pharmacology (CSF). email: rdelgado@infomed.sld.cu</p> <p>Pharmacology is an essential base in therapeutic. Pharmacological investigations contribute to identify new therapeutic targets and alternatives therapeutic. The present work seeks to intrude in this essential thematic, and it points out some examples about the main results reached by Cuba in the development of new drugs that aroused in appropriate identification of therapeutic targets; as well as others that are located in the</p>

	<p>biotechnological synthetic generic drugs, they are obtained and commercialized in Cuba. They constitute unquestionable achievements of the Cuban biotechnological and pharmaceutical development. Also in this presentation it will demonstrate a brief review of the potentialities that possess the principles investigation centers of Cuba and with particular emphasis in role of the Institution of the Western Scientific Pole of Havana. On the other hand they show the importance of the molecular design of new drugs and the obtaining of scientific results in this field for the service of the Cuban pharmaceutical industry and the National System of Health. This constitutes a clear example of the Cuban development in pharmacological science. The conference will also show the role that has developed in these years in the Cuban Society of Pharmacology (CSF) and their members in the whole island for their improvement and impact on the pharmacological sciences in the scientific activity that Cuba today can demonstrate to the rest of the world.</p>
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Poster Room / Sala de Carteles	12:30-15:30	SECCIÓN DE CARTELES / POSTERS SECTION WEDNESDAY / JUEVES, DECEMBER / DICIEMBRE 16
Chairs / Presidentes	Rodolfo López, Celia Magalys Casado, Yahelin Ferrer	
PFep 001- 107	PHARMACOEPIDEMIOLOGY / FARMACOEPIDEMIOLOGIA	
Chairs	Jun A Furones, Giset Jiménez, María Aida Cruz, Dulce María Calvo	
	<i>Poster Discussion and Scientific Exchange. Oral Presentation (5 min) of Selected Posters. / Discusión de Carteles e Intercambio Científico. Presentación Oral (5 min) de Carteles Seleccionados /</i>	
Poster No./ No. Cartel	ABSTRACT / RESUMEN	
PFep 001	<p>ANTIBIOTICS UTILIZATION STUDY IN A GYNECOLOGICAL PRIVATE HOSPITAL IN HIDALGO, MEXICO Chehue Romero A¹, Camacho Velázquez GA¹, Olvera Hernández EG¹, Reynoso Vázquez J¹, De la O Arciniega M¹.</p> <p>¹ Área Académica de Farmacia, Instituto de Ciencias de la Salud, Universidad Autónoma del Estado de Hidalgo, Carretera Pachuca-Tilcuautla S/N, Municipio San Agustín Tlaxiaca, Hidalgo, México. email: chehuea@uaeh.edu.mx, chehue_alex@yahoo.com.</p> <p>Introduction: Antibiotics are one of the most widely used therapeutic groups in the world. Studies have revealed the existence of an irrational use of antibiotics in clinical practice. Moreover, women are subject to suffer any infections at different stages of their life and because of they are subject to use antibiotics. Objective: Evaluate the antibiotics prescription in a gynecological private hospital in Hidalgo, Mexico. Material and Methods: A descriptive, retrospective, cross-sectional, and prescription-indication study from January to November 2007 was carried out, and it was non-probability sampling. With the purpose to analyze antibiotic prescriptions following data was considered: indication, dose, administration interval, administration route, pharmaceutical forms and treatment time. In order to characterize the study population a descriptive analysis was done, the Defined Daily Doses (DDD) per 100 bed day (BD) were calculated, and possible adverse drugs and potential interactions were identified. Results and Discussion: 309 clinic expedients were included. The most of patients were in a group age between 16 and 30 years (53.07%), with a middle socioeconomic level (81.87%), the most of case were women undergoing cesarean delivery (59.75%). The antibiotic most frequently used by intravenous route was cephalothin (8.26 DDD/100 BD). The mean pharmacological interaction was between cephalothin and gentamicin (cephalosporins may potentiate the toxic effects of aminoglycosides). Cephalothin could be implicated in the largest number of adverse potential reactions, which shows that it is necessary to increase the safety of these antibiotics. Conclusions: The most prescriptions were considered correct; however, it is recommended work on pharmacotherapeutic guidelines of antibiotics, and to make known these issues, and to promote the continued education between health care providers in order to foment the rational use of medicines. References: Jaramillo LE., et al. Protocolo de Estudio e Instrumentos Validados para Estudios de Utilización de Medicamentos en Consumo. MPS. 2005; 1-32. Web site: http://www.who.int/topics/en/</p>	
PFep 002	<p>CEFTRIAZONE INDUCED WEEKNES AND NAUSEA IN 46-YEAR OLD MALE PATIENT Vesna Radović</p> <p>STADA Hemofarm A.D. Belgrade, Serbia y Montenegro. email Address: veradovic@beotel.rs</p> <p>This report was received from a physician via the Agency of Russia and via our Regulatory Team on 2010-Jun-03. The male patient age 46 yr was treated from <i>Bronch. chronica bill.</i> He had taking Azaran (INN: ceftriaxone), power for solution for inj. or inf., 1000 mg. Also, he had taking other drugs: Famotidin (INN: famotidine), Azafen (INN: pipofezin), Vinpocetin (INN:vinpocetine), Sibazon (INN: diazepam) and Piracetam (INN: piracetame). Suspected drugs is Azaran (INN: ceftriaxone), power for solution for inj. or inf., 1000 mg. Therapy dates: from 2010-04-14 to 2010-04-18. Concomitant drugs: Famotidin (INN: famotidine), per os from 2010-04-08 to N/A</p>	

	<p>Azafen (INN: pipofezin), per os from 2010-04-12 to N/A Vinpocetin (INN:vinpocetine), i.v. from 2010-04-14 to N/A Sibazon (INN: diazepam), i.v. from 2010-04-14 to 2010-04-15 Piracetam (INN: piracetame), i.v. from 2010-04-14 to 2010-04-15 Patient was recovery.</p> <p>DICLOFENAC INDUCED NECROSIS CUTANEA IN 49-YEAR OLD FEMALE PATIENT <u>Vesna Radović</u></p> <p>STADA Hemofarm A.D. Belgrade, Serbia y Montenegro. email Address: veradovic@beotel.rs</p> <p>This report was received from a physician via the Agency of Russia and via our Regulatory Team on 2010-Jun-03. The female patient age 49 yr was hospitalized on the Department of Surgery at the local Clinic (2010-05-17) with diagnosis: <i>Postinjection skin necrosis</i> on the right gluteal region. Post-injection infiltration. The patient suffering from long time of osteochondrosis and <i>Discus henria</i>. The patient never had an allergy or an other adverse drug reaction. Periodically treated with injections of Diklofenak. The patient felt a strong burning and through 1 hour after injection Diklofenak of gluteal region appeared black tape on the skin in the direction of the spine, width about 8 cm. 2 days later appeared the pain and burning continued. On the local institution has been established diagnosis of allergy. Giving the solution of Gluconate calcium i.v. (06, 07 May). The patient was hospitalized 2010-05-17. She was treated conservatively: antibacterial, vascular and antiinflammatory therapy. Involved or prolonged inpatient hospitalisation. Suspected drugs is Diklofenak (INN: diclofenac), i.m., 75 mg. Therapy dates: from 2010-05-04 to 2010-05-04. Concomitant drugs: Aktovegin (INN: actovegin), i.m. from 2010-05-04 to 2010-05-09.</p> <p>PENICILLIN INDUCED PROCAINE (PSEUDOALLERGIC) REACTION IN 4-YEAR OLD MALE PATIENT <u>Vesna Radović</u></p> <p>STADA Hemofarm A.D. Belgrade, Serbia y Montenegro. email Address: veradovic@beotel.rs</p> <p>This report was received from a physician via the Agency of R. of Srpska on 2010-Jun-07. The male patient age 4 month was immediately after application of Penicillin (INN: benzylpenicillin sodium, procaine benzylpenicillin) had the appearance of crisis awareness with absent from view and muscle cramps. He had not temperature and previously lactate. The child was received Diazepam (INN: diazepam) rectiole and sent to children's department, where he continued treatment with Penicillin. ADR had not occurre. Suspected drugs is Pancillin (INN: benzylpenicillin sodium, procaine benzylpenicillin), powder for suspension for injection, 800000 IU, № 50. Daily doses is 800 000 UI. Therapy dates: from 2010-05-24 to 2010-05-29.</p>
PFep 003	<p>STUDY DETERMINANTS OF IMPACT KIDNEY DISEASE OF SRI LANKA (CASE STUDY AT ANURADHAPURA DISTRICT) <u>Sumith Krishantha Godamuna Witharanage</u></p> <p>University of Sabaragamuwa, Galle, Sri Lanka. email: sumith_12@yahoo.com</p> <p>A steep rise in kidney disease in farming communities in Sri Lanka has baffled doctors and researchers struggling to pinpoint the factors making people in several rice-growing districts vulnerable to the debilitating illness. Medical researchers say the numbers have been steadily climbing since the high prevalence of the disease was first noted eight years ago in North Central Province, where over half the population is engaged in agriculture. Besides North Central Province, the ailment is prevalent in the North-Western, the Eastern and Uva provinces. The problem first came to light in Anuradhapura [a district in the North Central Province] around 2000. It is adding that it seriously jeopardized the health of those who got it, and the high economic cost of treatment. It is a burden to the patient, family, community and health system. Sources said the 3,000 kidney patients are treated at Medawachchiya district hospital while more kidney patients are reported from Negampaha, Thambuttegama, Horowpothana, Kebithigollewa, Kekirawa and Anuradhapur teaching hospital. The most mystifying feature of the problem is that most of those</p>

	<p>affected are farmers, and mostly male members of farming families. According to health officials, many of them do not have the pre-existing conditions of hypertension or diabetes that usually lead to renal disease and failure. They have uncovered the exact etiology of the disease. They can only guess at what the cause might be. This study pointed out, what are the exact reasons for that affection. This study inspection about age of kidney patients, sex, weight, height, education, other diseases (diabetics, hypertension and feeble of body). What are the food eating and drinking of kidney patients and alcohol consumption. Anuradapura kidney patients were selected as population. Using systematic sampling method selected 10% from kidney patients as sample. Multivariate data analysis, regression analysis and chi-square test was used as analysis method. Questionnaire and their clinic card was used as method of data collection. According to analysis data, the possible causes range from drinking water from tube wells, to exposure to fertilizer used by farmers to eating fish, bred in tanks. Most of the victims are middle aged farmers also most of them alcohol consumers. People who are suffering from rat fever, diabetic and high blood pressure are considered as the vulnerable sections of the kidney diseases. <i>Key Words: Kidney disease, factors.</i></p>
PFep 004	<p>ADHERENCE AND COST OF THE PHARMACOLOGICAL THERAPY IN PRIMARY OPEN ANGLE GLAUCOMA Ariana Fernández García¹, Idalia Triana Casado², Ana María Gálvez González³, Rosendo Villar Valdés⁴</p> <p>¹MINSAP. Línea e I. Havana City. Email: ariana.fdez@infomed.sld.cu. ²Salvador Allende Hospital. Calzada del Cerro. Havana City. ³National School of Public Health. Línea e I. Havana City. ⁴Medical University. Havana City</p> <p>Introduction Glaucoma is an important cause of irreversible blindness all over the world. The scope of the cost associated to this disease considers the treatment as well as the impairment in life quality of the patient. The main objectives of this paper are to identify the adherence of the treatment of primary open angle glaucoma and estimate the cost of the pharmacological treatment in the studied population. Material and methods A transversal and descriptive study was carried out. The patients with primary open angle glaucoma that went to the glaucoma medical consultation at Salvador Allende hospital in Havana city, during February and March 2010 were considered the universe in this study. The methodological approach was the cost of the treatment of the disease. The perspective of this study was the patient's one. Results and discussion 45 patients were studied. The female sex was predominant (64.4%); 55.5% of the patients were white. 68.9% had a positive family history with a mean time of evolution of 9.2 years and their average age was 63.4 years. The most frequent pharmacological treatment consisted on timolol eye drops (64.5%), pilocarpine (11.1%) and a combined treatment of timolol and pilocarpine (8.9%). 53.3% of the patients do not fulfill the treatment, they forgot to instill the drops twice a week (58.3%) and the main reason for that is that they were doing some other activities (70.9%). The average cost per month of this pharmacological treatment has been 9.17 Cuban pesos. Beta blockers are considered medications of the first choice and the anti glaucomatous treatment is poor. Conclusions The incorrect adherence of the indications on the side of the patient with respect to the treatment determines the progressive irreversible loss of vision. It strikes directly on the economy of the health system, the patient and their family.</p>
PFep 005	<p>EPIDEMIOLOGICAL REVIEW ABOUT THE USE AND COST OF ANTIBIOTICS IN NOSOCOMIAL INFECTIONS IN THE INTERNATIONAL CENTER OF NEUROLOGICAL RESTORATION (CIREN) IN LAST TWO YEARS PERIOD Padron A¹, García M¹, Ricardo J¹, Pedroso I¹, Alvarez M¹, Valdes M¹, Grass D¹, Reconde D¹</p> <p>¹International Center of Neurological Restoration (CIREN), Ave 25 No 15805, Reparto Siboney, Playa, Havana City. Cuba. email: arnoldo.padron@infomed.sld.cu</p> <p>Introduction: The International Center of Neurological Restoration attended patients with neurodegenerative disease with neurological disability associated, and make too neurosurgical interventions to minimal access in some kind of these diseases. In all cases the possibility of infectious events is real and its necessary the antibiotics treatment with the consequent cost added. In this work we try to inquire the topic of pharmacoconomics, about this problematic in our institution. Material and Methods: We included all the infectious events that occurred during the last two years (2008-2009) in the different services of the hospital, defining the type of antibiotic used in each case and the cost for each of them. These data were included in a database, which allowed comparing statistical processing for years. Results and Discussion: The main antibiotics used were cephalosporins and quinolones with a moderate level in the national currency accounts and foreign exchange. Costs were similar in the two years studied. There was, first, that some infections were treated empirically because it was difficult to perform</p>

	<p>microbiological studies of crops and on the other hand using two or more courses of antibiotics in patients with multi-resistant bacteria. These conditions increased the amount and therefore the cost of treating patients with nosocomial infections. Conclusions: The cost of antibiotics used was moderate in foreign currency. We believe that it is possible to lower costs through better use of clinical and microbiological tools, to take a correct decision when indicating antibiotic therapy, achieving control of infections and complications in our patients.</p>
PFep 006	<p>THERAPY WITH TROFIN PREGNANTS PATIENTS WITH IRON DEFICIENCY ANAEMIA <u>Bermúdez IC</u>¹, Espada LD¹, Ferrer AS², Martínez YP¹, Dutok CS¹</p> <p>¹Oriente University. Natural Sciences Faculty. Department of Pharmacy. Patricio Lumumba s/n. Santiago of Cuba City. Cuba. email: isis@cnt.uo.edu.cu betisell@yahoo.es ²Oriente University. Natural Sciences Faculty. Department of Chemical. Patricio Lumumba s/n. Santiago of Cuba City. Cuba.</p> <p>Introduction: Trofin is a biopreparation elaborated by BIOCEN Centre in Havana city. It is a natural product that contains iron, protein, amino acids, bee honey and propolis. Trofin has been used in Cuba for the treatment of the iron deficiency anaemia in pregnant patients. The aim of our study was to compare the cost effectiveness of the relationship between Trofin and ferrous fumarate in pregnant patients with anaemia caused by iron deficiency. Material and Methods: An open aleatory clinical trial was carried out in 60 pregnant patients with anaemia caused by iron deficiency in the Eastern Maternity House from Santiago of Cuba between January and July 2008. Thirty (30) women were treated with Trofin (Group A) and 30 women with ferrous fumarate (Group B). The principle variables used were the haemoglobin and hematocrite levels in each patient, the secondary variable as the clinical evolution; the safety variable was regarding adverse reactions and the control variables: age, toxic habits, nutritional habits, consumption of vitamins with the treatment indicated and instruction level. The benefit and risk relationship was calculated and the cost effectiveness of the relationship was also evaluated. Results and Discussion: Our results showed that the treatment with Trofin was useful in achieving the reduction of the haemoglobin and hematocrite levels of pregnant patients affected with anaemia and none of the patients treated with Trofin presented adverse reactions. Ninety six point seven (96.7%) of the pregnant patients who received the treatment with Trofin had higher benefits and reduced risks. In addition, the cost effectiveness of the relationship with Trofin was greater than cost effectiveness relationship of the treatment with ferrous fumarate. Conclusions: The results demonstrated that Trofin is very useful for the treatment of the iron deficiency anaemia in pregnant patients with advantages economic superiors to the ferrous fumarate.</p>
PFep 007	<p>CONSUME AND COST OF DRUGS USE IN THE TREATMENT OF CARDIOVASCULAR DISEASES, IN THE WEST REGION OF THE PROVINCE OF HAVANA, BETWEEN MARCH 2005 AND DECEMBER 2009 <u>Cabrera Cepero JR</u>¹, Lara Bastanzuri MC²</p> <p>¹Regulatory Bureau to Health Protection, Havana, 47 Ave, % 120 & 122 St, Marianao, Havana, Cuba. email: josercabrera@infomed.sld.cu ²Center for the Development of Pharmacoepidemiology, National Pharmacovigilance Unit, 5^{ta} Ave and 44 St, Miramar, Playa, Havana, Cuba.</p> <p>Introduction: The planning of resources is a big problem particularly in developing countries including Cuba, so it's vital the best use of the limited budgets and the shortage of hard currency. Among the health conditions, that has demanded more resources in the last years are Arterial Hypertension, Congestive Heart Failure and Ischemic Heart Disease. This study was made in the Province of Havana, which is divided in 2 regions for distribution of drugs. The goal of this work was too characterized the patterns of consumption of drugs for the treatment of cardiovascular diseases in the west of the Province of Havana between March 2005 and December 2009. Material and Methods: A Drug Use Study was made. It was of consume, descriptive, observational and retrospective with elements of practical consequences. The data of the consumption of medicine for these diseases in 58 months was used. The Doses per Habitant per Day was used to establish the comparison of consumption in time, also to establish the comparison of the amount planned to sell for each of the drugs in study. Results and Discussion: The most consume drugs were the thiazides diuretics, the Angiotensin Converting Enzyme (ACE) inhibitors and the β-blockers in this order. Other authors in Costa Rica have reported similar reports in 2001 and in Venezuela in 2006. Conclusions: The thiazides diuretics, The ACE inhibitors and the β-Blockers were groups of drugs of higher consumption. In the 70% of the studied drugs there's no correspondence between the data of selling, the</p>

	needs of the pharmacies and the plans.
PFep 008	<p>AN APPLICATION OF THE AFFINITIES THEORY IN A HEALTH ECONOMIC PROBLEM Alonso Aguila LM¹, Gálvez González AM², Portuondo Sánchez CL³</p> <p>¹Department of Industrial Engineering, Polytechnic Institute “José Antonio Echeverría” CUJAE La Habana Cuba. email: lmalonso@ind.cujae.edu.cu ²National School of Public Health, La Habana Cuba. email: econ@ensap.sld.cu ³Pharmacoepidemiology Development Center. 5th Ave and 44 St, Miramar, Playa, Havana City, CP 11 300. Cuba. email: cportu@infomed.sld.cu</p> <p>Introduction: Logical systems have been enriched with the article “Fuzzy Sets” published by Lotfy Zadeh in 1965. Gradually several applications emerged in different fields of science and technology. In recent years the Theory of Affinities developed by Arnold Kaufmann and Jaime Jil Aluja has become one of the main applications of fuzzy logic to economics and management problems. This work shows the potential of this approach in modeling a problem associated with health economics. Material and Methods: The paper shows the possibility of applying the so-called “Maximum inverse correspondence algorithm” in the following problem: Establishing a matrix of m rows and n columns where the rows represent all municipalities of the country and the columns represent the negative health indicators ; the algorithm allows different thresholds for each indicator and form a binary matrix which is the basis for making groups taking into consideration the affinities in different municipalities as well as groups of negative indicators. Results and Discussion: The practical value of this proposal is to detect similarities not evident by trial and error techniques or intuition of the researcher. Conclusions: In terms of Health Economics it is extremely useful to have this tool because it facilitates making decisions with minimal human resources, materials and financial accounting. References: Elements for a theory of decision in uncertainty. Kluwer Academic Publishers 1999.</p>
PFep 009	<p>DRUGS THAT REPRESENTED THE BIGGEST COST FOR THE HOSPITAL “AMISTAD ARGELIA CUBA” IN DJELFA Cordero O¹, Lara MC</p> <p>¹Center for the Development of Pharmacoepidemiology, 5^{ta} Ave and 44 St, Miramar, Playa, Havana City, Cuba. email: osvaldo@mcds.sld.cu</p> <p>Introduction: This study is realized with the objective to identify the medicines that represented the biggest cost for the Hospital “Amistad Argelia Cuba” in Djelfa and to evaluate the prescription of the medicines in ophthalmic presentation that were used in the hospitalization room and to the departure. Method: The study is delimited in one year, from May, 2008 until April, 2009 there were included 188 medicines of the basic module. Is applies the Method of Pareto or ABC to identify the medicines who represented the biggest cost, the necessary information to apply this method is obtained of the countable record (System Versat Sarasola). Were selected 13 medicines of ophthalmic presentation that were used in the hospitalization room and to the departure to evaluate the prescription of the same ones. To realize this evaluation were checked 500 clinical reports, of the hospitalized patients, who had used at least one of these 13 medicines, 469 were useful for the investigation. There are prepared by the author protocols of treatments, certificate by adviser group of the hospital of Djelfa and the Ophthalmological institute “Pando Ferrer” used like reference in the evaluation of the prescription. Results: 90,74 % of the expense is determined by 39 medicines (groups A and B) and they represent 20 % of the medicines that form the module of the hospital. There were selected the 13 of ophthalmic presentation used in the rooms and to the departure, to evaluate the prescription, 4 of the group A and 9 of the group B and they represent 32,56 % of the expense. 1 411 prescriptions was realized, 19 were inadequate for errors in the opinion of selection and 33 for incorrect therapeutic scheme. The patients operate of Cataracts and for Excímer Láser, receive the biggest number of prescriptions and the biggest quantity not suitable prescriptions. The Prednisolona, Diclofenaco, Gentamicina and The Ciprofloxacina presented major number of inadequate indications. Conclusions: The antibiotics and not inflammatory ophthalmic medicines are those who represented the biggest cost for the Hospital “Amistad Argelia Cuba” in Djelfa in this period. Although of general form it is possible to conclude that the prescription is adequate, the application of a correct therapeutic scheme can improve it.</p>

PFep 010	<p>CONSUMPTION AND NECESSITY OF ANTIHYPERTENSIVE ANTIDIABETIC AND ANTI-ASTHMATIC DRUGS. VILLA CLARA 2003-2009 <u>Rodríguez Benítez M¹</u>, Lara C.</p> <p>¹Medicines Trader and distributor. Pollera and Circunvalacion road. Santa Clara, Villa Clara, Cuba.</p> <p>Introduction: The increment of the prevalence of non-transmissible illnesses in Villa Clara, the absence of studies that describes patterns of consumption of medications and the irregularities in the supply has motivated the following investigation. To describe the consumption of antihypertensive drugs, antidiabetic and asthma medications from 2003 to 2008, to estimate the necessities of supply for the consumption method, identifying the differences according to the 2009 plan and their cost, these were the objectives of the present work. Material and Methods: It was considered the group of utilized medications from 2003 up to 2008 in pharmacies, those that could not be indicated in other pathologies included in the study or being of new introduction in the market being excluded. The data were obtained of the consumption registrations by the Stock Managerial MISTRAL Caribbean of the Drugstore. The analysis of the consumption was expressed in DHD and the estimated necessities in physical units, both defendants in Excel. Results and Discussion: 3 pharmacological groups and 26 drugs were analyzed. The consumption increases for all the groups in the studied period. The prescription profile is not adapted for the asthma medications. In a general way the consumption method supposes superior figures to the 2009 Plan. Alone for 6 products the plan was adapted, what denotes difficulties in the quality of the planning. In 8 medications the cost of the dear total consumption decreased when using the consumption method, while the rest generated an increment of the cost. Conclusions: The prescription profile is adapted for the antihypertensive ones and the antidiabetic. The use of medications prevails for the symptomatic treatment of the bronchial asthma on those of preventive use, what indicates lack of control of the illness. In a general way the plan of the province is not adapted to the estimated necessities according to the consumption method. The cost of the medications for the drugstore increases when this method is used, being affected the economic plan of the company and the units of health that will spend of its budget bigger figures that those dedicated initially to acquire the medications.</p>
PFep 011	<p>IMPLEMENTATION OF A PHARMACEUTICAL CARE SERVICES TO DIABETIC PATIENTS FROM AN ENDOCRINOLOGY CLINIC <u>Marcel Llovet A¹</u>, Bermúdez Camps I²</p> <p>¹Regulatory Bureau for Health Protection. General García No. 227 % Lora y Masó, Bayamo City, Granma. Cuba. email: amarcel@grannet.grm.sld.cu ²Faculty of Natural Sciences, Department of Pharmacy, Universidad de Oriente, Santiago de Cuba city. Cuba.</p> <p>Introduction: Diabetes is a global public health problem. It is no exaggeration to describe diabetes as one of the major contributors to ill health and premature mortality worldwide. The number of people with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity. If the current trend continues it is estimated that by 2030 the number of people with diabetes will more than double. Pharmaceutical care is a professional practice in which the pharmacist is responsible for patient necessities with regard to medicines. Such a practice is carried out through the detection of drug related problems (DRP) for the prevention and solution negative outcomes associated with medication (NOM). This process should be carried out in collaboration with the patient himself and other professional health care staff, with the aim of achieving specific results that improve the patient's quality of life. Patients with diabetes can benefit greatly from pharmaceutical care. Materials and Methods: A study from Endocrinology consulting in the healthcare field "Jimmy Hirzelt" Bayamo municipality for a period of 24 months was carry-up, in order to implement a pharmaceutical care services to diabetic patients, which enabled us to identify, resolve and prevent Negative Outcomes associated with Medication (NOM) in these patients. The Dader Method and guidelines from the Third Consensus of Granada were used. The impact assessment was conducted service implemented through the measurement of clinical outcomes achieved with the pharmacist interventions, taking into account its impact and the degree of significance for them. Results and Discussion: Was organized and created a pharmaceutical care services to diabetic patients from Endocrinology outpatient department, making an adjacent local consultation, with personal and material resources required and the methodology for its operation satisfactorily. During the monitoring period 84 patients were treated, mainly in the female sample (75.0%) aged between 50 and 70 years (55.95%) and type 2 diabetes mellitus (98.48%). The development of the</p>

	<p>service identified 89 Negative Outcomes associated with Medication (NOM), classified according to the Third Consensus of Granada, being related to safety their highest peak. Of the 66 interventions were accepted on 90.90%, giving solution to 80.30% of the NOM, with the persistence of adverse reactions and self-medication major causes of non-solution. The rate of impact on pharmaceutical interventions was high, this being appropriate in more than 80% so that the impact of implemented service was ranked as high as it contributed to disease control and effective response to therapy, raising its quality of life.</p> <p>Conclusions: All patients included in the investigation were benefited with the pharmaceutical care service, to receive health education components, and the results reinforced the view of the need for pharmacists in the health provider team as the person skilled in the area of drugs, so it is recommended to extend the study to other health institutions and provinces all over the country.</p>
PFep 012	<p>EVALUATION OF THE PRESCRIPTION OF TRIHEXYPHENIDYL IN SANCTI SPIRITUS PROVINCE SUBSEQUENT TO A HEALTH TEAM INTERVENTION Fernández A, López I</p> <p>Provincial Enterprise of Pharmacies and Optics. Sancti Spiritus. Avenida de los Mártires 409 e/n Lepanto y Cuartel. Sancti Spiritus. Cuba. Phone: 32 4212. email: ailenfh@farmacia.ssp.sld.cu</p> <p>Introduction: A usage study of trihexyphenidyl in Sancti Spiritus province in 2008 showed errors in the therapeutic scheme and prescriptions of this drug in not justified indications. Several problems related to drugs were identified in patients. For this reason, from January to June, 2009 an intervention program was developed where instructions related to its prescription were issued and a re-evaluation was made by the specialist in internal medicine, the mental health consultant and the pharmacist in each municipality of all patients registered for this drug, with the objective to improve prescribing and consumption habits of trihexyphenidyl.</p> <p>At the end of the year 2009 a descriptive study of the prescription medicine was carried out in the province to assess the influence of the intervention. Materials and Methods: 167 patients registered in the province were analyzed. The data were obtained from medical certificates, pharmacotherapeutic profiles, and reports of home visits. The variables described were: sex, age, diagnosis, daily dose, drug involvement, adverse reactions and medical specialty that prescribed it. Results and Discussion: The results showed a slight decrease in the rates of patients registered for this drug in the province, there was a 19.4% decrease in the amount of patients due to treatment changes and closures for not taking the drug. All patients are consumers of trihexyphenidyl 2 mg, 93.4% of indications were for Parkinson's disease, the dose used was adequate in all cases, in both studies the medical certificates were predominantly issued by the internal medicine specialty, 32 adverse reactions were detected in 29 patients, being mouth dryness and constipation the most frequent ones. Conclusions: It was evident a marked improvement in the prescription of trihexyphenidyl what allowed us to consider the intervention satisfactory.</p>
PFep 013	<p>PRESCRIPTION AND CONSUMPTION OF METHYLPHENIDATE IN SANCTI SPIRITUS PROVINCE. MARCH 2010 Fernández A</p> <p>Provincial Enterprise of Pharmacies and Optics. Sancti Spiritus. Avenida de los Mártires 409 e/n Lepanto y Cuartel. Sancti Spiritus. Cuba. Phone: 32 4212. email: ailenfh@farmacia.ssp.sld.cu</p> <p>Introduction: To improve the preventive measures in relation to the control and legal use of drugs and to guarantee a proper use of psychotropic substances given the drug dependence that they can produce, it is important to achieve a rational use of methylphenidate, avoiding any deviation from it. In order to describe the use of methylphenidate by prescription in patients with files opened for its consumption, the following descriptive study was designed. Materials and Methods: 52 patients were studied, which represents the total of existing files for methylphenidate consumption in the province at the end of March, 2010. For the data collection there were reviewed the medical certificates with prescription of this medicine, home visit reports with interviews to patients and families and the pharmacotherapeutic profiles. The variables described were: sex, age, diagnosis, daily dose, time of consumption, drug involvement, and medical specialty that prescribed it, as well as improvement or not due to the medication, and treatment abandonment. Results and discussion: The predominant was the use of methylphenidate for the treatment of attention deficit disorders with hyperkinesias in 82.7% of patients, followed by attention deficit in 15.4%, summing 98.1% of medical certificates issued by Child psychiatry specialists. Only in one patient the drug was indicated for the treatment of primary hypersomnia (1.9%) in the specialty of neurology. Males were significantly predominant (82.7%) and the predominant age range was 6-10 years (65.4%), the</p>

	<p>daily dose most frequently prescribed was 10 mg (73.1%) and the time for medication usage between 1 and 4 years. Very few patients have reported no improvement with the treatment what did not significantly influence the treatment abandonment. Conclusions: The rational use and appropriate prescription of methylphenidate are evident.</p>
PFep 014	<p>ANALYSIS OF DRUGS ADVERSE REACTIONS REPORTS. NATIONAL INSTITUTE OF ONCOLOGY AND RADIOBIOLOGY. JANUARY 2003-MAY 2010 Arbesú Michelena MA, <u>Pérez Nova AL</u>, Cruzata Rittoles A, Cuétara Lugo EB, Roperero RJ</p> <p>Institute of Oncology and Radiobiology. Calle F y 29, Plaza de la Revolución. Havana City. email: marbesu@infomed.sld.cu</p> <p>Introduction: Reviewing the notifications of Adverse Reactions (AR) due to drugs administration, emitted by whole National Institute of Oncology and Radiobiology during 2003-2006, we found that there were few notifications (5 per year, less than expected according to drugs used in oncology). The lack of knowledge about Drugs Surveillance (DS) topics, the lack of time to fulfill the form to report it and the unsuitability of the form used: were the main causes of the restricted number of AR report. The present work is aimed to underline the roll of Pharmaco -Therapeutic Committee (PTC) in DS process. Material and Methods: An observational, descriptive study was performed. All notifications from 2003 to May, 2010: received by the PTC were analyzed in terms of: number of AR, quality of the notifications, pharmaco-therapeutic category, reporter, severity of symptoms and causality. Results: In 2007, a graduate in Pharmaceutical Sciences was included in DS activity, to instruct the personal about how to perform a report. Thus, an increase of 15 notifications per year was observed. In 2009, a pharmacologist was added to the PTC, quality markers were applied resulting in 68 notifications per year. Adverse effects due to cytostatic administration were highly documented; reactions were severe, with causality association being the most frequent the possible ones, reporters were: physicians, nurses and pharmaceutical personnel. Conclusion: Notifications increase was the result of interventions done by the qualified personal added to the PTC in the analyzed stages.</p>
PFep 015	<p>ACTIVE MONITORING OF ADVERSE DRUG REACTIONS IN A PEDIATRIC INTENSIVE CARE UNIT <u>Hernández A¹</u>, Chea N¹, Jiménez G²</p> <p>¹Hospital Mother and Child "A. A. Aballí "Bejucal Czda Km 71 / 2, Arroyo Naranjo, Havana city, Cuba. email: aylinbej@infomed.sld.cu ²Center for the Development of Pharmacoepidemiology, National Pharamcovigilance Unit, 5th Ave and 44 St, Miramar, Playa, Havana City, Cuba.</p> <p>Introduction: severe child in intensive care, has conditions that make it vulnerable to developing adverse drug reactions (ADRs), are subjected to several drugs that interact, such processes may have affected the pharmacokinetics, pharmacodynamics. These patients are nursing care and permanent, they perform clinical and laboratory examination often hence it is feasible to conduct a study of active pursuit of RAM. Material and Methods: Observational, descriptive, retrospective Pharmacovigilance, using intensive surveillance of suspected ADRs, which included patients admitted to the ICU due to suspicion of being admitted RAM or it is detected by physical examination, examination, examination laboratory. The reactions were classified according to the mechanism, frequency, severity, causality, and the drug groups were most in affected organs and systems. Results: The most affected were older than 5 years of age (48.7%), mainly boys (69.2%). The drug group contributed more notifications J (69.2%), predominantly of ceftriaxone and fosfomycin with four reports each, 69.2% were mild reactions, the organ system most affected skin with 33.3% and according to mechanism of 56.4% were B. Over 50% of the reactions were classified as possible and 53.8% of low frequency. Conclusions: The most affected were those aged 5 years and male patients, highlighted the group of antimicrobials, more than half of other factors could explain the RAM, the latter were mostly mild and low frequency.</p>
PFep 016	<p>MONITORING THE QUALITY OF FILLING PRESCRIPTIONS. CUBA, FROM JUNE TO DECEMBER 2009. CENTRE FOR THE DEVELOPMENT OF PHARMACOEPIDEMOLOGY (CDF) <u>Álvarez Crespo Alina R.</u>, Villarreal Broche Lourdes, Yera Alós Isis, García Milián Ana J, Alonso Carbonell Liuba.</p> <p>Centre for the Development of Pharmacoepidemiology Calle 44 esq 5ta ave. No.502. Playa, Ciudad de La Habana.</p>

	<p>Introduction: The prescription is a scientific measure, ethical and legal. In the legal order, the physician is responsible for the results of that intervention called prescription, which includes a correct filling of the prescription including with the aim of rational drug use, according to current regulations so that it is necessary each health center to know the trends in prescription of each of their physicians, and consequently, determine their learning needs. Objectives: Monitor the quality of filling the prescription in Cuba in the period from June to December of 2009. Método: A cross sectional study. The variables were the total prescriptions identifying the province badly made more difficult, as well as the main shortcomings. We also took into account the prescriptions that are issued for the various drugs on surveillance, in this case, antibiotics and psychotropic drugs. Results: 15.6% of the revised recipes were badly made. The main shortcomings were given in the absence of lack of strength and / or quantity of medication prescribed to 25.4%, followed by lack of medical stamp by 13.9%, among others. Regarding antimicrobial errors were more frequent given the lack of diagnosis, 8.4% for ciprofloxacin and 9.8% for azithromycin. Referring to psychoactive drugs in monitoring such as thioridazine, amitriptyline and imipramine had similar behavior regarding the omission of data from the patient or the person buying the medication. Conclusions: There are still deficiencies in filling the prescription and in compliance with current regulations remain the province of Cienfuegos, which reported as many recipes monitored with errors in the making.</p>
PFep 017	<p>PATTERN OF NIMOTUZUMAB PRESCRIPTION IN CUBA HOSPITALS. JULY, 2009 TO JULY-2010 García Ana J, Yero Isis B, Alonso Liuba, <u>Alvarez Alina</u></p> <p>Center for the Development of Pharmacoepidemiology. Calle 44 esq 5ta ave. No.502. Playa, Ciudad de La Habana.</p> <p>Introduction: Nimotuzumab is marketed by the Center for Molecular Immunology (CIM) for the treatment of tumors that are amenable to radiotherapy, especially the head and neck high-grade astrocytoma malignancy as monotherapy in children refractory to treatment oncospecific and treatment of glioblastoma multiforme in combination with radiation therapy in adults. Objectives: To identify diagnoses that led to the prescription of Nimotuzumab, humanized monoclonal antibody against factor receptor (EGFR) and to estimate their consumption. Method: We designed a prospective longitudinal study, prescription - an indication, with elements of consumption in the period July 2009-July-2010. Results: During this period nimotuzumab has been prescribed to 882 patients, who consumed 9691 bb. The provinces are reporting increased consumption Holguín, City of Havana and Camaguey. The main indications for the product are the head and neck tumors and CNS, lung, colon, prostate and cervix. Conclusions: The indications identified by the use of Nimotuzumab not match what was approved in registration.</p>
PFep 018	<p>PATTERN OF PRESCRIPTION OF ERYTHROPOIETIN. CUBA. 2009 García Ana J¹, Alonso Liuba², Yero Isis B³ Alvarez Alina⁴</p> <p>Center for the Development of Pharmacoepidemiology. Calle 44 esq 5ta ave. No.502. Playa, Ciudad de La Habana. email:anaj@mcds.sld.cu</p> <p>Introduction: iorR EPOCIM recombinant human erythropoietin produced in the Molecular Immunology Center (CIM) and obtained medical records in April 1998. The annual distribution has increased significantly since obtaining medical records and is currently indicated for the treatment of secondary anemia in patients with chronic kidney disease (dialysis and not on dialysis), with neoplastic diseases and chemotherapy treatments, programs autologous donations, infected with HIV, among others, treated with zidovudine and infant anemia. ior and estimate their consumption. Objectives: To identify the diagnoses that led to the prescription of EPOCIM Methods: We performed this prospective longitudinal descriptive research, which ranks in studies of drug use, and prescription - an indication, with elements of consumption in the period from March to December 2009. The variables are: provincial hospitals, months, medication, diagnosis, consumption. In the case of consumption this variable was calculated taking into account the number of bulbs per patient consumed. Cause renal anemia is the main indication for this product 84.1%, followed by that produced by the use of chemotherapeutic 8.3%. The bone marrow failure and anemia of prematurity are the most common diagnoses in other causes of limitation. Results: On average 11 bb consumed by patients. The provinces that consume more than the product are Camaguey, Las Tunas, Holguín and Granma. Conclusion: The pattern of use of erythropoietin corresponds to that reported in the literature, being the cause renal anemia its main indication.</p>

<p>PFep 019</p>	<p>ADVERSE REACTIONS REPORTED TO THE CONSUMPTION OF NATURAL PRODUCTS IN CUBA. 2003, 2005, 2007 Ana Julia García Milian¹, Liuba Alonso Carbonell², Yeny Ávila³, Pedro Lopez Puig⁴, <u>Ana Karelia Ruiz Salvador</u>⁵, Francisco Morón Rodríguez⁶</p> <p>¹ESP II Degree in Pharmacology, Master in Health Economics. Researcher and assistant professor. Center for the Development of Pharmacoepidemiology. ²Esp II Degree in Pharmacology, Master in health promotion. Assistant Professor. 1Centro For the Development of Pharmacoepidemiology. Calle 44 esq 5ta ave. No.502. Playa, Ciudad de La Habana. ³Department of Pharmacovigilance Specialist. Center for the Development of Pharmacoepidemiology. ⁴Esp II Degree in General Medicine, Masters in Primary Health Care. Assistant Professor. National School of Public Health. ⁵Esp II Degree in Pharmacology. Assistant Professor ⁶Professor. Doctor of Medical Sciences. Specialist degree in Pharmacology II.</p> <p>Summary: The natural medicinal product can be used to endless suffering, but like any medicine are not exempt from producing adverse reactions, in order to detect and classify them by applying these reactions causal relationship and gravity, a study that is classified as observational, descriptive, retrospective and longitudinal. It was considered as eligible for the study sample comprised of all natural products, which circulate in the country, who are reported adverse reactions in the years 2003, 2005 and 2007. We observe dominance in the frequency of occurrence of ADRs in females, the products were the most frequent garlic, oregano, the propolis and medicinal mud. It was concluded that minor reactions were the most frequent and were classified as probable.</p> <p>Keywords: consumption, natural medicinal products, adverse reactions</p>
<p>PFep 020</p>	<p>PHARMACOTHERAPY FOLLOW-UP SERVICE IN HOSPITALIZED PATIENTS OF THE NEUROLOGY SERVICE IN SANTIAGO DE CUBA. <u>Zúñiga A</u>, Piper O, Pupo M.</p> <p>Pharmacy Department. Universidad de Oriente.Hospital Juan Bruno Zayas. Santiago de Cuba. Universidad de Oriente. Patricio Lumumba s/n Santiago de Cuba. email:auroraz@cnt.uo.edu.cu</p> <p>A pharmacotherapy follow-up service was developed and evaluated in patients hospitalized in the Neurology Service of the General Hospital Dr. Juan Bruno Zayas located in the municipal of Santiago de Cuba in the province of Santiago de Cuba. The investigation was conducted using elements of the Dader Program and the IASER Method, sustaining them with the changes found in the Third Consensus of Granada, adapting them to the Cuban Health System. Fifty (50) patients satisfied the inclusion criteria during the pharmacotherapy follow-up with the majority being of the female sex (52%), age range from 36 to 51 years (48%), the pathology for hospitalization was Epilepsy (34%) and the associate pathology being Arterial Hypertension (46,15%). The identification of Negative Outcomes associated with Medication (NOM) was achieved by the creation of this service and was classified by the Third Consensus of Granada of which Safety was the category with the most NOM (70,46%). Forty one of the Forty four interventions were accepted (93,28%), with 100% appropriate pharmaceutical actions, and all of the patients and health care professional were satisfied with the service given. The impact of the service was classified as being High, using the aforementioned indicators. These results reemphasizes the necessity of pharmacists in health care groups as the professional most qualified in the area of medication, that will reduce pharmaceutical morbidity by the identification, prevention and resolution of Negative Outcomes associated with Medication.</p>
<p>PFep 021</p>	<p>PRESCRIPTION OF ANTIMICROBIAL DRUGS TO PEDIATRIC PATIENTS <u>Zúñiga A</u>, Calixte C, Pupo E</p> <p>Pharmacy Department. Universidad de Oriente.Hospital Juan B de la Cruz Martínez Maceira. Santiago de Cuba.Universidad de Oriente. Patricio Lumumba s/n Santiago de Cuba. email: auroraz@cnt.uo.edu.cu</p> <p>It is about a descriptive cross study that refers to the methodology of medication use corresponding to the prescription-symptom classification, with elements of a therapeutic plan in order to evaluate the prescription of antimicrobial drugs to pediatric patients showing infectious diseases in three departments of "Juan de la Cruz Martínez Maceira" Hospital, in Santiago de Cuba, during two months .The remaining</p>

	<p>sample make up 139 patients of which most were from one month old to one year old (75,51%) in Therapy service and others, from 8 to 21 days old (46,34%) in Newborn service. The most recurring pathologies were the Acute Respiratory Infections (51,79%). Among the patterns of the most prescribed antimicrobial drugs were CEFTRIAZONE (23,67%), CRISTALLIN PENICILLIN (19,32%) and AMIKACINE (14%). The results showed that 50,98% of the population in the study received medications that matched their pathologies, of which 83% indicated an adequate individualization of treatment and 67,74% an adequate combination of drugs. There was no significant statistical difference within the percentage of appropriate prescriptions (47,71%) and those that were not (52,28%) considering the three hospital departments together, although actually there were inappropriate prescriptions at all because of the unnecessary antimicrobial drugs.</p>
PFep 022	<p>SIMIFAL: A CONTRIBUTION TO HEALTH CARE QUALITY AND RESPONSIBLE SELF MEDICATION Herrera A. Mateu L, Díaz M, Pavón J. Pharmacy and Food Institute, University of Havana. 222 and 25 Ave. La Coronela. La Lisa. Havana City. Cuba. e-mail:ahllpiz@ifal.uh.cu</p> <p>Introduction: Drug Information Services from the Institute of Pharmacy and Food Sciences, (SIMIFAL) University of Havana, Cuba, was founded in 1993 in order to give access to objective and updated scientific information regarding the immense field of medications. Unlike the traditional systems of information and documentation, the SIMIFAL specialists, search, select, analyze and evaluate the documentation and finally give a specific and concrete answer to the user. The present paper shows the results achieved by the SIMIFAL from September 2009 to June 2010. Material and Methods: We received 153 consults by phone (116) and on-line (37). 24 of them were made from outside countries mainly from Mexico, Venezuela, Bolivia and Spain. Patients made 68% of the consults; that indicates a trend. Results and Discussion: Regarding the theme most of the consults were related to general information about Cuban and non foreign drugs and pharmaceuticals and drug interactions. The results confirm that this service is useful and practical with a pharmacotherapeutic level that guarantees an increment in the healthcare quality and an appropriate education to the patients that contribute to a safer and responsible self-medication.</p>
PFep 023	<p>CONCOMITANT THERAPY WITH TAMOXIFEN IN PATIENTS CONSUMING 20 MG TAB. AT INOR Chacón González B. Ropero RJ, Arbesú Michelena MA, Planché Aguiar L.</p> <p>Institute of Oncology and Radiobiology. Calle F y 29, Plaza de la Revolución. Havana City. email: marbesu@infomed.sld.cu</p> <p>Introduction: Breast cancer is the second leading cause of death in Cuba and the world. In order to treat this disease, considerations have been given to the use of a Gold Standard Patent, this is a tamoxifen 20 mg tablet to be given daily for five years. Patients under this treatment present associated pathologies that are treated with drugs, these patients may have a tendency to self-medicate with the occurrence, or not, of a possible drug overdose that will affect the patient's well-being. It is then utterly important to describe and study the variables and the causes associated to the use of tamoxifen. Material and Methods: We surveyed 100 patients, they had surgery during 2008 and were estrogen's receptor positive. The tributaries of the indication of Tamoxifen. As variables were analyzed: age, personal medical history, drugs used, causes, the indication origin, and occurrence, or not, of drug interactions that produced overdose or not. Results: The age group most represented was 51 years and older (65.3%), with a presence of 25.1% of those under 30 years. Hypertension and diabetes mellitus are the most common medical history (54%) and 38% did not suffer from another disease, but self-medicate. The drugs used were 87% correspond with the underlying diseases, 11 presented 29 self-medicate and drug interactions no apparent clinical manifestation. Conclusion: We found 78 deficiencies in the therapy of the patients studied, that led to 81 to make a targeted intervention with the doctor, the patient and companion.</p>
PFep 024	<p>CHARACTERIZATION OF THE ADVERSE MEDICINAL REACTIONS IN THE GRANMA PROVINCE DURING A YEAR (MAY 2009-MAY 2010) Guevara B¹</p> <p>¹Regulatory Bureau for the Protection of Health, Bayamo, Granma. email:bettygr@grannet.grm.sld.cu</p>

	<p>Introduction: The pharmaco-vigilance is one activity of appointed to health department to the identification, evaluation and prevention of the risks associated to the medicines one time commercialized. In Cuba there is a system of pharmaco-vigilance with a high rate of reports of adverse medicinal reactions (RAM). In Granma is not known the rate of notification of reports of RAM in the province, nor exist studies that characterize them. Materials and method: carried out a observacional, descriptive and transversal study, by using the method of spontaneous notification of report suspicions of adverse reactions and the base of data of pharmaco-vigilance, in an one-year period (May 2009- May 2010). Constituted objective of the work it calculate the rate of report of RAM in the province, it characterizes the population that presented adverse reactions according to demographic variables, identify the pharmacological groups and the medicines that with major frequency are involucrate in the reports of suspicion of RAM and classify the adverse reactions according to severity, frequency and harrow of imputability. Results and discussion: The rate of report of RAM to be 245 reports for each 100000 inhabiting. In the affected population they predominated the reports of the female sex (73.1 %), as well as the adult population (64.1%). The pharmacological groups with major reports of RAM to be the vaccines with 867 (42.3%), between those which the medicines more reported went, the Pandemrix (584) and the Pentavalent (171); the antiviral with 320 reports of the Oseltamivir (15.6%) and the Antibacterianos with 192, of these the medicines but reported went the Penicillins (37%), the Cefalosporinas (34.4%) and the Quinolonas (15.6%). The moderate reactions occupied the major percentage 1053 (51.3%), as well as the frequent reactions 1334 (65%) and predominated the probable thing 1385 (67.5%). Coclusiones: By means of this study knew the rate of report of RAM of the province and it is analyzed the conduct of the adverse medicinal reactions. Does to him necessary extend the study to decide us of own data and contribute to the quality of the pharmaco-vigilance system.</p>
PFep 025	<p>THE PHARMACOEPIDEMIOLGY DEVELOPMENT CENTER WEBSITE AS A CONTENT MANAGEMENT SYSTEM Portuondo Sánchez CL¹ ¹Pharmacoepidemiology Development Center. 5th Ave and 44 St, Miramar, Playa, Havana City, CP 11 300. Cuba. email:cportu@infomed.sld.cu</p> <p>Introduction: The Pharmacoepidemiology Development Center (PDC) has the objective of reaching a perfect use of medications in different levels of the Cuban National Health System. The necessity of producing and disseminate an objective information over medications for prescribers and consumers was the reason for which since 1998 this website was designed. The site shows bulletins of therapeutic actualization, books of consultations, the national formulary of medications, programs of diplomates issued, regulations made by the center and more information of interest. Material and Methods: The website was designed at the beginning on Front Page format, and it is hosted by Infomed as our service provider. The current site was designed with Drupal as <i>Content Management System</i>. It is an open source program that can manage content independently of the design. It shows a central column with an editorial and on both sides the blocks that are updated through blogs. Results and Discussion: The links at the top of the site access to basic drugs table, National Drug Program, National Formulary, program scripts “<i>La Dosis Exacta</i>” and discussion lists. Sections are shown Pharmacovigilance, Teaching, Research, Scientific Production, Therapeutic Consultation Service, news, and Program of Rational Use of Drugs in the blocks. Conclusions: The PDC website allows health personal to keep up with reliable information that responds to the necessities of our users. Given the structure and site design, access and content retrieval is feasible. References: Web site: http://www.cdf.sld.cu</p>
PFep 026	<p>IMPACT OFF SERVICE PHARMACOTHERAPY MONITORING DEVELOPED IN PATIENTS SUFFERING FROM CONGESTIVE HEART FAILURE. Lores D, Bermúdez I, Zúñiga A, Lazo Y.</p> <p>Institution: Principal Municipal Pharmacy . Santiago of Cuba. 4ta streets , number 4 . “Sueño” District. Santiago of Cuba CP 90400. Cuba. email: farma681@medired.scu.sld.cu</p> <p>Introduction: A service pharmacotherapy monitoring was developed with 30 patients suffering from Congestive Heart Failure, dispensed in the Principal Municipal Pharmacy Santiago de Cuba, in the period from October 2004 to January 2010. Objective: Evaluate the impact off service pharmacotherapy monitoring. Method: A prospective and intervention study was realized following the Dader methodology adapted off according to the experimental conditions and the impact of the service was determined through the established indicators. The results were analyzed through the correlational statistic. Results: 141</p>

	<p>suspects of negative outcomes related to medication and negative outcomes related to medication were detected, classified according Third Consensus of Granada, this being the non-quantitative safety problem (40.42%) and the non-quantitative ineffectiveness (29.07%) the one of greater incidences. The impact index of the accepted pharmaceutical interventions (98.56%), and the patient's satisfaction level (100%) were high. Conclusions: The impact index of the accepted pharmaceutical interventions and the patient's satisfaction level were high for this reason the impact of the pharmacotherapy service continuation carried out for the attention of said patients was regarded as high.</p>
<p>PFep 027</p>	<p>ADVERSE EVENTS ASSOCIATED WITH THE USE OF IOR@LEUKOCIM IN NEUTROPENIC PATIENTS WITH HEMATO-ONCOLOGIC DISORDERS Leyva Perdomo D., Hernández Rodríguez R, Vázquez Báez L, Rodríguez Hernández V. Universidad de Ciencias Medicas de Santiago de Cuba, Cuba. Faculty of Medicine, "Las Americas" Avenue, S / N. Santiago de Cuba, Cuba. email: doris@medired.scu.sld.cu</p> <p>The approval of a drug to be commercialized does not mean that its administration is not subject to risks. When a product is first introduced on the market, little is known about its long term effects ,so we have to take into consideration not only its effectiveness but also its safety. IOR@LeukoCIM is indicated for the shortenning of immunosuppression time in patients who received myelosuppressive chemotherapy for cancer therapy. It stimulates the bone marrow stem cells.Motivated for the need to assess the safety of this product, a cohort study was conducted to characterize the safety and adverse events associatted to the administration of IOR@LeukoCIM (Granulocyte Colony Stimulating Factor) in neutropenic patients with hemato-oncologic disorders. The dose of 5 micrograms / kilogram / day was administered to patients attending the Hematology Oncology Services at three different hospitals in Santiago de Cuba (Dr. Juan Bruno Zayas Alfonso, Conrado Benítez, and Saturnino Lora), in Cuba, from September 2007 to September 2008. Most of the 25 adverse events shown were classified as mild or moderate. There were no reports of severe adverse events and none of them required the discontinuation of therapy with the use of this drug. All patients recovered completely. The relation of causality most frequently observed was probable followed by possible and the least observed was definitive, in which category only were included leukocytosis, neutrophilia, and bone pain. There was an statistically significant association between cigarette smoking and adverse reactions. This investigational drug was considered safe in the dose, route of administration and indication used.</p>
<p>PFep 028</p>	<p>CUBAN NATIONAL FORMULARY ON WEB VERSION A NEW TOOL OF GOOD DRUG INFORMATION TO NATIONAL CUBAN HEALTH PROFESSIONAL AND SYSTEM Calvo Barbado DM¹, Delgado Martínez I¹, Kouri G², Castro R³, Rodríguez K⁴</p> <p>¹National Pharmacoepidemiology Development Center, Ave and 44 St, Miramar, Playa, Havana City. email: duche@infomed.sld.cu ²National Center of scientific Information-Network INFOMED, 27 ST, Vedado, Plaza de la Revolución, Habana City, Cuba. ³Center of Research and Drug Development, Ave 26, No. 1605 Boyeros y Puentes Grandes CP 10600, Plaza de la Revolucion, Habana City, Cuba. ⁴National Center of scientific Information-Network INFOMED, 27 ST, Vedado, Plaza de la Revolución, Habana City, Cuba.</p> <p>Introduction: Provide reliable drug information if one of the interventions and strategy that WHO consider to get a rational use of drug for any health system. The Cuban Health System as anyone need that the health professional take decisions based in good evidence and information, cause we need as a develop country an efficient and quality use of drugs. The first example of Theraputic Guide produced in our country was in 70's decades. During 80's re-editions of this sort of formulary was made. In 2003 the Pharmacoepidemiology Development Center (PDC) gather a group of professional that belong to their network and from the several Institutions of the Cuban health System an published the Cuban Generic National Formulary with re-edition in 2004 and a new edition in 2006. These 3 books contribute to improve the use of dugs and were well received by Cuban professionals. Although the printed book and his version in pdf, was difficult to manage and lack of useful for net-users, the needs of improve this version, the desire of incorporate new fields, and to make more interactive the National Formulary provide an opportunity to produce our web version or Drugs database of the Essential Medicines include in our National list. Material and Methods: The development of this tool gather the group of writers of the book who belong to the PDC, personal from the Vice-direction of Health Information Service of INFOMED, specialist from the National Pharmaceutical Center and Editors from Medicine Science</p>

	<p>Editorial House . The writers worked all a year gathered the information of each drug, and at the same moment the technologist find the proper tool to our formulary. In January of this year the editorial team, designer and the mains author of the project began the edition process and to test the CWIS program, the chosen tool for the project. Results and Discussion: The final product is an interactive drug database, with 24 fields (include pharmacokinetics, mechanism of action, price, if had any regulation to recipe or dispense, etc). More than 860 product with all information were produced. Conclusions: The Cuban health professional will have a new product or information service to make proper decision at time of the prescription . This is a new effort of the Pharmacoepidemiology Center to improve our medical care.</p>
<p>PFep 029</p>	<p>DESIGN OF THE EDUCATIVE INTERVENTION ABOUT PSYCHOTROPIC SUBSTANCES, IN STUDENTS OF TELECOMMUNICATIONS AND ELECTRONIC CAREER Pupo E¹, Labrada R¹</p> <p>¹Department of Pharmacy, Faculty of Natural Sciences, University of Oriente. Patricio Lumumba y Avenida de Las Américas. Santiago de Cuba, Cuba. CP 90500. email: epupo@cnt.uo.edu.cu</p> <p>Introduction: Drugs Utilization Studies are studies on marketing, distribution prescription and use of drugs in a society, with a special emphasis on the sanitary, social and economic consequences. These studies on university community show the high consumption and less knowledge, and we can use to obtain effective prevent strategic. Material and Methods: A traverse descriptive study of drug utilization of medications, of type consumption on substances psychotropic, in the major of Telecommunications and Electronic of the Ability of Electric Engineering, University of Oriente, during 2009. Results: According to the knowledge there is a prevalence of students Experts with Deficiencies with 60.97% of the total of the sample, fundamentally in those belonging to the 4th year, and regarding the consumption of psychotropic substances it was determined that in its majority they turned out to be Consumers for 91.70%, for a reason of 11:1, preferably of social type with 72.68%, being the secondary multiconsumers those that prevailed with 35.1%, the same as the non poliaddictive (83.51%), being the coffee, the alcohol and the psychodrugs the consumed substances, being obtained a low but significant self-medication with 18.57%, being the Diazepam the used medication. A direct relationship was not evidenced between the consumption and the knowledge, being the social push the cause of more consumption. The perception was valued in appropriate as well as the specific factors of risks and of protection, with a high consumption probability those of risk prevailed over the ones of protection. These data provided a non favorable student diagnosis, similar result to the educational diagnosis. It was proposed an intervention design related to the results from the specific student and educational diagnosis to their curricular and extracurricular profile in function of the obtained results. Conclusions: Obtained the drugs diagnosis of knowledge and consumption in the university students.</p>
<p>PFep 030</p>	<p>DESIGN OF THE EDUCATIVE INTERVENTION ABOUT PSYCHOTROPIC SUBSTANCES, IN STUDENTS OF JURY FACULTY Pupo E¹, Taboní L¹</p> <p>¹Department of Pharmacy, Faculty of Natural Sciences, University of Oriente. Patricio Lumumba y Avenida de Las Américas. Santiago de Cuba, Cuba. CP 90500. email: epupo@cnt.uo.edu.cu</p> <p>Introduction: Drugs Utilization Studies are studies on marketing, distribution prescription and use of drugs in a society, with a special emphasis on the sanitary, social and economic consequences. These studies on university community show the high consumption and less knowledge, and we can use to obtain effective prevent strategic. Material and Methods: A traverse descriptive study of drug utilization of medications, of type consumption on substances psychotropic, in the Jury Faculty community of University of Oriente, during 2009. Results: 63.41% of students Experts was obtained with Deficiencies, prevailing the 4th year (71.79%). 88.78% turned out to be Consumers, mostly social (56.10%) and habitual (25.85%). A secondary multiconsumers was obtained with 53.30% and 93.66% of the students they turned out to be non poliaddictive. In the self-medication level didn't prevail in a general way with 21.46%, it calculates significant due to it is psychodrugs, justifying this consumption due to the stress, where the Clorodiazepóxido and the Meprobamato, they were the psychodrugs more used respectively for 45.35%. The students in spite of possessing an appropriate perception in a general way on this thematic one, impact in this study the individual factors of risk for 30.0% followed by the social ones with 26.67% of the total of the sample. All these obtained results of each one of the indicators proposed in the investigation, it allowed us to evaluate the student diagnosis as Not Favorable. The development of the strategy of prevention was</p>

	<p>diagnosed against the undue use of drugs, inside the educational process in this major, that which was documented in records where the strengths and weaknesses of the career were evaluated, being obtained a favorable educational diagnosis. Conclusions: Obtained the drugs diagnosis of knowledge and consumption in the university students.</p>
PFep 031	<p>BEHAVIOUR OF REPORTS OF SUSPECTED ADVERSE REACTIONS TO MEDICATIONS CONSUMED. CUBAN MEDICAL MISSION. BOLIVARIAN REPUBLIC OF VENEZUELA. 2007-2008 Reinaldo Acosta ED1, Debesa GF1, Jiménez LG2, Dupuig BR1</p> <p>¹ Medical Cuban Mission, Venezuela. email:damaraacostareynaldo@yahoo.es ² National Coordinating Unit of Pharmacovigilancia. email: giset.jimenez@infomed.sld.cu</p> <p>Introduction: The Cuban medical mission in Venezuela, has a database where empty suspected adverse drug reactions, but with the output that has the system of absolute and relative frequencies is not sufficient to generate a signal, but consumption is an indicator of population exposed to drugs that are used to demonstrate, if the adverse event profile that has been reporting, is related or not drug use, suggesting the construction of an indicator that relates RAM and consumption forecasts for future decision making. Objective: To determine the behavior of reports of suspected adverse drug reactions in relation to the drugs most consumed in Venezuela, 2007-2008. Method: An observational descriptive cross-sectional research, drug utilization, which classifies consumer research with elements of practical consequences, to describe the behavior of the RAM report in relation to the most frequently used drugs in the Cuban Medical Mission in Venezuela, 2007 and 2008. Results: ferrous fumarate tablets was the drug that increased consumption experienced in the period (8.6 DID). Captopril was the most reported with 459 notifications. In adults, there were 1623 reports (73.0%) and 1090 females notifications (49.0%). Skin and mucous membranes was the most affected organ, 809 suspected (36.4%). Mild adverse effects predominated with 86.0% and 61.0% of the reports were classified as probable. Conclusions: Consumption of drugs was not the determining factor related to the reporting of suspected adverse drug reactions, this behavior could be related to other factors such as availability, prescription habits, lack of adverse effects, lack of role models, and laziness in the notification, among others. The design of an educational intervention strategy on pharmacovigilance, will consolidate the timely reporting of suspected ADRs in the Cuban medical mission.</p>
PFep 032	<p>POLYPHARMACY: THE MOST PREVALENT FRAILTY CRITERIA IN THE ELDERLY. Sansó F¹, Alonso P², Calvo DM³</p> <p>¹Clinical Surgical Hospital “Dr. Salvador Allende”. Cerro Ave and Domínguez St. Cerro. Havana City, Cuba. email:fsanso@infomed.sld.cu ²National Center of Medical Sciences Information. E St. between 19 St. and 21 St., Vedado. Plaza. Havana City, Cuba. email:patricia.alonso@infomed.sld.cu ³Center for the Development of Pharmacoepidemiology, National Pharmacovigilance Unit, 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba. email: dulce@mcds.sld.cu</p> <p>Introduction: Cuba is one of the oldest countries in the Americas. The country has gone from 11.3 percent of people aged 60 years or more in 1985 to 16.6 percent in 2009. The condition of “frailty” is inherent of the elderly group and is a risk of developing, worsen or perpetuate adverse health effects all of which are associated with increased risk of evolving into disability and dependency, and ultimately, to death. Polypharmacy is one of biomedical frailty criteria, defined in the Cuban context as daily consumption of three or more drugs regularly. To identify the contribution of polypharmacy to the prevalence of fragility in the elderly population attended by Basis Working Group "Palatino" in the health area "Antonio Maceo", Cerro Municipality, City of Havana, Cuba is the objective of this study.Material and methods: An observational, descriptive and cross-sectional study was conducted in the period January 2007- December 2007. For estimating the fragility prevalence, the Geriatric Scale of Functional Assessment was applied to all the elderly and they were then classified as frail and non-frail according to the present Cuban criteria. Results and discussion: 541 elderly adults were studied. Of the studied older people, 51.4 % were identified as frail. Polypharmacy was identified, by far, as the prevalent criterion of frailty (35,5 percent). Polypharmacy is also one of the conditions most frequently associated with frailty in the elderly according to other authors. It's assessment should cover beyond its quantitative behavior, and insist more on its quality. It's very different risk situations that could have an elder that consume more than three drugs on a regular basis, properly prescribed, than another self-medicated. Conclusions: Frailty in older people is a</p>

	highly prevalent condition in the "Palatino" People's Council population, in the expression of which significantly affects Polypharmacy.
PFep 033	<p>THE CENTER FOR ANALYSIS OF MEDICAL SUPPLIES, A STRATEGIC PILLAR, HEALTH INSURANCE CUBAN MEDICAL MISSION IN VENEZUELA. Debesa GF, Acosta RD, Roque ML, Trujillo FD, Fajardo CI, Vázquez LT, Socorro RW, Gonc ME.</p> <p>Cuban Medical Mission in Venezuela. email: patricia.alonso@infomed.sld.cu The Centre for Analysis of Medical Supplies was created to plan all the medical supplies that respond to the services of all existing specialties in the Cuban Medical Mission in Venezuela.</p> <p>For the first time in the history of the planning of medical supplies, is concentrated in a single center analysis of the behavior of these resources in specialties as diverse as dentistry, optical, waste materials, drugs and reagents, which provides strength to power conduct a comprehensive analysis of all these inputs that affect the quality of medical services. As part of the center, joins the specialty of Pharmacoepidemiology that provides tools for studies of consumption, which combined with sentinel surveillance and evaluation of planning by analyzing the forecasts of consumption, make this a novel process in working with medical supplies. The exhibition explains the mechanisms by which they are implemented in Venezuela consumption studies in all specialties and how to use these results in resource planning, using the computerization of all processes, which has resulted in a better planning and therefore better care for patients in the Medical Mission in "Barrio Adentro".</p>
PFep 034	<p>ADVERSE DRUG REACTIONS IN PREGNANT WOMEN, CHILDREN AND EDERLY PERSONS NOTIFIED TO PHARMACOVIGILANCE SYSTEM. MATANZAS. 2004-2008 Francisco W</p> <p>Regulatory Desk for Protection of Health. Céspedes Ave y Obispo st, Cárdenas. Matanzas. email: medicar.mtz@infomed.sld.cu</p> <p>Matanzas province has a Pharmacovigilance System directed to the detection of adverse drugs reactions (ADRs), but the behavior of those reactions are unknown in pregnant women, children and old person. In order to describe the main characteristics of them ADRs and identifying factors that explain its behavior took place an empiric research in which quantitative and qualitative methods were applied. The quantitative methods was an observacional, descriptive and transverse study where all the ADRs notified in Matanzas from 2004 to 2008 were evaluated. The variables were sex, age, type of ADRs, affected organ, pharmacological group, type of medication, among others. The source of data was the Vigibase of Cuba. The qualitative investigation applied the focalized group discussion technique, two groups were made, one of them was integrated for doctors, nurses, pharmacists and stomalogists, the other was formed by municipal pharmacoepidemiologists. In the period of study 3 ADRs of pregnant women were notified, 436 in children and 529 in old people. In the pediatric age, the female sex predominated (51.4%), the group from 1 to 4 years (29.8%), the rash (36.5%), as ADRs, the skin (50.2%) as system of organs, the antibacterials (53.9%) within pharmacologic groups, the procaine penicillin (9.6%) as responsible pharmaceuticals of ADRs. In geriatric age, the women predominate (59.5%), the group from 60 to 69 years (62%), the rash (15.9%), the digestive system (27.6%), the antibacterial (26.1%) and the captopril (7.8%). Most of the totality of the reports came from APS (98.5%) and they were made by doctors (56.6%). A marked infranotification of ADRs became evident in pregnant women, that the rash and antibacterial were the types of ADRs and pharmacological group that predominated in children and old person, as well as female sex was the most affected. The majority of ADRs were moderated, probably and frequent. The difficulty to establish the reaction drug-ADRs, lack of time constituted the main identified factors as possible causes of infranotification.</p>
PFep 035	<p>BEHAVIOR OF ADVERSE DRUG REACTIONS IN CHILDREN UNDER 15 YEARS. CUBA. 2003-2009 Mourelle Furones JA¹, Muñoz Quian B M², López Jiménez G.¹, Avila Pérez Jenny¹, Figueredo Ramirez D³, López Aguilera AF⁴</p> <p>¹Centre for the Development of Pharmacoepidemiology. esq 44th Street, to 5th Ave. No. 502, Miramar, Playa. Ciudad de La Habana. email: furones@infomed.sld.cu ²Provincial Health Department Havana. Department of Pharmacoepidemiology. ³National Control Center for Quality of Medicines ⁴Faculty of Medical Science "Julio Trigo" Medical University of Havana.</p>

	<p>Introduction: Children have pharmacokinetic and pharmacodynamic characteristics peculiar and rapidly changing that makes them a higher risk of adverse drug reactions (ADRs). Objectives: To describe adverse drug reactions (ADRs) in children under 15 years reported to the pharmacovigilance Cuban system from 2003 to 2009 and assess the factors that explain the behavior of the notifications. Material and Methods: An observational, descriptive and cross-sectional quantitative and qualitative methods use quantitative research in the universe consists of all ADRs reported spontaneously and included in the VIGIBASE of Cuba. The variables used: sex, age, level of care, specialty of the reporter's home province, diagnoses that led to the indication, medication, drug group, administration route, type of RAM, organ systems, frequency, severity, severity, association drug-RAM, sex and age of the fatal reactions. Qualitative research to design a questionnaire to be discussed at interview focused group. Results: Reports of RAM accounted for 18.5% of the total. Underreporting existed in the years 2004, 2005 and 2006 with a RR = 0.9, 0.87 and 0.58 respectively, compared with the reported rate of adults. ADRs were more common in females (50.7%) and 1 and 5 years (35.2%). Physicians (62%) and Primary Health Care (86.3%) reported the most. The pentavalent vaccine was the drug most reported (10.9%) and drug group, antimicrobials (39.4 /) and immunization most reported diagnosis (33.5%) and intramuscular (45, 3%), skin rash predominated (27%) and the skin as an organ affected (41.6%). Most were mild (49.1%), probable (83.8%) and common (66.7%). All children under 1 year (23, 63.9%) males (26, 72.2) and antimicrobials (11, 30.5%) contributed the greatest amount of RAM fatal. The disinterest and lack of knowledge about pediatric pharmacovigilance, difficulty in differentiating between disease toddler and RAM and poor compliance with treatment by relatives, were the major factors that accounted for the underreporting. Conclusions: ADRs in children accounted for one fifth of the total notifications to Cuba Pharmacovigilance system in the study period, with rates of underreporting compared with adults.</p>
PFep 036	<p>ADVERSE DRUG REACTIONS AMONG ELDERLY PEOPLE IN THE CUBAN SYSTEM OF PHARMACOVIGILANCE.YEARS 2003-2007 Furones Mourelle JA¹, Jova Bouly A P², Duque Rodríguez R², López Jiménez G.¹, Pérez Ávila Jenny¹, Cruz Barrios MA¹, Aguilera López AF³.</p> <p>¹Centre for the Development of Pharmacoepidemiology. esq 44th Street, to 5th Ave No. 502, Miramar, Playa. Ciudad de La Habana. email:Furones@infomed.sld.cu. ²Analysis and Planning Group of the Ministry of Public Health. Cuba. ³Faculty of Medical Science "Julio Trigo" Medical University of Havana.</p> <p>Introduction: The population over age 60 have an increased risk of suffering adverse drug reactions (ADRs). Objectives: To characterize the ADRs in the elderly, reported to the Pharmacovigilance system from 2003 to 2007 and assess the factors that can explain the behavior of the notifications. Material and Methods: A descriptive cross-sectional observational study, which used quantitative methods and qualitative research. In quantitative research, the universe were all reported ADRs in patients over aged 60 and included in the VIGIBASE, during the period study. Information was collected on age, sex of patients, professional reported, level of care, type of RAM, organ and severity, causality and drugs that led. In qualitative research, a questionnaire was designed to be discussed In an interview focused group, with professionals and technicians of the National Directorate of Older Persons and Social Assistance. Results: We found that notifications were reported 7793 ADRs in this age group, accounting for 18.7% of all reports made in Cuba in the period, 2003 was the highest number of notifications with 2318 (18.5 %), more frequent in women with 5083 reports (65.2%) and 60 and 69 years with 4405 (56.5%). The most common types of ADRs were the rash with 1009 (12.9%) and cough with 676 (8.6%), which affected in greater amount of skin with 1756 (22.5%) and gastrointestinal system in 1636 (21%). The Captopril was the drug most reported 958 (12.3%), followed by ciprofloxacin with 299 (3.8%) and drug group most affected were the antimicrobials with 1892 (24.2%). The events were mild in 56% and 73% probable. ADRs were reported by most physicians (70.5%) of primary care (84.6%). The lack of training in the pharmacology of the elderly in undergraduate and graduate, in addition to the lack of administrative control in pharmacovigilance, are the most important factors that explain the behavior of the notification of ADRs. Conclusions: Adverse reactions in the elderly were approximately one-fifth of all the Pharmacovigilance system notifications of Cuba from 2003 to 2007 and notification rates were higher than those of the population under 60 years.</p>

PFep 037	<p>CLIENT SATISFACTION ASSESSMENT AT VILLA CLARA DRUGSTORE. 2008-2009 Lorenzo G¹, Gómez LA² ¹Molecular Immunology Center. email: cim@capiro.vcl.sld.cu ²Villa Clara Drugstore. email : lalberto@vcl.quimefa.cu</p> <p>Villa Clara Drugstore is in charge of the distribution of medications, reagents, and other medical consumables in this province of the country. It has commercial relations with a wide variety of clients, but the most important ones are within the Health System. This work is aimed at evaluating the service quality that this Organization offered to Hospitals, Polyclinics, and Pharmacies of the province during the years 2008 and 2009. To this end a representative sample from these institutions in all Villa Clara municipalities was selected and the personnel in charge of medications in each unit were surveyed. Satisfaction index for each surveyed client was determined as well as the overall satisfaction index for polyclinics, hospitals, and pharmacies. Also matrix of attributes were made taking into consideration the aspects for which the least satisfaction index was achieved and a measures plan to obtain a better service was devised. On the other hand, the Drugstore's overall satisfaction index in each assessed year was determined. The service offered by Villa Clara Drugstore in the years 2008 and 2009 was assessed as GOOD, with a tangible improvement showed by the satisfaction indexes that increased from 84.8% in 2008 to 88.8% in 2009. The clients of the medications distribution process perceive medication availability as the main problem in the province.</p>
PFep 038	<p>PHARMACEUTICAL ASSISTANT PROGRAM ON THE COMMUNITY. MANZANILLO. 2010 Lastres Rodríguez GM¹, Arceo Naranjo R² ¹Pharmacy's and Optic's Enterprise, 210 at Luz Caballero Street, Manzanillo City, Granma's Province, Cuba. email: ellie2010 @grannet.grm.sld.cu ²Hermanos Cordové 's Pediatric Hospital Caymary's District, Manzanillo City, Granma's Province, Cuba.</p> <p>Men since their existence needed drug products to counteract their illness, however, although the efficacy of them in treatment for different pathologies, it had been demonstrated the abuse of drug products which are provoking several adverse reactions in some patients, but they are easily prevented with a good prescriptions practice and by following the patients. The checked of 138 certificate of controlled drugs prescribed by Family's Doctors belonging to two Heath's Center in Manzanillo, as well as, the systematically visits to patients who present non transmission chronic diseases, allowed the authors detected many problems refer to drug-related problems, such as prescribing errors, dosing errors, incorrect, inconvenient, or less-than-optimal dosing interval, adverse drug effects, drug-drug interaction, drug-food interaction. That's why, the development of this research with the objective of elaborating a Pharmaceutical Assistant Program on the Community of Manzanillo to improve the medical prescription and to increase the quality life of the ambulatory patients, taking into account as hypothesis: the application of a Pharmaceutical Assistant Program on the Community based on the wok as a whole among doctor-nurse-pharmacist in consults and by visiting outpatient it will be allow a rational prescription of drugs and a best life for them. During the investigation some scientific methods were used as theoretical and empirical ones and the statistical method too in order to obtain the diagnostic of the actual states of problem and for evaluating results. Good results were obtained such as: the errors in prescription decrease a lot and the adverse effects too. It had demonstrated the roll of pharmaceutical personnel who have the most training in drug products and can help the physicians in preventing drug misuse, drug abuse and irrational prescriptions. This work has a great economical and social impact.</p>
PFep 039	<p>REASONED THERAPY VIEWED FROM THE PERSPECTIVE OF PATIENTS IN LA LISA MUNICIPALITY IN 2010 Díaz I,¹ Martínez RP,¹ Betancourt Y,¹ Pulido L.¹ ¹Finlay-Albarrán Medical Faculty, Ave 25, No. 15005, Cubanacán, Playa, Havana City, Cuba. email: irisdiaz@infomed.sld.cu</p> <p>Introduction: Academic and medical institutions are promoting the methodology of Reasoned Therapy (RT). It involves step by step all the prescriptors of the problem and the solution. The method takes into account an adequate structure of the treatment in an oral and written ways. The objective of this research was to analyze the accomplishment of the variables information, instruction and advice (the fifth step of the RT). Material and Methods: A descriptive and observational study was made with descriptors from</p>

	<p>primary and secondary health care institutions. The sample was formed by all the patients who got the medications in Special Pharmacies in the municipality of La Lisa in may 2010. To establish the size of the sample a proportion of expected satisfactory answers of 0.662 of the variable instruction was taken into account in an experimental (pilot) survey. The probable reliability was of 0.05 and 0.1 of accurate estimation. As a result of all these information eighty six individuals participated in the survey. It had an evaluation scale of good, fair or bad for each variable. Results and Discussion: Of all the prescriptors evaluated in the survey 79.09 % of the information was evaluated as bad, including chronic and acute diseases and those given by primary and secondary health centers. The majority of the instructions were evaluated as fair or bad, 52.32% and 38.37% respectively. The worst results were for acute diseases and secondary health care centers. More than three of four of the advice were evaluated as bad (75.58%). The result was similar not only in both kinds of diseases. Conclusion: As a conclusion can be said that the fifth step of the Reasoned Therapy was accomplished with an evaluation of un satisfactory in our real clinical practice.</p>
PFep 040	<p>PROBLEMS ASSOCIATED TO THE PSYCHOACTIVE DRUGS USE IN EDERLY HOSPITALIZED PATIENTS Ortega IL¹, Verdecia ME²</p> <p>¹Pharmacy Department, Orient University, Ave. Patricio Lumumba, Without number, Santiago de Cuba City, Cuba. email:irma@cnt.uo.edu.cu ²"Saturnino Lora" Hospital of Santiago de Cuba, Ave. de los Libertadores, Santiago de Cuba City, Cuba.</p> <p>Introduction: Drug- related problems are common in the geriatric population due to polypharmacy and age- related physiologic, pharmacokinetic, and pharmacodynamic changes. Material and Methods: A prospective study was carried out, of intervention, with the purpose to identify the drug related problem and to prevent or to solve the negative outcomes associated with medication of the same ones; in old patients that consumed psychoactive drugs, and that they were hospitalized in "Saturnino Lora" Hospital of Santiago de Cuba, during the period from May-October 2009. The study was carried out according to the DADER Method of Pharmacotherapy Monitoring, adapted by the author and the theoretical budgets of the Third Consent of Granada were assumed, 2007, for the considerations related with the drug related problem and the negative outcomes associated with medication. Results and Discussion:Thirty five patients were included whose ages oscillated between the 60 and 90 years. Thirty six negative outcomes associated were identified, in 34 patients that represented 97.14% of incidence, for each patient, probably; it was exposed to 1.06 negative outcomes associated. A prevalence of the negative outcomes associated to the necessity was observed with 50%, followed by those associated with the security with 38.89% being represented the problems of effectiveness in 11.11%. The self-medication and the inadequate drug uses were the drug related problem that prevailed with 44.44% in each case, the probability of adverse effects was presented in 41.17% of the sample. Conclusions: The psychoactive drugs that were related with these results in more measure were the anxiolytic (36.11%), carbamates (19.44%) and the neuroleptics (22.22%). The 82.35% of the interventions were accepted, achieving you to solve 47.06% of the negative outcomes associated with medication.</p>
PFep 041	<p>TREATMENT OF THE PEPTIC ULCER BY <i>HELICOBACTER PYLORI</i> IN HOSPITALIZED PATIENTS Bermúdez IC¹, Cutie ET¹, Santiesteban XS²</p> <p>¹Oriente University. Natural Sciences Faculty. Department of Pharmacy. Patricio Lumumba s/n. Santiago of Cuba City. Cuba. email: isis@cnt.uo.edu.cu betisell@yahoo.es ²Surgical Clinic General Hospital "Juan Bruno Zayas Alfonso" Santiago of Cuba City. Cuba.</p> <p>Introduction: The peptic ulcer is a health problem with a tall prevalence in the population. This entity occupies in Cuba the second place in frequency between the alterations of the stomach and in Santiago of Cuba the first cause of admission in the hospital between all the gastric alterations. Material and Methods: A drug utilization study of the prescription indication type, with elements of a therapeutic plan and factors that determinate the prescriptions habits was carried out, to evaluate the treatment of the peptic ulcer by <i>Helicobacter pylori</i> in patients that they were hospitalized at the Surgical Clinic General Hospital "Juan Bruno Zayas Alfonso" in the period comprising January to September 2009, also to evaluate the knowledge degree of the doctors belonging to Gastroenterology service. The sample was constituted by 176 patients and 6 doctors who were characterized using biosocial and clinic variables. The prescriptions were evaluated utilized 4 indicators: indication, therapeutic plan, treatment individualization and</p>

	<p>medicaments combinations and the knowledge degree of the doctors was obtained with the knowledge test. Results and Discussion: The results demonstrated that this pathology is frequent in men (68,8%) between 47-60 years (42%), that they consumed coffee (85,79%) and they suffered rheumatic diseases (41%) and arterial hypertension (31%), The nausea (86,9%) and epigastria pain (72,1%) was the principles symptoms. The adequate prescriptions were the more frequent (89,21%) by the use of the triple-drug regimen with omeprazole, amoxicillin and metronidazole. The doctors of the service were little knowledge (50%) because the criterion for the indication maintained the use of the medicament that now it was substituted by the triple-drug regimen and they no knowledge well the adverse reactions and medicament combination provoked by this medicaments. Conclusions: The little knowledge of medical personnel it aim toward the necessity of intervening through activities of sanitary manners.</p>
PFep 042	<p>THERAPY WITH TROFIN IN PREGNANTS PATIENTS WITH IRON DEFICIENCY ANAEMIA Bermúdez IC¹, Espada LD¹, Ferrer AS², Martínez YP¹, Dutok CS¹</p> <p>¹Oriente University. Natural Sciences Faculty. Department of Pharmacy. Patricio Lumumba s/n. Santiago of Cuba City. Cuba. email: isis@cnt.uo.edu.cu betisell@yahoo.es ²Oriente University. Natural Sciences Faculty. Department of Chemical. Patricio Lumumba s/n. Santiago of Cuba City. Cuba.</p> <p>Introduction: Trofin is a biopreparation elaborated by BIOCEN Centre in Havana city. It is a natural product that contains iron, protein, amino acids, bee honey and propolis. Trofin has been used in Cuba for the treatment of the iron deficiency anaemia in pregnant patients. The aim of our study was to compare the cost effectiveness of the relationship between Trofin and ferrous fumarate in pregnant patients with anaemia caused by iron deficiency. Material and Methods: An open aleatory clinical trial was carried out in 60 pregnant patients with anaemia caused by iron deficiency in the Eastern Maternity House from Santiago of Cuba between January and July 2008. Thirty (30) women were treated with Trofin (Group A) and 30 women with ferrous fumarate (Group B). The principle variables used were the haemoglobin and hematocrite levels in each patient, the secondary variable as the clinical evolution; the safety variable was regarding adverse reactions and the control variables: age, toxic habits, nutritional habits, consumption of vitamins with the treatment indicated and instruction level. The benefit and risk relationship was calculated and the cost effectiveness of the relationship was also evaluated. Results and Discussion: Our results showed that the treatment with Trofin was useful in achieving the reduction of the haemoglobin and hematocrite levels of pregnant patients affected with anaemia and none of the patients treated with Trofin presented adverse reactions. Ninety six point seven (96.7%) of the pregnant patients who received the treatment with Trofin had higher benefits and reduced risks. In addition, the cost effectiveness of the relationship with Trofin was greater than cost effectiveness relationship of the treatment with ferrous fumarate. Conclusions: The results demonstrated that Trofin is very useful for the treatment of the iron deficiency anaemia in pregnant patients with advantages economic superiors to the ferrous fumarate.</p>
PFep 043	<p>THE CLINICAL OUTCOME OF PATIENTS TREATED WITH HEBERPROT-P. CUBA. 2007-2009. Yera Alós Isis Belkis¹, Alonso Carbonell Liuba², Alvarez Crespo Alina³, Debesa García Francisco⁴, Diaz Hernández Aleida⁵</p> <p>¹Esp II Degree in Biostatistics, Master in Health Economics. Assistant professor. ²Esp II Degree in Pharmacology. Master in Health Promotion Assistant Professor. Assistant Researcher. ³Esp I Degree in General Medicine. Instructor Professor. ⁴Pharmaceutical Sciences Lic.. Master in Health Economics. ⁵Tec Informatica. Center for the Development of Pharmacoepidemiology. Calle 44 esq 5ta ave. No.502. Playa, Ciudad de La Habana. isis @mcd.f.sld.cu.</p> <p>Introduction: P Heberprot a drug developed in Cuba, and only novel therapy for diabetic foot ulcer (UPD), in clinical studies have proven the safety and efficacy results in a small number of carefully selected data need to be enriched with the evidence obtained from the use of the drug in medical practice conditions habitual. Objetivos: To characterize patients treated with Heberprot-P in Cuba since June 2007 to December 2009 according to demographic, clinical and therapeutic evaluate the clinical outcome of patients treated with Heberprot-P Method: An observational, longitudinal, multicenter 2050 adult patients attending treatment in 85 health institutions. Results: The mean age of patients was 63.4 ± 11.7 years, 54.2% of the cases were women, 59.3% reported a history of hypertension and 22.9% of ischemic heart</p>

	<p>disease. In patients with ulcer predominated neuroinfecciosa UPD as ranked by Mc Cook (57.3%) and Grade 3 Wagner (53.5%). The time evolution of the lesions in 95.8% of cases was less than 1 year. The main reason for prescribing Heberprot-P was the UPD. 75.1% of patients achieved complete granulation of the injury, CI 95.0% (73.2 -77.0). An association was found between the complete granulation and the pathogenesis and clinical stage of the UPD. Conclusiones: In medical practice the Heberprot-P confirms the results achieved in pre-marketing stage regarding its effect on the formation of granulation tissue injuries .</p>
<p>PFep 044</p>	<p>SURFACEN SAFETY PROFILE IN INFANTS WITH HYALINE MEMBRANE DISEASE. CUBA. 2007-2009 Yera Alós Isis Belkis¹, Casaña Díaz Elaine², Fernández Limia Octavio², Morilla Andrés³, Martín Estevez Ana Ibis⁴ Debesa García Francisco⁵</p> <p>¹Esp II Degree in Biostatistics, Master in Health Economics. Assistant professor. isis @mcd.f.sld.cu. ²DrC. National Center for Agricultural Health. Carretera de Tapastey Autopista Nacional, Km. 22 1/2, Apartado 10, San José de las Lajas, La Habana. ³Esp II Degree in Neonatology . Ministry of Public Health Cuba. ⁴Specialist. National Center for Agricultural Health. Carretera de Tapastey Autopista Nacional, Km. 22 1/2, Apartado 10, San José de las Lajas, La Habana ⁵Pharmaceutical Sciences Lic. Master in Health Economics. Center for the Development of Pharmacoepidemiology. Calle 44 esq 5ta ave. No.502. Playa, Ciudad de La Habana.</p> <p>Introduction: The Surface is a natural drug, porcine, recommended for replacement therapy in conditions of pulmonary surfactant system dysfunction, Objectives: To describe the safety profile of SURFACEN in infants with respiratory distress in the context of clinical practice. Method: We conducted an observational, multicenter, postmarketing, which included 259 patients who were treated with SURFACEN Cuba in 17 institutions between March 2007 and March 2009. Results: 48.6% of patients reported at least one occurrence of an event during treatment. Among patients who reported adverse events, the highest percentage reported an event and the maximum of events reported in any patient was seven. Hyperoxia was the most reported event (33.9% of patients), followed by hypocapnia in 8.9%. Regarding the severity 63.2% of the events were classified as mild, 31.6% as moderate and 5.2% as severe. Conclusions: In medical practice the Surface features a safety profile that is dominated by events with a mild magnitude causal link that can be explained largely by hyaline membrane disease and clinical conditions that prevail in patients of this drug tax</p>
<p>PFep 045</p>	<p>PATTERN OF PRESCRIPTION LeukoCIM. HOSPITALS OF CUBA. JULY-DECEMBER 2009 García Ana J¹, Yero Isis B², Alonso Liuba³ Alvarez Alina⁴</p> <p>¹Esp II Degree in Pharmacology, Master in Health Economics. Researcher and assistant professor. ²Esp II Degree in Biostatistics, Master in Health Economics. Assistant Professor. ³ESP II Degree in Pharmacology. Master in Health Promotion Assistant Professor. Assistant Researcher. ⁴ESP I Degree in General Medicine. Instructor Professor. Center for the Development of Pharmacoepidemiology. Calle 44 esq 5ta ave. No.502. Playa, Ciudad de La Habana anaj@mcd.f.sld.cu</p> <p>Introduction: LeukoCIM, colony stimulating factor granulocyte (G-CSF or G-CSF) is produced by the Center for Molecular Immunology (CIM) and is marketed for use in cancer patients treated with myelosuppressive chemotherapy in patients with acute myeloid leukemia in chemotherapy induction or consolidation, who receive bone marrow transplant, patients with cancer underwent mobilization procedures and collection of hematopoietic progenitor cells with severe chronic neutropenia and profile-xis and treatment of neutropenia in patients with Vifian / AIDS. Objectives: To identify prescription diagnoses motivating factor granulocyte colony stimulating (G-CSF or GCSF) and to estimate their consumption Method: This prospective longitudinal descriptive study, limitation - an indication, with elements of consumption in the period July to December 2009. Results: During the last half of 2009 were treated with LeukoCIM 664, which consumed bb 5253 for an average of nine per patient bb. Lung cancer, prostate, breast, leukemia and multiple myeloma were the main diagnoses reported. Villa Clara, Granma and Havana are the provinces which included greater numbers of patients. Conclusions: The indications for colony stimulating factor identified are associated entirely with oncological diseases, although not all agree with the indications for which the product was approved.</p>

PFep 046	<p>DERMATOLOGICAL SIDE EFFECTS CAUSED BY ANTIBIOTICS. CUBAN SYSTEM OF PHARMACOVIGILANCE. 2007-2009 Alfonso I, Jiménez G, Pérez J, Chao A Centre for the Development of Pharmacoepidemiology, Pharmacovigilance Cuban Coordinating Unit, 44th Street and 5th Avenue, Miramar Playa, Havana City, Cuba. e-mail ismary@mcds.sld.cu , isma.alfonso@infomed.sld.cu</p> <p>Introduction: Each year there are more than 140,000 adverse reactions associated with the use of antimicrobials in the United States, the most common allergic type. This research aimed to characterize the dermatologic adverse reactions to antimicrobial notified to the National Coordinating Unit of Pharmacovigilance during the period 2007 – 2009. Materials and Methods: An observational study of Pharmacovigilance, descriptive and cross-sectional reports Spontaneous Reporting of Suspected Adverse Reaction database and Cuban Pharmacovigilance System. We analyzed reports of adverse reactions reported antimicrobial skin from the year 2007 - 2009, the primary endpoint was the dermatological adverse reactions reported. Results and Discussion: A total of 3 006 suspected adverse reactions to skin. Predominant in females and in adults for 60.2% and 53.7% respectively. Antimicrobials associated with increased number of reports were 18.5% RL penicillin, amoxicillin, cotrimoxazole 12.5% and 7.6%. The most frequently detected ADRs were rash (59.1%), erythema (11.9%) and urticaria (9.1%). Predominance of moderate adverse reactions (reporting 1935, 64. 4%) and 0.3% of severe reactions. were 87.5% and 81.8% likely to frequent.</p> <p>Conclusions. Predominant in females and in adults. RL Penicillin was the drug most associated with adverse reactions of the type rash. Moderate adverse reactions, probable and were most frequent in the study.</p>
PFep 047	<p>STRATEGY AND RESULTS OF THE PHARMACOVIGILANCE OF VACCINES FROM THE FINLAY INSTITUTE, 2009 Cuevas IE¹, Jiménez G²</p> <p>¹Instituto Finlay, Centro de Investigación- Producción de Vacunas. Ave. 27 No. 19805 e/198 y 202. La Lisa, La Habana, Cuba. E-mail: cuevas@finlay.edu.cu; ivancuevas@infomed.sld.cu ²Unidad Nacional Coordinadora de Farmacovigilancia. 44 y 5ta Ave, Miramar, Playa, La Habana, Cuba.</p> <p>Introduction: The objective of this work was to show to the strategy and the results of vaccine pharmacovigilance which sanitary registries ownerships hold the Finlay Institute. Materials and Methods: The biography of products at post licensure stage took shape and the balance risk/benefit was examined. It was possible thanks to agreements between institutions allowed the access to digital and auditable data bases from spontaneous notification of adverse events and the fulfillment of the good practices, standard operating procedures and rules of the regulatory authority. The data mining for search of rare and unexpected events for a same lot or of accidents, the update safety periodic reports and the systematic practice of complete information of security from subpopulations and special groups allowed us to fill in the safety profile of vaccines. Results and Discussion: It was confirmed that the trivalent leptospiric vaccine, the typhoid Vi vaccine and the tetanus toxoide vaccine, displayed a frequency of adverse events smaller of 0.1 reports by each 100,000 administered doses, while the other vaccines had values between 1 and 10 by each 10,000 vaccinated. Between 80% and 95% of the notifications were related causally to the vaccine, and only 0.89% of reports were of serious severity, almost all in smaller children of a year. The systemic manifestations were predominant. Conclusions: The presented results show the importance of pharmacovigilance from the industry as a proof of the stewardship of quality of valuable safety data of administration of vaccines. Key words: pharmacovigilance, vaccines, industry.</p>
PFep 048	<p>SURVEILLANCE OF ADVERSE EVENTS OF MENINGOCOCCAL AC POLYSACCHARIDE VACCINE DURING A VACCINATION CAMPAIGN. NÍGER 2009 Cuevas IE¹, Rodríguez MC¹, Mirabal M¹, Ruíz L²</p> <p>¹Instituto Finlay, Centro de Investigación- Producción de Vacunas. Ave. 27 No. 19805 e/198 y 202. La Lisa, La Habana, Cuba. email: cuevas@finlay.edu.cu; ivancuevas@infomed.sld.cu ²Brigada Médica Cubana en Níger.</p> <p>Introduction: Every year, a meningitis epidemic whips Western Africa and affects between 25,000 and 200,000 people, fundamentally infants. <i>Neisseria meningitidis</i> A and C has been identified like the main causal agents. Prophylaxis by vaccine constitutes the strategy par excellence for the prevention of the</p>

	<p>disease. The Finlay Institute, Research center, Development and Production of Vaccines, Cuba and the Institute of Technology and Immunobiologics Bio-Manguinhos, Brazil, had to the request of the World Health Organization to cover the necessities of meningococcal AC vaccine for African countries in sanitary emergency, and for that, had obtained the prequalification of the WHO. For this, was pending to complete the safety profile of this vaccine during their field use, which was the study objective. Materials and Methods: A study of monitoring of consecutive adverse events to the vaccination campaign was made in Niger. Two methods for the data collection of adverse events were used (spontaneous notification and intensive monitoring in hospitals). Results and Discussion: As result, a total of 81 adverse events was reported, of which only 11% were induced by the vaccine and considered “more likely related” to this. Conclusions: The obtained results show that the profile of security of this vaccine in its use in campaigns of vaccination in Africa corresponds to the described one in the sanitary registry of Brazil and the experiences of use of similar products in Spain.</p> <p>Keywords: meningococcal AC vaccine, adverse events, pharmacovigilance</p>
<p>PFep 049</p>	<p>HEALTH EDUCATION PATIENTS IN MATERNAL HOSPITAL SOUTH MARIANA GRAJALES Reyes I¹, Serpa L², Sánchez A¹, Bermúdez I¹</p> <p>¹ Universidad de Oriente. Departamento de Farmacia email: ireyes@cnt.uo.edu.cu ² Hospital Materno Sur Mariana Grajales ³ Patricio Lumumba s/n Altos de Quintero. Santiago de Cuba.</p> <p>A prospective and longitudinal research was carried out in the obstetrics service of the Sur Mariana Grajales Maternal hospital of the municipal of Santiago de Cuba in the period between November 2009 and April 2010, with the aim of implementing a Health Education service, using the Normalized Work Procedure structured under the Cuban norm (NC) 9001:2008. For the development of the service, the stages of the process and the methodologies of the work for each one of these was followed; the direct observation and the application of questionnaires allowed for the evaluation of attitude, conduct, level of knowledge and therapy fulfillment. A satisfaction poll was also applied. Out of the 90 patients included in the service, 51.1% were women who had recently given birth, and 48% were pregnant women. Patients with ages between 20 and 30 years and with pre-university level in education predominated (49%). Attitudes, conducts, level of knowledge and therapy fulfillment, reached a high level after the educative intervention; the essential method used was interview and the patients acquired satisfactory evaluations in higher percentages (88.8%). The behavior of the indicators of structure quality and the process and the results of the service offered was determined, and this showed that when this activity is carried out in a systematic and normalized way, improved attitudes and conducts as well as level of knowledge and therapy fulfillment by patients could be achieved. This could help elevate the adherence to treatments and at the same time improve in a continuous manner the services offered.</p>
<p>PFep 050</p>	<p>NORMALIZATION OF PHARMACOTHERAPEUTIC FOLLOW UP: A TOOL TO INCREASE THE QUALITY IN THE PHARMACOTHERAPY IN HOSPITALIZED PEDIATRIC PATIENTS Reyes I¹, Nambatya W¹, Zuñiga, A¹, Cleger Y², Batista Y², Bermúdez I¹, Mengana E²</p> <p>¹ Universidad de Oriente. Departamento de Farmacia. e.mail: ireyes@cnt.uo.edu.cu ² Hospital Infantil Norte Juan de la Cruz Martínez Maceira. Patricio Lumumba s/n Altos de Quintero. Santiago de Cuba.</p> <p>A longitudinal and prospective study was carried out in order to implement a pharmacotherapeutic follow up service to patients admitted in the hospital “Juan de la Cruz Martínez Maceira” in the city, Santiago de Cuba, applying a normalized work procedure designed to offer pharmacotherapeutic follow up to hospitalized patients, putting into consideration requirements of the Cuban norms NC ISO 9001:2008 , as well as methodologies well known by the international pharmaceutical community for the follow up. The service was offered to patients admitted in the services; Intensive care, Nephrology and Cardiology following the principal ethics as in the Helsinki declaration, also the inclusion, exclusion and exit criteria for the selection of the sample. The behavior of the indicators for the structure, process and result was determined as a way to demonstrate the impact of the service offered and also to determine the quality of the pharmacologic treatments in the pediatric inpatients. The service offered permitted the detection of 77 problems related to the medications as well as the resolution of 85, 71% of the negative results associated to these problems detected in the 3 services studied. The behavior to the indicators determined demonstrated not only the satisfaction of the patients but also the satisfaction of the members of the health</p>

	<p>team, the continued improvement in the service offered and the global efficiency of the pharmacotherapeutic follow up as a tool to raise the quality of life of the inpatients.</p>
PFep 051	<p>REPORTS ON BEHAVIOR IN NATIONAL COORDINATING UNIT OF PHARMACOVIGILANCE. CUBA 2003-2008 Ávila J¹ Jiménez G¹, Alfonso I¹ ¹Centre for the Development of Pharmacoepidemiology. Cuba. Calle 44, No 502 5th Avenue at 44 St.. Playa. Havana. Cuba Faculty Instructor Professor Manuel Fajardo. Pharmacy degree and a specialist in Pharmacovigilance . email: jenny@mcdf.sld.cu, javila@infomed.sld.cu</p> <p>Introduction: Every year the number of hospitalized patients who suffer an adverse reaction increase, in addition to being among the leading causes of death, increased hospital admissions and stays, becoming is not only a health problem but result also an economic problem. Material and Methods: Retrospective study to characterize Pharmacovigilance reactions suspected adverse secondary cares, which were reported to the National Coordinating Unit of Pharmacovigilance from the years 2003-2008. Results: The total number of reporting in secondary care in this period was 7319.15%, most provinces reported that Havana with Santiago de Cuba 1358 and 1890, physicians (51.6%) and pharmaceuticals (24.5%) reported the highest number of reports, adult the age group most commonly reported (61.2%), as antibacterial agents (34%) and between crystalline penicillin, 7.1% of the reports, also describes the reaction frequent organ system most affected, severity and causal classification of reported reactions and low frequency. Conclusions: We demonstrated that there is underreporting in the primary health care.</p>
PFep 052	<p>USE OF ANTIMICROBIALS IN THE MATERNAL HOME "LEONOR PEREZ CABRERA" SINCE JANUARY 2007 - JULY 2009 Pavón Pérez J, Díaz Molina M, Mateu López L, Herrera Llópiz A. Pharmacy and Food Institute, University of Havana. 222 and 25 Ave. La Coronela. La Lisa. Havana City. Cuba. email: jpavon@ifal.uh.cu</p> <p>Introduction: The inappropriate use of medicines is now a major health and economic problem, which is more sensitive in the case of vulnerable populations such as children, the elderly and pregnant women. Gestation is a long process, which can appear vaginal infections, renal, respiratory, etc. In such cases you must select the most appropriate antibiotic so that does not present a risk to the baby or the pregnant. In this paper we conducted a retrospective study during the period January 2007-July 2009, the characterization of the household population of pregnant mother "Ms Leonor Pérez Cabrera", site in the old Habana and the prescription of antimicrobials for the treatment of sepsis pregnant vaginal pathology, high incidence among this population. Material and Methods: The review of clinical history allowed the study of social variables maternal age, gestational age at admission, number of previous pregnancies, occupation, comorbidities, diagnosis that required the use of antimicrobials, most commonly used form of diagnosis and the most commonly prescribed antimicrobials. Results and Discussion: The results led to evidence that pregnant women predominated aged between 21 and 30 years, with gestational ages at admission between 21 and 30 weeks, and workers. The pathology that largely motivated the use of vaginal antimicrobial sepsis was diagnosed in a clinic in almost all cases and antimicrobials prescribed were azithromycin, metronidazole, clotrimazole and nystatin. Conclusions: The results confirm the need to evaluate the prescription quality of antimicrobials by means of medical utilization study.</p>
PFep 053	<p>IMPACT OF VITAMIN A IN GAMBIA CHILDREN WITH ACUTE DIARRHOEA DISEASE. Otero JC¹, Ciria A². ¹ Maternity Hospital "A. A. Aballí "Bejucal Czda Km 71 / 2, Arroyo Naranjo, Havana city, Cuba. email:juanqui@infomed.sld.cu ² Pediatric Hospital "William Soler", 100th Street, corner of Convent, Havana city, Cuba</p> <p>Introduction: Vitamin A is one of the micronutrients that are involved in diverse physiological processes in the human body. There is evidence of an increase of 25% risk of death in chronic diarrhoea processes and these can be reduced through the beneficial effects of vitamin A on the structure and / or immune system function. Randomized open trial. Material and Methods: Study performed at the Pediatric Hospital Bansang in The Gambia, Africa. We included 200 children diagnosed with acute diarrhoea admitted to the pediatric service in February 2008 to July 2008. In order to validate the role of vitamin A in acute diarrheal disease were administered to 100 children with this diagnosis one dose of 50 000 IU of this micronutrient and observed the evolution of these for about a month. Results: Of the 100 children with</p>

	<p>acute diarrhoea (group II) 17% evolved to the persistence of their digestive process unlike the other 100 children who were given a dose of vitamin A (group I) in which the 11 % progressed to persistent diarrhoea. Of the 88 children suffering from an infectious aetiology EDA for the group II 13.7% evolved to persistent diarrhoea differences of the 91 children in group I than after administration of vitamin A showed only a 4.4% recurrence. Conclusions: After administration of vitamin A in children with acute diarrhoea, the percentage to the persistence of reduced digestive table showing the association of vitamin A stored in the aetiology of infectious diarrhoea process.</p>
PFep 054	<p>CHARACTERIZATION OF THE PRESCRIPTION AND ADVERSE REACTIONS OF CIPROFLOXACINA AND SOUR NALIDÍXICO IN PRIMARY ATTENTION. PINAR DEL RÍO. 2009 Roque K¹, Díaz Y², Alfonso I³, Jiménez G³</p> <p>¹Dirección Municipal de Salud. Pinar del Río. email: keniar@princesa.pri.sld.cu ²Buró Regulatorio para la Protección de la Salud. Ciprian Váldez # 1 entre Martí e Isabel la Católica. Pinar del Río. email: yumara@minsap.pri.sld.cu ³Centro para el Desarrollo de la Farmacoepidemiología. E-mail: ismary@mcd.sld.cu</p> <p>Introduction: The irrational use of the antibiotics can take to resistance, adverse reactions and I increase of the cost, the quinolonas used in Cuba is not exempt of this problem. Objectives: to characterize the population in which was prescribed sour nalidixico and ciprofloxacina, to evaluate their prescription, to describe and to classify the adverse reactions, to identify level of knowledge of the prescriptores and to design strategy of educational intervention. Method: he/she was carried out an observational, descriptive and traverse study, inside EUM it was classified of the type prescription indication with elements of practical consequences, therapeutic outline and of factors that condition the prescription habits, jointly was carried out a study of farmacovigilancia of the type active surveillance of the adverse reactions, in the patients treaties with sour nalidixico and ciprofloxacina in the year 2009 in the county of Pinegrove of the River. A questionnaire of five questions was applied to measure the level of knowledge of the prescriptores: there was contraindication to ciprofloxacina and sour nalidixico in 35.0% of the patients, 76.1% of the prescriptions was inadequate, motivated by inadequate indication to the ciprofloxacina and for rule not adapted in the sour nalidixico, fundamentally, in 30.6% of the patients they took place RAM and in a great number they were epigastralgia, you nauseate and migraine, 71.7% of these RAM was light, 75.3 probable%, the RAM frequents they represented 75.9% and the avoidable ones 72.7%, mainly to the ciprofloxacina, the level of knowledge of the prescriptores was insufficient in 73.1% Conclusion: Prevalence of indications in the mature population, preponderance of inadequate prescriptions. The types of drug reactions prevalent adverse were the epigastralgia, nausea and migraine, the adverse probable, frequent, light and avoidable reactions stood out; the level of knowledge of the insufficient prescription prevailed.</p>
PFep 055	<p>CHARACTERIZATION OF STRAINS OF LEPTOSPIRA INTERROGANS ISOLATED FROM CLINICAL CASES OF NICARAGUA DURING THE EPIDEMIC CAUSED BY HURRICANE FELIX Blain K.¹, Batista N.¹, Oliva R.¹, Solis R. L.¹ and García L.¹.</p> <p>¹Finlay Institute. Ave. 27 No. 19805, La Lisa. Ciudad de la Habana, Cuba. AP. 16017, CP11600. email: Kblain@finlay.edu.cu</p> <p>Introduction: In 2007 there were several outbreaks of leptospirosis in the departments of Leon and Chinandega belonging to Nicaragua, as a result of the impact of Felix Hurricane. As part of the epidemiological study were isolated <i>Leptospira</i> strains from patients with symptoms. Objective: Evaluate the degree of virulence of clinical isolates from the departments of Leon and Chinandega, kinetics of growth under shaking culture conditions, dose required to cause lethal infection in the Syrian hamster animal model and cell antigenic profiles that are recognized by serum of people vaccinated with vax-SPIRAL. Methods: We analyzed 16 samples of blood cultures taken in acute phase of suspected cases of leptospirosis. All samples were inoculated in hamsters to estimate the degree of virulence. Samples were inoculated again were highly virulent in this model by the method of Fajardo et al to determine the median lethal dose and subcultured in liquid medium to study growth kinetics. Antigenic profiles were analyzed by whole cell electrophoresis and Western blotting using as a source of antibodies, sera from individuals vaccinated with vax-SPIRAL®. Results: The inoculation in the animal model identified a number of virulent and avirulent isolates. The lethal dose of virulent isolates ranged between approximately 32 and 4</p>

	<p>cells. The kinetics of growth was in correspondence with the patterns described for this type of microorganism. It revealed a large antigenic homology among all strains. Conclusions: The results of this study suggest that in the departments of Leon and Chinandega circulating strains of <i>L. interrogans</i> with a variable stability in terms of virulence, regardless of the serovar circulation and there is evidence of strong antigen recognition prevenient in sera from people vaccinated with vax-SPIRAL®</p>
<p>PFep 056</p>	<p>EDUCATIONAL INTERVENTION STRATEGY ON KNOWLEDGE ANTIHYPERTENSIVE THERAPY IN ELDERLY PATIENTS. NEW ESPARTA, VENEZUELA, 2008 Pons Herrera L¹, López Aguilera AF², Furonos Mourelle JA³</p> <p>¹ Policlínico Héroes del Moncada, City of Havana, Cuba. email: lph20078@hotmail.com ² Faculty of Medicine Julio Trigo, Medic University of Havana. St Bejucal km 7 ½, Havana City, Cuba. ³ Center for the Development of Pharmacoepidemiology. 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba</p> <p>Introduction: High blood pressure constitutes the first cardiovascular risk factor in geriatric patients, and then doctors that work in primary care have an important role in the management and control of the disease, that why we wanted to assess whether an educational intervention strategy improves the knowledge of general practitioners on antihypertensive therapy in patients 60 years and older, treated in primary care, at municipalities Antolin del Campo and Maneiro Arismendi, from New Esparta State, in the Bolivarian Republic of Venezuela, in 2008. Methods: The study consisted a quasi-experimental research, non-equivalent control group, the universe was constituted by 44 doctors in General Medicine specialists working in the selected municipalities. A sample, non-probabilistic, of 30 medical specialists in general medicine, 15 of them for the experimental group and the other 15 for the control group, all of them had worked in primary health care territory at least one year, an initial survey was applied to identify the knowledge about how achieve control of the disease and needs on high blood pressure learning. There was implemented an Educational Intervention Strategy on antihypertensive therapy. Results and Discussion: At the beginning the knowledge level was wrong in both groups, 47% in study group and 67% in control group, these results were reverted after the intervention, we observed that any doctors was wrong in study group and 61% of doctors from control group continued with insufficient knowledge about hypertension. Conclusions: The usefulness of the educational intervention was shown.</p>
<p>PFep 057</p>	<p>DESIGN OF A PHARMACEUTICAL BULLETIN OF PHARMACO-POPULARIZATION Rodríguez L¹, Gómez S, Milián M, León R</p> <p>¹EMCOMED. Sancti Spiritus e-mail: laritza@ss.quimefa.cu.</p> <p>Introduction: At present, knowledge is a strategic resource for contemporary social and economic development. The emergence of Internet and widespread intensive use of information technology has facilitated almost instantaneous cognition and global emerging issues and advances in public health. Material and Methods: We designed a bulletin that we call "Pharmacy to date" with a monthly release in Word format for easy emailing, and a minimum of printouts, and so gets into the hands of as many people as possible, whether health professionals or not. All information was gathered from the site of health (www.infomed.sld.cu). This bulletin consists of three sections named: "Drug of the month," "You know ..." and "Knowledge Management" each with a specific function. We selected for release each month those medicines that slow-moving in our drugstore, which may be caused by several causes: low demand products, products with risk of expire date or newly introduced for each medical speciality or clients who must know the existence, indications, dosage and adverse reactions of each of these drugs. Results and Discussion: To date, have reported more than 10 drugs that were recently incorporated in our province but were not known to doctors, and then had better consumption, avoiding losses due to our drugstore, such as: Atenolol 25 mg tab, Trofin solución, Albendazol tab, Cernevit ámp. It also had great success the other sections have been treated very interesting topics such as alcoholism, diets rich in omega 3 fatty acids and their advantages, CIMAVAG: new Cuban vaccine against lung cancer among others. The bulletin has been useful in the work of pharmacoepidemiological of each municipality.</p>

<p>PFep 058</p>	<p>TREATMENT ADHERENCE IN HYPERTENSION IN THE HEALTH AREA PINTO SALINAS ONE OF THE CUBAN MEDICAL MISSION, CAPITAL DISTRICT, VENEZUELA, 2009. Sabino LR1, Alonso CL2, Debesa GF1</p> <p>¹Cuban Medical Mission in Venezuela ²Center for the Development of Pharmacoepidemiology, National Pharmacovigilance Unit, 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba. email:liuba@mcdf.sld.cu</p> <p>Introduction: Non-adherence to drug treatment is a major public health problems today. Treatment adherence in patients with chronic diseases averages only 50% of studies, cardiovascular disease constitute the leading cause of mortality in industrialized countries, with hypertension one of its most important risk factors. Non-adherence is one of the causes of uncontrolled blood pressure in the Capital District of the Cuban medical mission in Venezuela. Objective: To describe treatment adherence in Hypertension in the health area Pinto Salinas one of the Cuban Medical Mission, Capital District, Venezuela, 2009. Method: We conducted an observational, descriptive and transversal study that as the use of Medicines is classified as therapeutic regimen on adherence to drug treatments for hypertensive patients. Results: 52.9% of patients showed no adherence to treatment. The Atenolol (61.5%), enalapril (61.3%) and hydrochlorothiazide (60%) were the drugs with less grip. The major cause of non-compliance with treatment was found to be forgetting (36.6%), those over 60 years (57.8%), loneliness (60%) and primary school level (48.9%). Patients with more than 10 years of diagnosed hypertension had a 33.3% non-adherence to treatment. 94.7% of adherents knew of complications and more than 80% were satisfied with treatment. Conclusions: Over half of patients do not adhere to treatment and medications involved were Atenolol, Enalapril and Hydrochlorothiazide. The reasons for non-adherence were forgot, loneliness, age over 60 years, male sex, a longer suffering from the disease and the primary school level.</p>
<p>PFep 059</p>	<p>SIGNIFICANT ADVERSE EVENTS WITH SYSTEMIC THERAPY IN COLORECTAL CANCER PATIENTS. EXPERIENCE AT NATIONAL INSTITUTE OF ONCOLOGY AND RADIOBIOLOGY Lami L¹, Areces F¹, Arbesu MA¹</p> <p>¹ National Institute of Oncology and Radiobiology, 29 and F St, Plaza, Havana City, Cuba. email: leo.lami@infomed.sld.cu</p> <p>Introduction: In Cuba, colorectal cancer (CRC) is the malignant neoplasm with the fourth-highest incidence and third-highest mortality. Systemic therapy based on citotoxic drugs such as 5-fluorouracil, oxaliplatin or capecitabine, plays a fundamental role in the control of the disease after surgery and also in the increase of the survival in metastatic cancer. However this therapy is tie together with profile of important toxicity whose prevention and treatment is part of Clinical Oncologist practice. Material and Methods: This study included patients aged >18 years, with a confirmed histological diagnosis of colorectal adenocarcinoma and admitted to INOR between January 1, 2009 and December 31, 2009 to be treated with chemotherapy after surgery or for the presence of metastatic disease. Patient characteristics, regimen, line of therapy, drug, cycle, treatment, toxicity (tox), and delay information were recorded. Delays were categorized as administration/other delays or toxicity-related delays. Results and Discussion: 68 patients received 575 cycles (Avg 8.5 cycle per patient). Avg. age = 62 years, 60% male and median ECOG PS = 1. Median survival = 17 mo. The top regimens (cycles) were: 1st line - Folfox4, de Gramont, Mayo, XELOX, Capecitabine Single Agent; 2nd line - Folfox4, Capecitabine Single Agent, XELOX. The most frequent adverse events were nausea, vomiting, peripheral sensory neuropathy, diarrhea and neutropenia, the majority grade 1–2, according to Common Terminology Criteria for Adverse Events (CTCAE) classification. Our data confirm this regimen's tolerability. Conclusions: In the systemic treatment of colorectal cancer, there is a wide variation in community oncologist prescribing patterns. We defined regimen tox based on criteria focusing on clinical decision making and showed the feasibility of measuring tox-related delays apart from other non-tox delays. Toxicity reported in this fashion may prove valuable for oncology administrators seeking to employ disease management strategies.</p> <p>References: Leonardo Lami, MD, Fernando Areces, MD, Juan J Lence, MD, María A Arbesú, MS. FOLFOX-4 Regimen as a First-line Therapy for Cuban Patients with Metastatic Colorectal Cancer. <i>MEDICC Review</i>, Summer 2009, Vol 11, No 3: 34-38.</p>

<p>PFep 060</p>	<p>PRESCRIPTION OF DRUGS FOR THE INFECTION OF THE URINARY TRACT IN THE GERIATRIC PATIENTS Pajarín Fernández L, Granados Hormigó A.E, Álvarez González R. M, Perdomo Leyva, Remedios Reyes R</p> <p>University of Medical Sciences of Santiago de Cuba. Faculty #1. Las Americas avenue. Sueño Neighbourhood. email:lianne@sierra.scu.sld.cu</p> <p>To prescribe a medication shows the aptitudes and expectations of the prescriber in connection with the evolution of the illness and with the role that the medications can play in the therapy. It was carried out a transverse descriptive study to evaluate the prescription of medications in the infections of the urinary tract in the elderly people "Carlos J. Finlay" health area in Santiago de Cuba, from January 1° to June 1° , 2010, motivated by the increasing of the prescription of certain antimicrobial groups in this entity, expression of difficulty in the quality of the treatment of the same one and the absence of statistics that allow to describe with accuracy the difficulties; this showed the existence of a readiness and appropriate accessibility to the medications; enough quantity of prescribers to offer the service, but most of these inadequate results in the evaluation of the knowledge, what becomes more evident in the interns and doctors of General's Integral Medicine specialty. The most prescribed medications were quinolones (ciprofloxacin and norfloxacin), sulfonamides (cotrimoxazole) and beta-lactams (cefalexin and amoxicillin) suitable for the infections of the high and lower, asymptomatic bacteriuria urinary tract. Most of the prescriptions of these medications were inadequate, for difficulties in the mainly individualization of the treatment. Adverse reactions medications were presented the majority of them were slight with definitive attributable and there was prevalence of the satisfaction of the users with the health service.</p>
<p>PFep 061</p>	<p>ADHERENCE IN THE TREATMENT OF ANTIHYPERTENSIVES Mateu López L, Díaz Molina M, Herrera Llopiz A, Pavón Pérez J.</p> <p>Pharmacy and Food Institute, University of Havana. 222 and 25 Ave. La Coronela. La Lisa. Havana City. Cuba. email: liliana@ifal.uh.cu</p> <p>Introduction: Studies on the prevalence of hypertension (HTA) in Cuba, show values between 20 and 40% of the adult population. At present it has many therapeutic for the treatment of hypertension and known health and hygiene criteria which help keep blood levels within normal limits. The lack of adherence to therapy is a common chronic diseases. In the case of arterial hypertension of noncompliant reached alarming levels, about 40% for drug treatment and between 60-90% in the hygienic-dietetic measures. Failure to do prescribed treatment ineffective leading to increased morbidity and mortality. Material and Methods: In this paper we conducted a study to assess adherence to antihypertensive treatment in a sample of patients in a health area of the municipality of San Miguel del Padrón, in San Francisco de Paula. For the study used the Morisky-Green test-Levine. Variables included were treatment adherence, sex, age and type of therapy. Results and Discussion: The results showed the prevalence of a large number of noncompliant dependencies found between the adherence variables and type of therapy. Conclusions: The effectiveness of antihypertensive therapy depends of the therapeutic compliance. The non adherence increases the likelihood of therapeutic failure, and to be responsible for unnecessary complications, leading to increased spending on health care.</p>
<p>PFep 062</p>	<p>EVALUATION OF QUALITY OF PHARMACEUTICAL SERVICE IN THE CONTROL OF PRODUCTS IN CLINICAL THERAPEUTICAL TRIALS AT THE CAMILO CIENFUEGOS GENERAL HOSPITAL Ramos L¹, Hernández M¹, Rodríguez H¹, Ruíz H², Leon O²</p> <p>¹Hospital General "Camilo Cienfuegos", Bartolomé Maso s/n, Sancti Spiritus, CP 60100. Cuba email: lramost@ucm.ssp.sld.cu ²UCM "Dr. Faustino Pérez Hernández", Circunvalante norte, Olivos 3 Sancti Spiritus, CP 60100. Cuba</p> <p>Introduction: A clinical controlled trial is an experimental method to show the efficacy and safety of a product under research (PUR). The services of a pharmacist play a fundamental role during the planning and conduction of a study, by warranting the quality demanded in the Good Clinical Practices (GCP). Our objectives are: assessing the quality of clinical services provided, and describing the main deficiencies detected during the monitoring carried out for clinical trials. Material and method: A retrospective</p>

	<p>descriptive study was made of clinical multicentre studies carried out in our province in the period from 2005 to 2010 . A review was made of the essential documents required by the ICH such as : the pharmacist's and the clinical researcher's files, the registries of quality and the clinical records of the patients included. Qualitative variables were used such as quality of service , which was categorized in acceptable and non/acceptable depending on the deficiencies found related with the direct control of the (PUR) such as storing conditions, violations of blinding, coincidence of prescriptions with products sold, and the presence of updated basic documentation on the worksite. Results: It was observed that in 80% of the trials the quality of pharmaceutical service was categorized as acceptable. Among the main difficulties we observed that in 60% of the trials there were problems with the storing and control of the PUR, in 100% there is no control of the concomitant treatment the patient is receiving, no trial has a protocol on the pharmacist's file, and the substitute pharmacist is not designated. Conclusions: We considered that there was a good quality on the services provided, with difficulties that can be resolved in several trials. The deficiencies found were due to the lack of training and experience of the pharmaceutical personnel involved in this high complexity research activity.</p>
<p>PFep 063</p>	<p>STUDY OF CONSUMPTION OF DANGEROUS DRUGS IN PARIRENYATWA HOSPITAL. JULY TO DECEMBER OF 2007. Ramos L¹, Parra D², Ruíz H¹</p> <p>¹UCM “Dr. Faustino Pérez Hernández”, Circunvalante norte, Olivos 3 Sancti Spíritus, CP 60100. Cuba. email: lramost@ucm.ssp.sld.cu</p> <p>Introduction: The term opiodes is used for the natural or synthetic exogenous substances able to be linked to the different receivers for the morfina. The opiodes drugs are considered dangerous drugs, their prescription is controlled. General Objetives: to describe the consumption of Morphine 10 mg in pills and 15 mg IV, Petidina 100 mg IV and Fentanyl 100 ug in Parirenyatwa Hospital July to December of 2007. Material and Methods It was carried out a retrospective descriptive study of consumption drugs, the data took of the books of registrations in pharmacy of dangerous drugs that were in their respective store rooms. We registered the monthly consumption by wards. A database was created, the statistical prosecution one carries out using the descriptive statistics of frequency. Results and Discussion: A total of 5870 ampoules of Fentanyl, 2239 ampoules of morphine of 15 mg, 7525 pills of Morphine 10 mg, 2848 ampoules Pethidine was consumed in that period. The bigger consumption of Fentanyl was observed at Intensive Therapy, Operations Gynecobstetrics and the Main Theatre. The distribution of the morphine 15 mg is wide, adults' intensive cares, Main Theatre, Orthopedics and Cardiovascular Surgery was those that showed a bigger number of consumed units. It was observed that the room of Oncology, Internal Medicine, Orthopedics, Cardiovascular surgery and general surgery those that consumed an adult were I number of units of morphine 10 mg tab. The rooms where a bigger consumption of Pethidine was observed they are gynecology, Main Theatre, general surgery, Cardiovascular Surgery, postpartum, orthopedics, burnt and casualty. Conclusions: the consumption of these drugs didn't follow a regular behavior in the course of the months and that the distribution for services is wide, it was possible to describe the total consumption of these drugs per months as well as for wards.</p>
<p>PFep 064</p>	<p>DRUGS ADVERSE EFFECTS IN PREGNANT WOMEN, REPORT TO THE PHARMACOVIGILANCE SYSTEM OF CUBA SINCE 2003 TO 2007. López L¹, Furones JA², Jiménez G³, Ávila J³</p> <p>¹Basics and Preclinical Sciences Institute “Victoria de Girón”, 31 Ave and 146 St, Cubanacán, Playa, Havana City, Cuba. email: luis.perez@infomed.sld.cu. ²Center for the Development of Pharmacoepidemiology, 5ta Ave and 44St, Miramar, Playa, Havana City, Cuba. ³Center for the Development of Pharmacoepidemiology, National Coordinator Pharmacovigilance Unit, 5ta Ave and 44St, Miramar, Playa, Havana City, Cuba.</p> <p>Introduction: Cuba report drugs adverse effects to the pharmacovigilance system of the World Health Organization (WHO) since 1994. There are many studies made in general population, ancients and childs but never in pregnant women. That's the reason we aimed to make this investigation. Material and Methods: Our observational, descriptive and transversal study was made to disistinguish the suspicion of drugs adverse effects (DAE) during pregnancy who were notified to the National Coordinator Pharmacovigilance Unit. The study comprised since 2003 to 2007. It was based in the spontaneous</p>

	<p>notification method of suspicion of DAE. The complete reports of the choiced period of time were selected. The information was obtained by the national pharmacovigilance database and we apply descriptive statistics. Results and Discussion: The predominant age group was between 20 to 30 years old (56.4%). Time of pregnancy was absent in the majority of the reports of DAE (87,5%). Santiago de Cuba (32,3%) and Granma (26,9%) were the principal notifiers provincias. Physicians (37,2%) and pharmaceutics (27,7%) were the health professionals who notify most. Drugs that provoke DAE more frecuently were prenatal tablets (27,7%) (no pregnancy risk cathegorized), ferrous fumarate (6,9%) (A cathegory), metronidazol (5,9%) (B cathegory). The most affected system of organs were digestive (48,1%). Constipation (20,8%) was the most frecuent DAE. Frequent (66%), mild (65,9%) and probable (63,8%) were the most predominant cathegories of DAE. The avoidable DAE constituted an 8,3% and the main avoidance causes were unequal indications and doses. Conclusions: Drugs without pregnancy risk cathegory were the drugs that provoked more DAE. The severity, causality and more affected provincias indexes, except frecuency, were similar to those described in general population of Cuba in the study's period of time. An small proportion of DAE were avoidable and they caused serious health damaged, provoking two deaths.</p>
<p>PFep 065</p>	<p>STRATEGY FOR THE IMPLEMENTATION OF DRUG DISPENSING SERVICE IN COMMUNITY PHARMACIES OF SANTA CLARA CITY. Jaramillo L¹, Bermúdez A¹, Martín Y².</p> <p>¹ Medical Sciences University “Dr. Serafin Ruiz de Zárate Ruiz”. Center of Studies, Documentation and Information on Drugs. Aqueduct Road, Santa Clara City, Villa Clara, Cuba. CP 50200. email: lisetjh@ucm.vcl.sld.cu, abdelbs@ucm.vcl.sld.cu ² Central University of Las Villas, Pharmacy Department. Camajuani Road, Km. 5 1/2 Santa Clara City, Villa Clara, Cuba. 54830. email: ymfadragas@uclv.edu.cu</p> <p>Introduction: The inclusion of dispensing inside the activities of Pharmaceutical Care, looks forward to evidence the responsible participation for the pharmacist in the achievement of positive results in treatments, based on the pharmacotherapeutical knowledge and bioethics principles that characterize this profession, humanizing the relationship between health professionals and patients. The implementation of this service by means of an appropriate strategy is crucial to achieve a rational use of drugs. Objectives: To propose a strategy for the implementation of Drug Dispensing Service in Community Pharmacies of Santa Clara city. Materials and methods: An investigation in systems and services of health (ISSS) was carried out, with a systemic approach and an observational, descriptive and cross-sectional study was done, using both quantitative and qualitative approaches according to the different phases of the investigation. The spatial context was the community pharmacies of Santa Clara city, from May, 2009 to May, 2010. Results and discussion: Characterization of Drug Dispensing showed that the readiness of human resources is partial and there are not enough material resources to execute this service. 95.2% of pharmacists possess high learning necessities about Dispensing of Drugs and its bioethical principles. On the other hand there are not adequate Working Normalized Procedures. The patient interview evidenced that they don't receive any information of its medication what shows that the service is not carried out, so the structure, the process and the results of the service are inadequate. All this justifies the design of the intervention strategy for the implementation of the Dispensing Service in community pharmacies, this strategy includes and introduction, objectives, vision, awaited general results, scenario analysis (DAFO Matrix), action lines and plan. Conclusions: the intervention strategy was valued as very adequate to the implementation of the Drug Dispensing Service.</p>
<p>PFep 066</p>	<p>SLOW INSULIN CONSUMPTION IN THE POLICLINIC ARMANDO GARCIA Pérez Y¹, Sánchez I¹, Ortíz L¹, Vázquez Z²</p> <p>¹University of the Oriente, Department of Pharmacy. Patricio Lumumba s/n Ave Las Américas. Santiago de Cuba. Cuba. CP: 90 500. ²Provincial Direction of Health. Pharmacoepidemiology. Ave. Los Libertadores s/n. Santiago de Cuba. Cuba.</p> <p>Introduction: Diabetes Mellitus is a chronic metabolic disorder, characterized by constantly elevated glucose levels in blood. Due to the high levels of slow insulin consumption in the province of Santiago de Cuba it was decided to create the present investigation. Materials and Methods: A specifically qualitive consumption study with elements of treatment compliance, in the area of health Armando Garcia in the period November 2006 – June 2007 was carried out through interviews with the patients of this area.</p>

	<p>Results and Discussion: Of which 95% consume slow insulin, even though the indication was adapted in the 100% of the patients. The relation buy/consumption that was predominated was equal to 1 in 92 patients. Of the 174 studied 75% demonstrated compliance with the pharmacological treatment however only 53% demonstrated correct insulin use. Conclusions: The obtained results demonstrate that difficulties exist with the use of this medicine. It is recommended the commencement of a study of the factors that condition the prescription habits, the revision by provincial pharmacoepidemiology of the indication practices and slow insulin office so that it is made by units and not by bulbs as it is in present time.</p>
PFep 067	<p>INTENSIVE PHARMACOVIGILANCE OF OSELTAMIVIR IN “CARLOS MANUEL DE CÉSPEDES” HOSPITAL Beltrán L¹, Corpas M¹, Sánchez Y¹.</p> <p>¹Carlos Manuel de Céspedes Provincial Hospital, Central Road km 1 , Bayamo City, Granma, Cuba. Email: farmhcmc.grm@infomed.sld.cu</p> <p>Introduction: Oseltamivir is an antiviral drug introduced in our country due to the A (H1N1) Influenza, that is why it is necessary to intensify drug supervision to identify adverse reactions related to its use. That was the reason why this investigation was carried out. Material and Methods: A descriptive and prospective study was carried out in Carlos Manuel de Céspedes Hospital, in Bayamo, from November 2009 to January 2010. Patients that were administered doses of Oseltamivir (75 mg a pill) were interviewed, and in case of suspicious adverse reactions the official model 33-36-1 was filled. The sample was characterized according to demographic variables, and the adverse reactions were identified, specifying the affected organs system, seriousness and frequency. The causality was determined through the Karch and Lasagna Algorithm. Results and Discussion: 224 patients were tested, out of them 61.6% showed side effects. Most of the adverse reactions were observed in female patients (97.1%), of the white race (65.9%) and the most affected ages were from 15 to 24 years old (52.2 %) and from 25 to 34 years old (35.5%). Reactions in the digestive system were predominant (78.3 %) followed by reactions in the central nervous system (15.2%), prevailing vomits, nausea, headache, and in a lower degree weakness, cramps, and palpitations. These results coincide with the ones reported in bibliography. 85.5% of the adverse reactions were minor and the rest moderate, with a definitive causality relation in 91 cases and probable in 47. According to frequency they were classified in frequent (97.1 %) and rare (2.9%). The rare adverse reactions identified were: itching, diarrhoea, and cough. They are all described on the information referring to the medicine. Conclusions: 138 adverse reactions were reported, mainly at the digestive system level, being nausea and vomit the most frequent. 85.5% of the adverse reactions were minor and frequent (97.1%)</p>
PFep 068	<p>ASSESSMENT OF SOME PROCESSES OF THE MEDICATIONS SUPPLY MANAGEMENT CYCLE. VILLA CLARA, JANUARY-DECEMBER 2009 Gómez LA¹, Lorenzo G², Lara MC³</p> <p>¹Villa Clara Drugstore. email : lalberto @vcl.quimefa.cu ;²Molecular Immunology Center. email: cim@capiro.vcl.sld.cu; ³Pharmacoepidemiology Development Center. email: cristina.lara@infomed.sld.cu</p> <p>Introduction: The medications supply management cycle is organized in processes that characterize the medication chain in the country. These processes are neither evaluated nor controlled in an overall and periodical form as there are neither integrated parameters identified by general consent nor identified strengths and areas that need improvements in their implementation. Objectives: To identify and assess the relevant parameters that characterize the quantification, acquisition and distribution processes as well as defining the strengths or areas that need to be improved in Villa Clara province, during 2009. Method: In order to identify the parameters, the criteria expressed by national and provincial experts that work with a nominal group dynamics were used. The “Kendall Coefficient of Concordance” was added to these criteria to determine their reliability. In order to assess quantification and acquisition processes the “Differential measurement method” and the “Client satisfaction index” were applied. Also, to prioritize the areas that require improvements within medication distribution the “Matrix of attributes” was used. Results: The quantification and acquisition were assessed as non adequate, when comparing the results of the quality simple indexes in the province with the national average basic indexes. Also, the distribution process was assessed as “good” by the clients. Conclusions: The quantification and acquisition processes in this province were implemented with less quality in comparison with the national average. Distribution assessment behaved differently, which yielded good results, and the clients identified “medication availability” as the main dissatisfaction in relation with this process.</p>

PFep 069	<p>EVALUATION OF THE EXECUTIVE SOLVENCY OF THE CENTRE FOR STUDIES, DOCUMENTATION AND INFORMATION OF DRUGS ¹Bermúdez-del Sol A, ¹San Gabino Y, ²Bravo Sánchez L.R,</p> <p>¹Medical Sciences University “Dr. Serafín Ruíz de Zárate Ruíz”. Centre for Studies, Documentation and Information of Drugs. Aqueduct Road, Santa Clara City, Villa Clara, Cuba. CP 50200. ²Pharmacy Department. Central University of Las Villas, Santa Clara City, Villa Clara 54830. email: cedimed@capiro.vcl.sld.cu; abdelbs@iscm.vcl.sld.cu</p> <p>Introduction: Drug Information is a real need, nowadays is not possible to carry out a rational therapeutics without and adequate information about the problems related to the use of drugs. In this context, the centres for information of drugs play an important roll since they are entities specialized which take care of the management, processing and distribution of this information so it is very important that those centres are able to maintain and adequate solvency in the execution of its activities as a guarantee of the accomplishment of its mission. The objective of this work is to evaluate the degree of executive solvency of the Centre for Studies, Documentations and Information of Drugs of Villa Clara province. Materials and Methods: An observational, descriptive, using three expert’s group’s external valuation study was carried out. Each group stated its collegiated criteria in an evaluation guide for each one of the basic activities of the centre, elaborated according verifiable indicators. For docent activity the group was formed by Central University of Las Villas professors, for research were taken investigators of the same university and form the Medical Sciences University of the same province and for the drug information activity it was selected a group of experts which evaluated the final reports of health projects financed by the CITMA. The degree of executive solvency was calculated using the average points given by the experts and expressed as: High (average: ≥90 points), Medium (average: ≥ 75 y ≤ 89 points) and Low (average: ≤74 points). Results and Discussion: The activities of drug information and research received 100 points and docent one received 97 points. The general average was 99 points. Conclusion: The Centre for Studies, Documentations and Information of Drugs of Villa Clara province has a high degree of executive solvency in their three basic activities.</p>
PFep 070	<p>LONG-TERM ADVERSE DRUG EVENTS AFTER TREATMENT WITH TRANSFER FACTOR. CITY OF HAVANA, 2009 Cruz Barrios MA¹, Medina Magaña Y², Furones Mourelle JA¹, Broche Villarreal L¹.</p> <p>¹ Center for the Development of Pharmacoepidemiology, 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba. email: maria.cruz@infomed.sld.cu ² Medic University of Havana, Cuba, 31 y 146 St, Cubanacán, Playa, Havana City, Cuba.</p> <p>Introduction: Transfer factor called Hebertrans is an immunostimulant used in a wide range of diseases. The safety of this drug has been assessed in several clinical assays prior to registration, but there are a few research studies aftermarket. The objective was to identify long-term adverse drug effects observed in patients treated with transfer factor. Method: An observational study of active surveillance was carried out in 201 patients treated with transfer factor five years ago and more years in hospital from City of Havana, to detect adverse events like haematic infections, cancer and another and then to classify them by cause. Data was collected by the pharmacoepidemiologist in each municipality, they visited patient in home to get the information. Results and Discussion: A total of 72 adverse events were reported, they were observed in 65 patients. The most frequent events were hypertension (33,3%), death (18%) and diabetes mellitus (15%); also were observed infarction (4,1%), hepatitis C (2,8%), hepatitis B (1,4%) and other events less frequents. None of the events was classified definitively caused by transfer factor, although the temporal relation between drug and event was adequate, in all cases the events could be explained by other causes, patients had several diseases and they had received hemoderivative drugs that could had produced the event. Conclusions: Transfer factor was a safe drug for the patients under observation.</p>
PFep 071	<p>PRESCRIPTION OF NEUROLEPTIC DRUGS IN THE HOSPITALIZED PATIENT Morales M¹, Larduet O², Dupotey N¹, Bring Y²</p> <p>¹Department of Pharmacy, Faculty of Natural Sciences, University of Oriente. Patricio Lumumba y Avenida de Las Américas. Santiago de Cuba, Cuba. CP 90 500. ²Psychiatry Hospital “Gustavo Machin”. Santiago de Cuba, Cuba email: maramg@cnt.uo.edu.cu</p>

	<p>Introduction: Drugs Utilization Studies (Medications) are studies on marketing, distribution prescription and use of medications in a society, with a special emphasis on the sanitary, social and economic consequences. These studies on Psychiatry allow to assess psychotropic use both in out care and in hospital care, as well as, to obtain the predicted morbidity of some diseases taking into account the consumption of specific drugs, and assessing the excessive or insufficient use of a specific one. The aim of this activity was to analyze prescriptions of neuroleptic drugs in all hospitalized patients. Material and methods: A drug utilization studies that considered prescription, consumption and pharmacological surveillance elements was carried out in the Psychiatric Hospital of Santiago de Cuba during 2008. We were compared the number of neuroleptic drugs used according to the hospitalization time and time of evolution as well as unwanted effect of treatment. Parametric and non-parametric tests, with a level of significance of 0,05 were the basis of the analysis.</p> <p>Results: We observed inadequate prescription in the 40% of patients. Haloperidol was used in the 60% of treatment, the Chlorpromazine plus Levomepromazine was used in the 30% of patients. The group of patients who stayed at hospital for over 60 days, they were showed unwanted effect such as constipation (48%) and dry mouth (36%). Conclusions: There was association between the number of neuroleptic drugs and the time of evolution of disease and unwanted effects.</p> <p>References: National Institute for Clinical Excellence. Schizophrenia: core interventions in the treatment and management of schizophrenia in the primary care (NICE guideline) [página de Internet]. London: NICE; 2002. [citado 2007 nov 11]. Available in: http://www.nice.org.uk/pdf/CG1NICEguideline.pdf</p>
PFep 072	<p>INCIDENCE CONSUMPTION OF DRUGS IN THE QUALITY OF LIFE OF A SAMPLE OF ELDERLY PEOPLE. Licea M.E¹, Díaz M.², Hernández L.³</p> <p>¹Institute of Pharmacy and Food, 222 and 25, La Lisa, C. Havana, Cuba. email:mlicea@ifal.uh.cu ²Institute of Pharmacy and Food, 222 and 25, La Lisa, C. Havana, Cuba. Tel: 267-9502 Superior ³Instituto Joseph A. Echeverria, street No11901entre 114 119 and 127, Marianao, C. Havana. Cuba. email: loira@quimica.cujae.edu.cu.</p> <p>Introduction: The elderly people are increasing more and more on the Cuban population. The statistics predict that by 2025 one in four Cubans will be elderly, so the educational activity plays a key role in improving the quality of life for this population group. In this work we aimed to assess the develop lifestyles that older people living in the city Bauta, Havana province and how they impact on your quality of life, considering the use of medications, most notably in these people. Materials and Methods: We conducted a survey of closed questions and direct a group of 60 elderly persons, belonging to 2 circles, grandparents and a nursing home, the health area of Pedro Polyclinic Esperon Bauta municipality. Results and Discussion: The characterization of the study population was conducted through interviews. Styles of life of older people are inadequate, as 88% of respondents perform physical activity, 92% reported not drinking and 72% do not smoke. The majority expressed acceptable living conditions with family support. A high percentage of older respondents (80%) reports taking medications logical situation by the group in question. Polypharmacy was found in 40% of respondents and a large number of drug interactions, are largely preventable with proper use of medications consumed. Educational activities were developed on healthy lifestyles and rational use of medicines. Conclusion: The lifestyles of the respondents are acceptable, but not drug use, which is high and shows a considerable proportion of people suffering from avoidable drug interactions. Key words: lifestyles; drugs interactions; polypharmacy.</p>
PFep 073	<p>CHARACTERIZATION OF ACUTE INTOXICATIONS IN TWO HOSPITALS OF VILLA CLARA PROVINCE Tejera ME¹, Martínez Y²</p> <p>Villa Clara Medical Sciences University. Acueduct Rd. and Circunvalation Rd. Santa Clara, Villa Clara, Cuba. email: mariata@ucm.vcl.sld.cu</p> <p>Introduction: acute intoxications represent a complex of syndromes which group diverse symptoms and signs which are the result of a sudden exposition to a potentially toxic dose of a chemical substance, they emerge in an unexpected way and their organic and functional disorder evolve rapidly to forms that can provoke death. Materials and Methods: an observational, descriptive, retrospective study was carried out of the acute intoxication cases attended in two hospitals of Villa Clara province (Arnaldo Milian and Jose L. Miranda) in two years: 2006 to 2007 with the objective of characterize the behaviour of the acute intoxications in this period. The study universe and the sample coincided and were 457 patients attended</p>

	<p>by this cause. The information was taken from the medical records and reflected in questionnaires confectioned to record the different variables which were later operationalized and deposited in a data base to be analyzed using software SPSS. Results and Discussion: results show that the predominant intoxications are the intentional ones in females from 15 to 19 years old and the non intentional ones in males from 1 to 4 years old by oral route (93,4%). The 84% of intoxications occurred in the house. Drugs are the most common cause of acute intoxication, specifically drugs used for the nervous system (40%). Only 5,2 % of patients showed complications. In the 48% of cases there was some kind of mistakes such as: indiscriminated use of forced diuresis, non decontamination and incomplete decontamination of the site of intoxication and the staying in the hospital oscillated from 1 to 10 days. Conclusions: Acute intoxications are a common cause of admittance in the two studied hospitals.</p>
PFep 074	<p>REPORTS OF DEATH AS ADVERSE REACTION TO DRUGS. CHARACTERIZATION, CUBA 2000-2008 Tase MJ¹, Jiménez G², Peña MA³, Hernández A⁴.</p> <p>¹Faculty of Medical Sciences “Julio Trigo López”, Bejucal Czda , Km 7 ½, Arroyo Naranjo, Havana City, Cuba. email: maria.tase@infomed.sld.cu ²Center for the Development of Pharmacoepidemiology, National Pharamcovigilance Unit, 5^{ta} Ave and 44 St, Miramar, Playa, Havana City, Cuba. ³Center for research and vaccine production. Ave 27 # 19 805, The Colonel, La Lisa, Havana City, Cuba. ⁴Maternal and Child Hospital “A.A.Abali”, Bejucal Causeway, Havana City, Cuba.</p> <p>Introduction: Drugs symbolize the ability to modify the natural course of most diseases but its limitations also may cause adverse effects and lead to death of the individual. Material and methods: Observational, descriptive, retrospective, pharmacovigilance, using the 256 reports of suspected fatal ADRs, received from 2000 to 2008 in the UNCFv. Were characterized according to age, sex, suspected drugs, drug group, body system affected, causation, frequency, potential determinants and preventable reactions. Results and discussion: The adults were the most affected (47%), literature reports that the elderly are most vulnerable to suffer RAM and its complications. The female sex predominated (53%), corresponding to that reported in the literature. The drug was associated mostly crystalline penicillin G (44 notifications), prevailing general events (37.5%) and within anaphylactic shock, these drugs are widely used not only exposing their therapeutic effects but also undesirable, including anaphylaxis , which can be fatal. The 50.4% of reactions were classified as probable and low frequency, the accountability could be established from the discussions of experts from the hospital and national, in addition to the autopsies in 32.4% of cases, confirming causality. Indications were found unsuitable preventable 15.8% and apparently the use of two or more drugs (58.1%) contributed to the occurrence of adverse reactions. Conclusions: ADRs Cuba affected more fatal to the female adult population, the highlights of antibiotic penicillin within them, apparently in the drug most associated with the cause, the risk increases when using more than one drug and a non-negligible percentage of these events were preventable.</p>
PFep 075	<p>THE QUALITY OF PHARMACEUTICAL SERVICES EVALUATION IN THE HEALTH COMMUNITY JOSÉ MARTÍ. SANTIAGO DE CUBA. JANUARY- MAY 2009 Briso Fernández M¹, Bermúdez Camps I², Vendrell Calzadilla N³</p> <p>¹Dirección Provincial de Salud Pública, Paseo esquina Luz Caballero. Cuba. ²Oriente University. Patricio Lumumba. Santiago de Cuba. Cuba. ³Empresa de Farmacia y Óptica. St D. Sueño. Santiago de Cuba. Cuba.</p> <p>Introduction: It was carried out a descriptive and operational cross-section investigation in the health services and systems with the objective to evaluate the quality of the Pharmaceutical Services in the health community José Martí during the period January through May 2009 taking point the official normative established in the country. Material and Methods: The evaluating process was developed with a sample composed of 52 doctors, 6 licentiates in Pharmacological sciences, and 14 Technicians in Product Pharmacy as well as 382 patients that were assisted at the 5 pharmacies of the health area studied. The quality was evaluated starting from the attributes of structure, process and results, establishing or standards, and the coefficient was calculated as well. Results and Discussion: The results demonstrated that the evaluated Pharmaceutical Services do not possess quality because they presented insufficient availability of the quality pharmaceutical professionals, with post-graduation formation and the accurate</p>

	<p>hold of work, lack of technical equipment and material resources as well as an inadequate achievement of the functions related to the use of medication that conditional the dissatisfaction of patients, doctors and pharmaceutical professionals of the to design a strategy in search of services quality based on the result of this work. Conclusions: The quality of the Pharmaceutical Services in the health community José Martí was inadequate, because all the services were inadequate at all.</p>
PFep 076	<p>PHARMACOVIGILANCE IN PATIENTS WITH HIV / AIDS Rodríguez M¹, Muronso I²</p> <p>1-Hospital Oncológico “Conrado Benítez”, Santiago de Cuba. email: farmaonco@medired.scu.sld.cu 2- Bindura Provincial Hospital. Zimbabwe.</p> <p>It was a descriptive-traverse study in patients with HIV/AIDS who plows taking antiretroviral therapy in the period from January to June 2008 in Bindura Provincial Hospital, Mashonaland Central with the objective to monitor the patients. Firstly the sample was characterized, then the percent of treatment adherence was determined, and the possible adverse reactions were detected. It was used a method of intensive monitor to hospitalized patients and modified to ambulatory patients. A sample was obtained of patient 179; they had from 14 to 70 year-old. Of the patient included only 1% have HTA, and 2.2 and 7.8 presented illnesses opportunists the biggest percent according to HC. The entire patient’s received the first line treatment: Dual combination and triple combination first 2 weeks and after first 2 weeks received triple combination two times a day³. And one patient received treatment with Efavirens after Triviro side effects. 14% of the patients presented adverse reactions, which were classified as probable: headache, peripheral neuropathy, vomits, Diarrhoea, stomach pain, rash. In the alone analyzed sample 0.5% tube less than 70 percent of adherence, the 92. 7% reaches but of 95 adherence%. The biggest percentage of patient was concentrated from 29 to 43 years old and the feminine patients prevailed. It were detected the more frequent side effects according to literature and with more percentage in the gastrointestinal and nervous system. 96% of the patient had more than 95% of adherence to the antiretroviral treatment. 92% of the patient had an appropriate consumption of antiretrovirales.</p>
PFep 077	<p>EVALUATION OF THE PRESCRIPTION OF ANTIBIOTICS IN THE URGENCY SERVICE OF A PEDIATRIC HOSPITAL Echavarría M¹, López R¹, Miranda M¹, Sedeño C¹</p> <p>¹Pharmacy and Food Institute of University of Havana , 23 Ave No 21415 between 214 y 222, La Coronela, La Lisa, Havana City, Cuba. email: midalys@uh.cu</p> <p>Introduction: Antibiotics (ATBs) are one of the most highly prescribed pharmacological groups. The excessive consumption and inadequate prescription of ATBs have serious consequences for public health, such as: the appearance of bacterial resistances, the exposure to toxic and secondary effects, the increase in morbidity, etc. It also represents an unnecessary increase in cost. We carried out a study on prescription - indication of antibiotics with the objective of evaluating these substances in the Urgency Service of the Pediatric Hospital Juan Manuel Marquez of the municipality ‘Marianao’ in Havana City.</p> <p>Material and Methods: We used a sample size of 382 pediatric patients diagnosed with sepsis during the study period (November 2007 - April, 2008). The interviews to doctor and the family of patient were used as a work method. Qualitative and quantitative were used to express the results of the investigation. The interviews and the models of picking up of data processed him statistically through no parametrics tests (squared Chi and the coefficient of correlation of Spearman) intervening the statistical package SPSS 12, 0 for Windows. Results and Discussion: These results showed that the antibiotics prescribed the most were Penicillin and Macrolide, the most frequent infections were those of the upper respiratory tract, the prescription was filled incorrectly in more of 50% of the cases. The therapeutic fulfillment was satisfactory and the answer to the treatment was positive in 77.5% of the cases. Conclusions: Traditional antibiotics have been replaced by new, wide-spectrum, more costly antibiotics. The levels of resistance of the main micro-organisms involved in the most prevalent infections. It is necessary to take action in order to attain a more rational prescription.</p>
PFep 078	<p>INFORMATION NEEDS ON THERAPEUTIC HEALTH PROFESSIONALS. CUBAN MEDICAL MISSION. CARONI MUNICIPALITY. BOLIVAR STATE. 2009 Linares IM¹, Calvo BD², Debesa GF²</p> <p>¹Cuban Medical Mission in Venezuela ²Center for the Development of Pharmacoepidemiology, National Pharmacovigilance Unit, 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba. email:dulce@mcdf.sld.cu</p>

	<p>Introduction: In Bolivar state found problems with the use of information technology in the search for scientific information by health professionals and therapeutic errors identified by performance indicators, health insurance area, the causes are unknown these deficiencies. Objectives: To identify sources of information on treatment and determine the relevance in the case of electronic and information needs therapy. Designing an educational strategy to meet those needs. Method: We conducted an observational, descriptive and cross-sectional Caroni municipality, Bolivar State, Venezuela Bolivarian Republic in the months from May to July 2009. Operationalized the variables are given output targets. A structured questionnaire was drawn up to apply for health professionals. A questionnaire was developed to evaluate the relevance of websites visited by the respondents. Results: 52% of respondents mentioned not having access to scientific information in the network. The most visited sites were Infomed, Medline, Lilac, while found to be most relevant Cochrane Library, Medline, Pubmed, Infomed and Finisterre. Books and print journals are preferred by professionals. The issues they care most about are drugs (27.7%) and therapy (23.4%). As for the drug groups, the greatest demand are: antimicrobials (20%), antihypertensives (19.6%) and antidiabetics (16.7%). Health problems that matter most are diabetes mellitus, hypertension and asthma. Conclusions: Health professionals from Caroni municipality does not have sufficient and timely information on therapeutics, as most mentioned not having access to search sites of scientific information. The preferred sources of information were sometimes outdated, in addition, the sites visited did not always match those that were considered most relevant.</p>
PFep 079	<p>ADVERSE EVENTS ASSOCIATED WITH THE VACCINE PREPARATION NGCGM3/VSSP/MONTANIDE ISA 51 IN PATIENTS WITH METASTATIC BREAST CANCER Cid M¹, Pérez M¹, De la Torre A², Pérez K,² Marinello P³, Suárez G³</p> <p>¹Institute of Medical Sciences “Dr. Serafín Ruíz de Zárate Ruiz”. Vicerrectorate of investigations. Clinical Trials Center. Carretera a Acueducto y Circunvalación. Santa Clara, Villa Clara, Cuba. E-mail: maykelpm@yahoo.es, maykelpm@iscm.vcl.sld.cu ²Universitary Hospital “Celestino Hernández Robau”. Santa Clara. Cuba. ³Center of Molecular Immunology. Havana. Cuba.</p> <p>Introduction:The gangliosides are among the better studied antigenic systems and they have its increased expression in the tumoral cell membrane. Several clinical trials with therapeutic vaccines containing N-Glycosylated gangliosides have been carried out in Cuba by the Center of Molecular Immunology. One of these studies is the clinical trial: Active immunotherapy specific for the vaccine preparation NGcGM3/VSSP/ Montanide ISA 51 in the treatment of patients with metastatic breast cancer (stage II). With the objective of evaluating the main adverse events related with this product, the clinical records of all the patients included in this clinical trial carried out in the Oncology Service of the University Hospital “Celestino Hernández Robau” of Villa Clara were checked. Materials & Methods: The number of adverse events reported by patients were gathered and classified according to the Common Terminology Criteria for Adverse Events (CTCAE) to the Cancer National Institute of the U.S.A. Results: A total of 389 adverse events were reported. According to their intensity degree the adverse events were classified as: slight intensity (77.37%), moderate (20.05%), severe (1.54%) and very severe (1.03%). Regarding the causality relation the non-related adverse events were predominant (73.0%). The most frequent events associated to the vaccine were related with the administration site and general symptoms similar to an influenzal state. Conclusions: The adverse event of higher intensity related with the product of investigation was the abscesses in the injection site. The group of the adverse events was neither a limitation doses nor a cause for treatment interruption.</p>
PFep 080	<p>DIABETOLOGICAL EDUCATION IN PATIENTS WERE HAD DEALINGS WITH HIPOGLICEMIANTS AND ANOTHER MEDICATIONS. UNIVERSITARY CLINICAL POLICLINIC. “LUIS A. TURCIOS LIMA”. PINAR DEL RIO 2009 Rojas N¹, Martínez H², Labrador N³.</p> <p>¹Universitary Clinical Surgical Hospital Dr Leon Cuervo Rubio, Km 1 central Road CP 20100 Pinar del Rio Cuba. Senior Imagenology, Instructor Professor of Pharmacology. email: jesusp@princesa.pri.sld.cu ²Clinical Center Turcios Lima, Velezcaviedes street, CP 20100 Pinar del Rio, Cuba. Doctor of Medicine, Instructor Professor of Pharmacology. ³Clinical Center Turcios Lima, Velezcaviedes street, CP 20100 Pinar del Rio, Cuba, Doctor of Medicine, Instructor Professor of Pharmacology</p>

	<p>Introduction: The Diabetes Mellitus has become a pathology of great incidence in the world, when aging the population and increase the risk factors, study becomes necessary, therefore, It investigation has the objective to orchestrate a strategy of intervention on Diabetological Education in patients were had dealings with hipoglicemiant and another medications. Material and Methods: At the end of the investigation. Another questionnaire and graphics were grouped to determine statistical significance or association of variables, and it was worked up with a level of 95 % of certainty. Results and Discussion: In the adult diabetic elders Group on the University Clinical. "Luis A. Turcios Lima" in 2009. The sign was composed by diabetics patients of 60 years old and more, an initial questionnaire and a little flat collector of data where they gathered following variables such as: Age, sex, diabetes type, non associated diabetics medications, Nutritional evaluation, associated to the diabetes illnesses, start age of debut, more common symptoms to the debut, and medicinal reactions with and without medicinal associations. At a later time an evaluation on the principal adverse reactions, was applied the questionnaire to validate the result of educational intervention, provoked by the synergism. Conclusions: All demonstrated to us the increased of adverse reactions and symptomatology not of Diabetes due use of medications such like Psicofarmacs, Antiparasitars, tighteners, Analgesics and permitted this decreasing unwanted effects in patients with Diabetes Mellitus, as well as welcomed bearing treatments, having present the need to use the hipoglicemiant in patient with chronic illnesses.</p>
<p>PFep 081</p>	<p>IMPACT OF DRUG INFORMATION SERVICE IN THE CENTRE FOR STUDIES, DOCUMENTATION AND INFORMATION OF DRUGS OF VILLA CLARA González N¹, Bermúdez A¹, García Y¹, Jaramillo L¹, San Gabino Y¹.</p> <p>¹Medical Sciences University "Dr. Serafín Ruiz de Zárate Ruiz". Centre for Studies, Documentation and Information of Drugs. Aqueduct Road, Santa Clara City, Villa Clara, Cuba. CP 50200. email: namirygs@ucm.vcl.sld.cu , abdelbs@ucm.vcl.sld.cu.</p> <p>Introduction: Drug Information Service (DIS) is frequently offered based on the clinical situation of a specific patient and as an integrated part within the programmes of Pharmaceutical Attention. Drug information is materialized in the Centre for Studies, Documentation and Information of Drugs (CSDID) of Villa Clara province. Materials and Methods: a retrospective study of DIS in CSDID was carried out and there were analyzed passive and active information in the period of January, 1999 to December, 2009. Results and Discussion: There were received 6373 pharmaceutical consults of passive information (average: 531 requests/year) and 98.8% was satisfactory responded. From a total of 3870 consults, 60, 7% were requested by health professionals (medical doctors, pharmacists, nurses, etc.), 1754 (27, 5%) by patients and 738 (11, 6%) by Medicine and Pharmacy students. There were presented 83 informative bulletins (70 of pharmacotherapeutical updating and 13 of patient education in the rational use of drugs). 1714 pharmacotherapeutical individual education activities are done and 119 on a grouper including totally 2648 patients. Conclusions: the great number of responded consults, the diversity in the requesters and the variety of subjects and the numerous educative activities show that the actions of DIS have contributed to guarantee the rational use of drugs.</p>
<p>PFep 082</p>	<p>USAGE OF PSYCHOTROPIC DRUGS IN ELDERS RESIDING IN A "10 DE OCTUBRE" MUNICIPALITY AREA Yodú Ferral N¹, Peña Fleites C¹</p> <p>¹"10 de Octubre" Medical School, Medical University of Havana, Calzada 10 de Octubre No 130 Cerro, Havana City, Cuba. email: yodu@infomed.sld.cu</p> <p>Introduction: Aging is a global process with socio-economical repercussions. Elders in Cuba, one of Latin America's most aged countries, amount to 17.4% of the population. Seniors must face diverse bio-psycho-social problems and this is probably why psychotropic drugs rank among the most consumed, most self-medicated and worst employed drugs in elders. Methods: To learn about the consumption habits of psychotherapeutic agents in an aged community (23.5%) in the municipality of "10 de Octubre", Havana City, an observational-descriptive, drug utilization study was conducted. A sample of 100 old adults was randomly selected and surveyed for a period of one year, from an initial universe of 216 elders (65 or more years of age) taking psychotropic agents and under the care of family doctors. Results and Discussions: The highest psychotropic drug consumption was observed in women (63%), with anxiolytics being the most used (71.2%). They were daily used in 86.1%. Diazepam had the first place with 23.4% followed by</p>

	<p>Nitrazepam and Meprobamate with 18.9% each. The referred causes of use were anxiety-nervousness (46.8%) and insomnia (26.6%). Although these treatments coincide with medical recommendations, it can be questioned if they were used rationally, after learning that 87.3% used these drugs for a very long time, 45.6% were self-medicated and 37.6% of this group got the medication through ways out of the control of the National Health System.</p> <p>Conclusions: The inadequate use of psychotherapeutic drugs in old adults could affect their satisfactory longevity; therefore it is necessary to find ways to solve this health problem.</p>
PFep 083	<p>UTILIZATION OF AZITROMICIN IN “MÁRTIRES DE CALABAZAR” PRIMARY HEALTH ATTENTION CLINICAL. 2008 <u>Neylim Blanco Hernández</u>¹, Yohandra Machado Pérez²</p> <p>¹Especialista de I Grado en Farmacología. Máster en Enfermedades Infecciosas. email: neylimb@infomed.sld.cu</p> <p>²Licenciada en Farmacia. Policlínico “Mártires de Calabazar” Ciudad de La Habana. Cuba. Policlínico “Mártires de Calabazar” Municipio Boyeros. Ciudad de La Habana. 2008</p> <p>Drugs - utilization study type of prescription-indication with elements of consumption and therapeutics scheme was realized about Azitromicin available in the four pharmacies appertaining to “Mártires de Calabazar” primary health attention clinical during three months of 2008. The prescription was review to evaluate its quality with regard to diagnosis and doses. The most important results include that the consumption of azitromicin was 2 DHD, the respiratory infections disease were the most frequent and more than quarter of prescribed doses were incorrect. Concluding 40% of Azitromicin prescription was erroneous.</p> <p>Key Words: Drug-utilization study, azitromicin, antibiotic, therapeutic antibiotic</p>
PFep 084	<p>PHARMACOVIGILANCE OF THE HEBERPROT-P AT THE TERRITORY CÁRDENAS-VARADERO-MARTÍ <u>Marín N</u>¹, Díaz J. I¹, Pérez L¹, Peña V¹.</p> <p>¹Hospital: "Julio M. Aristegui Villamil". Highway Cárdenas-Varadero, Km. 2. Cárdenas, Matanzas. email:director02@mtz.jovenclub.cu</p> <p>Introduction: The Heberprot-P is a pharmaceutical formulation based in the epidermal human growth factor recombinante, it formulate myself of 0,025 and 0.075mg for his administration the intralesional. Es once a product that favors the cicatrization of diabetic ulcers and reduces the risk of amputation, of the above was considered can present ourselves that we chased like objective to develop the pharmacovigilance the Heberprot-P at the territory Cárdenas Varadero Martí. Materials and Methods: A study to 24 patients hospitalized in Angiology's service during the first trimester of the present year the isquémicas or neuropáticas in estadios showed injuries 3 ó 4 of Wagner's scale with probability of amputation. At all was applied Heberprot-P at our institution to detail the more common frequency of patients with adverse events and to develop pharmacovigilancia's study. Results and Discussion: Of 24 processed patients, 12(50 %) developed adverse events, their 9(37.5 %) RAM light predominating ardor, local pain, shivers and fever, 3(12.5 %) RAM tax characterized for precordial pain. A low frequency appears of RAM tax and the properties and advantages the Heberprot-P When stimulating to granulation and accelerated in ulcers of diabetic foot; reduce the time of cicatrization and number of surgical interventions the same way that contributes to the rescue of the extremity. Conclusions: Farmacovigilancia's study demonstrated light appearing of RAM tax in low frequency, a report of cases treated at the territory in national data base. Have given graduates to do this application extensively to Salud's Attention Primary and demonstrated at our hospital a considerable reduction of the number of amputations in patients with ulcers of the diabetic foot thanks to Heberprot P.</p>
PFep 085	<p>INFLUENCE OF DRUGS AND TOXIC HABITS IN NEWBORNS IN CAMAGUEY PROVINCE, CUBA <u>Valdovinos Casado Niurys, Ferrándiz Ramírez Dania.</u></p> <p>¹ University of Camaguey. Cuba. niurys.valdovinos@reduc.edu.cu</p> <p>Elder, child population and fetus are very susceptible to drug side undesirable effects, so research in drug influence are among investigations that has been done in the search of born malformations and development. In this study could be determined influence of drug and toxic habits in low birth weight,</p>

	<p>prematurity, defects and respiratory depression in newborn, and established drug classes most involved in the development of these anomalies. A retrospective observational study was conducted in the Maternity Hospital of Camagüey province in the period between the October 15, 2007 and April 14, 2008. The study was conducted using the questionnaire method, 400 women were interviewed and took a random sample of 370 women aged between 20 and 30 years. Smoking had the greatest influence of toxic habits. It was found that 108 pregnant women were exposed to any medication during the period of gestation and controls, only 21 were exposed. Antimicrobials have the highest effect on the newborn, having a higher incidence of congenital malformations and prematurity. Another important pharmacological group was made up by hypnotics and sedatives, which has influence on the birth of children with respiratory depression when these drugs were administered in the third trimester of pregnancy. It took into account the effect of the quarter, which is nonspecific and depends largely on the type of medication.</p>
<p>PFep 086</p>	<p>HANDLING OF THE CLINICAL SEARCHING IN THE BASIC ATTENTION IN LAS TUNAS Montes de Oca N, Rojas S, Horta EM, Peña D, Rosales S, Trista Y</p> <p>Medical Sciences University Las Tunas. e-mail: norma@cucalambe.ltu.sld.cu</p> <p>Introduction: During the clinical searching, the investigator handles the natural conditions of the investigations, turning them into very different ideals regarding the usual practice. They are perspective studies, where the effect of the interventions in human beings is evaluated. The knowledge about the handling of this kind of investigation is important to achieve valid scientific results. Materials and Methods: A descriptive study of a cross section was carried out in 75 doctors from the five health areas of Las Tunas municipality with the objective of designing an educative strategy to increase knowledge about the handling of the clinical investigations carried out by these professionals during the period from September, 2009 to February, 2010. The variables were the characterization of the scientific potential, the handling of the clinical investigations regarding design and ethics of investigation, the level of knowledge and the main learning necessities of the studied sample, what was used to design an educative strategy validated by the experts' criteria. Results: The samples were predominantly of interns and 1st degree specialists, instructor-professors, and the category of master, identifying as an inadequate handling of the clinical investigations in the 71.7%; only 26% obtained a high level of knowledge, being methodology of investigation, ethics of clinical investigation, and good clinical practice the priorities in the learning necessities, what permitted to design an educative strategy validated through a group of experts, and which has the title of "Improvement of the handling of the clinical investigations in health basic attention". Conclusions: The characterization and diagnosis of the handling of the clinical investigations uphold the necessity to improve our professionals through an educative program with a view to achieve a good performance in the investigation and medical attention.</p>
<p>PFep 087</p>	<p>EFFECTIVENESS AND SAFETY OF SURFACEN IN THE PRESENT CIRCUMSTANCES IN CUBA Fernández-Limia O¹, Díaz E¹, Yera I², Morilla A³</p> <p>¹Centro Nacional de Sanidad Agropecuaria (CENSA). Carretera de Jamaica y Autopista Nacional, San José de las Lajas, La Habana, Cuba. email: octavio@censa.edu.cu ²Centro para el Desarrollo de la Farmacoepidemiología (CDF) ³Programa de Atención Materno Infantil (PAMI) MINSAP</p> <p>Introduction: SURFACEN is a porcine natural surfactant used to treat the Newborn Respiratory Distress Syndrome, (NRDS) known formerly as Hyaline Membrane disease. Since its approval for use in 1995 has been used increasingly and has helped with Neonatal Intensive Care Units (ICU) facilities the decline in infant mortality from this cause from 0.8 in 1994 to 0.1 per thousand live births in 2008. However, since the first clinical trial (CT) conducted in 1994 and a further comparative CT with Beractant made in Mexico, after more than 10 years of use is not aware of the effectiveness and frequency of adverse events associated with the use of the drug today. Material and methods: As we set out to make a CT of pharmacovigilance (Phase IV) prospectively in 13 provinces and 17 neonatal ICU in the country. We included 259 newborns with SDRN to whom SURFACEN was applied at 100 mg / kg dose by tracheal instillation in one or more applications depending on the patient requirements. Results and discussion: The results show a rapid and sustained increase in arterial blood oxygenation index measured by PaO₂/FiO₂ almost immediately after applying the surfactant, the number of applications were 2.0 ± 1 and the output indicators as ICU stay was 11.9 ± 11.4 days, mechanical ventilation 7.1 ± 8.9 days and mortality 19.7%. Most striking was the reduction of mortality to almost half compared with the previous</p>

	<p>EC and that was the cause SDRN only 13.7% of deaths. The observed complications were: late pneumonia 22.8%, <i>ductus arteriosus</i> reopening 13.9%, pneumothorax 12.4%, bronchopulmonary dysplasia 11.4%, other complications were below 7%. We conclude that survival is higher than in previous studies and tends to increase, most deaths are not caused by SDRN, oxygenation after treatment was comparable to that reported and is considered adequate and the complication rate is very similar the previous EC, other adverse events were related with the rapid increase in arterial blood oxygenation. Conclusions: In general SURFACEN has high effectiveness and safety and has contributed to the decline in infant mortality by SDRN in Cuba.</p>
PFep 088	<p>DELIRIUM AS SIDE EFFECTS CAUSED BY MEDICIN IN ANCIENTS. 2004-2009 García O, Alfonso I, Hydes E</p> <p>CITED, 27 y G. Plaza de la Revolución. Havana City, Cuba. Email: ogarnao@infomed.sld.cu</p> <p>Introduction: The ancients are a special populations when we talks about medicines, because they are more susceptibles to present side effects, more frecuently than the rest of the populations. This study show the characteristics of this populations and focus in the delirium as adverse reactions. Materials and Methods: First was an exploratory study about ancients and adverse reactions by medicines, specific delirium and diferents sustances that provoke this sindromes. After an descriptive, transversal and retrospective study of the reports of confusional sindromes as side effect in ancients since 2004 to 2009 at database and Cuban Pharmacovigilance System. Results and Discussion: The results showed that pharmacodinamic and pharmacocinetic changes, in relations with the ages, provoke side effects in this populations, The adverse reactions by medicin are the principal cause of delirium and they are many medicine that provoke confusions, principals in ancients. The study of the reports of this side effects, show a very small reporting. Conclutions: This study showed a few reports of delirium as side effects of medicines, provoked meanly by the non agnoleadgments of the relations between many sustances and this sindrome, be really necessary to educate the healthcare persons about it.</p>
PFep 089	<p>EVALUATION OF THE PRESCRIPTION OF ANTIMICROBIALS FOR SYSTEMIC USE IN PATIENTS ADMITTED TO THE INTEGRAL DIAGNOSTIC CENTER RAUL MAZA MÉRIDA. DELTA AMACURO. 2008 Pérez LO P¹, Furonos MJ²</p> <p>¹Cuban Medical Mission in Venezuela ²Center for the Development of Pharmacoepidemiology, National Pharmacovigilance Unit, 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba. email: furones@mcdf.sld.cu</p> <p>Introduction: In order to evaluate the prescription of systemic antimicrobials in patients admitted to the CDI Raul Maza Delta Amacuro Mérida state during 2008 and assess the factors influencing the pattern of use was made in an investigation with quantitative and qualitative methods. Methods: The quantitative study was observational, descriptive and transversal that since EUM is classified as a prescription and therapeutic schemes and elements of practical consequences. The qualitative study was a discussion group for this purpose 2 groups one with physicians at the DTC and another who performed the medical guard. Results: We evaluated 162 patients who were treated with antimicrobials in the study period. Information was gathered on diagnosis, prescribed antibiotics, route of administration, type, change and duration of treatment was assessed scheme, the quality of treatment and clinical evolution, we found that the diagnoses more motivated to prescribe antibiotics were the disease acute diarrhoea, acute fever and pneumonia and antibiotics were most commonly prescribed penicillin, metronidazole, ceftriaxone, route of administration used was an intravenous 70.5%, the prevailing treatment duration less than three days with a (56.2 %) and choice of antibiotic was inappropriate and wrong: Conclusion: The evolution of patients after discharge was satisfactory in most patients (96.6%). We conclude that there is an inappropriate use of systemic antibiotics.</p>
PFep 090	<p>CONSUMPTION OF PRESCRIBED DRUGS DURING PREGNANCY IN LAS TUNAS N Orive Rodríguez, Y Núñez Rojas, F Varona de la Peña, G Martínez González, AF Raad López</p> <p>Provincial Center of Medical Genetics, PO Box 27, Las Tunas 75100, Las Tunas, Cuba email: nora@cucalambe.ltu.sld.cu, cpgmt@infomed.sld.cu</p>

	<p>Introduction: Pregnancy is a critical period where medication should be managed with caution, particularly during the first trimester. The risk for drug-induced birth defects demands the health care providers to accurately assess the potential benefits of therapy in terms of safety for the fetus and the newborn. Drug consumption is one of the criteria taken into account by genetic counsellors when evaluating prenatal genetic risks in pregnant women. Design: A longitudinal, prospective study was carried out, as part of the Pre-Conceptional and Prenatal Genetic Risk Program of the Provincial Network of Genetics in Las Tunas, to follow up every pregnant woman who was classified with an increased genetic risk for teratogenicity due to medication during 2009 and 2010 in the sixteen health areas. A registry was designed to collect information regarding maternal age, gestational age, prescribed drug, dose and fetal and/or newborn outcome, among other variables. Results: 126 women have been included in the registry so far. The average gestational age in the sample was 13 weeks and 84.7% received the medication during the first trimester. The duration of treatment was variable, with 2.9% undergoing permanent therapy, 4.8% having single dose and 70.2% receiving one week regimens. Antivirals (Tamiflu) and antibiotics represented the most frequently used drugs in the sample, with 35.9% and 11.7%, respectively. Only one defect has been diagnosed so far, a brachial cyst in a newborn.</p> <p>Conclusions: The consumption of pharmaceuticals during pregnancy has not posed an increased risk of teratogenicity in the sample studied. Though the safety of prescribed drugs is thoroughly assessed during preclinical and clinical studies, it is important the surveillance during pregnancy and after birth to detect both known and unexpected effects in the fetus and the newborn.</p>
PFep 091	<p>IDENTIFICATION OF THE ADVERSE AVOIDABLE REACTIONS, IN THE STATE OF MIRANDA, VENEZUELA, FROM OCTOBER 2007 TO OCTOBER 2009 Aguilera Aguilra O¹, Alfonso Orta I², Jiménez López G², Groning Roque E³</p> <p>¹Regulatorio Buro for health proteccion. General Garcia No.227 up. Between. Lora and Maso streets, Bayamo City, Cuba. email:dr.aguilera@grannet.grm.sld.cu; brpsgrm@grannet..grm.sld.cu ²Center for the Development of Pharmacoepidemiology, National Pharamcovigilance Unit, 5^{ta} Ave and 44 St, Miramar, Playa, Havana City, Cuba.</p> <p>Introduction: The researches about the so called drug adverse avoidable reactions ,are useful to focus the most severe incidents that take place out of the hospitals in the world, though these could be real consequences of failures in the use of those medicaments closely related to the primary or specialized attention or in the middle of both assistance levels. Objective: To identify the drug adverse avoidable reactions (DAR) that have been previously noticed by doctors in the Mission “Barrio Adentro” in the state of Miranda, Venezuela, from October 2007 to October 2009.Material and Methods: It has been made an observational study such as descriptive and transversal of pharmaco-vigilance with an interventional proposition, taking into account the method of spontaneous notification of adverse reactions during the period of time from October 2007 to October 2009 in the state of Miranda, Venezuela. In the “avoidable” aspect of DAR, the adverse reactions have been potentially classified as “unavoidable” following Schumock and Thornton’s questionnaire modified by Otero and Cols.Results and Discussion: There has been 965 drug adverse avoidable reactions; the 31 per cent of all made notifications. The antimicrobials group was more associated to the notifications (34%). Captopril produced only the 11.2 per cent. The minor adverse reactions were the 71,4 per cent. The inappropriate indication of medicaments keeps being the main cause in the avoidable aspect, in this case the 21.3 per cent. The 71.4 per cent of all adverse reactions were classified as probable. Conclusions: The outstanding group is for females and aged persons between 19 and 65 years old. The most reported have been the antimicrobials group and in the case of medicament the captopril. There have been different kind of minor adverse reactions, frequents and casuals to others. The main cause that has been shown in the “avoidable” aspect was the inappropriate indication of the medicament joined to the skin rash as the most frequent reported adverse reaction.</p>
PFep 092	<p>POLYPHARMACY IN THE ANCIENT IN THE COMMUNITY Alonso P¹, Sansó FJ², Fernández EJ³, Calvo DM⁴</p> <p>¹National Center of Medical Sciences Information. E St. between 19 St. and 21 St., Vedado. Plaza. Havana City, Cuba. email:patricia.alonso@infomed.sld.cu ²Clinical Surgical Hospital “Dr. Salvador Allende”. Cerro Ave and Domínguez St. Cerro. Havana City, Cuba. email: fsanso@infomed.sld.cu ³Faculty of Medical Sciences “Dr. Salvador Allende”. Buenos Aires St. Cerro. Havana City, Cuba. ⁴Center for the Development of Pharmacoepidemiology, National Pharmacovigilance Unit, 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba. email: dulce@mcdf.sld.cu</p>

	<p>Introduction: Cuba is among the nations with demographic transition. In 2009 the percentage of elderly was over 16% of the total population. Polypharmacy is one of the "capital geriatric problems" and sometimes can be considered an addiction. It is one of the most common situations, with negative implications on morbidity and mortality in old age. In considering the frailty in the elderly population, we found that polypharmacy is one of the most common criteria; however, there is no research to deepen polypharmacy in subpopulations of frail older adults. To characterize the state of polypharmacy in the frail elderly population attended by Basis Working Group "Palatino" in the health area "Antonio Maceo", Cerro Municipality, City of Havana, Cuba is the objective of this study. Material and methods: An observational, descriptive and cross-sectional study was conducted in the period January 2008- December 2009. Those frail elderly adults that met the criteria "polypharmacy" were identified and characterized. The variables studied were sex, age, educational level, number of medications, consumption origin and drug groups. Results and discussion: 302 frail elderly adults were studied, 61.59% met the criterion of frailty "Polypharmacy." In this group females were majority (65.1%). The age group 75-79 years (24.2%) and "primary education" education level (38.2%) were predominant. On average, daily consumption was four drugs. 62.9% had a prescription method, 40.2% of these additionally consumed other drugs and 62.37% were self-medicated. The average daily consumption of prescribed drugs was superior compared to those consumed without prescription. The most prescribed drugs were antihypertensive drugs (37.1%) and diuretics (36.0%) and in the case of self-medication the most consumed were vitamins and minerals (65.2%) and opioid analgesics (13.0%). Conclusions: The criterion of frailty polypharmacy is a condition of a high prevalence in the population studied in which the prescription has strongly influence.</p>
<p>PFep 093</p>	<p>SIMPLE DOSE OF MEBENDAZOLE USED IN LIGHT INTESTINAL INFECTION BY ASCARIS AND TRICHURIS. LAS TUNAS, MARCH FROM DICEMBER 2009 Laird RM¹, Reyes E², Merino RM³, Pérez S⁴, Montes de Oca N⁵</p> <p>¹University of Medical Sciences, Las Tunas, Youth Ave, Las Tunas city, Cuba. email: rebecam@cucalambe.ltu.sld.cu ²Provincial Center of Hygiene, Epidemiology and Microbiology, Lucas Ortiz # 13 Las Tunas city, Cuba. e-mail: eduardoreyes@cucalambe.ltu.sld.cu ³University of Medical Sciences, Las Tunas, Yuoth Ave, Las Tunas city, Cuba. e-mail:vdi@cucalambe.ltu.sld.cu ⁴University of Medical Sciences, Las Tunas, Youth Ave, Las Tunas city, Cuba. e-mail:sahily@cucalambe.ltu.sld.cu ⁵University of Medical Sciences, Las Tunas, Youth Ave, Las Tunas city, Cuba. e-mail: norma@cucalambe.ltu.sld.cu</p> <p>Introduction: The use of simple dose of wide spectrum antihelminthic drugs is one of the epidemiological bases for intestinal geohelminth control, besides health education and environmental sanitations. Materials and methods: A transversal analytical study was carried out with the objective to evaluate the effectiveness of 300 mg simple dose of mebendazole in the treatment of intestinal geohelminth in Las Tunas, from March to December 2009. Fifty children between eight and nine years old from five primary school of Las Tunas municipality with light intensity of infection by Ascaris and Trichuris diagnoses by Kato Katz procedures and familiar consent were study. All the children received the drug and the variables to consider were adverse reaction and the result of coproparasitological exam by Kato Katz smear. Chi square was used for analysis parasitological results after and before drug administration. Results and Discussion: In all cases the parasitological analysis of feces was negative after the use of the drug. Nauseas and vomiting were presented in just 12% and 2% of the cases, respectively according with the bibliography. Conclusion: The use of simple dose of mebendazole in simple dose of 300 mg was considered effectiveness in the treatment of light infection of intestinal geohelminth Ascaris and Trichuris.</p>
<p>PFep 094</p>	<p>QUALITY OF THE PRESCRIPTION OF AMITRIPTILINE IN DEPRESSION OF THE ELDERLY. JOSÉ MARTÍ DISTRICT . JANUARY TO JUNE , 2009 Álvarez González RM, Pajarín Fernández L, Granados Hormigó A E, Remedios Reyes R.</p> <p>University of Medical Sciences of Santiago de Cuba. Faculty #1. Las Americas avenue. Reparto Sueño, Santiago de Cuba. email:odet@medired.scu.sld.cu</p> <p>The rational use of drugs in the elderly not only implies to control the excessive and unnecessary use of</p>

	<p>medicaments but also to propitiate the use of drugs whose effectiveness to improve the quality of the life has already been demonstrated the psicodrugs occupy the third place in their consumption. Amitriptiline has been considered as one of the compounds of reference for the pharmacological treatment of depression, but any information is reported about the quality of its prescription in this population group, which constitutes our research problem, motivating us to carry out the present work. A descriptive, transversal study was done to evaluate the quality of the prescription of Amitriptiline as health service, in elderly patients with diagnosis of Depression, treated with this medicaments and whose prescriptions were picked up in the Main Pharmacy of the area of primary attention of José Martí district Santiago de Cuba municipality, in the period from January 1ro to June 1ro, 2009. The methodology suggested in the National School of Public Health in Cuba was applied to evaluate the quality of prescription in centers of primary attention taking in to considerations its three dimensions: structures, process and results. For each dimension criteria and subcriteria, value rates and standars were built. The evaluation of the structure was appropriate because it was found that the criteria of availability of material and humans resources were appropriate. For the evaluation of the process and results, 19 prescriptors of the medicament were used and 58 elderly patients who were consumers of Amitriptiline. It was found that both the test of knowledge and the competence were inapropiated because the process was evaluated in the same way. The results of the satisfaction of the users were appropriate and that of the prescriptors inapropiate.</p>
<p>PFep 095</p>	<p>METHODOLOGICAL PROPOSITION FOR THE DEVELOPMENT OF CLINICAL PHARMACIST'S GRADUATE IN THE HOSPITALITY PHARMACEUTICAL'S SERVICES, PINAR DEL RIO 2010 <u>Sanchez R¹</u>, Ramirez F², Rojas N³</p> <p>¹Faculty of Medicine school Km 1 ½ Central Road CP 20100 Pinar del Rio Cuba, Senior Biology, Assistant Professor of Pharmacology, Master's Degree in Sciences. email: roselia@princesa.pri.sld.cu ²Universitary Clinical Surgical Hospital Dr Leon Cuervo Rubio, Km 1 central Road CP 20100 Pinar del Rio Cuba, Senior Pharmacist, Instructor Professor of Pharmacology. ³Universitary Clinical Surgical Hospital Dr Leon Cuervo Rubio, Km 1 central Road CP 20100 Pinar del Rio Cuba, Senior Imagenology, Instructor Professor of Pharmacology</p> <p>Introduction: In the team of health, the Clinical pharmacist's function is to advise the doctor in various aspects of the Pharmacotherapy, such: The regimens' establishment of doses detection and prevention of problems once medicaments were related to, adverse medicinal reactions, information to patients and besides related professionals of health. The Scientific problem was based on ¿How contributing to the Perfection of the Clinical Pharmacist's in the Hospitality Pharmaceutical's services and this makes the need of overcoming possible post gradual. Material and Methods:The utilized Methods were: Logic historic that corresponding with the data gathered on the theme and Empiric this one based on the revision of documents. The Investigation comes from Descriptive, and Retrospective type, and it made in Pinar del Rio Medicine School in the period of time of 2009 to 2010. With the objective the Designing a Methodological Proposition.</p> <p>Result and Discussion: The Program has duration of 260 hours to give Seminars in a year, with the mode of Conference and other forms of organization like Practical Lessons. The subject matters for the modules are itemized in The Pharmaceutical's Attention to the hospitalized patient in the clinical medication distribution for unitary dose, Nourishing parenteral's and intravenous mixtures. Conclusions: Labour of the pharmacist in the Preparation and Implementation of aspects explained, advantages and disadvantages, Farmacoservilance, Farmacoepidemiology, Gerency and Hospitality Organization, ethic and Communication, Chemical Pharmaceutical, and Physiopathology applied to the adverse Pharmaceutical reactions. The System of evaluation is indicated besides to culminate the Graduate.</p>
<p>PFep 096</p>	<p>SECURITY OF PARACETAMOL IN CUBA. 2003-2008 <u>Legón Pérez Tatiana¹</u>, Jiménez López G², Alfonso Orta I², Díaz Mato I¹, Chao Cardeso A²</p> <p>¹ Institute of Sciences Medical Dr. Salvador Allende Calzada del Cerro. Habana City, Cuba. email: Tatiana.legon@infomed.sld.cu ² Center for the Development of Pharmacoepidemiology, National Pharamcovigilance Unit, 5ta Ave and 44 St, Mirama, Playa, Havana City, Cuba.</p> <p>An observational, descriptive and retrospective study was realized to characterize the behavior of the adverse reactions related to paracetamol, including in the data base of the National Coordinating Unit of Pharmacovigilance, in the period included from January of the 2003 to December of the 2008. Once</p>

	<p>identified the main's adverse reactions associated to the use of paracetamol and organs' systems more affected it was determined his distribution by sex and groups of ages. In addition, severity and causality were classified accordantly to the avoidable reactions and their causes. Of the 612 notified reactions, the cutaneous eruptions were those of greater quantity (52.2%), corresponding this result with the system of organs more affected, and then it was the skin (54.4%). Feminine sex and the group of age between the 16 and 39 years, presented/displayed the majors percents of undesirable effects, with 62.9% and 30.2%, respectively. The behavior, as far as severity and causality, was not different from what it was reported in other studies because the slight reactions predominated (56.7%) and probable (80.2%). As far as the avoidable, the 69.1% of the reactions were catalogued like no avoidable, in as much, the errors in the indication of paracetamol constituted the main evitable cause.</p> <p>Key words: paracetamol, acetaminophen, overdose, hepatotoxicity, evitability, pharmacovigilance.</p>
PFep 097	<p>IMPACT OF SERVICE PHARMACOTHERAPY MONITORING IMPLEMENTED IN PATIENTS SUFFERING DIABETES MELLITUS TYPE-2 Lazo Y, Zúñiga A, Bermúdez I, Lores D</p> <p>Facultad de Tecnología de la Salud. Carretera del Caney Km 2 ½. Santiago de Cuba. email: ylazo@medired.scu.sld.cu</p> <p>Introduction: A service pharmacotherapy monitoring was implemented with 30 patients suffering from Diabetes Mellitus type 2, dispensed in the Principal Municipal Pharmacy Santiago de Cuba, in the period from January 2009 to January 2010. Objective: Evaluate the impact off service pharmacotherapy monitoring. Method: A prospective and intervention study was realized following the Dader methodology adapted off according to the experimental conditions and the impact of the service was determined through the established indicators. The results were analyzed through the correlational statistic. Results: 98 suspects of negative outcomes related to medication and negative outcomes related to medication were detected, classified according Third Consensus of Granada, this being the non-quantitative safety problem (42.85%) and the non-quantitative ineffectiveness (30.61%) the one of greater incidences. The impact index of the accepted pharmaceutical interventions (97.95%), and the patient's satisfaction level (100%) were high. Conclusions: The impact index of the accepted pharmaceutical interventions and the patient's satisfaction level were high for this reason the impact of the pharmacotherapy service continuation carried out for the attention of said patients was regarded as high.</p>
PFep 098	<p>VACCINATION AGAINST INFLUENZA A H1N1 AND THE RISK OF BIRTH DEFECTS. Y Núñez Rojas, N Orive Rodríguez, F Varona de la Peña, Y Bermúdez Velásquez, AF Raad López, Y Muñoz Martínez, G Martínez Rodríguez, OR Serrano Barrera Provincial Center of Medical Genetics, PO Box 27, Las Tunas 75100, Las Tunas, Cuba. email: yakelinnr@cucalambe.ltu.sld.cu</p> <p>Introduction: Pregnant women have been affected by influenza A H1N1 pandemics with particular severity worldwide. In Cuba, health authorities undertook a vaccination strategy focused on the main risk groups, which considered pregnancy as one of the inclusion criteria. Thus a surveillance program was established by the Genetics Network to assess the potential effects on those women who received the Pandemrix shot during the first trimester of pregnancy. Design: A longitudinal, prospective study was carried out to follow up every pregnant woman who was vaccinated against influenza A H1N1 during the first trimester of gestation (up to 13.6 weeks). They were remitted to the Provincial Center of Medical Genetics, where they were evaluated by ultrasound and by a genetic counsellor. A registry was established to record the maternal age, health area, gestational age when vaccinated and at the evaluation and ultrasound findings, among other variables. The results were compared to a sample of unvaccinated pregnant women studied in the same period of the previous year. Results: 34 out of 451 vaccinated pregnant women have been diagnosed with some condition, minor or major, by ultrasound and in the control group the figures were 21/205, for an Odds Ratio of 0.71. The median values in the affected previously vaccinated women versus affected unvaccinated women were 26,8 and 24,0 years for maternal age, 21,2 and 22,3 weeks of pregnancy when studied by ultrasound and 11,3 weeks, on average, for gestational age when shot. 64,7% of findings in the vaccinated group were located in the kidneys and 62,2% were renal ecstasy, either unilateral or bilateral. Conclusions: Vaccination against influenza virus A H1N1 did not increase the risk of birth defects when applied during the first trimester of gestation in the sample studied.</p>

PFep 099	<p>ORGANISATIONAL DESIGN FOR THE DRUG INFORMATION NET OF THE MUNICIPALITY OF SANTA CLARA Bermúdez-del Sol A, Santiesteban D, <u>García –Guevara Y</u></p> <p>Medical Sciences University “Dr. Serafín Ruiz de Zárate Ruiz”. Center of Studies, Documentation and Information on Drugs. Aqueduct Road, Santa Clara City, Villa Clara, Cuba. CP 50200. email: yaimagg@ucm.vcl.sld.cu, cedimed@capiro.vcl.sld.cu , ltorres@uclv.edu.cu</p> <p>Introduction: health system in Villa Clara province has not given sufficient attention to drug information, considering that this specialized service is a way to contribute to the rational use of drugs, so it is necessary to achieve the integration between the organisational design and the availability of resources in order to get coherence and correspondence to offer an adequate information service. The objective of this work is to propose the organisational design for the drug information net in the municipality of Santa Clara.</p> <p>Materials and Methods: an investigation in systems and services of health was done, from January to May 2010; it was an observational, descriptive, transversal type study. It was executed in two phases: diagnose which determined the availability of resources (humans and materials) and the needs of formation of the human resources and a second one dedicated to the design of the organisational structure of the drug information net. There were evaluated 11 communitarian pharmacies (30%), all hospital pharmacies (100%) and all the Centres of Information of Medical Sciences (100%) of the studied municipality.</p> <p>Results and Discussion: human resources are not in function of drug information service and even though in some pharmacies they are really deficient, in a general way an analysis and redistribution of them would be enough as a solution. Informatics resources are the most affected ones, but the centres of information of medical sciences have them and there is the disposition of putting them in function of the pharmacists. Human resources were sufficient even though a high percentage has high needs of formation. The organisational design was constituted by: strategic cusp, technical structure, medium line and operative centres. Conclusion: It was achieved an organisational design for the net of drug information in the municipality of Santa Clara.</p>
PFep 100	<p>CLINIC EVOLUTION OF THE TREATMENT OF HEBERPROT-P AND SECURITY OF THE MEDICINE FOR PATIENTS IN HOLGUÍN, GRANMA, AND SANTIAGO DE CUBA 2007-2009 <u>Ramírez Y¹, Yera Alós I²</u></p> <p>¹Regulatory Bureau for the Protection of Health. General García St. # 227/ Lora y Maso, Bayamo City, Granma, Cuba. email: yeraldisgrm@infomed.sld.cu ² Center for the Development of Pharmacoepidemiology, National Pharamcovigilance Unit, 5^{ta} Ave and 44 St, Miramar, Playa, Havana City, Cuba.</p> <p>Introduction: Heberprot-P is medicine that was developed into the Genetic Engineering and Biotechnology Center of Cuba, the only one for the therapy of the ulcer of diabetic foot (DFU) which in clinical essays demonstrated his efficacy and security, in the short run in carefully selected people's little number. Data which need to be enriched with the obtained results of the usage of the medicine in the habitual medical practice conditions. Material and Methods: observational, analytic, longitudinal and multicentric research with 405 adults patients, who came to receive the treatment into the 13 institutions of Holguín, Granma and Santiago de Cuba provinces where the medicine is administrated from June, 2007 to June, 2009. The principal clinical evolution variable was the complete granulation of the lesion at the end of the treatment, the variables related with the security of the medicine were: type of adverse event, system of affected organ, reference, gravity and cause of the grave events. Results and Discussion: the 68.9% of the patients achieved complete granulation of the lesion (IC 95,0 64,2 % - 73,5%). It was observed association between the complete granulation and the etiopathogeny of the DFU so as the clinic stage. The 35.3% of the patients presented at least one adverse event during the treatment, there was detected 366 adverse events related to 30 different types, detected the shivering as the most frequent event, followed of pain at the place of administration of the medication and chills. The 97.8% of the reported events were classified as non grave. Conclusions: Heberprot-P is a treatment which in the habitual clinic practice has certify its potentialities to overcome the complete granulation in the DFU so as in de ulcers located in other anatomic localizations. The main type of the adverse event notified and affected organ system are in close relation to the action mechanism of the medicine and the way of its application. The novelty of the medicine and the own complication of the diabetics mellitus justify the casual relation of the detected</p>

	<p>grave events. The close observation of the elements of the clinic evolution in patients and security of the medicine has contributed to conforming the profile pharmacoepidemiology, of the Heberprot-P in Holguín, Granma, and Santiago de Cuba province.</p>
PFep 101	<p>CHARACTERIZATION OF THE PRESCRIPTION AND ADVERSE REACTIONS OF TIORIDACINA IN PATIENT PSYCHIATRIC HOSPITALIZED. PINEGROVE OF THE RIVER. SEPTEMBER 2009 – FEBRUARY 2010 Díaz Y¹, Roque K², Alfonso I³, Jiménez G³</p> <p>¹Buró Regulatorio para la Protección de la Salud. Ciprian Váldez # 1 entre Martí e Isabel la Católica. Pinar del Río. email: yumara@minsap.pri.sld.cu. ²Dirección Municipal de Salud. Pinar del Río. email: keniar@princesa.pri.sld.cu. ³Centro para el Desarrollo de la Farmacoepidemiología. email: ismary@mcdf.sld.cu</p> <p>Introduction: The use of the tioridacina has been restricted to the alternative treatment of the schizophrenia, in patients that have not responded appropriately to other antipsychotics. In the last years a high incidence of cardiovascular adverse reactions has been presented to the tioridacina what has caused that in several countries it has been suspended or restricted its use, not being appreciated this behaviour in Cuba and specifically in the county of Pinegrove of the River. Materials and Methods: It was carried out an observational, descriptive and traverse study, inside the EUM of the type prescription indication with elements of practical consequences and therapeutic outline, together to an intensive monitoring of adverse reactions in patient psychiatric hospitalized treaties with tioridacina of September 2009 to February 2010, of the county Pinegrove of the River. Results and discussion: of the 123 included patients 82.9% was mature, 84.6% of the indications was not adapted. The dose and the administration interval used in all the patients were adapted. 78.9% of the patients presented contraindications to the drug The prescription of the drug was inadequate in 96.4% of the patients. Suspicions of adverse reactions took place in 39 patients (31.7%) of the total; being the dysfunctions extrapiramidales those that prevailed with 23.1%, the system nervous power station was the affected system of organs. A prevalence of the light, conditional and not described adverse reactions existed. 84.6% of the reactions were avoidable. Conclusions: It was detected a prevalence of the indication in mature women. The inadequate prescriptions not prevailed to expense of indications approved in the national form and to the existence of contraindications for this medication. The main detected adverse reactions were effects extrapiramidales, asthenia and migraine. The systems of more affected organs were the central and psychiatric nervous system. The light, conditional adverse reactions prevailed, not described and avoidable.</p>
PFep 102	<p>ADVERSE DRUG REACTIONS IN CHILDREN IN CAMAGÜEY PROVINCE, CUBA Bárzaga Z¹, Novoa D¹, Caballero N¹, Choonara I², Fernández E³, López A¹</p> <p>¹Department of Pharmacoepidemiology, Camagüey Province, Cuba. zebaa@finlay.cmw.sld.cu ²Academic Division of Child Health, University of Nottingham, Derbyshire Children's Hospital, Derby, UK. email: imti.choonara@nottingham.ac.uk ³Faculty of Pharmacy, University of Havana, Cuba. email: efdez@infomed.sld.cu</p> <p>Introduction. Adverse drug reactions (ADRs) are a significant problem in children throughout the world. Systematic reviews have shown that almost one in ten children in hospital will experience an ADR. ADRs in children attending outpatients are less frequent (1-2%). Although many ADRs are mild, a small number are severe and unfortunately some are fatal. Cuba is an active participant in the WHO Programme for International Drug Monitoring. Camagüey Province has a particular interest in children who experience ADRs and this research describes the results of the National Pharmacovigilance Programme within this province of Cuba. Materials and Methods. To determine the incidence of ADRs in children in Camagüey Province, all suspected ADRs reported to Provincial Pharmacovigilance Centre during 2008 were analysed. Each report was classified in relation to the severity of the ADRs, the causality and collated. Results and Discussion. Over a 12 month period, there were 124 reports involving suspected ADRs in children. Within these 124 reports there were a total of 152 suspected ADRs. Most ADRs were mild (98, 79%). There were, however, two fatalities and five other severe ADRs. Antibiotics were the group of medicines most likely to be associated with ADRs. The overall report rate of suspected ADRs was 634 per million children per year which is considerably higher than the only comparative studies in Sweden and the UK. This figure is likely to be a significant underestimate of the actual number of ADRs. Conclusion. ADRs in children are more frequent than previously reported. A successful pharmacovigilance</p>

	programme can be established in lower middle income countries.
PFep 103	<p>DIAGNOSIS AND PHARMACOLOGICAL TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) <u>Díaz Molina M</u>, Fernández Manzano E, Pegueros Santos Y</p> <p>Pharmacy and Food Institute, University of Havana. 222 and 25 Ave. La Coronela. La Lisa. Havana City. Cuba. email: mdiaz@ifal.uh.cu</p> <p>Introduction: Attention Deficit disorder with or without hyperactivity (TDHA) is one of the most frequent psychological disorders among the Cuban pediatric population; it affects between 3 and 5% of that population. TDAH diagnosis requires meticulous evaluation of the child habits and living conditions, the history of the symptoms and their impact on the child's family and school relationship. Methylphenidate is the only indicated psychostimulant for the THDA pharmacologic treatment. Its therapeutic efficacy is considered to be between 75 to 80%, and improvements in the behavioral, motor and cognitive performance and higher self-esteem and social and familiar adaptability have been found in patients taking this drug. Methods: The main criteria for the TDAH diagnosis and treatment are identified in this paper. A collection data model based on the Connors survey was used to establish the diagnosis. Results and conclusions: The physician interviewed showed an adequate level of information about this theme; however a diversity of diagnosis criteria was found.</p>
PFep 104	<p>ANTIHYPERTENSIVE PHARMACOLOGICAL TREATMENT IN A GROUP OF PATIENTS OF JAMAICA <u>Yoldi T</u>, Pons N, González I.</p> <p>Institute of Pharmacy and Food, University of Havana.</p> <p>Introduction: The arterial hypertension is a cardiovascular illness with high prevalence on a worldwide basis. Approximately the 33.8% of the population of Jamaica over 30 years suffers of arterial hypertension. The most affected region is the province of St. Catherine. Objective: Describe the antihypertensive drug therapy used in patients with high blood pressure in Jamaica. Method: The sample was constituted by 60 mestizos and black hypertensive patients from the hospital of curative services of Spanish Town, St. Catherine. Continuing the criterion of selection established by the WHO and the JNC VII a survey was applied and the medical histories were revised. The possible drug interactions were determined. Results: Dosage of the antihypertensive was adequate, and in all cases was prescribed by a doctor. The most appropriate drug both monotherapy and combination therapy was enalapril, whose mechanism of action is mediated by the Renin-angiotensin system. We found that 55% of patients were taking other medications. The groups of non antihypertensive drugs most used were non steroidal anti-inflammatory drugs (NSAIDs), hypoglycaemic agents, antibiotics, antianginal drugs and cardiac glycosides. The use of antihypertensive medications along with non steroidal anti-inflammatory drugs affected the control of hypertension.</p> <p>Conclusions: The antihypertensive medications indicated corresponded to the established standard reference of Jamaica. It has been reported that individuals of the black race present low levels of renin; because of this the use of ACE inhibitor therapy should be research as a therapy of election.</p>
PFep 105	<p>INTOXICATIONS REPORTED FOR TOXIC PLANTS IN A SERVICE OF TOXICOLOGICAL INFORMATION Macías B, Berenguer CA, <u>Pérez L</u>.</p> <p>Centro de Toxicología y Biomedicina. Toximed. Dirección: Km. 1 ½ Autopista Nacional. Teléfono: 641000, 643864. Santiago de Cuba. Cuba. email: bebe@toxi.scu.sld.cu ; antidotos@toxi.scu.sld.cu</p> <p>From last century, in many countries the accidental or voluntary exhibition to toxic substances has been frequent cause of the appearance of sharp and chronic pathological processes, constituting this way the second cause of death, after the infectious illnesses. The intoxications have always prevailed for medications and insecticides, but other intoxications that you/they have gone winning peak in the last decades exist and they are the provoked ones for vegetable substances. Objectives: To determine the incidence and mortality of intoxications for plants reported in the service of pharmaco-toxicological Consultancy of TOXIMED. Methods: The registration of intoxicated patients was used assisted in the Service of Pharmaco-toxicological Consultancy, from the year 1998 and until December of the 2007, for an universe of 290 patients. Of each registration data like Sex were obtained, fundamental clinical</p>

	<p>Manifestations, Circumstances of the intoxication, Name of the toxic plant, origin Place of the one intoxicated, the patient's final evolution. Results: Of the study universe it was identified that 24 consultations of patients were assisted intoxicated by toxic plants (8.3%), 18 (75%) of the masculine sex and 6 (25%) of the feminine sex. The voluntary intoxications prevailed for drugs consumption (54%), being the Trumpet the plant that more intoxicated it contributed to our registrations. The biggest percent of having intoxicated was of the county Santiago from Cuba (75%), prevailing the patients of the municipality Santiago from Cuba (38.9%). There were 4 patients' deceaseds (16.7%). Conclusions: The population of the oriental region of the country uses the plants in a traditional way, due to the knowledge that is transmitted of generation in generation, but in many occasions plants are used a little or anything studied from the pharmacological and toxicological point of view, for what becomes necessary to continue with the study of these plants and to carry out popularization works to diminish the morbidity and mortality for toxic vegetables.</p>
PFep 106	<p>MISTAKES IN THE PRESCRIPTION OF ANTIHYPERTENSIVES IN “CARLOS MANUEL DE CÉSPEDES” PROVINCIAL HOSPITAL Corpas M¹, Sánchez Y¹, Beltrán L¹, López C¹.</p> <p>¹Carlos Manuel de Céspedes Provincial Hospital, Central Way km , Bayamo City, Granma, Cuba. email farmhcmc.grm@infomed.sld.cu</p> <p>Introduction: High blood pressure is the most common condition that affects humans health worldwide. It is estimated that 691 million people around the world suffer from this disease. Due to the wide variety and the amount of drugs available to treat this pathology it is necessary to make a proper selection of them to guarantee treatment effectiveness. Taking into account that there are still difficulties regarding this problem this study was carried out.</p> <p>Materials and Methods: A descriptive and prospective study with 54 high blood pressure patients, selected at random, admitted in the rooms of Internal Medicine of Carlos Manuel de Céspedes Provincial Hospital, in Bayamo, Granma, was carried out from May to April, 2010. A control of the illness was determined at admission, having into account the blood pressure figures of these patients. To identify the mistakes in the antihypertensive therapy, the therapeutical scheme was checked, taking into account the following variables: suboptimal therapeutic, overdose prescription, use of non prescribed medicine, risky medical interactions, among others. In the end the mistakes related to the control of the sickness were listed. Results and Discussion: 96.3% of the patients were under control, which can be explained because during the admission at the hospital the treatment is strictly taken, and non pharmacological measures are applied. In 14.8% cases mistakes were detected, prevailing the suboptimal therapeutic, because in 9.3% of the patients (under control and not controlled) lower doses of antihypertensive drugs were used. In 3.8% of the cases, inhibitory drugs of the enzyme angiotensina converter in patients suffering from diabetes without other counter-indication were not used, although those patients were under control. In one of the cases a risky drug interaction was detected (Espironolactona + Potassium Chloride), which cause a hiperpotasemia in the patient. Conclusions: Most of the high blood pressure patients checked kept their sickness under control. Suboptimal therapeutic was the main mistake detected, which partially influenced the sickness control.</p>
PFep 107	<p>MARKETING AUTHORIZATION OF Heberprot-P, A CUBAN PRODUCT FOR THE DIABETIC FOOT ULCER TREATMENT Rodríguez-Silva A¹, López-Saura P¹, Berlanga J¹, Cosme K¹, Barcardi D¹, Trujillo R¹, Sotolongo J¹, Pujol V¹, Ferrero W¹, Jiménez D¹, Chuay C¹, Aznar E², Suárez S², Hernández N¹, Sánchez JC¹, de la Cruz T¹, Montané M¹, Vega JL¹, Pérez E¹, Vega M¹, Costa L¹, Santana H¹, Besada V¹, González LJ¹, Heredia I¹, Quiñones Y¹, Ubieta R¹, Delgado A¹, Aguila A¹, Gutiérrez D¹, Portuondo I¹, Gutierrez A¹, Chuay D¹, Carballo LA¹, Mauri M¹, Silva R¹, Martínez D¹, López-Mola E¹, Herrera L¹.</p> <p>¹Centro de Ingeniería Genética y Biotecnología (CIGB). Ave 31, E/ 158 y 190. Cubanacán. La Habana. Cuba. email: arlene.rodriguez@cigb.edu.cu ²Centro Nacional de Biopreparados (BIOCEN). Carretera de Beltrán, km 1 ½, Bejucal, La Habana. Cuba.</p> <p>Introduction: Heberprot-P is a safe and efficacious parenteral formulation based on recombinant human Epidermal Growth Factor (rhEGF) developed in Cuba for the treatment of advanced diabetic foot ulcers. Ischemic and neuropathic patients have been successfully treated. Here we describe the marketing authorization process carried out with this product and the results obtained. Materials and methods: For the marketing authorization process the Heberprot-P dossier was prepared according to the Common</p>

	<p>Technical Document (CTD) format. Likewise, the requirements and registration procedures of each specific country where the approval was intended to obtain were also considered. Results and discussion: The first marketing authorization was obtained in Cuba, as conditional, in June 2006, definitive in October 2007. It was followed by registration in Algeria in June 2008, Argentina in February 2009, Uruguay in May 2009, Dominican Republic in December 2009 and Venezuela in February 2010. In Cuba the marketing authorization has been already renewed, and in Venezuela the product was first approved as Service Drug with a renewal process every 6 months until the definitive registration. In Cuba more than 98,000 vials have been distributed, and more than 140,000 vials have been exported to other territories. It has made possible the treatment of more than 10,000 patients mainly in Cuba and Venezuela where National Programs for the treatment of the diabetic foot ulcer have been implemented. Conclusions: Heberprot-P has been registered in 5 countries in 4 years. The dossier in the CTD format has been a valuable tool for the marketing authorization processes even in those countries not following this format as a requirement. Sales have been significant in countries with a National Program implemented for the management of the diabetic foot ulcer where a large number of patients have been treated.</p>
<p>PFep 108</p>	<p>CONSUMPTION AND FORECASTS OF ESSENTIAL DRUGS LISTING IN POPULAR MEDICAL PRACTICE OF CUBAN MEDICAL MISSION. BOLIVARIAN REPUBLIC OF VENEZUELA, 2006 TO 2009. Sandra Lorenzo Betancourt¹, Juan Antonio Furores Mourelle², Alfredo González Rodríguez¹, Gisele Coutin Marie¹. ¹Provincial Centre of Hygiene, Epidemiology and Microbiology, Las Tunas. Email:sandra.lorenzo@infomed.sld.cu. ² Center for the Development of Pharmacoepidemiology. Calle 44 esq 5ta ave. No.502. Playa, Ciudad de La Habana.</p> <p>Introduction: The popular clinics constitute the first level of access from the Venezuelan population to the Cuban Medical Mission. The insufficient or excessive supply generates problems to the doctor and the population. Previous consumption studies that analyze this situation in an integral way don't exist. Objective: To describe the consumption of essential drugs listing of the popular clinics of the Cuban Medical Mission in Venezuela from the 2006 to the 2009, to identify the level of consumption of the states and to predict it for the year 2010. Method: It was carried out an observational, descriptive, longitudinal study, of use of consumption medications for DHD. The universe was all the medications of the essential drugs listing of the popular clinics, being excluded those that don't have defined DDD; the sample was of 76 drugs. The data are obtained of the registrations of exits of warehouses. For the presage the exponential smoothing was used with three parameters. Results: The groups more consumed were the B (blood and blood forming organs) with 253.59 of DHD, C (cardiovascular system) with 80.93 and the A (alimentary Tract and metabolism) with 40.03 of DHD. The consumed medications were more for folic acid with 216.30 DHD, ferrous fumarate with 27.96 DHD and enalapril with 21.13 DHD. The states of the stratum of high consumption level for the group that affects the blood and vitamins (consumption superior to 78.98) they were Zulia, Trujillo, Merida, Apure, Yaracuy, Carabobo, Guárico and Delta Amacuro; for the group of cardiovascular and diuretic (consumption superior to 25.41) they were Zulia, Trujillo, Falcon, Yaracuy, Carabobo, Cojedes, Hurry, Guárico, Miranda, Vargas, Anzoátegui and Delta Amacuro, for group of AINE, analgesic and antigout preparations (consumption superior to 12.06) they were Zulia, Trujillo, Yaracuy, Hurry, Vargas, Delta Amacuro and Amazons and for the anti-infective group (consumption superior to 9.60) they were Zulia, Trujillo, Cojedes, Yaracuy, Apure, Delta Amacuro and Amazonas. Conclusions: The consumption of the medications of the essential drugs listing has an irregular behavior, with prevalence of the groups B, blood and blood forming organs; C, cardiovascular System and A, alimentary Tract. The states with a bigger consumption level in most of the studied groups were Zulia, Trujillo, Yaracuy, Apure and Delta Amacuro. Consumption is predicted for 2010 superior to that of the last year.</p>
<p>PFep 109</p>	<p>PARACETAMOL AS A MODIFIER OF LIVER ENZYMES IN PATIENTS WITH DENGUE. GENERAL MEDICAL CENTER OF SOUTHERN CALIFORNIA. CARACAS, VENEZUELA, APRIL-AUGUST 2010 Rafael Dupuig Barroso, Enma Damara Acosta Reynaldo. Institución a la que pertenecen ambos autores: Hospital General Juan Bruno Sayas Alfonso. Santiago de Cuba. email: dupuig@medired.scu.sld.cu, rdupuig@yahoo.es</p>

	<p>Paracetamol is a highly hepatotoxic drug and an overdose requires a careful monitoring to prevent liver failure. Usually in patients with hemorrhagic dengue fever, and/or classic liver enzymes: transaminase glutamic pirúvica (TGP), transaminase glutamic oxalacética (TGO) and gamma glutamyl transpeptidase (GGT), elevate and if add an excessive dose of paracetamol to treat fever, this could be the mayor increase of these enzymes. A descriptive study of cross section to identify biochemical disruptions caused by prescription of maximum dose of paracetamol in patients with a diagnosis of dengue was held in the General Diagnostic Medical Centre in the South of California, Caracas and Venezuela, in a period of time from April - August 2010. The universe was make of 48 patients and match with the sample. Among the patients that consumed paracetamol, 71.6% (34 cases), presented high TGP, TGO and GGT and in the ones that were prescribed maximum drug dose, there was a mayor increase of these enzymes. There was no remarkable influence of age and sex .In patients with hemorrhagic dengue, liver enzymes were elevated more than in the case of classic dengue and the mayor experienced alteration was the GGT.</p>
PFE 001-132 PFE-001-131	EXPERIMENTAL PHARMACOLOGY / FARMACOLOGIA EXPERIMENTAL
Chairs	Roberto Menéndez, Odalys Blanco, Idania Rodeiro, Ivones Hernandez y Mariela Guevara
	Discusión de Carteles e Intercambio Científico. Presentación Oral (5 min) de Carteles Seleccionados / <i>Poster Discussion and Scientific Exchange. Oral Presentation (5 min) of Selected Posters.</i>
PFE 001-056	PRODUCTOS NATURALES / NATURAL PRODUCTS
PFE 001	<p>ANTINOCICEPTIVE EFFECT OF <i>Geranium schiedeanum</i> Schl. IN A MODEL OF VISCERAL PAIN IN MICE <u>De la O-Arciniega M¹</u>, Gayosso-De Lucio JA¹, Castro-Torres IG², Bautista-Ávila M¹, Velázquez-González C¹. ¹Área Académica de Farmacia, Instituto de Ciencias de la Salud, Universidad Autónoma del Estado de Hidalgo. Pachuca de Soto, Hidalgo, México. email: mina@uaeh.edu.mx ²Facultad de Química Farmacéutica Biológica, Universidad Veracruzana. Xalapa de Enríquez, Veracruz, México.</p> <p>Introduction: In order to contribute to the knowledge of Mexican medicinal plants, the present study was designed to investigate the antinociceptive effect of <i>Geranium schiedeanum</i> Schl., which is used in Mexican traditional medicine for the treatment of kidney pain and as antipyretic. Material and Methods: All experimental procedures followed the Guidelines on Ethical Standards for Investigations of Experimental Pain in Animals. Male CD1 mice (30-35 g) were used. The antinociceptive effect was evaluated in an experimental model of visceral pain induced by i.p. injection of 0.6% acetic acid in mice (writhing test). The mice (n=6) were treated intragastrically with the acetone-water (7:3) extract of aerial parts of <i>G. schiedeanum</i> Schl., (AWGs) at different doses (100, 178, 316 or 562 mg/kg), and compared with the antinociceptive effect of indomethacin (10 mg/kg), or vehicle physiological NaCl-solution (10 mL/ kg). The total number of abdominal constrictions was recorded in periods of 5 min during 30 min immediately after acetic acid administration. Results and Discussion: AWGs showed a dose-dependent antinociceptive effect. The higher doses of AWGs (316 and 562 mg/kg) showed the maximum antinociceptive effect (61.25 and 81.79% of inhibition, respectively) compared with vehicle, reducing significantly ($P<0.05$) the number of abdominal constrictions. Conclusions: These results suggest that <i>G. schiedeanum</i> Schl., may have analgesic potential for treatment of pain and lend a support for traditional use of this plant as analgesic agent. References: Cariño-Cortés R, et al. <i>J. Ethnopharmacol.</i> 2010; 130 (2): 216-221.</p>
PFE 002	<p>ACUTE ORAL TOXICITY OF RAW JUICE OF <i>Agave lechuguilla</i> Torrey (lechuguilla) IN CD1 MICE <u>Almaguer Vargas G¹</u>, Resendiz Esparza E¹, Montejano Rodríguez JR¹, Trejo García M¹, Martin Gress JM¹, Chehue Romero A¹</p> <p>¹Universidad Autónoma del Estado de Hidalgo, Instituto de Ciencias de la Salud. Área Académica de Farmacia, Carretera Exhacienda la Concepción s/n, Tilcuautla, Hidalgo México. email: georginaalmaguervargas@yahoo.com.mx</p>

	<p>Introduction: Numerous adverse reactions and the high cost of medicinal products, have resulted in 80% of the world's population use medicine herbal. Frequently the efficacy and toxicity of medicinal plants are unknown. Hidalgo state is not exception, it a state where is attributed to the agave different properties which include the bactericides, antiinflammatory, and antitumour. Therefore it is necessary search test in order to determine the toxicity of plant and ensure the provision of safe and effective, and provide a better quality of life for people who consume traditional therapy. Material and methods: Each females and males groups of 5 CD1 mice were administrated orally with raw juice of agave lechuguilla in dose of 5,50,500 and 2000mg/kg as a single dose. They were weight day 2, 3, 7 y 14 and observed frequently on the day of treatment. All surviving animals were sacrificed at the end of each test and then autopsied and examined macroscopically for any pathological changes in mice's liver, heart, spleen and gonads. Results and discussion: The method of investigating acute toxicity which has been tested in practice shown macroscopically that groups of females presented alterations at renal (petechiae and infarction areas) and liver (cirrhosis, stroke and blood congestion areas). In addition to those observed in spleen (enlarged spleen) to 2000mg/kg. While in males groups, renal edema was presented in four quantities used, cirrhosis of the liver to higher doses and infarction in spleen areas (2000mg/kg PV). Conclusions: In this study acute toxicity of agave lechuguilla was determinate that raw juice is not acute toxicity. However, the macroscopically analysis of the mice's organs who administered the raw juice, it is shown toxic effect.</p>
<p>PFE 003</p>	<p>KNOWLEDGE AND THE CONSUME OF THE MEDICINAL PLANTS AMONG STUDENTS FROM THE HEALTH AREA OF THE UNIVERSITY OF HIDALGO MEXICO Delgado Pérez J¹, Montejano Rodríguez JR¹, <u>Almaguer Vargas G¹</u>, Resendiz Esparza E¹, Galnares Necochea L¹, Esquivel Gómez JI¹</p> <p>¹Autonomous University of Hidalgo State, Institute of Health Sciences. Pharmacy Academic Area, Highway Conception ex hacienda s / n, Tilcuautla, Hidalgo, Mexico. email: georginaalmaguervargas@yahoo.com.mx</p> <p>Introduction: The Hidalgo's Mexico state is distinguished by its herbal used history. At the same time, it has been considered as one of the poorest states of the country in which there is an existence of mortality treatable diseases. Due to this fact, it is necessary to find other alternatives from the ones used now days. One of these alternatives is to: encourage people to use medicinal plants from a rational point of view. The present work is based on the knowledge and the consume of the medicinal plants among students from the health area. Material and methods: The methods were surveys. And it was applied to 219 students for the health area of the University of Hidalgo Mexico. The survey consisted of 12 questions. Results and discussions: The result of the present work showed that the 89.5% of the people surveyed know about the medicinal plants and the 68.5% have used once in their life time. The most well known plants were; manzanilla (<i>Matricaria chamomilla</i>); hierbabuena (<i>Mentha spp</i>); ruda (<i>Ruta graveolens</i>), savila (<i>Aloe spp</i>) and ajeno (<i>Artemisia absinthium</i>). These plants are used in different percentage, for stomach ache in 30.13 %; muscle pain 14.6 %; flu symptoms 8.6% and for cough 5 %. These medicinal plants are consumed by children in 21.9 % and grandparents in 14.1 %. 30.5% of these medicinal plants can be found in supermarkets, 19.6 % in their own homes. These plants are considered effective in 86.3 %, without side effects in 86.3%. Conclusions: Students of the health care area and their families consume medicinal plants because that are accessible, efficient , and with little side effects.</p>
<p>PFE 004</p>	<p>INHIBITION OF TRPA1 RECEPTOR ACTIVATION BY LUTEIN IN DIFFERENT <i>IN VITRO</i> AND <i>IN VIVO</i> MODELS <u>Szöke É¹</u>, Kemény Á¹, Horváth Gy², Molnár P², Szolcsányi J¹, Helyes Zs¹</p> <p>¹Department of Pharmacology and Pharmacotherapy, University of Pécs, Szigeti str 12., Pécs, Hungary. email: eva.szoke@aok.pte.hu ²Department of Pharmacognosy, University of Pécs, Szigeti str 12., Pécs, Hungary</p> <p>Introduction: Activation of Transient Receptor Potential ion channels, such as Vanilloid 1 and Ankyrin repeat domain 1 (TRPV1 and TRPA1) and the release of pro-inflammatory neuropeptides mediate neurogenic inflammation. We found that lutein, a natural tetraterpene carotenoid, inhibits neurogenic inflammation induced by TRPA1, but not TRPV1 activation, and that lipid rafts in the neural membrane are involved in TRPV1 functions. The aim of these experiment was to investigate the mechanisms by which lutein modulates TRP channels and inhibits neurogenic inflammation. Material and Methods: The water-soluble random methyled beta-cyclodextrin (RAMEB) complex of lutein was studied on TRPV1 and TRPA1 activation on cell bodies and peripheral nerve terminals. Cultured rat trigeminal neurones and</p>

isolated trachea preparations were treated with the respective selective agonist, capsaicin (330 nM) or mustard oil (200 microM). $[Ca^{2+}]_i$ was measured with microfluorimetry, CGRP release with RIA. Capsaicin (2.5%) and mustard oil (3%)-induced neurogenic oedema and inflammatory cell accumulation in the mouse ear was determined with micrometry and histology. **Results and Discussion:** Mustard oil-induced Ca^{2+} -influx in trigeminal sensory neurones and CGRP release from the nerve terminals were significantly inhibited by RAMEB-lutein (100 microM). Ear oedema was also diminished by RAMEB-lutein (100 microg/ml). In contrast, this carotenoid complex did not influence capsaicin-evoked responses. **Conclusions:** These data demonstrate that lutein inhibits Ca^{2+} influx and CGRP release in vitro, as well as neurogenic inflammatory responses in vivo induced by TRPA1, but not TRPV1 stimulation. Based on these results and the structure of lutein, its ability to modulate lipid rafts in the membrane can be suggested.

PFE 005 ANTI-INFLAMMATORY AND CYTOTOXIC ACTIVITY OF FLAVONOIDS ISOLATED FROM *Oncidium sphacelatum* Lindl. (Orchidaceae)

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Introduction: *Oncidium sphacelatum* orchid is known as May flower, which grows in tropical areas of Mexico. Previous phytochemical studies have indicated the presence of pectolinarin and scutellarein-6-methyl ether-7-rutinoside, but not studies on its biological activity have been reported. As part of our systematic search for bioactive compounds, now we present the results of anti-inflammatory and cytotoxic activity of flavonoids from *O. sphacelatum*. **Material and Methods:** The anti-inflammatory activity evaluation was carried out using the model of TPA (12-*O*-tetradecanoyl-13-acetate-phorbol) in mouse ear. The cytotoxic activity was evaluated by the method of sulforhodamine B (SRB) in human cancer lines. **Results:** From AcOEt extract was yielded a solid which was subjected to an acetylation reaction. The purification of the reaction mixture allowed to obtain the 5,6-diacetate-4'-methoxy-7-*O*-acetylrutinosideflavanone, which is a new compound in the literature. Pectolinarigenin and pectolinarin acetate were also isolated, the presence of these compounds are reported for the first time for the genre.

Anti-inflammatory activity

Compounds	Doses (mg/ear)	Inhibition (%)
Indomethacin	0.36	78.76
5,6-diacetate-4'-methoxy-7- <i>O</i> -acetylrutinosideflavanone	0.31	47.89
Pectolinarin acetate	0.31	-4.63

The data represent the average of three animals.

Citotoxyc activity

Compounds	Inhibition of cell growth (%)				
	Cellular line				
	U251	PC-3	HCT-15	MCF-7	SKLU-1
50 µM/mL					
Doxorubicin	100	100	100	100	100
5,6-diacetate-4'-methoxy-7- <i>O</i> -acetylrutinosideflavanone	29	44.93	34.2	56.1	39.3
Pectolinarigenin	56.95	55.38	99.24	72.92	87.61
Pectolinarin acetate	40.59	35.85	74.9	56.64	22.63

U251= central nervous system glia, PC-3=prostate, HCT-15=colon, MCF-7=breast, SKLU-1=lung.

Discussion and Conclusions: From the flavonoids evaluated in the TPA model the one that exhibited the highest activity was 5,6-diacetate-4'-methoxy-7-*O*-acetylrutinosideflavanone with an inhibition of 47.89%. Pectolinarigenin is a compound with proven anti-inflammatory activity. The results obtained in the SRB model showed that 5,6-diacetate-4'-methoxy-7-*O*-acetylrutinosideflavanone inhibited 56.1% of cell growth in line MCF-7, pectolinarigenin had activity on all evaluated lines with percentages of inhibition between 55.38 and 99.24%. Pectolinarin acetate inhibited 74.9 and 56.64% of cell growth in lines HCT-15 and MCF-7, respectively.

<p>PFE 006</p>	<p>ENFOQUE DE MÍNIMA ENTROPÍA (-ΔS) EN INTERVENCIONES COMPLEJAS FÁRMACO-DIETÉTICAS EN POBLACIONES HUMANAS <u>Abuín A</u>¹, Batista M¹, Reyes M³, Portales V³, Robaina R³, Blanco J⁴, Gonzáles A¹, Quintero Y¹, Alfonso R⁵, Pérez R⁵, Alfonso M², Porrata C⁶, Pianesi M⁷</p> <p>¹Universidad de Ciencias Médicas de Matanzas “Dr. Juan Guiteras Gener.” ²Centro de Atención al Diabético Cárdenas. ³Policlínico Carlos Verdugo. ⁴Clínica de Rehabilitación Playa. ⁵Instituto del Arroz y Granos. ⁶Instituto Finlay, ⁷ UPM Italia.</p> <p>La medición de la efectividad de las intervenciones clínicas usualmente tienen en cuenta aspectos muy reducidos a la población humana y raramente se analizan los importantes aspectos del ecosistema que son claves en la modificación de los parámetros y variables en estudio. Las intervenciones fármaco-dietéticas que se recomiendan a los pacientes diabéticos son un ejemplo de este tipo de trabajo y pudieran ser analizadas de forma holística si se incluyen en los estudios algunos enfoques termodinámicos globales, como la entropía de sistemas. La entropía es la medida del grado de desorden de los sistemas y puede ser utilizado para evaluar la estabilidad de los sistemas incluyendo la red de procesos que modifican a las enfermedades y la eficiencia energética de sus intervenciones. La Diabetes Mellitus puede considerarse como una patología donde se pierde el orden (+Δ S) necesario para mantener el ritmo de la glicemia. Una intervención dieto-farmacológica que disminuya la entropía (-ΔS) del subsistema ambiental, el subsistema del metabolismo energético de los individuos y las fronteras entre ambos subsistemas puede considerarse como una intervención exitosa.</p> <p>Para poner a prueba este enfoque se evaluó un programa de intervención nutricional-farmacológico en 397 pacientes Diabéticos que se trataban farmacológicamente con combinaciones de hipoglicemiantes orales e insulina. El componente dietoterapéutico consistió en una intervención educativa con los principios de la dieta Macrobiótica Ma-Pi organizada en el Policlínico “Samuel Fernández” de la Ciudad de Matanzas. Las principales modalidades educativas fueron charlas interactivas colectivas, consultas individuales efectuadas por dietistas clínicos entrenados y capacitados, y un curso práctico de cocina. En todos los casos se contó con el asesoramiento metodológico propuesto por el proyecto nacional del Instituto Finlay.</p> <p>Para evaluar la evolución de la entropía del sistema antes y después de la intervención, se tuvo en cuenta los siguientes principios orden:</p> <p style="padding-left: 40px;">orden o entropía constructiva, orden o entropía de regulación, orden temporal o crono-entropía, orden morfológico o entropía de matriz estructural.</p> <p>Como resultado la intervención fármaco-dietoterapéutica con la Dieta Macrobiótica Ma-Pi se evidenció un importante efecto restaurador de orden negentrópico (-ΔS) en la Diabetes Mellitus en los cuatro principios de orden del sistema analizados. Demostrándose que con este enfoque no solo se puede estudiar el impacto clínico-farmacológico a nivel comunitario sino que también se pueden evaluar con la metodología científica actuales aspectos contextuales claves en la Diabetes Mellitus como son el beneficio en la restauración del orden natural ecológico, social y económico del sistema analizado.</p>
<p>PFE 007</p>	<p>EFFECTS OF ORAL TREATMENT (60 DAYS) WITH D-004, A LIPID EXTRACT FROM ROYSTONEA REGIA FRUITS, ON RAT PROSTATE HYPERPLASIA AND OXIDATIVE MARKERS <u>Ovarzábal A</u>¹, Jiménez S¹, Curveco D¹, Pérez Y¹, Molina V¹ and Mas R¹</p> <p>¹Center of Natural Product, National Center for Scientific Research, Ave 25 and 158, Cubanacán, P.O 6880, Havana City, Cuba. email: ambar.oyarzabal@cnic.edu.cu</p> <p>Introduction: Short-term (14 days) oral treatment with D-004, a lipid extract obtained from Cuban royal palm (<i>Roystonea regia</i>) fruits, has been proven to prevent testosterone-induced prostate hyperplasia and increased prostate oxidative stress, but no study has documented if such effects persist after longer treatment. This study investigated the persistence of the effects of D-004 orally given for 60 days for preventing prostate enlargement and increase of oxidative markers in rats with testosterone -induced prostate hyperplasia.</p> <p>Material and Methods: Rats were randomized into three groups (30 rats per group): a negative control</p>

	<p>group and two testosterone-injected groups: a positive control (orally treated with the vehicle) and a D-004 (400 mg/kg/day)-treated group. Subgroups of each group (10 rats per group) were sacrificed, under ether anesthesia, at 15, 30 and 60 days on treatment, respectively. At sacrifice, prostates were removed and weighed. Mean prostatic weights and prostate/body weight ratios were calculated. The whole organs were taken for obtaining the prostate homogenates used in the assessment of oxidative markers. Results and Discussion: Prostate weights of positive controls significantly and markedly increased over the time, while persistent and significant reductions of such increases were seen in D-004-treated rats. Also, D-004 significantly reduced the testosterone-induced increase of prostate conjugated diene generation and sulphhydryl groups concentrations, achieving a complete reduction from the day 30 after starting the treatment. Conclusions: The effects of oral treatment with D-004 (400 mg/kg/day) on testosterone-induced prostate enlargement and increased prostate oxidative markers persisted over 60 days of treatment. Keywords: D-004, prostatic hyperplasia, oxidative markers, long term, rats.</p>
<p>PFE 008</p>	<p>PROTECTION OF THREE SEaweEDS AQUEOUS EXTRACT AGAINST CELL DEATH INDUCED BY FECL₃ Batista-González AE¹, de O e Silva AM¹, Mancini-Filho J¹, Portari-Mancini DA³ and Vidal Novoa A¹ ¹ Department of Biochemistry, Faculty of Biology, University of Havana, Cuba ² Lipid Laboratory, Faculty of Pharmaceuticals Science, University of Sao Paulo, Brazil ³ Butantan Institute, Sao Paulo, Brazil</p> <p>Introduction: Seaweeds have been studied by years in relation with their pharmacologic properties. In this line, antioxidant activity of seaweeds has been a main area of research with polyphenols playing an important role contributing to the antioxidant action. Materials and Methods: In this work, three seaweeds of <i>Halimeda</i> genus were evaluated in Vero cell culture, where FeCl₃ induced cell death, and cell viability was measured by MTT reduction assay. Total polyphenolic content in aqueous extract of lyophilized was 2.789 ± 0.099, 2.634 ± 0.034 and 1.448 ± 0.038 µg/g for <i>Halimeda monile</i>, <i>Halimeda opuntia</i> and <i>Halimeda incrassata</i>, respectively expressed as gallic acid equivalents. For cell assays different quantities of seaweeds expressed as polyphenolic compounds (1-10 µg) were evaluated. Results and Discussion: Aqueous extract of <i>Halimeda opuntia</i> and <i>Halimeda monile</i> didn't induce significant cell death at 1-10 µg of polyphenolic compounds, and <i>Halimeda incrassata</i> induced slight cell death at 6-10 µg of polyphenolic compounds. With FeCl₃ treatment cell viability was 6 %, and when cells were treated with FeCl₃ and aqueous extract of seaweeds, cell viability was improved to 46 % for <i>Halimeda monile</i>, 45 % for <i>Halimeda opuntia</i> (10 µg of polyphenolic compounds) and 36 % for <i>Halimeda incrassata</i> (6 µg of polyphenolic compounds). Ascorbic acid, used as positive control, improved cell viability to 20%. Conclusion: The aqueous extract of the three seaweeds showed a protective effect against cell death induced by FeCl₃, and this effect could be related with the presence of polyphenolic compounds with antioxidant activity.</p>
<p>PFE 009</p>	<p>PHARMACOLOGICAL ACTIVITY OF MEDICINAL PLANTS FROM CUBA, MARTINIQUE, AND THE CARIBBEAN García AI, López M, Morejón Z, Morón FJ, Victoria MC, Boucourt E, Martínez MJ, Bacallao Y, Acosta de la Luz.</p> <p>Central Laboratory of Pharmacology, Dr. Salvador Allende School of Medical Sciences. Carvajal entre Agua Dulce y A, Cerro, Ciudad de La Habana, CP 12000, Cuba. email: anai904@fallende.sld.cu</p> <p>Introduction: Caribbean countries share to a great extent a common flora, especially medicinal plants of traditional use. Within this context, we take part into the ethnopharmacological validation of the use of such species from the region inside TRAMIL network. Our objective was to know the pharmacological effect of the use of some medicinal plants from Cuba, Martinique and the Caribbean. Material and Methods: The parts of the plants to be evaluated were collected, botanical identification was made, as well as the preparation of herbarium/voucher specimens; plants selected were the following: <i>Annona squamosa</i> L. (custard apple), <i>Citrus aurantium</i> L. (Seville orange), <i>Citrus aurantifolia</i> (Christm.) Swing (lemon), <i>Cordia martinicensis</i> (Jacq) Roem. & Schult, <i>Persea americana</i> Mill.(avocado), <i>Hyptis verticillata</i> Jacq., <i>Musa x paradisiaca</i> L.(banana), <i>Bidens pilosa</i> L. (rosemary), <i>Lepidium virginicum</i> L. (common cress) y <i>Tamarindus indica</i> L. (tamarind). Some pharmacological studies were developed in order to evaluate analgesia in writhing <i>noniceptive</i> response <i>induced</i> by intraperitoneal acetic acid (writhing test) and induced by tail flick; topic antiinflammatory activity with <i>Crofton</i> oil-induced ear edema and intestinal motility activity with intestinal transit in mice. Results: All plants studied showed peripheral analgesic</p>

	<p>activity and topic antiinflammatory activity; <i>H. verticillata</i> and <i>M. paradisiacal</i> did not show central analgesic activity; no action on intestinal motility was shown. Conclusions: Presence of analgesic and topic anti-inflammatory activity was shown, as well as a lack of action in intestinal motility in plants studied. This contributed to the validation of their traditional use in diseases in which painful and antiinflammatory symptoms occur, as opposed to constipation and diarrhea.</p>
PFE 010	<p>PRECLINICAL ANTIMICROBIAL OF TOTAL EXTRACTS FROM THE <i>Petiveria alliacea</i> L LEAVES (II) Ochoa AP¹, Marín JM¹, Hidalgo AR¹, González ZG² ¹Pharmacy Department, Faculty of Natural Sciences, Universidad de Oriente, Patricio Lumumba s/n, Santiago de Cuba, Cuba. email:aochoa@cnt.uo.edu.cu ²Centre of Industrial Biotechnology Studies, Faculty of Natural Sciences, Universidad de Oriente, Patricio Lumumba s/n, Santiago de Cuba, Cuba.</p> <p>Introduction: During the investigations with the <i>Petiveria alliacea</i> L. (Anamú), we observed that the vegetable extracts studied, are not contaminated with microorganisms when it is exposed to non controlled storage conditions; therefore two antimicrobial evaluations of total extracts were carried out. One from the dry leaf with 30% hydroalcoholic solution, not obtaining positive results and the other from the fresh drug, with low inhibition zone; therefore we decided to continue this evaluation, with 7 total extracts, 4 soft [proportions 1:4 (B1),1:6 (B2),1:8 (B3),1:12 (B4)] and 3 blended [proportions 1:4 (E1),1:6 (E2),1:8 (E3)] ; from the fresh leaves and using as a solvent 80% hydroalcoholic solution; with the purpose of getting a better antimicrobial response. Materials and Methods: The antimicrobial evaluation was carried out using the Kirby- Bauer Method with strains of <i>Escherichia coli</i>, <i>Staphylococcus aureus</i>, <i>Enterococcus faecalis</i>, <i>Pseudomonas aeruginosa</i> and <i>Candida albicans</i>; according to recommendations from the National Norms Committee of the Standard Clinic Laboratory. Results and discussion: The 7 extracts are active against <i>Pseudomonas aeruginosa</i> and <i>Staphylococcus aureus</i>, comparable with Ciprofloxacin in the first bacteria, antifungal activity was not obtained. The minimum inhibitory concentration for the soft extracts was higher than 100mg/mL and for the blended higher than 50mg/mL; the minimum bactericide concentration for the soft extracts were more than or equal to 400mg/mL and for the blended more than 200 mg/mL, in the base of the fresh drug. Conclusions: The antimicrobial activity increases with the concentration of the extracts ; the most concentrated extracts B4 and E3 possess a higher antimicrobial spectrum, the highest antimicrobial activity against <i>P. aeruginosa</i> is obtained in the blended extracts E1,E2 and E3; the blended extracts are considered more potent and active then the bland extracts.</p>
PFE 011	<p>ANTIATHEROGENICITY OF SEAWEEDS: ANTIOXIDANT ACTIVITY OF <i>H. INCRASSATA</i> (ELLIS) LAMOROUX IN THE INHIBITION OF LIPOPROTEIN OXIDATION AND SMOOTH MUSCLE CELL MIGRATION Costa A¹, Mondejar D¹, Batista A E¹, Brömme D², Soto Y³, Vázquez A M³, Zaldívar C¹, Vidal A¹ ¹Department of Biochemistry, Faculty of Biology, University of Havana, Cuba ²Department of Oral Biological and Medical Sciences, Faculty of Dentistry, University of British Columbia, Canada ³Department of Antibody Engineering, Center of Molecular Immunology</p> <p>Oxidative stress is considered a key causal factor during atherosclerosis progression so natural antioxidants are attractive for disease modulation. In this context, marine algae are a privileged reservoir of antioxidants with very low toxicity (1). In the present work we evaluated the antiatherogenic effect of <i>H. incrassata</i> seaweed during lipoprotein oxidation and smooth muscle cell migration in relation to its antioxidant activity. <i>H. incrassata</i> aqueous extract had a protective action against lipoperoxidation induced by Cu²⁺ ions or the free radical generator AAPH. Lower doses were required to inhibit TBARS formation for native LDL as compared to heparin precipitated LDL (hep-LDL) (IC₅₀ = 0.8 mg/mL vs 4.2 mg/mL in oxidation by Cu²⁺). Phenolic compounds contribute to the observed effect as polyphenol rich fractions were very active against lipoprotein oxidation (> 90% inhibition of Cu²⁺ mediated hep-LDL oxidation at 1 µg gallic acid equivalents,GAE). <i>H. incrassata</i> aqueous extract also dose-dependently inhibited PDGF-BB induced smooth muscle cell migration of MOVAS cell line in a transwell and wound healing model (43% and 53.1 % inhibition at 0.1 mg lyophilized/mL respectively). The <i>in vitro</i> atheroprotective effect could be related to the antioxidant activity of the seaweed evaluated in this study: DPPH* radicals scavenging (IC₅₀ = 0.27 mg lyophilized/mL and 1 µg GAE for free phenolic acid fraction (FFA)); reducing activity (2 mg lyophilized/mL and 35 µg GAE for FFA fraction to reach an absorbance of 0,155); and oxygen radical</p>

	<p>absorbance (ORAC) capacity (7.8 trolox equivalents at 0.5 mg lyophilized/mL and 16 trolox equivalents at 8 µg GAE). The results support the antioxidant activity and antiatherogenic properties of <i>H. incrassata</i> and represent a further step for the introduction of the seaweed for a phytotherapeutic application.</p> <p>1- Characteristics and nutritional and cardiovascular-health properties of seaweeds. Aránzazu Bocanegra, Sara Bastida, Juana Benedit, Sofia Ródenas, Francisco J. Sánchez-Muniz. <i>J Med Food</i> 12 (2) 2009, 236–258</p>
<p>PFE 012</p>	<p>ANTIPROTOZOAL ACTIVITY OF SOME CUBAN MEDICINAL PLANTS Fernández-Calienes A¹, Mendiola J¹, Monzote L¹, Sariego I¹, García M¹, Scull R², Gutiérrez Y², Acuña D¹, Rojas L¹, Payrol JA².</p> <p>¹Departamento de Parasitología, Instituto de Medicina Tropical “Pedro Kourí”, Autopista Novia del Mediodía Km 6 ½, La Lisa. Apartado Postal 601, Marianao 13, Ciudad de La Habana, Cuba. email: ayme@ipk.sld.cu.</p> <p>²Departamento de Farmacia, Instituto de Farmacia y Alimentos, Universidad de La Habana. Calle 222 entre 23 y 27, La Coronela, La Lisa, Ciudad de La Habana, Cuba.</p> <p>Introduction: Protozoa can cause serious health problems worldwide and more efficacious drugs are needed. Plants that have been used in traditional medicine are more likely to yield pharmacologically active compounds. Many research groups screen plant extract searching new promising therapeutic candidates for infectious diseases. We evaluate antiprotozoal activity of ethanolic extracts from 33 medicinal species used in Cuban traditional medicine. Material and Methods: Plant species were identified and collected in the Cuban National Botanical Garden. Hydroalcoholic extracts were prepared. <i>In vitro</i> activities were tested against <i>Trichomonas vaginalis</i> trophozoites, <i>Leishmania amazonensis</i> (promastigotes and amastigotes) and <i>Plasmodium falciparum</i> intraerythrocytic stages. Extract concentration inhibiting 50 % of parasite growth (IC50) was determined. To assess the selectivity of antiprotozoal activity, cytotoxicity was determined in parallel against human MRC-5 cells and Balb/c mice macrophages. Selectivity index (SI) was calculated as a ratio between the 50% cytotoxic concentration (CC50) and the IC50. Balb/c mice infected with <i>Plasmodium berghei</i> or <i>L. amazonensis</i> were used as models for malaria or cutaneous leishmaniasis. NMRI mice intraperitoneally infected with <i>T. vaginalis</i> trophozoites were used as experimental model for trichomonocidal activity evaluation. Mice were treated intraperitoneally (or subcutaneously for malaria) at doses of 500, 200 and 100 mg/Kg of extract. Untreated mice were included as controls. Results and Discussion: Eight species were selected for their promising activity (IC50 < 50 µg/mL) and specific (SI > 5) <i>in vitro</i> antiprotozoal activity: <i>Bixa orellana</i>, <i>Bambusa vulgaris</i>, <i>Cucurbita maxima</i>, <i>Hura crepitans</i>, <i>Manguifera indica</i>, <i>Parthenium hysterophorus</i>, <i>Pluchea carolinensis</i> and <i>Punica granatum</i>. Only <i>B. orellana</i> showed <i>in vivo</i> activity against all tested protozoa; <i>P. carolinensis</i> and <i>P. granatum</i> were respectively active against <i>Leishmania</i> and malaria models, whereas, <i>C. maxima</i> showed significant activity against <i>T. vaginalis</i> in the experimental animal model. Conclusions: Our study reveals the antiprotozoal potential of Cuban medicinal plants. Four extracts were selected for further follow-up because of their <i>in vitro</i> and <i>in vivo</i> activities against at least one of the studied protozoa.</p>
<p>PFE 013</p>	<p>MURRAYA PANICULATA: IN VITRO AND PHYTOCHEMICAL EVIDENCES OF ITS ANTIOXIDANT PROPERTIES Casado CM, Gutiérrez YI, López R</p> <p>Pharmacy and Foods Institute. University of Havana. 222 and 23 Ave. La Coronela. La Lisa. Havana City. Cuba. email: celia@uh.cu; celiamecm@ifal.uh.cu</p> <p>Introduction: Medicinal plants have become a source of new and more efficient antioxidants to which pharmacology can appeal to neutralize free radicals produced by cells. Moreover antioxidants have been related to several illnesses, it has been accepted that those plants that have been traditionally used by their anti-inflammatory effects, could have a therapeutic action due, at least partly, to the presence of compounds able to react with free radicals involved in this kind of ailments. Tincture obtained from <i>Murraya paniculata</i> fresh leaves, used as analgesic frictions, which possesses, according to previous results, anti-inflammatory properties, presents, taking in to account the consulted bibliographical reports, an important group of secondary compounds that could be also associated to the antioxidant effect of this phytopharmaceutical. Materials and methods: <i>Murraya paniculata</i> and the obtained formulation were subjected to a phytochemical study. <i>In vitro</i> evaluation of its antioxidant properties was made by means of FRAP (Ferric Reduction Antioxidant Power) methodology and a qualitative DPPH (1,1-diphenyl-2-picrylhydrazyl) analysis on TLC (Thin Layer Chromatography). Results and discussion: We can presume</p>

	<p>the presence of alkaloids, terpenoids, coumarins, flavonoids, among others in the vegetable drug and the extract analyzed. The obtained results in FRAP analysis showed us a reduction power above 200μM. DPPH analysis evidenced antioxidant capability for total extract and also for some groups of secondary compounds, which could be separated using the TLC technique, this assay also showed a time dependant decoloration reaction which must be proportionally related with the antioxidant activity. Conclusions: This result let us conclude that <i>Murraya paniculata</i> possesses antioxidant property under the rehearsed experimental conditions.</p>
<p>PFE 014</p>	<p>EFFECTS OF CONTINUOUS ORAL ADMINISTRATION OF <i>Boldoa Purpurascens</i> Cav. ON SEVERAL PHYSIOLOGICAL VARIABLES OF RATS González D¹, Pérez M¹, Boffill M², González D.M.³, Monteagudo E²</p> <p>¹Institute of Medical Sciences “Dr. Serafín Ruiz de Zárate Ruiz”. Vicerrectorate of investigations. Clinical Trials Center. Carretera a Acueducto y Circunvalación. Santa Clara, Villa Clara, Cuba. email: maykelpm@iscm.vcl.sld.cu ²Experimental Toxicology Unit. Medical College of Villa Clara. Santa Clara, Cuba. ³Pharmacy Department. Central University of Las Villas. Santa Clara, Cuba.</p> <p>Introduction: There are many medicinal plants used traditionally by our population which are attributed diuretic properties, among them <i>Boldoa purpurascens</i> Cav. Scientific validation of these traditional practices is a perentory need because the safety of these plants can not be limited only to the popular wisdom. To test the diuretic effect of a liophilized aqueous extract from <i>B. purpurascens</i>, known as nitro blanco, a non clinical study was conducted evaluating several physiological variables after a repeated application of 14 days. Material and Methods: There were used 5 rats (preliminary study) to prove the diuretic effect of the prime matter which will be subsequently used for the obtention of extracts and 40 rats for the repeated dose study (main study, 14 days) and there were analyzed some haemathological and biochemical parameters at 7 and 14 days of treatment. It was observed a high diuretic activity of the plant at the dose of 400 mg/kg BW when compared to historical control treated with furosemide. Results and Discussion: During the clinical evaluations there were no observed behavior abnormalities and body weight gain was according to the species normal values in both groups. Statical analysis of haemathological values showed differences in haemoglobin and haematocrit but both parameters were inside the normal rank of variations. Biochemiela values showed a lowering in the glucose values and an increase of potassium ones at 14 days of administration. Conclusion: It is concluded that a 14 days oral adminsitration of <i>Boldoa purpurascens</i> Cav has a diuretic effect at the dose essaied. It continuous adminsitration diminish significativly the values of haemoglobin and haematocrit and affects potassium homeostasis and diminsh those of glucose at 14 dyas of adminsitration.</p>
<p>PFE 015</p>	<p>A NEGATIVE CHRONOTROPIC ACTIVITY MEDIATES THE TOXIC EFFECT OF A LOW MOLECULAR WEIGHT FRACTION FROM <i>Zoanthus sociatus</i> Domínguez-Pérez D^{1*}, Díaz-García CM^{2†*}, Fuentes-Silva D³, García-Delgado N⁴, Taboada-Crispi A⁵, Kairuz Hdez-Díaz HA⁵, Sierra Y⁶, Varela C⁷, Sánchez-Soto MC², Pedroso A⁸, Pérez-Saad H⁹, Rodríguez-Romero A⁴, Hiriart M², Castañeda-Pasarón O⁴.</p> <p>*Domínguez-Pérez D and Díaz-García CM contribute equally to this work. †Posgrado en Ciencias Biológicas de la Universidad Nacional Autónoma de México. email: danydp@uclv.edu.cu, cmanlio@ifc.unam.mx</p> <p>¹Universidad Central “Martha Abreu” de Las Villas. Departamento de Biología. Carretera a Camajuaní, Km 5.5, 54830, Santa Clara, Cuba. ²Instituto de Fisiología Celular, Universidad Nacional Autónoma de México. Neuroscience Division, Neurodevelopment and Physiology Department. Circuito Exterior S/N Ciudad Universitaria, Coyoacán, 04510 México D.F. ³Instituto de Química, Universidad Nacional Autónoma de México. Idem (2). ⁴Departamento de Biología Animal y Humana, Facultad de Biología, Universidad de La Habana. Calle 25 No. 455, Plaza de la Revolución, Ciudad de La Habana, CP 10400, Cuba. ⁵Universidad Central “Martha Abreu” de Las Villas. Centro de Estudios de Electrónica y Tecnologías de La Información. Idem (1). ⁶Centro de Estudios de Proteínas. Facultad de Biología, Universidad de La Habana. Idem (4). ⁷Acuario Nacional de Cuba. Avenida 3^{ra}, Esquina 62, Miramar Playa, Ciudad de La Habana. ⁸Instituto de Endocrinología, MINSAP, Cuba. Calle Zapata esquina C, Vedado, Municipio Plaza, Ciudad de La Habana.</p>

	<p>⁹Instituto de Neurología y Neurocirugía, MINSAP, Cuba. Calle D No. 139 esquina 29,10400, Ciudad de La Habana.</p> <p>Introduction: Cnidarian venoms often contains a group of small molecules, mostly peptides, with neurotoxic and cardiotoxic activities. The phylum has a great potential in the research of novel cell excitability modulators since its biodiversity have not been fully explored yet, and particularly, Cuban marine platform constitutes an excellent source of such species. Materials and Methods: Total bodies of <i>Zoanthus sociatus</i> were homogenized by autolysis in distilled water, then filtered and centrifuged, and the supernatant was lyophilized. After a gel filtration step, the low molecular weight fraction was then freeze-dried and the acute toxicity and Irwin test were assessed in OF-1 mice (doses were calculated upon protein content). RP-HPLC C18 was performed as a criterion of purity and molecular weights were determined by mass spectrometry. Electrocardiograms were recorded in control and i.p inoculated mice and the comparison between average beat-to-beat intervals was analyzed. Results and Discussion: The gel filtration chromatogram at 280 nm reveals two major peaks, the second with the highest absorbance and corresponding to the low molecular weight fraction, ranging from 2–7 kDa, and resembling those peptide toxins described in the phylum. Moreover, the RP-HPLC chromatograms show that this peak accounts for compounds with retention times below 30 min in a 1 %ACN/min gradient. The pharmacological effects are mostly autonomic and cardiotoxic, causing death in a dose-dependent manner with a LD₅₀ of 792 µg/Kg and a dose-lethality curve slope of 17. Preliminary results indicate that after 5 min, the fraction increases in a 20% the average RR interval at a non lethal dose of 600 µg/Kg, and it recovers in a 13 % approximately after 20 min post-treatment. Conclusions: The low molecular weight fraction from the crude extract of <i>Z. sociatus</i> exerts a negative chronotropic effect in cardiac pacemaker, which could lead to cardiac arrest at lethal doses.</p>
<p>PFE 016</p>	<p>ANTI-INFLAMMATORY AND CITOTOXIC ACTION OF THE THYME (<i>THYMUS VULGARIS</i>) Ferrándiz Ramírez Dania¹, Valdovinos Casado Niurys</p> <p>¹ University of Camagüey. Cuba. email: dania.ferrandiz@reduc.edu.cu</p> <p>The use of the medicinal plants is so remote than the mankind older origins. One of the fields that awake bigger interest in the investigation pharmacognostic is the study of vegetable species with anti-inflammatory properties. The objective of this work is the evaluation <i>in vivo</i> of the flavonoides in experimental models of inflammation and the realization of citotoxic assays. The used method was the inflammation subchronic induced by repeated application of TPA as irritating agent, taking place in the experimentation animals an inflammatory response and cutaneous hypertrophy. The activity of the fluid extract of the thyme is tested according to the protocol. This compound is applied by topical way to dose of 0,25 mg/ear. The reference drug is also applied by topical way to dose of 0,05 mg/ear. The anti-inflammatory activity is evaluated by means of the calculation of the percentage of edema inhibition. Given the result of the fluid extract in the inflammation model is appreciated that the compound presents inhibitory activity of 61%, being able to reduce the inflammation leukocytic in a significant way. For the citotoxic assay PMNs peritoneales of rats was used obtained after glycol injection, picked up by laundry in the peritoneal cavity and incubated in presence of the one compound to assay to a concentration of 10 µM. They are considered citotoxic those compounds that reduce the viability of the PMNs below 95%. The result obtained in the citotoxicity assay showed a percent of viability of 97,4%, being corroborated the non citotoxicity of this compound.</p>
<p>PFE 017</p>	<p>ANTIMICROBIAN ACTIVITY OF DIFFERENT EXTRACTS OF PLANTS Boucourt E, Martínez MJ, López M, Morejón Z, García AI, Victoria, MC, Morón F Central Laboratory of Pharmacology, Faculty of Medical Sciences “Dr. Salvador Allende”. Carvajal street between A and Agua Dulce, Cerro. Havana City. Cuba. CP 12000 email: elisabr@fallende.sld.cu</p> <p>Introduction: In this work was evaluated the antimicrobial activity of different species of plants reported in traditional medicine: <i>Plantago major</i> L. (<i>Llantén</i>), <i>Lepidium virginicum</i> L. (<i>Mastuerzo</i>), <i>Phania matricarioides</i> (Spreng.) Griseb (<i>Manzanilla de la tierra</i>), <i>Alpinia zerumbet</i> (Pers.) B.L. Burt & R. M. Sm. (<i>Colonia</i>), <i>Cocoloba uvifera</i> L. (<i>Uva caleta</i>), <i>Citrus aurantium</i> L. (<i>Naranja agria</i>), <i>Citrus aurantifolia</i> (Christm) Swing (<i>Limón</i>), <i>Cissus verticilada</i> (L.) Nicolson & C.E. Jarvis (<i>Bejuco ubí</i>), <i>Psidium guajaba</i> L. (<i>Guayaba</i>), <i>Lycopersicum esculentum</i> Mill. (<i>Tomate</i>). Materials and Methods: It was used the method of diffusion in solid environment to determine the potence of extracts in relation to: <i>Staphylococcus aureus</i>,</p>

	<p><i>Bacillus subtilis</i>, <i>Escherichia coli</i>, <i>Pseudomonas aeruginosa</i>, <i>Klebsiella pneumoniae</i>, <i>Enterobacter cloacae</i> microorganisms and <i>Candida albicans</i> of international reference (ATCC). As positive control were used estreptomycin and nistatine; as negative sterile distilled water. Results and Discussion: It was not demonstrated halo of inhibition of growing in the microorganisms studied in the extracts of Llantén, Mastuerzo, Manzanilla de la tierra, Colonia, Uva caleta y Tomate. The juice of limón and sour naranja agria demonstrated antimicrobial action in relation to <i>S. aureus</i>, <i>B. subtilis</i>, <i>E. coli</i>, <i>P. aeruginosa</i>, <i>K. pneumoniae</i> and not presented that activity in from of <i>E. cloacae</i>, <i>C. albicans</i>. The aqueous extract of guayaba leaves presented this action only with a <i>S. aureus</i>, <i>K. pneumoniae</i>.; the leaves of Bejuco ubí heated in oil showed positive answer with <i>S. aureus</i>. Conclusion: The vegetable extracts of <i>Plantago major</i> L., <i>Lepidium virginicum</i> L., <i>Phania matricarioides</i> (Spreng.) Griseb, <i>Alpinia zerumbet</i> (Pers.) B.L. Burt & R. M. Sm., <i>Cocoloba uvifera</i> L., <i>Lycopersicum esculentum</i> Mill., don't have antimicrobial activity with different microorganisms studied. It was shown antimicrobial action with certain microorganisms evaluated of the preparation of <i>Citrus aurantium</i> L., <i>Citrus aurantifolia</i> (Christm) Swing, <i>Cissus verticillata</i> (L.) Nicolson & C.E. Jarvis, <i>Psidium guajaba</i> L.</p>
<p>PFE 018</p>	<p>PROTECTIVE EFFECT OF <i>Bidens pilosa</i> L EXTRACT IN HEPATOTOXICITY INDUCED BY PARACETAMOL IN RATS Monteagudo E¹, Méndez R², Boffill M¹, Pérez M², López O²</p> <p>¹Experimental Toxicology Unit Medical College of Villa Clara. Aqueduct Rd. and Circunvalation. Santa Clara, Villa Clara, Cuba. email:emiliomj@iscm.vcl.sld.cu ²Clinical Trials Center. Medical College of Villa Clara. Aqueduct Rd. and Circunvalation. Santa Clara, Villa Clara, Cuba.</p> <p>Introduction: <i>Bidens pilosa</i> L, known as romerillo blanco, is widely used by the Cuban population. It is chemically composed by flavonoids (quercetin) with proved antioxidant proprieties. Materials and Methods: a preclinical study was carried out to evaluate the hepatoprotective effect of <i>Bidens pilosa</i> L in the toxicity induced by paracetamol. Male adults MNRI mice were used to evaluate the effect of oral administration of three-level dose (150, 300 y 600 mg/Kg weight) of <i>Bidens pilosa</i> L extract, 30 minutes before and 2 hours after the hepatotoxicity was induced by paracetamol (600 mg/Kg, oral, unique dose) establishing as endpoints: the evaluation of: clinical signs, enzymatic activity (alkaline fosfatase, alanine aminotransferase, and aspartate aminotransferase) and histological changes produced in hepatocytes. Results and Discussion: there were no abnormalities in the animal's behavior. The analysis of plasmatic concentrations of the three enzymes in treated groups showed high statistic significance with respect to control group (paracetamol). Values within the reference values range for the specimen were obtained. Anatomopathological results confirmed the cellular protection, either macroscopic or microscopically, in the livers of treated animals. Conclusions: the administration of <i>Bidens pilosa</i> L extract showed a protective effect on the liver against the toxicity induced by paracetamol, with no relation between dose and pharmacologic action.</p>
<p>PFE 019</p>	<p>VASCULAR ACTIVITY OF <i>DICHROSTACHYS CINEREA</i> (MIMOSACEA) FRUITS ON ISOLATED AORTIC RINGS OF RATS Hernández E, Ribalta V, Torres L, Sueiro M, Armas Y</p> <p>Pharmacy Department, Chemistry and Pharmacy Faculty. Central University of Las Villas. Santa Clara, Villa Clara. Road to camajuani km 5 ½. email: enoelh@uclv.edu.cu</p> <p>Introduction: The objective of this study was to explore its vascular effects and possible(s) mechanism(s) that could be related. Methods: <i>Plant material:</i> Natural dry fruits were collected in the forest surrounding Botanical Garden of Central University of Las Villas. Plant sample was identify as <i>Dichrostachys cinerea</i> (Mimosaceae) by Orestes R. Méndez a taxonomic expert of above Institution and deposited under register code UCLV-9493. <i>Phytochemical procedure:</i> Aqueous extract (AE) were obtain by following method. AE: 30 g of dry fruits was boiled with distilled water (100 ml) in a balloon for 15 minutes. Preliminary chemical composition of AE was determinate as previous reported (Adikay, 2009). <i>Animals:</i> Wistar rats 250-300 g was use in this study. <i>Isolated tissue studies:</i> Aortic rings, cut into 5 mm, were used to test the relaxant effects of the aqueous extract of <i>D. cinerea</i> fruits (Dc.F). Phenylephrine (1.0 µM) was used for elicited contraction as previous reported (Rattman, 2009) and after AE was added (50-120 µg/ml) in cumulative manner to organ bath. Pilocarpine, a m₃ muscarinic agonist (300 µM) and isoprenaline, a B₂ adrenergic agonist (10 µM) were used as positive control. <i>Isolated conditions:</i> The aortic rings was suspended in 10 ml organ bath filled with Krebs-Henseleit solution (pH=7.4) maintained at 37 °C and</p>

	<p>continuously aerated with carbogen gas. Two grams of basal tension was applied for all preparations and equilibrated period of 1 h before any drug exposure. <i>Viability tissue test</i>: KCl (30 mM) was used for elicited contraction and checks the functional tissue state. <i>Statistics</i>: Values are expressed as means ± S.E.M. One-way Anova test was used for statistical analysis, with $P < 0.05$ considered significant. Results: <i>Phytochemical screening</i>: The positive result was found for flavonoids, tanins, saponins and alkaloids. The Dc.F produced a concentration-dependent relaxation on phenylephrine (1.0 μM)-induced contractions of rat thoracic aortic preparations. The vasodilatory responses were not altered in the presence of Propanolol (100 μM), a non-specific beta adrenergic blocker but complete abolished by Atropine (10 μM), a non-selective muscarinic blocker, or Methylene Blue(100 μM) a guanylate cyclase inhibitor. Conclusions: These results suggest that the vasodilator effects of Dc.F extract are mediated possibly through muscarinic receptor (m₃) agonism in accordance with the alkaloids detection in aqueous fruits extract.</p> <p>References: 1-Adikay, S., B. Koganti, and K. Prasad. Effect of alcoholic extract of roots of <i>Dichrostachys cinerea</i> Wight-Arn against cisplatin-induced nephrotoxicity in rats. <i>Natural Product Radiance</i>, 2009. 8(1):p. 12-18.</p> <p>2- Rattmann, Y.D., et al., Activation of muscarinic receptors by a hydroalcoholic extract of <i>Dicksonia sellowiana</i> Presl. Hook (Dicksoniaceae) induces vascular relaxation and hypotension in rats. <i>Vascular Pharmacology</i>, 2009 50: p. 27–33.</p>
PFE 020	<p>PHARMACOLOGICAL EVIDENCES ON THE ANTIOXIDANT ACTIVITY OF <i>MORINDA CITRIFOLIA</i> L. FRUITS</p> <p>Álvarez Jiménez E¹, Miranda Martínez M², Scull Lizama R², Abreu Payroll J²</p> <p>¹Farmacia Comunitaria (U – 626). Empresa Provincial de Medicamentos del Oeste. Ciudad de la Habana. Cuba. email: esthera@infomed.sld.cu</p> <p>²Instituto de Farmacia y Alimentos. Universidad de la Habana. Ciudad de la Habana. Cuba.</p> <p>Introduction: <i>Morinda citrifolia</i> L. (Noni) has had a great impact in current phytotherapy due to its wide and grateful use, in traditional medicine, for numerous affections, it is known in Cuba since the first half of XIX century with the common name of “Moorish of the India”. Although there are a high number of properties that have been attributed to this species, there are a few scientific results that endorse it. Materials and Methods: It was carried out a phytochemical screening on the samples corresponding to different stages of the fruit, it was also carried out a heavy metals determination and also DPPH scavenger capacity and catalase enzymatic activity on water and alcoholic extracts. Results and discussion: Fruits phytochemical composition was similar on different stages with probable presence of lactons, reducers compounds, phenols and tannins, flavonoids, triterpens and steroids. Among the studied minerals, the most abundant were zinc and copper, although its values don't present significant differences between the fruits stages and they are inside the established limits for other fruits and vegetable drugs in general. The mature fruit water extract present the biggest DPPH scavenger capacity and catalase activity, continued by the fermented fruits water extract and the green one, which showed a significantly smaller capacity. The alcoholic extracts presented the smallest capacity, being demonstrated the antioxidant effect of this species fruits. Conclusions: Results of this study evidence that it's the mature fruit the one that present the biggest DPPH scavenger capacity and catalase activity, with significantly superior values to green and fermented ones, being demonstrated the antioxidant effect of the fruits of the species, but in mature stage and not fermented as it is generally used in Traditional Medicine.</p>
PFE 021	<p>NEW PROPERTIES OF <i>PEDILANTHUS TITHYMAOLOIDES</i> L POIT</p> <p>Hiran Cabrera Suárez¹, Armando Cuellar², Ana Iris Frías³, Neivys García Delgado³, Yanier Núñez Figueredo⁴</p> <p>Laboratorio Central de Farmacología, FCMH “Dr. Salvador Allende”, Carvajal s/n y Agua dulce, Cerro, Ciudad de la Habana, Cuba. email: iranacs@infomed.sld.cu</p> <p>Introduction: <i>Pedilanthus tithymaloides</i> L Poit is known as Itamo real and traditional medicine show some properties, today they prepare a tincture of Itamo real to treatment mouth affections, some works research had shown new properties related with some substance isolated from their leaves, in order to try this presentation has as a Objective: To explain old and new pharmacology properties related with some substances isolated from leaves of <i>P tithymaloides</i>. Material and methods: they joint a numerous chemistry and pharmacology work research from our group and other authors about Itamo real and analysis all data, Results: they could explain some pharmacological and toxicological properties attributed</p>

	<p>by traditional medicine to this plant and other weren't known at the moment, and they could know some pharmacological properties from some substances presents at the leaves of this plant CONCLUSIONS: Itamo real is a plant with more toxicological properties than other pharmacological properties and some substance show properties not related with traditional uses.</p>
PFE 022	<p>ANTIPROTOZOAL ACTIVITY OF CUBAN PROPOLIS EXTRACTS Idalia Sariego¹, Monzote L¹, García M¹, Cuesta-Rubio O², Campo M², Márquez I², Piccinelli A³, Rastrelli L³</p> <p>¹Departamento de Parasitología, Instituto de Medicina Tropical “Pedro Kouri”, Autopista Novia del Mediodía Km 6 ½, La Lisa. Apartado Postal 601, Marianao 13, Ciudad de La Habana, Cuba. email: idalia@ipk.sld.cu</p> <p>² Instituto de Farmacia y Alimentos, Universidad de La Habana. Calle 222 entre 23 y 27, La Coronela, La Lisa, Ciudad de La Habana, Cuba.</p> <p>³ Università degli Studi di Salerno, Italia</p> <p>Introduction: Natural products and their derivatives have historically been invaluable as a source of therapeutic agents. In the present work, we analyzed the antiprotozoal effects of eighteen Cuban propolis extract (brown, red and yellow) collected in different geographic areas, using <i>Leishmania amazonensis</i> (as a model of intracellular protozoa) and <i>Trichomonas vaginalis</i> (as a model of extracellular protozoa).</p> <p>Material and methods: Propolis samples were extracted with methanol and were dissolved in dimethyl sulfoxide to perform the experiments. The <i>in vitro</i> activity against <i>L. amazonensis</i> amastigotes was expressed as a percent of reduction of the infection rate, in comparison to the control, by counting with the microscope after Giemsa staining. The trichomonocidal activity was determined using the colorimetric method with MTT, as well as the assessment of the cytotoxicity of propolis samples on macrophages.</p> <p>Results and discussion: All propolis extracts evaluated caused inhibitory effect on intracellular amastigotes of <i>L. amazonensis</i>. However, cytotoxicity on peritoneal macrophage from BALB/c mice was observed. Low effects on <i>T. vaginalis</i> growing by propolis extracts were shown; although five samples decreased the viability of trophozoites at concentrations lower than 10 µg/mL. No correlation between the type of propolis and activity was found. Conclusions: Cuban propolis extracts demonstrated activity against both models used of intracellular and extracellular protozoa, corroborating the potentialities of propolis as a natural source to obtain new antiprotozoal agents.</p>
PFE 023	<p>EFFECT OF CENSA 002 AQUEOUS EXTRACT AND ITS MAJOR FRACTION ON THERAPEUTIC TARGETS ASSOCIATED WITH TYPE 2 DIABETES. Sánchez J¹, Marrero E¹, Faure R¹, Mitjavila MT², Harvey A³</p> <p>¹Dep. Chemistry, Pharmacology and Toxicology. National Centre for Animal and Plant Health (CENSA). San José de Las Lajas, La Habana, Cuba.</p> <p>²Dep. of Physiology. Faculty of Biology. University of Barcelona, Spain.</p> <p>³ Strathclyde Institute for Drug Research (SIDR), University of Strathclyde, Glasgow, Scotland, UK. email: jsanchez@censa.edu.cu</p> <p>Introduction: Diabetes mellitus (DM) is a major health problem all over the world, there are approximately 194 million adults aged 20–79 years with diagnosed DM, with type 2 diabetes (T2DM) accounting for 90–95% of all diagnosed cases, and that number is expected to increase to 333 million over the next 20 years. Oxidative stress, lead to insulin resistance, β-cell dysfunction, impaired glucose tolerance and ultimately to T2DM. DM induces the NF-κB signaling cascade activation and subsequent overexpression of inflammatory enzymes, such as phospholipase A₂ (PLA₂) and cyclooxygenase 2 (COX-2). There are many traditional treatments for DM, mainly based on plant extracts, however, few of these have received scientific or medical scrutiny. Hence, the aim of this study was to evaluate the effect of CENSA002 aqueous extract and its major fraction on therapeutic targets associated with T2DM. Material and Methods: CENSA002 aqueous extract and its major fraction, were evaluated in the following T2DM targets: Dipeptidyl peptidase (DPP-IV) activity, glucose uptake in 3T3-L1 adipocytes and in others anti-inflammatory and antioxidant targets related with this disease: sPLA2 and COX-2 enzymatic activity inhibition; lipid peroxidation in rats brain homogenate tested by MDA measurement and superoxide anions generation in a cellular line of 264.7 RAW macrophages stimulated with PMA, detected by Nitrobluetetrazolium method. Results and Discussion: Results showed that CENSA002 extract and its major fraction have anti-diabetic effects on T2DM targets: as DPPIV inhibitor and stimulator of glucose</p>

	<p>uptake in adipocytes, suggesting a role for glucose transporters GLUT1 and GLUT4, which are expressed in 3T3-L1 adipocytes; also showed anti-inflammatory activity evidenced by sPLA2 and COX-2 enzymatic activity inhibition and antioxidant properties, achieved by the scavenging ability against superoxide anion and protective effect on oxidative damage to lipids. Conclusions: These results showing for first time the therapeutic potential of CENSA002 aqueous extract as candidate for development of new drugs for treatment of T2DM. References: Sánchez et al., 2005. Pharmacognosy Magazine 1(3): 101-105. Sánchez et al., 2005. Medisan 9(4) (ISSN 1029-3019). Marrero E, Sánchez J, et al., 2006. Fitoterapia 77: 313-315.</p>
<p>PFE 024</p>	<p>ANTIMICROBIAL ACTIVITY OF THE EXTRACTS AND COMPOUNDS FROM <i>MORINDA ROYOC L. (RUBIACEAE)</i> Borroto J¹, Salazar R², Quirós Y¹, Hernández M¹, Waksman N², Trujillo R¹.</p> <p>¹Centro de Bioplantitas, Unviersidad de Ciego de Avila, Cuba. email: jborroto@bioplantitas.cu. ²Departamento de Química Analítica, Facultad de Medicina, U.A.N.L. México. email: salazar1212@yahoo.com.mx</p> <p>Plants are a tremendous source of natural diversity in the multitude of compounds that they synthesize, many of which have been shown to be useful as therapeutics for treating a variety of human illnesses and maladies. Anthraquinones (AQs) are an important group of secondary metabolites occurring in bacteria, fungi, lichens and higher plants like <i>Morinda royoc L.</i> roots. The aim of the present study was to evaluate the potential antimicrobial activity of dichloromethane extracts of <i>ex vitro</i> and <i>in vitro</i> roots and callus culture of <i>Morinda royoc L.</i>, for the treatment of respiratory diseases. Dichloromethane extracts obtained from <i>ex vitro</i> and <i>in vitro</i> roots and callus culture, of <i>Morinda royoc L.</i> as well as eight anthraquinones isolated from these extracts were tested for their antimicrobial activity against seven isolates of <i>Candida</i> spp.: <i>C. albicans</i> 501, <i>C. albicans</i> 53, <i>C. albicans</i> 498, <i>C. tropicalis</i>, <i>C. glabrata</i>, <i>C. krusei</i> and <i>C. parapsilosis</i> and three Gram-positive bacteria (<i>Staphylococcus aureus</i> methyciline resistant, <i>Staphylococcus aureus</i> ATCC 12598 and <i>Enterococcus faecales</i>) and four Gram-negative bacteria (<i>Escherichia coli</i>, <i>Acinetobacter baumannii</i>, <i>Pseudomonas aeruginosa</i> and <i>Klebsiella pneumoniae</i>) using broth microdilution test. The crude extracts were active against all <i>Candida</i> species whereas morindone was found to be the best active compound. The lowest minimal inhibition concentration (MIC) values obtained by the microdilution test were 1.95 µg/mL as to the crude extracts as morindone. The dichloromethane extracts of callus culture, <i>ex vitro</i> and <i>in vitro</i> roots of <i>Morinda royoc L.</i>, showed strong inhibitory activity against <i>S. aureus</i>, <i>E. faecales</i>, and <i>E. coli</i>. The lowest MIC values obtained by the microdilution test were 31.25 µg/mL and 15 µg/mL for crude extracts and morindone respectively. No extracts or isolated anthraquinones were found to be active against <i>A. baumannii</i>, <i>P. aeruginosa</i>, <i>K. pneumoniae</i> at the maximum concentration analyzed (1000 µg/mL). These results provide promising baseline information for the potential use of these crude extracts as well as the morindone in the treatment of bacterial and fungal infections. Also, the results suggest that <i>in vitro</i> cultures of <i>Morinda royoc L.</i> could be a source of secondary metabolites to be used as antimicrobial agents. Keywords: antimicrobial activity, <i>Rubiaceae</i>, anthraquinone, morindone.</p>
<p>PFE 025</p>	<p>“IN VITRO AND IN VIVO INHIBITORY ACTIVITY AGAINST <i>PLASMODIUM BERGHEI</i> OF CUBAN MARINE SPONGES (<i>AGELAS</i>, <i>MYCALE</i>, <i>NIPHATES</i>, <i>CLATHRIA</i> AND <i>POLYMASTIA</i>) PRODUCTS” Mendiola B J¹, Regalado E L², Laguna A², Valdés O², Fernández-Calienes A¹, Acuña D¹, Thomas O P³.</p> <p>¹Institute of Tropical Medicine “Pedro Kouri” (IPK), P.O. Box 601, Havana, Cuba. email: mendiola@ipk.sld.cu</p> <p>²Center of Marine Bioproducts, Loma y 37, CP 10400, Havana, Cuba. ³Université de Nice-Sophia Antipolis, Laboratoire de Chimie des Molécules Bioactives et des Arômes, UMR 6001 CNRS, Institut de Chimie de Nice, Faculté des Science, Parc Valrose, 06108 Nice Cedex 02, France.</p> <p>Introduction: The emergence of multi-drug resistant strains of <i>Plasmodium</i> makes many of the available drugs useless. Since malaria is a disease of worldwide implications and almost half of the world’s population is currently at risk for malaria infection, discovery and development of new, safe and effective antiprotozoal agents for combating malaria is one of the highest priority needs. In this regard, marine sponges have provided the most promising classes of marine antimalarial lead compounds. Herein, we report the eligible antimalarial activities among eighteen sponge species; their crude and 49 derived fractions, which were subsequently explored concerning their secondary metabolites contents. Material</p>

	<p>and Methods: Crude extracts were prepared after ultrasonic extraction of a freeze-dried portion of sponge specimens collected at Boca de Calderas, Cuba, with a mixture MeOH/CH₂Cl₂ (1:1) and fractionated through RP-C₁₈ columns into aqueous and organic fractions. These samples were submitted to three <i>in vitro</i> biological assays: inhibition of <i>Plasmodium berghei</i> growth, cytotoxicity against the human lung fibroblasts line MRC-5 and inhibition of hemozoin formation, according to previously described methodologies*. Chloroquine and artemisinin were references. Fractions were analyzed by HPLC-DAD-MS and some of them were identified by spectroscopic techniques. Selected samples were administered to mice to determine their parasite suppressive activity. Results and Discussion: Crude and organic fractions from <i>Niphates digitalis</i>, <i>Neofibularia nolitangere</i>, <i>Agelas cerebrum</i>, <i>Mycale laxissima</i>, <i>Niphates erecta</i>, <i>Clathria echinata</i> and <i>Polymastia nigra</i> showed IC₅₀ lower than 100 µg/ml. <i>A. cerebrum</i>, <i>N. erecta</i>, <i>C. echinata</i> and <i>P. nigra</i> showed the most promising <i>in vitro</i> antiprotozoal activities as they were the less cytotoxic for human cells. The best inhibition against hemozoin formation was displayed by <i>M. laxissima</i>. Known antimalarial compounds were identified in <i>A. cerebrum</i>, but the ion comparisons for the other active species with the Marinlit database revealed that no coincident molecules are present. Low available purity of the samples could be related to limited <i>in vivo</i> activity of the fractions. Conclusions: This is the first report of the study of antimalarial assessments for these sponge species collected in Cuba that demonstrated that promising compounds could be isolated. Further investigations may pursue to identify lead compounds. References: *Regalado E L., Mendiola J, Laguna A, Nogueiras C, Thomas O P. Polar alkaloids from the Caribbean marine sponge <i>Niphates digitalis</i>. Natural Product Communications 2010, in press.</p>
<p>PFE 026</p>	<p>PHYTOCHEMICAL AND TOXICOLOGICAL STUDY OF PROPOLIS IN THE TOWN OF CABAIGUÁN 2008 – 2009 Lorenzo Barrios, LM¹</p> <p>¹General Hospital, Cabaiguán, Sancti Spiritus, Cuba. Email: letty@dmsc.ssp.sld.cu</p> <p>Introduction: We conducted a cross-sectional pilot study (study phytochemical and toxicological studies) in the Agricultural Research Center, Central University of Villa Clara. In order to meet these tests were used two samples of propolis from the apiary located in the Agricultural Cooperative Martyrs Cabaiguán Neiva municipality, provided in the month of February, one of which had been collected previously and was in conditions that are not required for the substance and the other sample was collected at the time of the job. Materials and Methods: To characterize the propolis collected from the standpoint of photochemical and toxicological studies, independent variables were studied chemistry, acute toxicity, dermal and irritability irritability ophthalmic) respectively. The data were processed using statistical methods. Results and Discussion: The results were the phytochemical study of propolis recently collected evidence of the presence of metabolites, coumarins, triterpenes and / or steroids, resins, reducing sugars, phenolic compounds, tannins and amines, lipids and essential oils. Improperly stored in propolis only showed the presence of reducing sugars, resins, lipids and / or essential oils. Conclusions: The acute toxicity study results showed that the newly collected propolis was no fatality. However, in the toxic effects were improperly stored until death. The study of skin irritability possible to classify the product as slightly irritating. The study of ophthalmic irritability showed that propolis has no irritating effects.</p>
<p>PFE 027</p>	<p>ACUTE ORAL TOXICITY OF THE SOLANUM TORVUM PLANT (PRENDEJERA) Pérez L, Alfonso A, Betancourt J, Aguilera P, Salas H, Puente E, Mora Y. Cedeño N.</p> <p>Institución: Centro de Toxicología y Biomedicina. Toximed. Dirección: Km. 1 ½ Autopista Nacional. Teléfono: 641000, 643864. Santiago de Cuba. Cuba. email: bebe@toxi.scu.sld.cu ; antidotos@toxi.scu.sld.cu</p> <p>A rehearsal acute oral toxicity was carried out following the (CTA) Method of the Classes which constitutes an alternative trial to the conventional one; its advantage resides in the use of a smaller number of animals for the investigation. The rehearsal was applied in the decoction of the plant <i>Solanum torvum</i> with the objective of establishing possible organic and functional lesions in the pattern animals employed which were the Sprague Dawley rats. The administration was carried out via oral through a unique dose of 2000 mg kg of corporal weight. 48 hours post-administration, at not presenting any clinical signs of death of the trialed animals which evidenced an attributed toxicity to the substance under study; it was proceeded then to the observation, during 14 days. Being concluded that the evaluated substance did not produce any clinical signs which evidenced neither toxicity nor animal deaths; besides no alterations were reported in the corporal weight of the experimental models; also macroscopically, it was not observed any alterations</p>

	of diagnostic value; for those reasons, the decoction via oral used in an unique dose, it is framed as WITHOUT CLASSIFYING , in the animal pattern and dosage used under the observed experimental conditions.
PFE 028	<p>THE ANTI-INFLAMMATORY ACTION TO THE DECOCTION OF THE <i>SOLANUM TORVUM</i> PLANT Pérez L, Puente E, González Y, Larramendi D.</p> <p>Centro de Toxicología y Biomedicina. Toximed. Dirección: Km. 1 ½ Autopista Nacional. Teléfono: 641000, 643864. Santiago de Cuba. Cuba. email: bebe@toxi.scu.sld.cu ; antidotos@toxi.scu.sld.cu</p> <p>The need of obtain a new active principle for the treatment of inflammation as a sign of diverse illnesses is, at the present time, one of the challenges of most clinics investigations, and one of the sources of greater pharmacologic value are the medicinal plants. For such reason, a trial was conducted in search of the anti-inflammatory action to the decoction of the <i>Solanum torvum</i> plant, administrated orally to Spague Dawley rats, applying to them the Formalin test at 1%, in order to evaluate the variation of inhibitory answer of the inflammation to different doses used, describing the changes of clinical and physiological parameters after administration and establishing a dose-answer comparison of the positive control drugs used in the animal model under consideration. The anti-inflammatory activity of the evaluated plant decocted was divided in three experimental groups that received only one administrations of the product to a 600, 300, 150 mg/Kg's dose levels respectively, using the <i>Indometacina</i> and Ibuprofen as positive controls. The study result showed that the decoction of the <i>Solanum torvum</i> plant in a 600 mg/ Kg dose inhibits inflammation al a 72,03% without altering the clinical and physiological parameters, being the answer higher that the drugs used as positive controls. All of which makes us come to the conclusion that we are in the presence of a plant with proven anti-inflammatory properties that would be the base to become a new pharmaceutical product with this therapeutic property.</p>
PFE 029	<p>EVALUATION <i>IN VITRO</i> OF THE RADIOPROTECTOR EFFECT OF THE AQUEOUS EXTRACT OF <i>MANGIFERA INDICA</i> L (VIMANG) Rosario LA¹, Rodeiro I², Almeida E³, Leyva O⁴, Alonso A³, Rodríguez Y⁴, Arencibia DF⁵.</p> <p>¹Institute of Pharmacy and Food Science (IFAL, U.H), 27 avenue and 222 street. Lisa Municipality. Havana City. Cuba. email: lrosario@ifal.uh.cu, darencibia@finlay.edu.cu ²Center of Biopreped Marine (CEBIMAR), Loma street between 35 and 37 avenue. Plaza de la Revolución Municipality. Havana. Cuba. ³Center for Application and Development of Nuclear Energy (CEADEN), 30 street between 5th and 7th street. Playa Municipality. Havana City. Cuba. ⁴Center for Pharmacist Chemistry (CQF), 200 at 21 Ave. Playa Municipality. Havana City. Cuba. ⁵Researches Vicepresidency (Finlay Institute), 17 avenue between 198 and 200 street. Playa Municipality. Havana City. Cuba.</p> <p>Introduction: The natural product, Vimang to obtains starting from the bark of <i>Mangifera indica</i> L, it constitutes a interesting candidate for the character radioprotector evaluation if one keeps in mind that the pharmacological studies indicated that this product is effectiveness like antinflammatory, analgesic, immunomodulator and antioxidant, all characteristics of an ideal radioprotector. Material and Methods: The aim of this work was evaluated the radioprotector effect of the aqueous extract of <i>M. indica</i> L (Vimang), front gamma radiation, by means SOS chromotest bacterial assay (radiation doses were used 150 Gy) in the pre, co and post-treatment variants, as well as the lipid peroxidation inhibition assay and the mitochondria enzymatic activity of human red cells (radiation doses were used 250 Gy), that are the cells more affected during the radiotherapy sessions. Results and Discussion: The execution of the SOS Chromotest indicated that the extract is antigenotoxic against the ionizing radiations in the range of concentrations rehearsed in the pre variants and co-treatment without significant differences among them neither with the negative control, contrary to the post-treatment variant where the extract in study didn't show an effect radioprotector in the range of concentrations 50 - 500 g/mL. The realization of the human red cells assay indicated that evaluated product inhibits the lipid peroxidation, when it is used between 500 and 1 000 mg/mL and it diminishes the damages caused to the mitochondria and its enzymes, when being used in a similar range of concentrations. Conclusions: These results demonstrate that the extract is able to protect the nuclear material of the damages induced by the gamma radiations possibly to its antioxidant capacity (SOS chromotest assay, pre and co-treatment). Equally it was demonstrated that the extract also has protective effect at level of cellular membranes and mitochondrial enzymatic systems.</p>

PFE 030	<p>RHIZOPHORA MANGLE L. A PROMISSORY VEGETAL SPECIMEN BY THE DEVELOPMENT OF MEDICAMENTS BY HUMAN HEALTH Luz María Sánchez Perera, Octavio Fernández Limia, Dulce María Soler Roger, Arturo Escobar Medina, Janet Sánchez Calero, Tania Pérez Bueno, Betty Mancebo; Ada Ibis Regalado, Evangelina Marrero, Pastor Alfonso.</p> <p>National Centre of Animal and Vegetal Health, CENSA, Apdo. 10, CP 32 700, San José de las Lajas, La Habana, Cuba</p> <p>The wound healing of skin is a problem of first necessity because it affects to numerous population groups in the world. Actually, it was recognised the importance of Species reactive of Oxygen (EROs) in the physiology of divers humans illness and the action of several antioxidants in the prevention and treatment of cardiovascular illness, cancer, SIDA and include other associate to old process. The gastroduodenal ulcers affect a high percentage of world population with the important roll of <i>Helicobacter pylori</i> in the aetiology of this illness that produced a finding of news therapies who contribute of decreasing of recidivism and gastric cancer. The finding of pharmacological action in Natural Products use scientific validation of effectiveness and security has an actual and increasing roll in development and developing countries. For also it had been an alternative in the development of World Pharmaceutical Industry. <i>Rhizophora mangle</i> L. is a vegetal with high distribution in Cuba and Caribbean countries ant it has ethnopharmacological properties. National Centre of Animal and Vegetal Health had been studied this specie who contribute to theory and theological sustentation by the development of some drugs with this plant. CIKRON – H a liquid formulation and semisolid formulation registered in Human Medicine as antiseptic and wound healing. RHIZONAT, tablets to the treatment of gastroduodenal ulcers. The results obtain with these products give impact at they in Medical Pharmaceutics Industry, due to their security, effectiveness a relative low cost of production that permit the competitive with generic drugs. The present work contents an abstract of a high pharmacological evaluation in the development of these phytodrugs.</p>
PFE 031	<p>ETHNOPHARMACOLOGICAL AND PRECLINICAL STUDY OF DIURETIC EFFECT OF THE MOST USED PLANTS BY CUBAN POPULATION Pérez M¹, Boffill MA², Morón F³, Monteagudo E², Sueiro ML⁴, Lorenzo G⁵</p> <p>¹Vicerrector of Research. Medical Sciences University of Villa Clara. Circunvalation Rd. and Acueduct Rd. Santa Clara, Villa Clara, Cuba. P.O.: 50200. email:maykelpm@ucm.vcl.sld.cu ²Experimental Toxicology Unit. Medical Science University of Villa Clara. ³Medical Science University of Havana. Cuba ⁴Central University “Marta Abreu de las Villas”. Santa Clara. Villa Clara. Cuba. ⁵Molecular Immunology Centre. Villa Clara branch. Cuba.</p> <p>Introduction: There exists a wide number of synthetic drug which are used with diuretic purposes however, Cuban population has always used for the same goal, a variety of decoctions and infusions which have been taught generation from generation through an ethnobotanic approach. Materials and Methods: A preclinical study was carried aut to experimentally confirm the diuretic effect given to the main plants used by Cuban population. They were previously identified in an ethnopharmacological research. There were elaborated extracts, juices and decoctions from the ones reported as diuretic, which were orally administrated to a dose of 400 mg/Kg on the basis of determining the total solids to male albino rats weighing between 180 and 220 g. Dose was completed with physiologic saline solution to reach and hydrosaline overweight with a constant total volume of administration of 40 mL/Kg PV either for treated or control groups (positive, furosemide 20 mg/Kg; negative NaCl 0.9%) Urinary excretion during ½, 1, 2, 3, 4, 5 and 6 hours post administration was measured. Result and Discussion: Twelve plants were identified as the most reported by Cuban population taking into consideration their diuretic function. They were <i>Justicia pectorales Jacq.</i>, <i>Cassia alata</i> L., <i>Parthenium hysterophorus</i> L., <i>Ocimum basilicum</i> L., <i>Citrus aurantium</i> L., <i>Allium cepa</i> L., <i>Oreganum vulgare</i> L., <i>Costus pictus</i> D. Don, <i>Zantoxylum fagara</i> L., <i>Nectandra coriacea</i> (Sw), <i>Urera baccifera</i> L. and <i>Persea americana</i> Miller. <i>Ocimum basilicum</i> L., <i>Urera baccifera</i> L., <i>Persea americana</i> Miller., <i>Cassia alata</i> L. and <i>Zanthoxylum fagara</i> L. Each of them was submitted to experimental validation of the diuretic effect, <i>Persea americana</i> Miller and <i>Cassia alata</i> L. had high single dose diuretic effect. Conclusions: The action of <i>Persea americana</i> Miller and <i>Cassia alata</i> L was the most remarkable, showing a high activity and significant differences (p<0.05) in relation with the negative control group and a similar behavior to the reference used diuretic drug.</p>

<p>PFE 032</p>	<p>DIURETIC ACTIVITY OF THE MOST USED PLANTS BY CUBAN POPULATION Pérez M¹, Boffill MA², Morón F³, Monteagudo E², Sueiro ML⁴, Lorenzo G⁵</p> <p>¹Vicerrectorate of Research. Medical Science University of Villa Clara. Circunvalation Rd. and Acueduct Rd. Santa Clara, Villa Clara, Cuba. P.O.: 50200. email:maykelpm@ucm.vcl.sld.cu ²Experimental Toxicology Unit. Medical Science University of Villa Clara. ³ Medical Science University of Havana. Cuba ⁴ Central University “Marta Abreu de las Villas”. Santa Clara. Villa Clara. Cuba. ⁵Molecular Immunology Center. Villa Clara delegation. Cuba.</p> <p>Introducción: In Cuba exists about 179 medicinal plants which are known because of their diuretic properties according to their traditional use, although in just some cases their effects have been proved experimentally. To value the diuretic activity attributed in the most useful plants used by Cuban population: <i>Ocimum basilicum</i> L, <i>Parthenium hysterophorus</i> L, <i>Justicia pectoralis</i> Jacq, <i>Oreganum vulgare</i> L, <i>Allium cepa</i> L, <i>Citrus aurantium</i> L, <i>Cassia alata</i> L, <i>Zanthoxylum fagara</i> L, <i>Nectandra coriacea</i> Sw, <i>Costus pictus</i> D. Don and <i>Caesalpinia bahamensis</i> Lam. Material and Methods: Diuretic activity was studied using 8 experimental groups of 8 SD rats each which were fasted for 17 hours and water was suppressed one hour before the starting of the experiment. Extract administration was carried out by gavage (16 G cannula) at doses of 400 mg/kg BW (based on total solids) diluted in a total administration volume of 40 ml/kg BW intended to hyperhydrate the animals to simulate an oedema situation which is proved that enhance the evaluated substance response. Animals were placed in metabolic cages and accumulated urine volume was measured at ½, 1, 2, 3, 4 y 6 hours postadministration. At 6 hours of administration the urinary excretion, both action and diuretic activity were mathematically calculated. Results and discussion: Only 2 plants showed high diuretic activity: <i>Cassia alata</i> L (50.40±11.57 mL/Kg) and <i>Persea americana</i> Miller (54.68±13.47 mL/Kg), in both cases being superior to 0,90. Comparing with negative control, both plants differ statistically (p<0,05) which is evidenced in the increasing of excreted urine volume in both groups. When comparing those plants with positive control (furosemide, 20 mg/kg BW) the behaviour is similar (p>0,05). The 6 hours results are similar to those previously experimentally proved by our research group of <i>Boldoa purpurascens</i> Cav. (58,2±5.74 mL/Kg), <i>Carica papaya</i> (54,08 ±10,23 mL/Kg), <i>Bidens pilosa</i> (50,22 ± 7,72 mL/Kg), <i>Rhoeo spathacea</i> (47,98 ± 8,26 mL/Kg), <i>Costus cylindricus</i> (52,89 ± 9,57 mL/Kg) and <i>Capraria biflora</i> (42,71± 8,10 mL/Kg). Conclusion: We could notice that urine volumes increased in all groups were treated in relation to the negative control group. Diuretic activity was higher in experimental groups: <i>Cassia alata</i> L and <i>Persea americana</i> Miller, similar to the diuretic of reference.</p> <p>References: 1-Boffill MA. Plantas medicinales usadas en cuba con efecto diurético comprobado experimentalmente. Medicentro 2008;12(1) [serie en Internet]. 2008 Ene [citado 12 Feb 2010];11(2):[aprox. 4 p.]. Disponible en: http://www.vcl.sld.cu/sitios/medicentro/paginas%20de%20acceso/Sumario/ano%202008/v12n1a08/plantas81.htm 2- Boffil M, Lorenzo G, Monteagudo E, Sueiro M, Martínez Y, Matos J, Loy S. Diuretic Activity of five medicinal plants used popularly in Cuba. Pharmacology online. [serie en Internet]. 2006 Marz [citado 6 Ago 2007];3(1):[aprox. 7 p.]. Disponible en: 2007;11(1):2007:[aprox. 6 p.]. Disponible en: http://www.unisa.it/download/1966_145_226226808_40.Bofill.pdf</p>
<p>PFE 033</p>	<p>ETHNOPHARMACOLOGICAL VALIDATION OF PHANIA MATRICARIOIDES (SPRENG.) GRISEB Victoria MC¹, Morón F¹, García AI¹, Cabrera H¹, Morejón Z¹, López M¹, Frías AI², Delgado N², Boucourt E,¹ Acosta L,¹ Martínez MJ,¹ Bacallao Y,¹ Fuentes V³.</p> <p>¹ Central Laboratory of Pharmacology (LCF), Faculty of Medical Sciences “Dr. Salvador Allende,” Carvajal s/n entre Agua Dulce y A, Cerro, Havana City, CP 11200, Cuba. email: mcvictoria@infomed.sld.cu ² Faculty of Biology, University of Havana, Calle 25 entre H e I, Vedado, Havana City, Cuba. ³ Research Institute on Tropical Fruit Cultivation, Güira de Melena, Havana Province, Cuba.</p> <p>Introduction: Decoction of <i>Phania matricarioides</i> fresh aerial parts use to be administered traditionally for digestive and skin health problems. No published studies were found about this species. Materials and Methods: It was collected fresh aerial parts of the plant and a 30% decoction was made; a phytochemical screening was performed. Pharmacological studies were done in: writhing test induced by acetic acid (0.75%, 0.1 mL/10g); tail flick by water (55 °C) immersion (1, 5, and 10 g/kg, p.o.); <i>Croton</i> oil induced ear oedema (decoction 30%, 1 g/kg, p.o) and metanolic extract, 2 mg total solids dissolved in absolute ethanol, topic administration); intestinal transit (1, 5, and 10 g/kg, p.o.) in mice; and <i>in vitro</i> antimicrobial activity</p>

	<p>(decoction 50%, 100 µL/well) in <i>S. aureus</i>, <i>B. subtilis</i>, <i>E. coli</i>, <i>P. aeruginosa</i>, <i>K. pneumoniae</i>, <i>E. cloacae</i>, <i>C. albicans</i>. Toxicological study (decoction 50%) was done in acute toxic model (CTA) in rats (maximal volumen: 2 mL/100g) and dermal irritability (0.6 mL/patch) in rabbits. Results and Discussion: It was detected the presence of saponins, phenolic compounds, tannins, flavonoids, nucleus of flavonoids and catechins, quinones, compounds lactones, triterpenes and steroids, reducing sugars, and alkaloids. Decoction (5 and 10 g/kg p.o.) inhibited significantly nociceptive response in writhing test, but not in the tail flick model. Ear edema was decreased 43.72% orally and 42.5% topically; intestinal transit did not change; no inhibition zone was observed for microbial growth. CTA did not show deaths or toxicity signs, and there were no dermal edema or erythema. Conclusions: The results suggest that the traditional use of the aerial parts decoction for skin diseases may be supported by the topical antiinflammatory effect and the lack of acute oral toxicity and dermal irritability.</p>
<p>PFE 034</p>	<p>UNIVERSITY EXTENSION WORK ON THE USE OF MEDICINAL PLANTS SCIENTIFICALLY VALIDATED Martínez MJ, Boucourt E, López M, Morejón Z, Victoria MC, García AL, Morón F</p> <p>Central Laboratory of Pharmacology, “Salvador Allende” Faculty of Medical Sciences. Carvajal Street, between A and Agua Dulce, Cerro. Havana City, Cuba. CP 12000. email: juliama@infomed.sld.cu</p> <p>Introduction: The university extension work was carried out in order to support the actions for pharmaceutical and innocuousness of medicinal plants for traditional uses. It has been performed in the Elders Community that belongs to the Elders Club and to the University for Elders (UAM in Spanish) from the Lisa Municipality of the Capital. This project has been developing since 2003. Materials and Methods: Scientific knowledge was disseminated in the community by delivering theoretical and practical classes, creating medicinal plants gardens in schools and communitarian houses, promoting contests where popular knowledge acquired by the Elders were manifested and the distribution of a practical manual entitled “Caribbean Medicinal Plants for Primary Health Care” as complementary bibliography. Results and discussion: A number of 520 elders from the University extension branches (UAM in Spanish) and 2 Elders Clubs have been benefited with the scientific knowledge that guarantees the ethnobotanical use of medicinal plants for different health conditions in Primary Health Care. The main works developed are shown such as contest, dissertation, publications, medicinal plants gardens, and classes). Conclusions: The communitarian work on university extension has allowed increasing the knowledge about ethnopharmaceuticals based on a scientific basis in using medicinal plants to combat different diseases effectively and safely.</p>
<p>PFE 035</p>	<p>CYTOTOXIC ACTIVITY OF 1-O-ALKYLGLYCEROLS OF DIFFERENT CHAIN LENGTH.</p> <p>Marian Hernández, María Del Carmen Abrahantes, Yolanda Valdés, José Luis León</p> <p>Pharmacology and Toxicology Dept., Food and Pharmacy Institute. University of Havana. email: marianhc@uh.cu</p> <p>1-O-alkylglycerols have been studied from two decades ago in our country, due to their potential activity over inflammation, metastasis and angiogenic processes. Obtained by chemical synthesis in Basic Chemistry Department of Pharmacy and Food Institute, at University of Havana, their properties have been demonstrated by our workgroup. Their cytotoxic action appears to depend of carbonated chain length. The aim of this study was to evaluate the cytotoxicity of a family of alkylglycerols of different chain length in several cell lines to determine and compare their GI50 and TGI, and to analyze structure-activity relationship. That was carried out using sulphorrodamine B (SRB) assay, and the more cytotoxic candidate was selected for western blot protein determination (ERK, Akt, Caspase-3) and to evaluate cell cycle influence by flow cytometry. Our result showed that longer chain length favors cytotoxic activity of alkylglycerols, and the longest compound assayed showed apoptotic characteristics in melanoma and breast cells, by treating with GI50 concentration of alkylglycerol.</p>

<p>PFE 036</p>	<p>EVALUATION OF DIURETIC ACTIVITY FROM <i>Dichrostachys cinerea</i> (L.) Wight & Arn. LEAVES AND BARK AQUEOUS EXTRACTS Sueiro Oyarzun ML¹, Ribalta Ribalta V¹, González Armas Y¹, Hernández Barreto E¹</p> <p>¹Pharmacy Department, Chemistry and Pharmacy Faculty, Central University of Las Villas, Santa Clara City, Cuba. email: msueiro@uclv.edu.cu</p> <p>Introduction: Diuretics are drugs capable of increase of urine, so they are useful in the treatment of diseases related with the retention of fluids. <i>Dichrostachys cinerea</i> (L.) Wight & Arn. is commonly called “marabou” and belongs to the family <i>Fabaceae</i> is a deciduous thorny shrub or small rounded tree found in tropical and subtropical condition. Traditionally plants are used as vermifuge, dysentery, diuretics, headache, toothache, etc. but only a few of this effects has been experimentally valuated. The objective of this investigation was to experimentally proof the diuretic action of aqueous extracts of the dried leaves and bark of <i>Dichrostachys cinerea</i> in normal rats. Material and Methods: Primary phytochemical analyses were made to all extracts (leaves and bark). Diuretics effect was carried out in Wistar rats (170 – 210 g body weight (BW) using <i>in vivo</i> Lipschitz test model. The volumes of urine, urinary concentration of sodium and potassium ions and pH were the parameters of the study. Furosemide (20 mg/kg) and Hydrochlorothiazide (10 mg/kg) were used as positive controls. Aqueous extracts (leaves and bark) were administered to experimental rats orally at doses of 200, 400 and 800 mg/kg BW. Results and Discussion: Urine volume was significantly (p<0.05) increased by 400 and 800 mg/kg doses of aqueous all extract (leaves and bark) in comparison to Hydrochlorothiazide (positive control). While the excretion of sodium was increased by all extracts, potassium excretion was only increased by the aqueous extract (leaves and bark) at doses of 400 and 800 mg/kg. There was no significant change in pH values. Conclusions: We can conclude that aqueous extracts (leaves and bark) of <i>Dichrostachys cinerea</i> at doses of 400 and 800 mg/kg produced notable diuretic effect which appeared to be comparable to that produced by the reference diuretic hydrochlorothiazide.</p>
<p>PFE 037</p>	<p>PHOTOPROTECTIVE EFFECT <i>PHYLLANTHUS ORBICULARIS</i> HBK IN <i>E. COLI</i> CELLS. Vernhes M¹, González-Pumariega M², Alonso A¹, Baly L¹, Menck C.F.M³, Sánchez-Lamar A².</p> <p>¹ Center of Technological Applications and Nuclear Development (CEADEN), Street 30. No 502, e/ 5 and 7, Miramar, Playa, Havana City CP 6122, Cuba. email: mariolys@ceaden.edu.cu ² Department of Vegetable Biology, Faculty of Biology, Havana University. Street 25 No 455, e/ I and J, Vedado, Havana City CP 10400, Cuba. ³ Department of Microbiology, Institute of Biomedical Science, University of Sao Paulo, Av. Prof Lineu Prestes, 1374, Sao Paulo, SP, 05508-900, Brazil.</p> <p>Over recent years, the incidence of various sickness and disorders related to solar ultraviolet (UV) irradiation has increased alarmingly. Most of these diseases are associated to the genotoxic effects of this radiation. The main UV-induced DNA lesions are pyrimidine dymers. Among UV wavelengths, UVC radiation is one of the most aggressive to DNA. One approach to protect human health against the harmful effects of UV radiation is to use natural products, such as photoprotectors. In this work, we evaluated the protective effect of plant extract <i>Phyllanthus orbicularis</i> HBK in <i>E. coli</i> cells against UVC light-induced damage. A fluorescent version of SOS assay was used and UVC dose was 5 J/m². Increasing extract concentrations were assessed (0.01-2.0 mg/ml). Different approaches in order to elucidate possible antigenotoxic mode were performed. Cells were treated with extract before, during and after UVC irradiation (A) and otherwise, after UVC irradiation cells were incubated in the presence of plant extract (B). The percentages of remaining genotoxicity (%RG) and the colonies formed from irradiated cells treated and not with extract were determinate. For approaches A and B the genotoxicity induced by UV radiation was significantly decreased at 0.1-2.0 mg/ml and 0.01-1.0mg/ml respectively. Also, the clonogenic capacity of cells was increased. The results indicated that <i>Phyllanthus orbicularis</i> extract is able to protect the <i>E. coli</i> cells against UVC radiation. This protective effect could related with the DNA repair's systems. Also the bioantimutagenic capacity of this extract against UV radiation was demonstrated.</p>

<p>PFE 038</p>	<p>PRECLINICAL TOXICOLOGICAL VALIDATION OF MEDICINAL PLANTS FROM CUBA AND THE CARIBBEAN López M¹, Morejon Z¹, Martínez MJ¹, Boucourt E¹, Garcia AI¹, Bacallao Y¹, Fuentes V², Acosta L¹.</p> <p>¹Central Laboratory of Pharmacology, Faculty of Medical Sciences Dr. Salvador Allende. " Carvajal s / n e / A and Agua Dulce. Cerro. Ciudad de La Habana, CP 12000, Cuba. ²Fruit Station. Guira de Melena. Havana Province. email: marisolb@infomed.sld.cu</p> <p>Introduction: Medicinal plants are widely used by the population of our country as well as in the Caribbean zone. Because of this and as part of TRAMIL this work aims to scientifically validate the toxicological safety of their use. Materials and Methods: The parts of the plants to be evaluated were collected, botanical identification was made, as well as the preparation of herbarium/voucher specimens; plants selected were the following: <i>Annona squamosa</i> L. (Sugar apple), <i>Annona reticulata</i> L. (Custard apple), <i>Citrus aurantium</i> L. (Sour orange), <i>Citrus aurantifolia</i> (Christm.) Swing (lemon), <i>Cordia martinicensis</i> (Jacq) Roem. & Schult, Mill <i>Foeniculum vulgare</i> (fennel), <i>Lepidium L. virgicum</i> (Cress), <i>Psidium guajava</i> L. (Guava), <i>Solanum americanum</i> Mill (nightshade), studies of acute oral toxicity by the method of CTA and repeated dose and acute dermal studies irritability, depending on the traditional use of the plant. Results: None of the plants studied in oral toxicity tests showed clinical signs or symptoms, except in the case of the aerial parts decoction of repeated doses of <i>Lepidium virgicum</i> L. in which one animal died. In the case of skin irritation symptoms was only found slight erythema and edema in the application of natural juice from the fruit of <i>Citrus aurantifolia</i> (Christm.) Swing. Conclusions: We demonstrated the safe use of medicinal plant extracts studied oral and topical, just throwing the <i>Lepidium virgicum</i> L a low toxicity and <i>Citrus aurantifolia</i> (Christm.) Swing mildly irritating.</p>
<p>PFE 039</p>	<p>MARINE BIOACTIVE SUBSTANCES: ITS EFFECTS OVER INMUNE SYSTEM, INFLAMMATION AND PAIN Llanio, Mirtha. email: llanio@infomed.sld.cu</p> <p>Marine bioactive substances have few years of discovery, and have been little explored. However, in this time several actions have knowledge of marine compounds over different systems and diseases. One of they targets are leucocytes cells and therefore acts over inflammation diseases and pain. We are going to summaries our explanation through Manoalide actions because was the first one discovery and which have been more research, but others marine isolated compounds also acts over inflammation and pain. Manoalide is a sesterterpene isolated from the marine sponge <i>Luffariella variabilis</i> which inhibits irreversiblement phospholipase A₂ enzyme from different sources as bee, rattlesnake and cobra venom, human synovial, etc. This compound inhibits phospholipase C isolated from guinea pig uterus in a calcium-dependent manner, and has effect on calcium levels reducing the increase of cytosolic free calcium in human polymorphonuclear leukocytes (PMNs), it is an inhibitor of calcium channels too. Manoalide inhibits arachidonic acid release in human neutrophils. Adhesion is also affected with a decrease in the surface expression of MAC-1 in human monocytes. This compound also inhibits the release of IL-1β and TNFα from LPS-stimulated human monocytes. The inhibition of eicosanoid release by Manoalide has been demonstrated in different cellular systems. Thus Manoalide decrease the release of LTs and PAF from human neutrophils and the production of PGE₂ in murine macrophages. This marine compound potently inhibits the generation of superoxide from PMA-stimulated rat PMNs. All these actions could explain the anti-inflammatory and analgesic activity of Manoalide which inhibits PMA-induced mouse ear oedema and zymosan-induced peritoneal writhing in mice.</p>
<p>PFE 040</p>	<p>ANTIOXIDANT ACTIVITY AND GENERAL TOXICITY OF HIDROALCOHOLIC EXTRACTS OF EUCALIPTUS ROBUSTA L. BARK Vega N, Ojito K*, Rivero A and Domínguez D</p> <p>Department of Biology. Faculty of Agricultural Science. Central University "Matha Abreu" of Las Villas. Carretera a Camajuani, km 5.5, Santa Clara, Villa Clara, Cuba. email:kojito@uclv.edu.cu</p> <p>Introduction: Recent works confirm the importance of natural antioxidants in the protection against chronic and degenerative disorders caused by oxidative stress. Flavonoids are secondary metabolites of plants with low toxicity and a great antioxidant effect. In the last years they have received a great attention because of their potentialities as drugs. Eucalyptus belonging to Myrtaceae family, is native from Australia, and contains around 600 species. His leaves content flavonoids, phenolic acids and aldehydes</p>

	<p>with antioxidant activity. One of the specie most represented in Cuba is <i>Eucalyptus robusta L.</i> This study was focused on the characterization of flavonoids in hidroalcoholic extracts of <i>Eucalyptus robusta L.</i> bark. Materials and Methods: The <i>E.robusta</i> bark was dried and crushed to obtain a powder. The methanolic and ethanolic extracts (1:20 w/v in both cases) were obtained by ultrasonication and vacuum filtration. Later, the flavonoids were identified by TLC (thin layer chromatography) and HPLC. The total content of flavonoids was determined by the assay $\text{NaNO}_2\text{-AlCl}_3$ using quercetine as standard. The antioxidant activity was determined by the free radical scavenger activity of the 2-2'-azino-bis (3-ethylbenziazoline-6-sulfonic acid) (ABTS) using quercetine and ascorbic acid as standards. An assay of general toxicity of the extracts was performed with <i>Artemia salina</i>. Results and Discussion: The extracts showed by TLC and HPLC the following flavonoids classes: flavonols-3-glicosydes, flavones, flavones without 5-OH and 3, 5-metoxilated flavonols. Ethanolic extracts exhibited the higher values in total flavonoids content (8.87 mg quercetine/ml of extract). The antioxidant activity was elevated in all the extracts and close to that obtained in this condition for quercetine, besides this activity was bigger than ascorbic acid. Neither of the extracts shows high general toxicity ($\text{LD}_{50} > 1000 \text{ mg/ml}$) towards <i>Artemia salina</i> larvae. Conclusions: Our work shows that eucalyptus bark has a great diversity in flavonoids classes with an improved antioxidant activity and low toxicity.</p>
<p>PFE 041</p>	<p>ANTIPROLIFERATIVE AND CYTOTOXIC EFFECTS OF DEFENSIVE SECRETIONS AND A SYNTHETIC ANALOGUE, FROM MILLIPEDE <i>RHINOCRICUS DUVERNOYI</i>. Mora González N¹, Ferrer Carmenates G¹, Casado Hernández I¹, Tacoronte Morales JE², Tiomno Tiomnova O² and Leyva Simeón JL².</p> <p>¹Centro de Inmunología y Productos Biológicos (CENIPBI), Universidad de Ciencias Médicas de Camagüey. Carretera Central Oeste s/n, Apartado Postal 150. CP 70100, Camagüey. Cuba. Email: nestor@iscmc.cmw.sld.cu ²Centro de Ingeniería e Investigaciones Químicas (CIQ). Vía Blanca, e/ Palatino e Infanta, Cerro. CP 12000, Ciudad de La Habana. Cuba.</p> <p>Introduction: Identification of agents with pharmacological activity against cancer has depended largely on the screening of natural products and their analogs. The aim of this study was to evaluate the antiproliferative effects of defensive secretions from Cuban millipede specie <i>Rhinocricus duvernoyi</i> and 2-methyl-3-methoxybenzo-1,4-quinone, a synthetic analogue of one of the majors metabolites identified in the secretions. Material and Methods: Millipedes were collected from several geographic regions of Cuba. Cytotoxicity was assayed by MTT [3-(4,5-dimethylthiazol-oyl)-2,5-diphenyltetrazolium bromide] and Neutral Red Uptake methods. The cells lines employed were T-47D (human breast carcinoma), SK-mel-3 (human melanoma) and Vero (African green monkey kidney derived cell line). Cytotoxicity of secretions extracts was determinated at 50, 100, 200 and 400 $\mu\text{g/mL}$ and benzoquinone was evaluated at eight different concentrations in the range of 69,4–350 $\mu\text{mol/L}$, employing a decimal geometric dilution. DNA damage was evaluated by <i>in vitro</i> Comet Assay and apoptosis induction was determined by analysis of DNA fragmentation in agarose electrophoresis. Results and Discussion: An evident antiproliferative effect was found in the extracts of defensive secretion of millipede in SK-mel cell line. Synthetic 2-methyl-3-methoxybenzo-1,4-quinone inhibited the growth of SK-mel and Vero cells markedly, while T47D cell line was much more resistant to cytotoxic effect of the benzoquinone. The method of Neutral Red Uptake was more sensitive than MTT to evaluate antiproliferative activity of the benzoquinone. DNA fragmentation as preliminary signal of apoptosis, was showed in SK-mel and Vero cells but not in T-47D. The resistance of cell line T-47D to cytotoxicity and DNA fragmentation induced by 2-methyl-3-methoxybenzo-1,4-quinone could be influenced by p53 status, since T-47D is mutated in p53 gene. Genotoxicity assays showed DNA damage induced by the benzoquinone in all cell lines. Conclusions: The results showed that defensive secretion of millipede <i>Rhinocricus duvernoyi</i> and 2-methyl-3-methoxybenzo-1,4-quinone exhibits significant antiproliferative activities <i>in vitro</i>.</p>
<p>PFE 042</p>	<p>SENSITIVE ASSAY SYSTEM ANTIVIRAL TO DETERMINED THE CAPACITY OF NATURAL PRODUCTS AGAINST HERPES SIMPLEX VIRUS TYPE 1 AND TYPE 2 Monteagudo R¹, Fidalgo O¹, Bolaños G¹, Echemendía O¹, Almora E¹, Lago V¹.</p> <p>¹Institute "Finlay". 27 Ave No. 19805, La Lisa, A.P. 16017. Cod. 11600. Havana City, Cuba. Teléfonos: 271-8221, 271-8177. email: rmonteagudo@finlay.edu.cu</p> <p>Introduction: Traditionally hundred of plants in the world have been used in the medicine to combat the viral infections. Different natural products can be employed as a therapeutic alternative against the</p>

	<p>infections caused by herpes simplex virus. In the present study is described a highly sensitive assay system for in vitro evaluation of antiherpes simplex virus agents using 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyltetrazolium bromide (MTT) and African green kidney (Vero) cells. Material and Methods: Confluents Vero cells were infected with either herpes simplex 1 virus (HSV-1) strain and herpes simplex 1 virus (HSV-2) strain of 100 CCID₅₀ in the presence of various concentrations of test natural compounds. The optical density of formazan was used to determine cell viability. The 50% cytotoxic concentration (CC₅₀) and the 50% antiviral effective concentration (EC₅₀) of the test compound were calculated. Results and Discussion: A total of 11 extracts derived from different plant species were studied. Four plants extracts were found to have antiviral activity. The results indicate that this MTT assay is useful for screening anti-HSV-1 and anti-HSV-2 agents.</p>
<p>PFE 043</p>	<p>PROTEOMIC ANALYSIS OF THE VENOM FROM THE SCORPION <i>RHOPALURUS JUNCEUS</i> Rodríguez R¹, Corona F², Zamudio F.Z², L.D. Possani², C.V.F. Batista²</p> <p>¹Centro de Desarrollo de la Montaña (CDM), Limonar, El Salvador, Guantánamo, Cuba. email: rodolfo@cdm.gtmo.inf.cu Department of Molecular Medicine and Bioprocesses, Institute of Biotechnology, National Autonomous University of Mexico, Avenida Universidad, 2001, Apartado Postal 510-3, Cuernavaca 62210, Mexico</p> <p>Introduction: The Nipe - Sagua - Baracoa mountainous area extends for the whole oriental end of Cuba. One of the distinctive features of this area is their scorpions and high endemic grade, constituting the territory of bigger biological diversity of the country with significant values in the landscape order and of conservation. This communication reports the chemical and biological characterization of peptides present in the venom of the Cuban scorpion <i>Rhopalurus junceus</i>. Materials and Methods: The venom of <i>R. junceus</i> was obtained by electrical stimulation, from scorpions collected from four geographically isolated localities in Macizo Nipe Sagua Baracoa (2). The soluble venom was directly submitted to an analytical C18 reversed phase (HPLC). The fractions obtained were performed for LC-MS/MS. Results and discussion: Fractions of the entire chromatogram were collected for molecular mass determination. In this venom 42 different molecular mass components were identified, are included the mass finger print (MFP) analysis earlier obtained from the soluble venom. The results of the HPLC separation of components obtained from the soluble venom of the Cuban scorpion <i>R. junceus</i>, their molecular masses and the most relevant amino acid sequence data obtained. By simply inspection and comparison of these data with those available in the literature for this venom (1). Conclusions: A critical analysis of data obtained by mass spectrometry is a fast, not too expensive and reliable method to isolate and identify a particular peptide from a complex venom mixture of an unknown related species of scorpion. Another interesting conclusion concerns the evidence that among related species of scorpions of the genus <i>Rhopalurus</i> many components have similar sequences and functions.</p> <p>References: (1). Rodríguez de la Vega, R.C., Possani, L.D., 2005. Overview of scorpion peptides specific for Na⁺ channels: biodiversity, structure-function relationships and evolution. <i>Toxicon</i> 46, 831–844.</p>
<p>PFE 044</p>	<p>ANTI-INFLAMMATORY ACTIVITY OF A NEW EXTRACTS OF <i>Pedilanthus tithymaloides</i> (L.) Poit López González T¹, Bermúdez Camps IB¹, Padró Rodríguez L¹.</p> <p>¹Pharmacy Department of the Orient University, Patricio Lumumba s/n, prolongación de Quintero, Santiago de Cuba, Cuba. email: tlopez@cnt.uo.edu.cu</p> <p><i>Pedilanthus tithymaloides</i> (L.) Poit, is a tropical American plant with a reported wide range of healing properties, namely emetic, anti-inflammatory, antibiotic, antiseptic, antihemorrhagic, antiviral, antitumoral, and abortive. In Cuba, this species, known as Itamorreal, is traditionally used as a tincture in the treatment of stomatological infections, as stomatitis and gingivitis, but so far, its empirical use was not yet supported by scientific studies. In the present study air dried stems and leaves of <i>P. tithymaloides</i> were powdered with a blender and macerated with EtOH solution. The obtained suspension was decanted, washed with the extraction solvent, filtered, and the final volume gauged to 100 mL to obtain a tincture of pH 7.8, refraction index 1.35, and density 0.98, and total solids 2.2% w/v. The extract was evaluated using the rat paw oedema assay to supplant for carrageenan to the doses of 250, 750 and 1000 mg / kg of corporal weight. Were administered the Indomethacin (10 mg/kg) as positive control, and EtOH solution as negative control respectively. The results observed in the rat paw oedema assay showed a significant inhibitory activity of the tincture in carrageenan induced paw inflammation, for the administrated doses of</p>

	<p>500, 750 and 1000 mg/kg without being observed adverse effects. The results of the present investigation suggest that the anti-inflammatory activity of the tincture of <i>P. tithymaloides</i> used in Cuban traditional medicine, and recognized by the Ministry of Health (MINSAP), could be explained, at least in part, by their antioxidant properties.</p> <p>Key words: extracts, <i>Pedilanthus tithymaloides</i>, anti-inflammatory activity.</p>
PFE 045	<p>ANTIOXIDANT PROPERTIES OF <i>DICHROSTACHYS CINEREA</i> (MIMOSACEA) LEAVES AND BARK</p> <p>Ribalta V¹, Hernández E¹, Torres L¹, Sueiro M¹, Armas Y¹</p> <p>¹Pharmacy Department, Chemistry and Pharmacy Faculty. Central University of Las Villas. Santa Clara, Villa Clara. Road to camajuani km 5 ½. email:venancior@uclv.edu.cu</p> <p>Introduction: The objective of this study was to evaluate the effects of <i>D. cinerea</i> in antioxidant test.</p> <p>Materials y Methods: <i>Plant material:</i> Leaves and bark were collected in the forest surrounding Botanical Garden of Central University of Las Villas. Plant sample was identify as <i>Dichrostachys cinerea</i> (Mimosaceae) by Orestes R. Méndez a taxonomic expert of above Institution and deposited under register code UCLV- 9493. The collected leaves and bark were washed with distilled water and stored at 38 °C until dried.</p> <p><i>Phytochemical procedure:</i> Aqueous (AE) and methanolic (ME) extracts were obtain by following method. AE: 30 g of dry powder boiled with distilled water (100 ml) in a balloon for 5 minutes, ME: 30 g of dry powder was macerated with 100 ml methanol (80%) for 48 hours. Alls extracts were filtrate, evaporate and residues keep were refrigerated. Preliminary chemical composition of AE and ME was determinate as previous reported (Adikay, 2009). <i>Total phenolic compounds determination:</i> Total phenols content was determinate as Galic acid equivalents (GAE) method (Yen, 2008). <i>Antioxidant properties of D. cinerea:</i> The DPPH method was used as previous reported (Ohinishi, 1994) with slight modification. Different doses of leaves and bark ME and AE were tested, rutin and ascorbic acid were used as positive control.</p> <p><i>Statistics:</i> Values are expressed as means ± S.E.M. One-way Anova test was used for statistical analysis, with <i>P</i> < 0.05 considered significant. Results and Discussion: <i>Phytochemical screening:</i> The positive results was found for flavonoids, tanins, saponins and mucilage for AE, and flavonoids, coumarins, tanins, saponins and steroids for ME. <i>Total phenolic compounds determination:</i> Highest phenolic contents were observed for methanolic (69 mg/g) and aqueous (49 mg/g) extracts of leaves than bark (ME: 16 mg/g, AE: 4.4 mg/g).</p> <p><i>Antioxidant activity:</i> The leaves ME and AE antioxidant activity was higher than all bark extracts at same doses, and also was similar that rutin and ascorbic acid in 25-100 ug/ml dose range.</p> <p>Conclusions</p> <p>In conclusion this study showed as first time the powerfull antioxidant activity of <i>D. cinerea</i> extracts and demonstrate that this plant possess potential health benefits on different diseases related with oxidative stress.</p> <p>References</p> <ol style="list-style-type: none"> Adikay, S., B. Koganti, and K. Prasad. Effect of alcoholic extract of roots of <i>Dichrostachys cinerea</i> Wight-Arn against cisplatin-induced nephrotoxicity in rats. <i>Natural Product Radiance</i>, 2009. 8(1):12-18. Yen, G.C. Hsieh, C.L. Antioxidant activity of extracts from <i>Du-zhong</i> (<i>Eucommia ulmoides</i>) toward various lipid peroxidation models in vitro. <i>Journal of Agricultural and Food Chemistry</i>, 1998. 46: 3952–3957. Ohinishi M., et al. Inhibitory effects of chlorogenic acids on linoleic acid, peroxidation and haemolysis, <i>Phytochemistry</i>, 1994. 36: 579-583.
PFE 046	<p>DNA DAMAGE IN NMRI MICE TREATED WITH THE AQUEOUS EXTRACT OF THE MARINE PLANT <i>Thalassia testudinum</i></p> <p>Ansoar Rodríguez Y¹, Díaz Llera S¹, Frión Herrera Y¹, Morffi Figueroa J¹, Rodeiro Guerra I², Menéndez Soto del Valle R², Martínez D²</p> <p>¹Departamento de Farmacología y toxicología, Instituto de Farmacia y Alimentos, Universidad de la Habana, Ave. 25 e/ 214 y 222, La Lisa, Ciudad Habana, Cuba. email: yansoar@uh.cu; sdllera@infomed.sld.cu</p> <p>²Centro de Bioproductos Marinos, CEBIMAR, Loma 37, Vedado, Ciudad Habana, Cuba.</p> <p>Introduction: <i>Thalassia testudinum</i> is a marine plant traditionally used in Cuba as antiinflammatory agent and to healing up burns. Phytochemical studies have revealed that polyphenols are the main constituents of <i>T. testudinum</i> aqueous extract (TAE) such as Thalassiolins A, B, C, proantocianidins, catequines and p-</p>

	<p>hydroxi-benzoic acid), followed in lower quantities by steroids, triterpenoids and saponins. The present study evaluates the genotoxic activity of TAE in hepatocytes of both sexes NMRI mice using the comet assay and correlates this endpoint with the levels of malondialdehyde (MDA). Materials and Methods: Experimental groups (n=7 for both sexes) were: TAE (2000 mg/kg p.c., i.g.) during 24, 48 and 72h; distilled water i.p. (as solvent control, i.p.), ciclophosphamide (40 mg/kg p.c., i.p.). After treatment a sample of hepatic tissue was obtained from each animal and processed to obtain dispersed hepatocytes which were processed for comet assay. A blood sample was also taken to determine MDA level in serum. Results and Discussion: TAE induced increasing frequencies of DNA damage with respect to duration of treatments in female animals. Strands breaks also increased in male mice after 24 and 48 h but decreased after 72 h after treatment. The treatments significantly reduced MDA levels in serum. Conclusions: TAE shows genotoxic activity in hepatocytes of treated mice and it is probably due to one or several of its phytochemical components although not associated with oxidative damage.</p>
<p>PFE 047</p>	<p>GENOTOXICITY AND RADIOPROTECTION OF NEMOROSONE THROUGH SOS Chromotest Frión Herrera Y¹, Almeida E², Diaz Llera S¹, Ansoar Rodríguez Y¹, Morffi Figueroa J¹, Cuesta Rubio O³.</p> <p>¹Departamento de Farmacología y Toxicología, Instituto de Farmacia y Alimentos, Universidad de la Habana, Ciudad de La Habana, Cuba. email: sdllera@infomed.sld.cu ²Centro de Aplicaciones Tecnológicas y Desarrollo Nuclear. Ciudad de La Habana. Cuba ³Departamento de Farmacia, Instituto de Farmacia y Alimentos, Universidad de la Habana, Ciudad de La Habana, Cuba.</p> <p>Introduction: Increasing efforts are directed toward finding applications for natural products and their derivatives in the treatment of human diseases. Nemorosone is a polyisoprenylated benzophenone isolated from <i>Clusia rosea</i> floral resins and the major constituent of brown Cuban propolis which has cytotoxic activity against different tumor cell lines. Genotoxicity and radioprotection against gamma radiation of this natural product were evaluated using the bacterial assay SOS Chromotest. Materials and Methods: The nemorosone concentrations tested ranged from 0.1 to 2 mg/mL. Nemorosone pretreated cells were irradiated at a dose of 150 Gy. SOS response induction factor (FI) and percentage of remanent genotoxicity (%GR) were calculated after treatments. Results and Discussion: FI values indicated no genotoxic effect of nemorosone at the evaluated concentrations. A dose dependent decrease of %GR with increasing concentrations of nemorosone suggests a protective activity of this propolis' constituent against gamma radiation. Radioprotective activity evaluation in mammals cells are in process. Conclusion: Nemorosone has a potent radioprotective activity in bacterial cells.</p>
<p>PFE 048</p>	<p>IN VIVO ACUTE AND 28 DAYS SUBCHRONIC STUDIES OF MANGIFERIN Prado Y¹, Rodeiro I², Pérez C¹, Merino N³, Arencibia A⁴, Duque Y³, Benferano C⁴, Delgado R³</p> <p>¹Faculty Medicine Science: Dr. Enrique Cabrera, Pharmacology Department, Habana City, Cuba. email: maryviz@infomed.sld.cu ²Marine Bioprepared Center, Pharmacology Department, Havana City, Cuba. email: idania.rodeiro@infomed.sld.cu ³ Biomolecular Chemistry Center(CQB), Natural Products Department, Havana City, Cuba. ⁴ Hematology and Immunology Institute, Havana City, Cuba.</p> <p>Introduction: Mangiferin, 1,3,6,7-tetrahydroxyxanthone-C2-₂-D-glucoside, is one polifenol of natural origin of the xanthone derivatives and C-glucosylxanthones (<i>Mangiferina indica</i> L.). This compound presents well documented anti-oxidant properties, anti-diabetic, anti-HIV, anti-cancer, immunomodulatory, antialergic and anti-inflammatory. The safety Mangiferin was assessed in acute and 28 days a subchronic studies, with objective to evaluate its toxic potencial of substance in roedores. Material and Methods: A single dose acute study of mangiferin was administered 200 and 2000 mg/kg by oral gavage (v. o.), and by i.p. through the acute classic method. A 28 days subchronic study of mangiferin was administered 250, 500 and 1000 mg/kg by oral gavage (v. o.) and one group with vehicle, that studies included mincronucleus genotoxicology test. Results: Oral and i.p (200 mg/kg) administration of Mangiferin did not show any sings or clinic symptoms, hystopathological damage neither in the acute essay. There was not evidence of weight variation in rats, although there was a little weight decrease in mice. No animal death by this essay. On the other hand (2000mg/kg), via i.p. occur small weight changes in both rats and mice. Cornerment, piloerection, spontaneous motor activity decrease, slanting eyes was observed. Liver damage (steatosis) in the highest dose was founded. All mice and two rats (1F and 1M) died. A 28 days of subchronic study (250, 500, 1000mg/kg bw/day, oral gavage) in rats reported no significant adverse effects in mortality,</p>

	<p>signs and clinical symptoms, clinical chemistry, and hematology. The histopatologic analysis demonstrated pancreatic damage in the doses 1000mg/kg in almost all animals of both sex. Mangiferin 1000mg/kg dose through assay micronucleus in bone marrow erythrocytes in subchronic study induced statistically significant increases in micronucleated PCEs as compared to vehicle controls in both sex. Conclusions: The results this toxicological evaluation demonstrated that more clinical essays must be done to proof the safety of the product.</p> <p>Key words: Mangiferin, toxicologic evaluation, subchronic essay, micronucleus test, acute toxic classes</p>
<p>PFE 049</p>	<p>ANTIOXIDANT, ANTI-INFLAMMATORY AND CYTOTOXIC ACTIVITY OF EXTRACTS AND FLAVONOIDS OBTAINED FROM <i>Phyllanthus orbicularis</i> HBK (<i>Euphorbiaceae</i>) Gutiérrez Gaitén Y¹, Miranda Martínez M¹, Martínez Vázquez M², Figueroa Hernández JL³, Bello Alarcón A¹, López Pérez R¹.</p> <p>¹Instituto de Farmacia y Alimentos, Universidad de la Habana, Ave 23 e/ 214 y 222 # 21425, C.P. 13600, La Coronela, La Lisa, Ciudad de la Habana, Cuba. email: ygutierrez@infomed.sld.cu, yamiletgg@ifal.uh.cu</p> <p>²Instituto de Química. Universidad Nacional Autónoma de México, Circuito exterior, Ciudad Universitaria, Coyoacán, C.P. 04510, México, D.F.</p> <p>³Facultad de Medicina. Universidad Nacional Autónoma de México, Circuito exterior, Ciudad Universitaria, Coyoacán, C.P. 04510, México, D.F.</p> <p>Introduction: <i>Phyllanthus orbicularis</i> HBK is a Cuban endemic plant. From the biological point of view it have antiviral activity against human hepatitis B virus, herpes simplex virus type 1 and 2, bovine herpes, as well as antimutagenic and antioxidant properties. With the purpose of enlarging the knowledge about the therapeutic potential of this plant, we present here a research on the antioxidant, anti-inflammatory and cytotoxic activity of extracts and isolated flavonoids from this vegetable species. Materials and Methods: Antioxidant activity was carried out through FRAP and Superoxide Radical Scavenger Activity techniques. Anti-inflammatory activity evaluation was carried out using TPA model in mouse ear. Cytotoxic activity was evaluated using Sulforhodamine B (SRB) method in human cancer lines (colon, breast, leukemia, CNS, prostate and lung). Results and discussion: Methanolic extract show the biggest antioxidant activity, significantly higher than vitamin C and similar to the standard (DOS). In TPA model the methanolic acetilate and hexanic extracts had bigger anti-inflammatory effect (59.80 and 42.74% respectively) compare to AcOEt and MeOH extracts. Rutin decaacetate and Quercetin (flavonoids) were the ones that show inhibition percentages above 50% (64.12 and 66.80% respectively). Results in SRB model evidenced that methanolic acetilate extract was more active in CNS (100%), breasts (72,48%) and lung (79,00%) lines. The hexanic extract was selective toward breast cellular line (56.57%), the other extracts didn't have appreciable activity. Rutin decaacetate, Quercetin and Quercetin pentaacetate had activity on all the cell lines evaluated with inhibition percentages between 62.8 and 100%. Conclusions: Methanolic extract was the one who evidenced higher antioxidant activity. In TPA assay, methanolic acetilate and hexanic extracts, rutin decaacetate and quercetin were those that showed higher anti-inflammatory activity; in SRB model the methanolic acetilate and hexanic extracts were active, being selective toward some cellular lines, however, Rutin decaacetate, Quercetin and Quercetin pentaacetate were active on all the assayed lines.</p>
<p>PFE 050</p>	<p>EFFECT OF D-004, A LIPID EXTRACT FROM <i>ROYSTONEA REGIA</i> FRUITS AND OMEGA-3 IN THE FORCED SWIMMING TEST IN MICE Carbajal D¹, Ravelo Y¹, Molina V¹, Mas Rosa¹ and Arruzazabala ML¹.</p> <p>¹Center of Natural Products, National Center for Scientific Research, Ave 25 and 158, Cubanacán, P.O 6880, Havana City, Cuba. email: yazmin.ravelo@cnic.edu.cu</p> <p>Introduction: Depression is one of the main causes of morbidity and mortality in the adult population. There are several pharmacological options to treat depression. Fish oil rich in fatty acids omega-3 (FAω3) has been shown to produce some benefits for treating depression. D-004, a lipid extract obtained from Cuban royal palm (<i>Roystonea regia</i>) fruits containing a mixture of free fatty acids, has shown a moderate antidepressant effect in animal models. This study was aimed to compare the effects of D-004 with FAω3 in a forced swimming test model in mice. Material and Methods: Male mice were randomized into six groups (12 mice per group): one control group treated with vehicle, two treated with D-004, at 250 and 500 mg/kg, two with FAω3 (250 and 500 mg/kg) and a reference group intraperitoneally injected with</p>

	<p>imipramine (10 mg/kg). D-004, FAω3 and vehicle were orally administrated by gastric gavage during 15 days. Immobility time assay was performed. Results and Discussion: All treatments (D-004, FAω3 and Imipramine) significantly reduced immobility time as compared to control group. No significant differences between the same doses of D-004 and FAω3 were found. Conclusions: D-004 and FAω3 were similarly effective for reducing the immobility time in the forced swimming test in mice.</p> <p>Key words: D-004, <i>Roystonea regia</i>, fatty acids omega-3 (FAω3), depression, forced swimming test.</p>
PFE 051	<p>TRADITIONAL USE OF PLANTS IN THE POPULATION OF SANTA CLARA'S MUNICIPALITY. Bermúdez del Sol A¹, Kanga F², San Gabino Y¹</p> <p>¹Medical Sciences University "Dr. Serafín Ruiz de Zárate Ruiz". Centre for Studies, Documentation and Information of Drugs. Aqueduct Road, Santa Clara City, Villa Clara, Cuba. CP 50200. ²Pharmacy Department. Central University of Las Villas, Santa Clara City, Villa Clara 54830. email: ydanellysp@ucm.vcl.sld.cu , ydanelly78@yahoo.es, abdelbs@ucm.vcl.sld.cu</p> <p>Introduction: Ethnobotanical studies constitutes the baseline for the development of programmes forwarded to obtain maximum knowledge about the use of traditional medicine, the enrichment of culture and the best use of the medicinal plants patrimony. Survey methods are generalized for this type of investigation, taking into account that the selected sample reach the most notable knowers of the zone. The objective of this work is to identify the plants traditionally used by the population of Santa Clara city.</p> <p>Materials and Methods: A field investigation which included 7 neighborhoods from Santa Clara's municipality in the province of Villa Clara was carried out. Survey method was employed where a questionnaire was elaborated and validated including the classical and required elements for this type of study. The questionnaire was applied to people from both urban and rural neighborhoods applying an intentional sampling to select key informers (salesmen and quacks of each zone) which included both sexes of different ages.</p> <p>Results and Discussion: The 102 surveys applied showed a total of 98 medicinal plants, grouped in 91 species, belonging to 57 families from those the most represented were <i>Lamiaceas</i> , <i>Rutaceas</i> and <i>Asteraceas</i>. Most used parts from plants were leaves (58%) and roots (10%) followed by fruits, flowers and seeds. Most cited preparation form was decoction.</p> <p>Conclusion: There were identified the principal plants traditionally used by the population of Santa Clara city which were attributed therapeutical properties for diverse pathological conditions.</p>
PFE 052	<p>EVALUATION OF <i>IN VITRO</i> ANTIFUNGAL SUSCEPTIBILITY OF G-1 AGAINST FILAMENTOUS FUNG Morales Y¹, Medina R¹, García M¹, Hidalgo P¹, Casanova M¹.</p> <p>¹Chemical Bioactive Center. Carretera a Camajuaní km 51/2 Santa Clara Villa Clara Cuba. email: yennyymm@uclv.edu.cu</p> <p>Introduction: The demonstrate activity of 2-bromo-5-(2-bromo-2-nitro-vinil)-furano (G-1) against <i>Trichophyton sp.</i> and <i>Microsporium spp.</i> has risen the interest for know his "<i>in vitro</i>" activity against filamentous fungi detected in ocular infections due to they can infect the eye in a opportunistic situation. For this reason were determined the Minimum Inhibitory Concentration (MIC) and the Minimum Fungicidal Concentration (MFC) of this product against 25 isolates of molds (<i>Aspergillus spp.</i>, <i>Fusarium spp.</i>, <i>Cladosporium spp.</i> and <i>Trichoderma spp.</i>).</p> <p>Material and Methods: The antifungal susceptibilities tests were evaluated by a broth macrodilution method approve for the Clinical and Laboratory Satandards Institute (CLSI) in his M38-A rule. The inoculum size was adjusted with a Neubauer chamber.</p> <p>Results and Discussion: The range of MICs were between 2-16 μg/mL. The MFCs values concur with MICs values in the 100% of them. The lowest MICs (2μg/mL) were shown in a isolate of the genu <i>Fusarium sp.</i> and <i>Cladosporium sp.</i>.</p> <p>Conclusions: In this study was demonstrated the "<i>in vitro</i>" activity of G-1 against isolates of filamentous fungi with environmental and agricultural origin that can cause ocular mycoses.</p>
PFE 053	<p>ANTIOXIDANT AND NEUROPROTECTIVE EFFECTS OF BM-21 EXTRACT FROM <i>Thalassia testudinum</i>, ON ACRYLAMIDE INDUCED NEUROTOXICITY IN MICE Morales RA, García T, Garateix A, Fernández MD, Palmero A, Regalado EL, Laguna A, Menéndez R</p> <p>Centro de Bioproductos Marinos, Agencia de Medio Ambiente, Ministerio de Ciencia, Tecnología y Medio Ambiente, La Habana, Cuba. email: roberto.menendez@infomed.sld.cu</p>

	<p>Acrylamide (ACR) is neurotoxic to experimental animals and humans. Several processes, such as peripheral and central axon swelling, inhibition of axonic transport, deficient intracellular energy production, etc, have been implicated in its neurotoxicity. Recently, there is evidence demonstrating that oxidative stress is also involved. BM-21 an aqueous ethanolic extract from the marine plant <i>Thalassia testudinum</i> leaves contains polyphenols (18.0 ± 1.5 %) and among them, thalassiolin B is the main component (5.8 ± 0.3%). Previous studies have demonstrated that both, BM-21 and thalassiolin B exerted skin protective and DPPH scavenging activity. All these prompted us to probe the extract for its antioxidant effects and its neuroprotective action against ACR-induced neurotoxicity in mice. <i>In vitro</i> studies showed that BM-21 scavenged OH[•] (IC₅₀ 0.167 mg.ml⁻¹), ABTS^{•+} (IC₅₀ 0.143 mg.ml⁻¹), O₂^{•-} (IC₅₀ 0.154 mg.ml⁻¹) and RO₂[•] (IC₅₀ 0.131 mg.ml⁻¹) and inhibited spontaneous (IC₅₀ 0.018 mg.ml⁻¹) and metal induced lipid peroxidation (IC₅₀ 0.091 mg.ml⁻¹) in brain homogenates. <i>In vivo</i> studies showed that subcutaneous administration of ACR (70 mg.kg⁻¹) for 4 weeks progressively induced neurological and systemic toxic symptoms. However, administration of BM-21 (40 and 400 mg.kg⁻¹, p.o.) during ACR treatment significantly prevented weight lost, death and abnormalities in behavioral indexes (gait score and rota-rod test). Besides, BM-21 significantly prevented the ACR-induced decrease in sciatic nerve conduction velocity and compound action potential amplitude and the increase in latency and duration. Our results also showed that BM-21 (400 mg.kg⁻¹) significantly attenuated the ACR-induced increase of total hydroperoxides and prevented the reduction of GSH and SOD, GR and GPx activities in the sciatic nerve. Also, brain antioxidant status was increased after BM-21 administration. In conclusion, our results showed that treatment with BM-21 antagonized the effects induced by ACR towards the normal value of controls. This effect may be either direct by inhibiting lipid peroxidation and scavenging free radicals or indirect by enhancing the endogenous antioxidant enzymes.</p>
PFE 054	<p>NEUROPROTECTIVE EFFECTS OF BM-21, EXTRACT FROM <i>Thalassia testudinum</i>, ON FOCAL ISCHEMIA IN RATS García T¹, Rivera F², Dajas F², Morales RA¹, Garateix A¹, del Vallín T¹, Merino N³, Palmero A¹, Regalado EL¹, Laguna A¹, Menéndez R¹ ¹Centro de Bioproductos Marinos. Agencia de Medio Ambiente, Ministerio de Ciencia, Tecnología y Medio Ambiente, La Habana, Cuba. ² Instituto Clemente Estable, Uruguay. email: roberto.menendez@infomed.sld.cu</p> <p>Our results have previously demonstrated that oral pretreatment with BM-21 (200 and 400 mg.kg⁻¹) protects against global cerebral ischemic injury in gerbils. Human cerebral ischemia most often results from a transient or permanent occlusion of the middle cerebral artery (MCA). Thus, MCA permanent or transient occlusion in rats is considered the animal model to more closely mimic the clinical situation. In consequence, the protective effects of the oral administration of BM-21 (400 mg.kg⁻¹) were investigated in permanent middle cerebral artery occlusion (pMCAO)-induced focal cerebral ischemia in rats. Our results showed that serial administration of the extract; once-a-day for 9 days prior to ischemia, decreased infarct volume (77.5 %; p<0.003), cerebral edema (66.9 %; p<0.006) and neurological signs 24 h after ischemia. In the histopathological study, no cell damage was evident by the cresyl violet staining in the cerebral cortex and striatum regions of sham-operated rats whereas in ischemic animals extensive neuronal loss was found. However, neuronal damage was markedly decreased by treatment with BM-21 being mostly comparable with rats without ischemia. Stress oxidative parameters were also examined. Twenty four hours after occlusion brain total SOD activity and GSH content were significantly reduced while MDA concentration was increased. However, BM-21 significantly improved all these parameters. Besides, oral administration of BM-21 to normal rats following the same dosage schedule increased the resistance of brain homogenates to “in vitro” kainate and metal-induced lipid peroxidation. Taken together, the present results sustain those previously observed in global ischemia in gerbils and indicated that BM-21 markedly reduced brain infarction, neuronal injury and significantly improved behavioral outcomes during focal ischemia in rats. As evidenced by our results it seems likely that BM-21 enhanced the antioxidant status of brain and hence decreased the extent of neuronal damage produced by the oxidative stress and lipid peroxidation in focal ischemia.</p>
PFE 55	<p>ANAMU (<i>Petiveria alliacea</i> L.), AN IMMUNOSTIMULANT MEDICINAL PLANT Lemus Z¹, Hung M¹, Batista A², De la Guardia O³, Alfonso A² ¹ Pharmaceutical Laboratory “Oriente”, Prolongation of Fifth Street s/n, “30 de Noviembre”, Santiago de Cuba city, Cuba. email: zoe@lfo.quimefa.cu</p>

	<p>² Toxicology and Biomedicine Center, Autopista Nacional km 1 ½, Santiago de Cuba city, Cuba. ³ North Infantile Hospital “Juan de la Cruz Martínez Maceira”, Ninth Street s/n, Sueño, Santiago de Cuba city, Cuba.</p> <p>Introduction: For the benefit of the immunodepressed patient in our country by means of an oral immunostimulant medication of natural origin, it was established as a main objective of the present work to demonstrate the capacity of the medicinal plant of traditional use named in Cuba as Anamú (<i>Petiveria alliacea</i> L.) to reinforce the immune system, considering that it is a very abundant and sustainable natural resource in Cuba and many other countries of Tropical America, and so it can be used as the base of a drug tablet.</p> <p>Material and Methods: There was realized a wide bibliographical revision of topics like etnomedicine and preclinical trials reported about Anamú (<i>Petiveria alliacea</i> L.) and in addition several experimental studies were carried out in our country with regard to the immunopharmacology and toxicology of the medicinal plant. At the end the pharmaceutical development of the tablet was attacked, using methods of experimental design to arrive to the formulation prototype, validated by means of a pharmaceutical chemical study in which thin layer chromatography and spectrophotometric methods were used. Results and Discussion: The etnomedical and preclinical reports obtained from the literature and our proper pharmacological and toxicological experimental studies confirmed the efficacy of the plant Anamú (<i>Petiveria alliacea</i> L.) as an specific Immunostimulant herbal drug and the security of its employment at the dose levels utilized in the tablet. So too the results obtained in the pharmaceutical development of the tablet allowed to corroborate the quality of this dosage form, as well as its stability, checked by one year under ambiental conditions. Conclusions: The significance of the results obtained led to the approval of the product Tablets of Anamú for its Registration as a Medication of Natural Origin for Human Use by the Center for the State Control of the Medications of Cuba (CECMED).</p>
PFE 056	<p>CITOPROTECTIVE EFFECTS OF BM-21 “IN VIVO” IN TWO HEPATOTOXICITY MODELS Hernández I¹, Rodeiro I¹, Morales RA¹, Merino N², del Vallín T¹, Martínez D¹, Rodríguez AT³, García A¹, Palmero A¹, Lagunas A¹, Regalado EL¹, Menéndez R¹</p> <p>¹Departamento de Farmacología, Centro de Bioproductos Marinos. email:cebimar@infomed.sld.cu . CITMA, Agencia de Medio Ambiente. Loma y 37, Vedado. Ciudad de la Habana. ² Centro de Investigaciones y Evaluaciones Biológicas. IFAL, UH. ³ Laboratorio Clínico, Hospital Salvador Allende. MINSAP.</p> <p>In recent years naturally occurring herbal compounds such as phenolic acids, flavonoids, and high molecular weight polyphenols have gained considerable attention as citoprotective agents. BM-21, an aqueous-ethanolic extract of the marine plant <i>Thalassia testudinum</i>, content phenolic compounds. Accordingly, we have previously found that BM-21 prevented the <i>in vitro</i> <i>ter</i>-butylhydroperoxide induced cell damage in rat hepatocytes. The extract reduced the rise in malondialdehyde (MDA) production and the significant depletion of cellular reduced glutathione (GSH). This suggests that the citoprotective effect <i>in vitro</i> involved, at least partially, an antioxidant action of the BM-21. In the present work we studied the <i>in vivo</i> hepatoprotective effects of the extract in two models of hepatotoxicity in mice. In the model of death by paracetamol BM-21 reduces the mortality induced by this agent. Thus, single intraperitoneal administration of paracetamol (1 g.kg⁻¹) produced about 90 % mortality while single (50 - 500 mg.kg⁻¹) 90 min prior to paracetamol administration) and repeated at similar doses (once-a-day for 15 days) oral pre-treatment of animals with BM21 significantly reduced the death rate. Maximal protection occurred at a dose of 100 mg.kg⁻¹. Amelioration of cellular injury was evident by the H & E staining. Also, the extract significantly reduced MDA and GSH liver content. In the model of Acrylamide (ACR) the extract administered together with the hepatotoxic agent at a dose of 400 mg.kg⁻¹, revealed hepatoprotective activity as is obvious from biochemical studies. BM-21 diminishes significantly the mortality, body weight lost and the activity of serum GPT and GOT and reduced MDA, total hydroperoxides and GSH concentration in liver. In conclusion, our present results showed that BM-21 behaved as a citoprotective agent at the level of the hepatic tissue after single and repeated oral administration. The hepatoprotective effects observed in both experimental models is likely to be related to its antioxidative properties since after their administration the extract normalized the values of MDA, HPT and GSH in the hepatic tissue.</p>

<p>PFE</p> <p>057-131</p>	<p>PHARMACOLOGICAL BIOMODELS / BIOMODELOS FARMACOLOGICOS</p>
<p>PFE 057</p>	<p>EVALUATION OF SPRAGUE DAWLEY RATS AS BIOMODELS TO DETECT DAMAGE ON DNA IN LEUKOCYTES OF PERIPHERAL BLOOD AND HEPATIC CELLS, BY MEANS OF THE COMET ASSAY <u>Vidal A</u>¹, Arencibia DF², Rosario LA³.</p> <p>¹Faculty of Biology, Havana University (U.H). 25 avenue between H and J street. Plaza de la Revolución. Municipality. Havana City. Cuba. email: alexis.vidal@infomed.sld.cu ²Researches Vicepresidency (Finlay Institute), 17 avenue between 198 and 200 street. Playa Municipality. Havana City. Cuba. ³Institute of Pharmacy and Food Science (IFAL, U.H), 27 avenue and 222 street. Lisa Municipality. Havana City. Cuba.</p> <p>Introduction: The induction of strand breaks (SB) or alkali-labile sites formation on DNA have been parameters broadly used for the genotoxicity detection and their implications have been demonstrated in degenerative illnesses, the cancer, and recently linked to the oxidative stress. This article had as objective to carry out a comparison to the spontaneous basal frequency and induced with cyclophosphamide, the induction of strand breaks or alkali-labile sites formation on DNA of leukocytes of peripheral blood and hepatic cells of Sprague Dawley rats of both sexes, by means of the Comet Assay. Material and Methods: We administered 10 rats/sex/group for 14 days, using a negative control group (not administered), two substance-vehicle controls and positive control cyclophosphamide administered with 50 mg/kg, by intraperitoneal route. The last time of administered was performed the alkaline electrophoresis them gel individual cells from leukocytes of peripheral blood and hepatic cells to demonstrate the possible damage to the DNA. Results and Discussion: Under our experimental conditions it is more feasible the biomodels utility in the determinations of damage in leukocytes of peripheral blood in both sexes; with significant differences when comparing the results starting from the hepatic cells. Also our encouraging results with the use of the cyclophosphamide, allowed us to affirm that it is possible to use this mutagen in the induction of damage in the primary structure on DNA. Conclusions: These rat line constitute a good <i>in vivo</i> experimental model to demonstrate the primary damage in the DNA given the low spontaneous frequency of the analyzed indicators. Also this study will allow to use the best procedure for genotoxicity studies by means of the Comet assay, in drugs that have not still been evaluated in this thematic.</p>
<p>PFE 058</p>	<p>GASTRIC IRRITATION OF SODIUM DICLOFENAC: COMPARATIVE STUDY OF SLOW-RELEASE FORMULATION IN RABBITS <u>Lagarto A</u>, Bueno V, Martínez A, García R, Lara M, Fernández A, Gabilondo T, Valdés O, Carrillo C, Montero C.</p> <p>Drug Research and Development Center. CIDEM. 17 No. 6208 e/ 62 y 64, Playa, código postal 11300, Ciudad Habana, Cuba. email: alicia@cidem.sld.cu</p> <p>The aims of the study was to evaluate the gastric irritation potential of a slow-release Cuban formulation of sodium diclofenac comparatively with the import product, by means of an acute test and repeated dose test in New Zealand rabbits tried with an oral dose of 59 mg/kg. National formulation of diclofenac produced slight gastric irritation in the acute test. This result was similar to the observed with Voltaren. The administration of national formulation of diclofenac for 5 days in rabbits produced gastric irritation. We observed gastric mucous erosion similar to the Voltaren treated group. The effects causes by both formulations on the gastric and duodenal mucous were similar in the acute test and repeated dose test, being feasible the employment of the national slow-release formulation in clinical rehearsals.</p>
<p>PFE 059</p>	<p>SCIENTIFIC, REGULATORY AND ETHICAL CONSIDERATIONS FOR INCREASING EFFICIENCY IN PLANNING NON-HUMAN PRIMATE TOXICOLOGICAL STUDIES OF PHARMACEUTICALS <u>Casacó A</u>¹, Beausoleil I¹, Gonzalez B², Luaces P¹, León A², Arteaga ME², Prado P³, Rodríguez V³, Pérez A⁴, Guevara G⁴, Bada AM², Ledón N¹, Fuentes D², González C², Hernandez O², Orphee R², Blanco D², García-Osuma M², Ballester-Labrada A⁵.</p>

	<p>¹Centro de Inmunología Molecular. ²CEMPALAB. ³Centro de Neurociencias de Cuba. ⁴CIMEQ. ⁵Centro de Investigaciones Clínicas, Havana, Cuba. email: casaco@cim.sld.cu</p> <p>Introduction: The purpose of this study is to better characterize the hematological, biochemical, respiratory, cardiovascular and electroneurophysiological parameters in young adult <i>Cercopithecus aethiops sabaesus</i> of both sexes. The rhesus and cynomolgus monkeys are widely used as experimental primate models. However, only few articles have been published testing toxicological effects of pharmaceuticals on African green monkey. Furthermore, some non-clinical toxicological guidelines recommend histopathological data to support the safety of the drug for all non-rodent toxicology studies.</p> <p>Material and Methods: The present study was carried out with the recompilation of all parameters recorded before the first drug administration in five sub-chronic or chronic toxicological studies performed on 66 <i>Cercopithecus aethiops sabaesus</i>, born in Cuba.</p> <p>Results and Discussion: This study provides hematological, biochemical, respiratory, cardiovascular and electroneurophysiological data for both, choosing animals to be included into experiments and monitoring these parameters during the study. Conclusions: We conclude that this study provides valuable integrated data for determining the health status, including electroneurophysiological parameters, data not previously reported for this species, of the African green monkey.</p> <p>References: Casacó A, Beausoleil. Considerations for reducing the euthanasia procedure in toxicological studies of biopharmaceuticals using non-human primates. <i>Toxicology</i>, 264: 131-133, 2009. Casacó A, Beausoleil, et al. Hematological, biochemical, respiratory, cardiovascular and electroneurophysiological parameters in African green monkeys (<i>Cercopithecus aethiops sabaesus</i>). Its use in non-clinical toxicological studies. <i>Journal of Medical Primatology</i>, 39 Issue 3: 177-186, 2010.</p>
PFE 060	<p>ANALGESIC ACTIVITY OF NEW COMPOUNDS IN EXPERIMENTAL ANIMAL MODELS AND “in vitro” TESTS López-Sacerio A¹, Marrero-Ponce Y¹, Tytgat J²</p> <p>¹Pharmacy Department. Chemistry- Pharmacy Faculty. Central University of Las Villas. Carretera a Camajuaní km 5.5, CUBA. email: areyls@uclv.edu.cu ²Toxicology Lab. KU Leuven. Belgium</p> <p>Introduction: Pain is the most frequent nursing diagnosis and the most common problem for which patients asks for help on clinical services. So, the search for new alternative analgesics drugs is required. Main goal of this work is to evaluate the possible analgesic activity of new compounds by means of <i>in vivo</i> and <i>in vitro</i> tests. Materials and Methods: To this end, four compounds at the doses of 100, 150 and 200 mg/kg were evaluated for the antinociceptive activity using the hot plate and acetic acid induced abdominal constrictions in mice. Analgesic activity was also evaluated using patch clamp technique in <i>X. laevis oocytes</i> and the whole-cell currents from oocytes were recorded from 1 to 2 days after injection. For the expression in <i>Xenopus oocytes</i> the mNa_v/pLCT vector was linearized with NotI. Results: The results of the analyses showed significant analgesic activity in all the models studied. Finally, the electrophysiological recordings are indicative for the existence of interactions between Na_v 1.6 channel and our compounds. Conclusion: We conclude that the four compound are involved in the analgesic answer and are useful for the treatment of painful conditions.</p>
PFE 061	<p>SYSTEMIC AND SKIN TOXICITY IN SPRAGUE DAWLEY RATS TREATED DURING 26 WEEKS WITH CIMAVAX-EGF VACCINE Mancebo A¹, Casacó A², González B¹, Ledón N², Sorlozabal J², León A¹, Gómez D¹, González Y¹, Bada AM¹, González C¹, Ramirez H²</p> <p>¹National Center for Laboratory Animals Breeding (CENPALAB), Habana, Cuba. email: axelm@cenpalab.inf.cu ²Center of Molecular Immunology (CIM), Habana, Cuba</p> <p>Introduction: CIMAvax-EGF consists of human recombinant Epidermal Growth Factor (EGF), coupled to P64k, recombinant carrier protein from <i>N. meningitis</i>, and Montanide as adjuvant. The vaccine immunization induces specific antibody production, inhibiting the EGF/EGF-R interaction through EGF deprivation. The objective of this study was to determine if rat is a relevant species for studying of CIMAvax-EGF vaccine and to assess the CIMAvax-EGF toxicity in SD rats after intramuscular administration of repeated doses (6 months). Materials and Methods: Rats were randomly distributed into</p>

	<p>four groups: Control, Control plus adjuvant, Treated with 1X and 15X of human total dose. Animals were immunized weekly during 9 weeks, plus 9 immunizations every 14 days. Rats were inspected daily for clinical signs. Body weight, food and water consumption, and rectal temperature were measured during the administration of doses. Blood samples were collected for hematological, serum biochemical determinations and EGF titles at the beginning, three months, and at the end of experimentation. Gross necropsy and histological examination of tissues were performed on animals at the end of the assay. Results and Discussion: Vaccine provoked the apparition of antibodies against EGF in the rats, demonstrating rat species relevance in these studies. CIMAvax-EGF and the vehicle produced clinical signs of toxicity in the administration site. Neither body weight gain nor food and water consumption were affected. Vaccine induced neutrophil elevation and some biochemical alterations. Conclusions: This study showed evidences that weekly intravenous administration during 26 weeks of CIMAvax-EGF at doses up to 15x human dose is well tolerated in rats and it has a clinical importance since this long lasting study in relevant species allows to treat cancer patients with tumours during long periods with relative weight safety margin.</p>
<p>PFE 062</p>	<p>THE MOUSE AS BIOMODEL IN GENOTOXICITY ASSAYS, TWO YEARS OF EXPERIENCE, FINLAY INSTITUTE, CUBA Arencibia DF¹, Rosario LA², Vidal A³.</p> <p>¹Researches Vicepresidency (Finlay Institute), 17 avenue between 198 and 200 street. Playa Municipality. Havana City. Cuba. email: darencibia@finlay.edu.cu ²Institute of Pharmacy and Food Science (IFAL, U.H), 27 avenue and 222 street. Lisa Municipality. Havana City. Cuba. ³Faculty of Biology, Havana University (U.H). 25 avenue between H and J street. Plaza de la Revolución. Municipality. Havana City. Cuba.</p> <p>Introduction: For the evaluation of new products is necessary to know the frequency of spontaneous and induced variables studied in genetic toxicology in the biomodel used. The aim of this work was to evaluate and to compare the spontaneous and induced indexes in mice of both sexes of Balb/c, NMRI, OF-1 and C57/BL6/cenp lines keeping in mind the epididymal sperm concentration, spontaneous frequency of sperm heads abnormal, number of erythrocytes in bone marrow with micronuclei, cytotoxicity index (ratio of young erythrocytes / mature erythrocytes), total of cells with structural chromosome aberrations, mitotic index (number of cells at the stage of division metaphase cell) and the percentage of peripheral lymphocytes undergoing DNA damage as level 1, 2, 3, 4 from low to high damage. Material and Methods: This study was carried out for to determine the most efficient line, on the base of the significant appearance of lower spontaneous indexes and high induced indexes to mutagenic substances like the cyclophosphamide in the comet alkaline <i>in vivo</i> assay, micronuclei assay, chromosome aberrations assay and sperm head morphology assay according to the standardized protocols and adjusted by Arencibia <i>et al.</i> 2009 and 2010. Results and Discussion: We obtained as a result that the Balb/c line in both sexes differs significantly with the other lines where they met the highest lower and induced spontaneous indexes with cyclophosphamide, keeping in mind the measured indicators. Also the line C57/BL6/cenp was the less efficient and less sensitive one to the mutagen, being obtained the lowest higher and induced spontaneous results. Conclusions: This work will allow using the best line of mice like biomodel in the genotoxicity and antigenotoxicity assay according to low spontaneous indexes and sensibility to detect mutagenic substances in a narrow range, being used these assays in the evaluation of natural products, drugs and vaccines.</p>
<p>PFE 063</p>	<p>WHITE LEGHORN POULTRY AS BIOMODELS IN PRECLINICAL STUDIES OF CANCER VACCINE Fuentes D¹, Machado Y², Arteaga ME¹, Ocaña R¹, García A¹, Suárez E², Pérez R², Montero E².</p> <p>¹National Center for Laboratory Animal Breeding (CENPALAB). Finca Tirabeque km 2 ½ Carretera a Cacahual, Bejucal, Havana, Cuba. email: dasha@cenpalab.inf.cu ².Center of Molecular Immunology (CIM). 216 Street & 15, Playa, Havana, Cuba.</p> <p>Introduction: Animal models offer a system that enables a better understanding of basic biological questions. The understanding of cancer vaccines immunopharmacology is rather limited. Variables such as optimum vaccine doses, schedule of administration, routes of administration, and booster frequency, would foster their clinical development. Gangliosides are sialic acid containing glycosphingolipids that are ubiquitously distributed on vertebrate plasma membranes. The 1E10 (Racotumomab) is a monoclonal anti-</p>

	<p>idiotype tumor vaccine against an IgM mAb, named P3 that reacts specifically with NeuGc-containing gangliosides. Ab3 antibodies were not detected in the sera of mice treated with 1E10 mAb, but 1E10 antibodies were detected in the sera of humans and chickens. For this reason, the main objective of this work was to evaluate the advantage of White Leghorn poultry as biomodels in preclinical studies of cancer vaccine.</p> <p>Material and methods: We explored the influence of vaccine doses, schedule of administration and booster frequency on the antibody response in chickens. Animals were primed in one, two or four anatomical sites simultaneously. Doses from 400 µg (1×), 800 µg (2×) and 1600 µg (4×) equivalent of the 1E10-Alum vaccine were administered. Boosting studies were performed administering 400 µg (1×) equivalent of the 1E10-Alum vaccine. Antibodies were determined by ELISA assays. Pre-immune serum was used as negative control. Results and Discussion: Priming with four times the 1E10-Alum dose increment the specific antibody response demonstrable since 2 weeks after the antigen challenge and 2 weeks later, surprisingly, a dose resulting suboptimal administered at a single site, induced a robust immune response if fractionated to be administered in four sites. These results evidenced that optimizing immunopharmacological determinants contribute to earlier, stronger and prolonged anti-1E10 antibody persistence. Conclusions: It demonstrates the potential optimization of the vaccine using White Leghorn poultry as biomodels in preclinical studies.</p>
<p>PFE 064</p>	<p>EVALUATION OF SPRAGUE DAWLEY RAT AS BIOMODEL IN TWO ANTIGENOTOXICITY ASSAYS Moreno D¹, Arencibia DF², Rosario LA³.</p> <p>¹National Center of Biosafety, 28 street, number 502, between 5th and 7th avenue. Playa Municipality. Havana City. Cuba. email: davis@orasen.co.cu, darencibia@finlay.edu.cu ²Researches Vicepresidency (Finlay Institute), 17 avenue between 198 and 200 street. Playa Municipality. Havana City. Cuba. ³Institute of Pharmacy and Food Science (IFAL, U.H), 27 avenue and 222 street. Lisa Municipality. Havana City. Cuba.</p> <p>Introduction: The new drugs discovery with antigenotoxic effect constitutes in our days a prioritized line of research. Reason why the researchers has headed to the <i>in vivo</i> biomodels development which it is carried out the damage in a consistent form. Material and Methods: In this article we decide to evaluate the Sprague Dawley rats in both sexes as biomodel in the induction of the primary structure damage on DNA by means of alkaline comet assay and the induction of micronuclei in bone marrow cells by cyclophosphamide and bleomycin. Which were formed 5 experimental groups per sex, the first administered with NaCl 0,9 % by intraperitoneal (i.p) route, the second and third groups were administered with cyclophosphamide by i.p route, with designs of different treatments at doses of 50 mg/kg. The fourth and fifth groups were administered with bleomycin by i.p route, equally in two designs of different treatments at doses of 40 mg/kg. Results and Discussion: At the end of the experience bigger induction of the strand breaks (SB) or alkali-labile sites formation on DNA damage was obtained with the use of the cyclophosphamide and bleomycin, both in the design of 48 and 24 hours administration before the sacrifice. This constitutes under our experimental conditions the two better experimental designs to increase in a considerable forms the frequency spontaneous present in this species of rat. In the mironucleis assay was obtained high results of induction with the use of cyclophosphamide was administered 48 and 24 hours before sacrifice in both sexes. That which constitutes in our experimental conditions the best design to induce the micronucleis formation in bone marrow cells of rats, increasing considerably the spontaneous frequency to present in this species. Conclusions: These results are useful in studies of drugs evaluation that they have not been explored in to the <i>in vivo</i> antigenotoxicity and genotoxicity environment.</p>
<p>PFE 065</p>	<p>REGULATORY ASPECTS ON THE TOXICOLOGICAL EVALUATION OF THERAPEUTIC VACCINES DESTINED TO THE TREATMENT OF CANCER Rodriguez J</p> <p>National Center Coordinating of Clinical Trials, 200 at 21 Ave, Atabey, Playa, Havana City, Cuba. email: julian@cencec.sld.cu</p> <p>Introduction: Given the high index of mortality that presents the cancer and the lack of therapeutic alternatives to give solution to this problem of health, it has brought the necessity to develop new treatment options for the patient with cancer. Inside these, the therapeutic vaccines constitute one of the most novel therapies, being located inside the first investigation lines that are developed at the present time. For such</p>

	<p>a reason the Objective of this work is to offer a general panoramic on the main regulatory requirements of toxicological evaluation for therapeutic vaccines dedicated to the treatment of the cancer</p> <p>Materials and Methods: An extensive bibliographical search was carried out using upgraded sources like magazines, specialized books and Internet of which were extracted guidelines, regulations related with the topic development of medications. Results and Discussion: As results of the revision 20 normative (10 of the EMEA, 6 of the FDA, 2 of the ICH, 1 of Cuba and 1 of the OMS) were consulted. In the 2009 the ICH incorporated inside its guidelines of security the guide S9 in which it's settle down the main preclinical requirements that should contemplate the toxicological evaluation of the new medications destined to the treatment of the cancer, this document was harmonized by the main regulatory agencies of drugs of the world. Equally was observed that exist a group of normative that are specify for biological and biotechnical products. Conclusions: The state of the art related with the requirements for the toxicological evaluation of the therapeutic vaccines dedicated to the treatment of the cancer was shown. Exists a group of toxicological investigations that are common for prophylaxes and therapeutic vaccines. The selection of the battery of specific toxicological studies for therapeutic vaccines constitutes a scientific challenge that requires from an analysis case by case of the vaccine's candidate in development.</p> <p>References: Web sites: http://www.who.int/vaccine_safety/en/, http://www.ema.europa.eu/htms/human/humanguidelines/nonclinical.htm http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/default.htm, http://www.ich.org/cache/compo/276-254-1.html http://www.cecmec.sld.cu/Pages/Reg_EvalDC.htm</p>
PFE 066	<p>EVIDENCE OF PHARMACOLOGICAL EFFECT IN THE STUDY TO REPEATED DOSE BY SUBCUTANEOUS ROUTE OF THE STIMULATING FACTOR OF GRANULOCYTE COLONIES IN RATS</p> <p>Arteaga ME¹, Fuentes D¹, Hernández O¹, Hernández J¹, Hernández Y¹, Subirós N¹ and Casacó A².</p> <p>¹Centro Nacional para la Producción de Animales de Laboratorio (CENPALAB), Calle 3ra y Carretera de Tirabeque, Sur del Reparto La Unión, Bejucal, La Habana, Cuba. email: melena@cenpalab.inf.cu</p> <p>²Centro de Inmunología Molecular (CIM). Reparto Atabey. Playa, Ciudad Habana, Cuba.</p> <p>Introduction: The humanized granulocyte colony-stimulating factor (G-CSF) is a product, obtained by means of technology of DNA recombinant; it is used in the treatment of patient with tumors subjected to radiations and chemotherapy. In the present work, the pharmacological effects were determined from the administration to repeated dose during 14 days of the G-CSF by subcutaneous route in Cenp:SPRD rats; housed individually in cages TECNIPLAST type T3, under controlled environmental conditions.</p> <p>Materials and Methods: Animals of both sexes were used conforming 4 experimental groups with 10 animals, applying as treatment: a physiologic saline solution; vehicle; low dose 8 µg/kg (1X) and high dose 80 µg/kg (10X). A part of the animals was sacrificed at 14 days and the rest lapsed 7 days after the last administration, with the purpose of evaluating the reversibility of the effects of the assay substance. They were carried out haematological exams and of sanguine chemistry at the beginning of the assay and before the sacrifice of the animals, where they were carried out histopathological studies. Results and Discussion: Neither Deaths nor clinical alteration were observed; the animals maintained a curve of normal body weight. The results of the haematology parameters and sanguine chemistry evidenced alterations in the group treated with high dose at 14 days of the administration; with the population of leukocytes increase (neutrophils), as well as an increase in the serous concentration of the alkaline phosphatase. In the autopsy, an increase was appreciated in the absolute and relative weight of the spleen with marked extramedullar granulopoiesis in the animals treated of high dose group in the day 14 of the assay; that it diminished significantly when suspending the treatment. Conclusion: The administration of G-CSF during 14 days in rats causes clinical and anatomical changes attributable to the pharmacological action of the assay substance and reversible when concluding its administration.</p>
PFE 067	<p>COMPARATIVE EVALUATION OF ACUTE AND CHRONIC TREATMENT OF NASAL NEURO-EPO AS A NEUROPROTECTANT A GERBILS BIOMODEL OF ISCHEMIC STROKE</p> <p>González S¹, Mengana Y¹, Rodríguez Y², Cabal C³, González E³, Olivera A⁴, Rojas AR³, García JC¹</p> <p>¹Centro Nacional para la Producción de Animales de Laboratorio. Calle 3ra y Carretera de Tirabeque, Sur del Reparto la Unión, Bejucal, La Habana, Cuba. email: susettglez@cenpalab.inf.cu, susettglez@gmail.com</p> <p>² Instituto de Ciencias Básicas y Preclínicas Victoria de Girón. Avenida 146 No. 3102 esquina a 31, Cubanacán, municipio Playa, Ciudad de La Habana, Cuba</p>

	<p>³Centro de Neurociencias de Cuba (CNEURO). Avenida 25 No. 15 202 esq. 158 Playa, Ciudad de la Habana Cuba.</p> <p>⁴Centro de Investigaciones Médico Quirúrgicas (CIMEQ). Calle 216 y Avenida 11 B. Reparto Siboney, Playa, Ciudad de la Habana Cuba.</p> <p>Introduction. Cerebrovascular diseases are the third leading cause of death in our country and the leading cause of disability. To date there are no adequate and specific treatment for this disease. Previous results obtained by our group in the Neuro-EPO treatment with nasal in acute phase of cerebral ischemia in the Mongolian gerbil model, demonstrate the safety and efficacy of this new drug [1-3]. We will now study the effect of chronic treatment in Neuro-EPO in order to improve the results previously obtained.</p> <p>Materials and Methods. We worked with 105 female animals in a range between 70-80 grams body weight, divided into three experimental groups: Group 1 Injured + Placebo, Group 2 Injured + 4 days of treatment with Neuro-EPO and Group 3 Injured and treated the first Group 2 week continuing treatment every other day for 11 weeks. Studies were conducted behavioral, biochemical and histological effects. Evolutionarily experimental groups were evaluated by MRI. Results. Significant differences (p <0.05) in survival between Group 1 vs Group 2 and Group 3 in the first seven days. The scale showed a better neurological neurological status of the animals corresponding to Group 3. We discuss the values of specific activity of GST and its response to chronic treatment with Neuro-EPO. The relationships between the damage in brain tissue and their correlation with magnetic resonance imaging. Conclusions. Shown for the first time in Cuba evolutionary images of cerebral ischemia in a biomodel. It demonstrates the neuroprotective effect of EPO Neuro-nasal on the mechanisms of neuroplasticity in a model of focal ischemia in Gerbils.</p> <p>References. 1- Sosa I, Mengana Y, García JD, Subiros N, Cruz J, Muñoz A, et al. Recombinant human erythropoietin as a neuroprotective therapy in brain ischemia. <i>Biocología Aplicada</i> 2008;25:223-9. [2] Sosa IT, J.C. GR, J.D. GS, J. S, N. SM, C. GT, et al. INTRANASAL ADMINISTRATION OF RECOMBINANT HUMAN ERYTHROPOIETIN EXERTS NEUROPROTECTIVE EFFECTS ON POST-ISCHEMIC BRAIN INJURY IN MONGOLIAN GERBILS. <i>Pharmacologyonline</i> 2006;1:100-12. [3] Rodríguez JCG, Teste IS. The Nasal Route as a Potential Pathway for Delivery of Erythropoietin in the Treatment of Acute Ischemic Stroke in Humans. <i>The scientific world journal</i> 2009;9:970-81.</p>
PFE 068	<p>TOXICITY IN RATS OF THE 1E10 VACCINE AFTER REPEATED SUBCUTANEOUS INJECTION</p> <p>González Torres Y¹, Vásquez AM², Casacó Parada AR², Bada Barro AM¹, González Navarro B¹, Fuentes Morales D¹, Arteaga Pérez ME¹.</p> <p>¹ Center of Experimental Toxicology, National Center for Laboratory Animals Breeding (CENPALAB), Havana, Cuba. email: yanagt@cenpalab.inf.cu</p> <p>² Center of Molecular Immunology (CIM), Havana, Cuba</p> <p>Introduction: Cancer has become a serious problem for mankind because of its high grade of incidence and mortality. Specific active immunotherapy is a therapeutic approach against this disease, allowing the targeting of immune response against malignant cells with a higher grade of effectiveness. Materials and Methods: The objective of this work was to determine the possible toxic effects due to the repeated dose subcutaneous administration for 14 days of the therapeutic vaccine 1E10. It was established three groups of 5 Sprague Dawley rats per sex: Control (Saline), Vehicle (Alumina Gel), and Treated (1E10 vaccine). Animals were daily observed to detect toxicity signs, and rectal temperature was measured before and after the administration of the substances. There were carried out haematological and blood chemistry exams on all animals at the beginning and at the end of the assay, and histopathological examination was performed on day 14th. Results and Discussion: There were not detected any significant variations neither in corporal weight nor rectal temperature or haematology parameters. Blood chemistry analysis showed an increased of bilirubin and creatinine in all groups, not been associated to the vaccine administration. Animals of Vehicle and Treated groups showed multiple white ring-shaped formations in the subcutaneous cellular tissues at the administration site, possible due to the action of the adjuvant (Alumina Gel). Conclusions: Obtained results indicated the absence of toxic effects in rats due to the administration of 1E10 vaccine.</p>

PFE 069	<p>ASSESSMENT OF HYPERLIPIDEMIC EXPERIMENTAL MODELS González Y, Boffill M, Castillo O, Betancourt E, Tamayo M, Alfonso B, Blanco F, Verdecía B. Experimental Toxicology Unit . UCM.VC Aqueduct Street and Circunvalation. Santa Clara City. Villa Clara. Cuba. email: yiselgm@ucm.vcl.sld.cu</p> <p>Introduction. Atherosclerosis is a disease caused by many factors. Hypercholesterolemia and a plasmatic increase in lipids are some of the risk factors of this disease. One of our main researching fields is the assessment of several hyperlipidemic experimental models in order to determine the most efficient that permits studying different substances with reducing lipid properties. Materials and methods. Four models were studied .Three were based on hyperlipemic or hypercaloric diet intake and another on an acute induction method of hyperlipemic symptoms .In the first model, we used 10% of chicken fat that was applied on Sprague Dawley rats for 90 days . In the second one, 20% of swine fat was combined with 30 % of sucrose for 2 months .The third chronic model was done by combining 20% of casein and 20% of swine fat on Wister rats for 30 days. A fourth model was carried out to reach hyperlipidemic symptoms consisting of applying non-ionic detergent (Synperonic F108) on C 57 BL/J6 mice. Results. The first described model was not useful for establishing dislipidemic state. By combining saturated fats and sucrose we obtained a considerable increase in cholesterol levels. However, there was no change in plasmatic TAG concentration. Moreover, mixing casein and saturated fats significantly increased cholesterol and TAG values on laboratory animals. Likewise, we obtained values greater than normal ones in non-ionic detergent –induced hyperlipidemic model. Conclusions. Casein and saturate fat model turned out to be the most efficient for developing chronic model of hyperlipidemias. On the other hand, the acute model proved to be useful for assessing pharmacological power.</p>
PFE 070	<p>NEONATALLY STREPTOZOTOCIN INDUCED TYPE 2 DIABETIC MODEL: AN ADEQUATE TOOL FOR TESTING ANTIDIABETIC DRUGS Oliva Y, Sánchez J, Marrero E, Fernández O</p> <p>Dep. Chemistry Pharmacology and Toxicology. National Centre for Animal and Plant Health (CENSA). San José de Las Lajas, La Habana, Cuba. email: yuleivys@censa.edu.cu</p> <p>Introduction: Diabetes is the most relevant and complex metabolic disease all over the world and its prevalence is rapidly increasing. At least 177 million people worldwide have diabetes, and it is predicted to double by 2030. There are 90-95 percent of those people belonging to type 2 diabetes (T2D). To better study both the pathogenesis and potential therapeutic agents, appropriate animal models of T2D are needed. Streptozotocin (STZ) is a glucose analog with diabetogenic effect due to its specific damaging action to pancreatic beta cells. T2D induced in rats by neonatal STZ administration (so-called “n-STZ models”) has been recognized as potentially appropriate for investigations in diabetes pharmacotherapy. The aim of this study was to evaluate this model of T2D in our conditions. Material and Methods: Two-days-old female and male Sprague-Dawley rats pups was injected intraperitoneally with STZ, at a single dose of 90 mg/kg, in 0.1M citrate buffer, pH 4.5. Control group was injected with an equal volume of citrate buffer. After 6 weeks, blood glucose concentration was measured after 18 h of fasting; and in an oral Glucose Tolerance Test (GTT), using 2 g/kg of glucose by gavage, at 30, 50, 90 and 120 min after glucose administration using a commercial glucometer (GlucoDr, Korea) (C, n = 8; n-STZ, n = 10). The experiment was performed as approved by the International Committee for Animal Care and in accordance with national regulations for animal experimentation. Results and Discussion: The results showed significant statistical differences between the control and n-STZ treated groups, in glucose at fasting (p < 0.05), and in the GTT at 30 (p < 0.05) and 50 min (p < 0.01). The weight of n-STZ treated animals increased significantly compared with that of the control group (p < 0.05). Conclusions: Neonatally streptozotocin induced diabetic model is reproducible in our conditions and it can be potentially used for pharmacological evaluation of drug candidates.</p>
PFE 071	<p>A METHOD FOR RELATIVE POTENCY DETERMINATION OF NEW IN-HOUSE REFERENCE BATCHES OF ALLERGEN PRODUCTS, BY PARALLEL SKIN PRICK TEST Labrada A¹, Oliva Y¹, Mateo M¹, Castro RL¹, Más A¹, Navarro I²</p> <p>¹ Allergens Dept. National Center of Bioproducts, Havana, Cuba; ² Policlinic Capdevila, Boyeros, Havana, Cuba. email: yunia.oliva@biocen.cu</p>

	<p>Introduction: In-House Reference Preparations (IHRP) of allergen products should be biologically standardized, preferably, on the basis of skin reactivity. Biological Units (BU) are defined regarding reactivity to Histamine; nevertheless, for establishing a new IHRP batch, both the old and the new IHRP should be tested in parallel. The aim of this work was to establish a parallel skin test for this purpose.</p> <p>Methods: Freeze-dried allergen extracts of <i>Dermatophagoides pteronyssinus</i> (Dp), <i>D.siboney</i> (Ds) and <i>Blomia tropicalis</i> (Bt) (BIOCEN, Cuba) were used. SPT was performed using three nominal concentrations for each batch: 200K; 20K and 2K BU/ml; and the wheal diameter (d) and area were measured. A dose-response regression line was built for each batch. The test was regarded valid for $d > 3\text{mm}$ at 20K BU/ml, and if it passed the linearity ($r > 0.90$) and parallelism tests ($p < 0.05$) for both regression lines. Relative Potency (RP) was calculated using the parallel lines statistical method. The first consecutive 10 valid patients were selected for RP calculations for each IHRP, and the final value was calculated as a weighted mean according to the inverse variance method. Results: The RP results were: for Dp: 0.82 (CI: 0.39-1.72); Ds: 1.29 (0.83-2.02); Bt: 1.29 (0.98-1.68). These values were in good agreement with the absolute potency results as determined using Histamine hcl 10mg/ml, and with the in-vitro RP values as measured by IgE inhibition ELISA. The overall precision of the method was $a[\log_{pr}] = 0.116$, better than for the absolute potency test. Conclusion: this method is suitable for assigning potency values to new IHRP batches.</p>
PFE 072	<p>ASSESSMENT OF THE <i>IN VIVO</i> GENOTOXICITY OF THE 1E10 MONOCLONAL ANTIBODY BY MEANS OF THE BONE MARROW MICRONUCLEUS TEST</p> <p>Curbelo A¹, Casacó A², Mancebo A¹, Arteaga ME¹, González C¹, Rivero Y¹, Legró M¹, Ocaña R¹, García-Somines J¹, Bada AM¹, Lemus M¹, Escalona MA¹</p> <p>¹Center of Experimental Toxicology, National Center for Laboratory Animal Breeding, Bejucal, Havana, Cuba. email: ailemys@cenpalab.inf.cu ²Center of Molecular Immunology, P.O. Box 16040, Havana, 11600, Cuba</p> <p>Introduction: Monoclonal antibodies (mAb) has become a primary tool in immunotherapeutic passive strategies, being reported their use in many malignant diseases and rejection of transplanted organs. Center of Molecular Immunology has developed the 1E10 mAb. With the objective of assessing the genotoxicity of this mAb it was performed the bone marrow micronucleus test in Cenp:NMRI mice. Material and Methods: It was established three dose levels (100, 200 y 400 µg/animal) and two control groups (negative: patient solution, positive: cyclophosphamide 40 mg/Kg body weight). All substances were administered via intraperitoneal injection scheduled in two treatments at 24-hour intervals, and samples were collected 24 hours following the final treatment. The proportion of immature among total (immature + mature) erythrocytes was determined for each animal by counting 500 erythrocytes, and 1000 immature erythrocytes per animal were scored for the incidence of micronucleated immature erythrocytes (MNPCE). Results: Statistical analysis of the results allowed establishing that 1E10 did not showed significant increase of the MNPCE in two sexes, and in female mice is observed significant decrease in the proportion of immature among total erythrocytes at the 400 µg/animal dose. Conclusions: The study showed that the 1E10 mAb did not produce mutagenic effects in bone marrow and induce cytotoxic effects in female mice at the 400 µg/animal dose.</p>
PFE 073	<p>EFFECTS OF AMPICILLIN ON THE GENTAMICIN-INDUCED NEPHROTOXICITY IN RAT</p> <p>Habibian Dehkordi S¹, Moradi M¹, Moshtaghian J², Karimi I³, Sharifi S⁴</p> <p>¹Department of Pharmacology, School of Veterinary Medicine, University of Shahrekord, Iran. email: habibian@vet.sku.ac.ir, habibian_dehkordi@Yahoo.com, ²Department of Biology, School of Basic Sciences, University of Isfahan, Isfahan, Iran. ³Department of Pathology, School of Veterinary Medicine, University of Shahrekord, Iran. ⁴Department of Surgery, School of Veterinary Medicine, University of Shahrekord, Iran.</p> <p>Introduction: Gentamicin is a broad spectrum antibiotic which is widely used for the therapy of serious infections caused by gram-negative aerobic bacteria. Its clinical use, however, is limited due to the risk of drug-induced nephrotoxicity. Agents which reduce its nephrotoxic effect could help to make gentamicin therapy safer. Present study aimed to study the effect of ampicillin on gentamicin induced nephrotoxicity in rat. Material and Methods: For this purpose, 40 male rats with body weight ranged from 290 to 310g were randomly divided in four groups. In groups one and two gentamicin was given IM for 9 consecutive days at the dose of 5 or 10mg/kg, respectively. Rats in group three received 10mg/kg gentamicin</p>

	<p>intramuscularly and 50mg/kg ampicillin subcutaneously for successive 9 days. Rats in group four (control group) received no drug. 3 days after last injection, rats were anaesthetized and blood samples were collected. They were then sacrificed and histopathological samples of liver and kidney were taken on 10% formalin buffer. Results and Discussion: The level of BUN and creatinine increased in experimental groups 1 and 2 compared to control and experimental group 3, however, this elevation was only significant in group two ($p < 0.05$). histopathologic investigation of kidney in experimental groups one and two showed tubular hemorrhage, interstitial nephritis, acute tubular necrosis. There was no histopathological abnormality in liver of any group. The protective effect of ampicillin could be ascribed to its inhibition of β-glucuronidase an enzyme which is located in renal lysosomes and which is activated by gentamicin and other aminoglycosides Conclusions: It can be concluded that in rats the nephrotoxicity of gentamicin is affected adversely by the presence of ampicillin</p>
<p>PFE 074</p>	<p>PULMONARY RESPONSES OF RATS EXPOSED TO TITANIUM DIOXIDE NANOPARTICLES INJECTED INTRATRACHEALLY Habibian Dehkordi S¹, Emami R², Moshtaghian J³</p> <p>¹Department of Pharmacology, School of Veterinary Medicine, University of Shahrekord, Iran. email: habibian@vet.sku.ac.ir, habibian_dehkordi@Yahoo.com, ²Department of Clinical Sciences, Shahrekord Branch of Islamic Open University, Shahrekord, Iran. ³Department of Biology, School of Basic Sciences, University of Isfahan, Isfahan, Iran.</p> <p>Introduction: Titanium dioxide (TiO₂) nanoparticles are in wide commercial use worldwide. The present study was carried out to evaluate if pulmonary toxicity and fibrosis can be induced by nano-TiO₂ particles. Material and Methods: For this purpose, 60 male rats were randomly divided in four groups. Rats in groups one, two and three were intratracheally instilled with 25, 50, or 100 mg/kg of 4-8 nm TiO₂ primary particles, respectively. Rats in group four (control group) received the same volume of normal saline, intratracheally. On days 15, 30 and 45 after injection, 5 rats from each experimental each groups were anaesthetized. Radiographic pictures were taken and rats were then sacrificed. Blood samples were collected and blood pictures and serum activity of LDH and ALP were determined according to routine laboratory methods. Samples of lungs were collected on 10% formalin buffer, subsequently. Results and Discussion: The results showed significant difference of total WBC, Lymphocytes, monocytes, Granulocytes percentages and serum activity of LDH and ALP on day 15 of experiment. Moreover, histopathologic and radiographic examination of lung tissues indicated that the pulmonary response to exposure to TiO₂ particles in rats manifested as dose-dependent inflammatory lesions, which mainly consisted of infiltration of inflammatory cells and interstitial thickening. Conclusions: These results suggest that exposure dose may have important role in pulmonary toxicity. Moreover, the present study showed that inflammatory effects of TiO₂ nanoparticles sustained for a limited time and rat recovered from these effects after a length of time.</p>
<p>PFE 075</p>	<p>EFFECT OF H₂S-CONTAINING BATHS ON EXPERIMENTAL DERMATITIS AND ARTHRITIS IN MICE Boros M¹, Helyes Zs¹, Kemény Á¹, Sándor K¹, Cseharovszky R¹, Grósz J¹, Szolcsányi J¹, Sebők B³, Kerécs T³, Debreceni B², Debreceni L⁴, Pintér E¹</p> <p>¹Department of Pharmacology and Pharmacotherapy, Faculty of Medicine, University of Pécs, H-7624 Pécs, Szigeti u. 12., Hungary ²Department of Biochemistry and Medical Chemistry, Faculty of Medicine, University of Pécs, H-7624 Pécs, Szigeti u. 12., Hungary ³Zsigmondy Vilmos Harkány Medicinal Spa Hospital, 7815 Harkány, Zsigmondy Vilmos setány 1., Hungary ⁴Independent researcher. email: erika.pinter@aok.pte.hu</p> <p>Introduction: Balneotherapy, as an effective treatment of inflammatory diseases has long been known, but its mechanism is still unclear. The Harkány medicinal water contains carbonile-sulfide, which is well-absorbed and converted to hydrogen-sulfide (H₂S). H₂S stimulates capsaicin-sensitive afferents and release sensory neuropeptides, therefore it might modulate neuroimmune interactions. We investigated the effects of Harkány medicinal water and a commercially available H₂S-containing product (Sulfivit) in allergic contact dermatitis and arthritis models. Material and Method: Delayed-type hypersensitivity reaction in the paw skin was induced by oxazolone in sensitized mice. Inflammation of the tibio-tarsal joint was evoked by complete Freund's adjuvant (CFA) injected into the left hindpaw and tail root. Paw volume was</p>

	<p>measured with plethysmometry and the mechanonociceptive threshold with dynamic plantar aesthesiometry. Histological examination, inflammatory cytokine (IL-1β, TNF-α) measurements and spectrophotometric mieloperoxidase (MPO) determination were performed. Mice were bathed in 37°C Harkány water, Sulfivit or distilled water (control) for 20 min/day during the studies. Results and Discussion: Oxazolone caused a 50-60% paw swelling, cutaneous oedema, leukocyte accumulation and cytokine increase in the control group. These inflammatory parameters were significantly reduced by both H₂S-containing baths, but the skin MPO activity was not altered. CFA-induced paw oedema, enlargement of the synovial tissue, infiltration of inflammatory cells and the level of TNF-α were decreased both by Harkány medicinal water and Sulfivit, but hyperalgesia and IL-1β production was not affected. Conclusions: We conclude that H₂S-containing baths exert anti-inflammatory effects in these mouse models of dermatitis and arthritis, predominantly by reducing oedema and inflammatory cell accumulation. The release of anti-inflammatory neuropeptides from the activated sensory nerves might be involved in these actions.</p>
PFE 076	<p>SYNTHESIS AND PHARMACOLOGIC STUDY OF A NEW HETEROCYCLIC FAMILY: THE β-CARBOLINO-BENZAZEPINONES AND ITS ACTIVITY IN THE CENTRAL NERVOUS SYSTEM Xuárez Marill Lisbet¹, Dodd Robert H² y Thomet Urs³</p> <p>¹Instituto de Farmacia y Alimentos, Departamento de Química Básica, Universidad de la Habana, Cuba. email: lisbet@ifal.uh.cu ²Institut de Chimie de Substances Naturelles (ICSN), Gif-sur-Yvette, Francia. ³bSys GmbH, Benkesenstrasse 254, CH-4108 Witterswill/ Switzerland.</p> <p>Introduction: The β-carboline heterocyclic skeleton is present in many naturally-occurring substances. Their 3-alkyl carboxylate derivatives, mostly synthetic, are known to interact strongly with the benzodiazepine receptor of the Central Nervous System (CNS).¹ This communication describes the preparation of a novel type of ligand β-carbolino-benzazepinones using a multi-step procedure. The results of electrophysiological tests showed that these new compounds interact with the CNS especially at the level of the GABA_A receptor.² Material and Methods: All the synthesized compounds were characterized by the combination of different spectroscopic techniques and chemical analysis. The obtained β-carbolino-benzazepinones were tested <i>in vitro</i> by determining the electrophysiology of the effects (at 1μM concentration) on the GABA-induced electrical current in the different sub-types of the GABA_A receptors expressed in <i>Xenopus</i> oocytes. Diazepam and DMCM (both at 1μM) were used as positive and negative controls, respectively. Discussion: Various CNS active β-carbolino-benzazepinones were prepared from 9-[(dimethylamino)sulfonyl]-<i>N</i>-benzyl-9<i>H</i>-β-carbolino-3-carboxamide by the following synthetic sequence: ortho-metalation, carboxamide N-alkylation of the 4-iodo-β-carbolino derivative obtained, intramolecular cyclisation by CH-ortho palladium catalyzed activation and final efficient elimination of (dimethylamino)sulfonyl protective group in acid medium. The results of the electrophysiological tests demonstrated that the synthesized compounds showed agonist profiles as well as selectivity to the different sub-types of GABA_A receptor. Conclusions: In the present work a general method for preparation of β-carbolino-benzazepinones was developed. The key reaction was the intramolecular cyclisation of <i>N</i>-benzyl-9-[(dimethylamino)sulfonyl]-4-iodo-9<i>H</i>-β-carbolino-3-carboxamide by CH-ortho palladium catalyzed activation. The biological results demonstrated that in electrophysiological tests, these new ligands showed the characteristic agonist properties of the benzodiazepines, contrarily to 3-carboxy-β-carbolines, which generally presents an inverse agonist profile.</p> <p>References: 1. Cox, E. D., Cook, J. M., <i>Chem.Rev.</i>, 1995, 95, 1797. 2. Thomet U., bSys GmbH, Witterswill, Switzerland.</p>
PFE 077	<p>ANXIOLYTIC AND SEDATIVE EFFECTS OF JM-20, A NOVEL BENZODIAZEPINE COMPOUND ON MICE AND RATS Nuñez Y, Carrillo C, Ochoa E, Verdecia Y, Pardo G, Delgado R</p> <p>Departamento de Farmacología Molecular. Centro de Investigación y Desarrollo de Medicamentos. Ave 26 No. 1605 entre Boyeros y Puentes Grandes, municipio Plaza de la Revolución, CP 10 600, Ciudad de La Habana, Cuba. email: yaniernf@infomed.sld.cu</p> <p>Introduction. Anxiety affects one eighth of the total population and has become a very important area of research in psychopharmacology in the current decade. Recently, research has been conducted to identify</p>

	<p>safer, more specific, and perhaps lower cost therapies. The purpose of this study was to characterize the putative anxiolytic-like effects of JM-20 a novel benzodiazepine compound obtained by Chemistry Faculty of Havana University. Materials and Methods. Male mice (18—22 g) were treated orally with 2, 4 or 8 mg/kg of these preparations 30 min before the experiments for the evaluation of the sedative/hypnotic activity (sleeping time induced by sodium tyopental 30 mg/kg, i.p., open-field test, aggressive behavior induced by isolation), anxiolytic activity (elevated plus maze (EPM)) and anticonvulsant activity (induced by pentylenetetrazole 85 mg/kg, sc); and on stereotyped behavior induced by amphetamine in rats (150-200 g). Results and Discussion. JM-20 in all doses assayed showed a significant increased the latency period of tonic seizures and percentage of survival in the convulsing experimental model, increased the sleeping time induced by barbiturates and the time spent in the open arms of the EPM. On the other hand, JM-20 decreased significantly the aggressive behavior in isolated mice, the stereotyped behaviour induced by amphetamine and the open-field conduct. Conclusions These results indicate that JM-20 is an effective anxiolytic agent probably mediated through CNS benzodiazepine receptors.</p>
<p>PFE 078</p>	<p>CYTOTOXICITY INDUCED BY GLUTAMATE AND H₂O₂ IN PC-12 CELLS AS <i>IN VITRO</i> MODEL FOR EVALUATED OF NEUROACTIVES PRODUCTS García-Pupo L, Nuñez Figueredo Y, Delgado R</p> <p>Molecular Pharmacology Lab, Drug Research and Development Center. 26 Ave. # 1605 e/ Boyeros and Puentes Grandes, Nuevo Vedado, C. Habana, Cuba</p> <p>Introduction: In cases of central nervous system (CNS) trauma, stroke, epilepsy, and in certain neurodegenerative diseases, increased concentrations of extracellular glutamate result in the overactivation of local ionotropic glutamate receptors that trigger neuronal cell death, either by rapid necrosis or delayed apoptosis of the neuron depending on the severity of the insult. In several of those diseases, especially in cerebral ischemia, neuronal death is also mediated by oxidative stress. Therefore, standardization of glutamate excitotoxicity and oxidative-induced cellular death models would be extremely useful, in order to evaluate neuroprotective compounds and therapeutic candidates. Materials and Methods: In this work we studied the effects of glutamate and hydrogen peroxide treatment in cell vitality. L-glutamic acid was dissolved in different mixes of culture media DMEM/bovine fetal serum 10% with alkaline buffer. PC12 cells (murine pheocromocitome cells line) were treated with glutamate (8-128 mM) or hydrogen peroxide (30-70 μM) for 24 and 4 hours, and cellular vitality were estimated by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay and IC₅₀ was calculated. Results and Discussion: When glutamate treatment was prepared using a mix of DMEM/bovine fetal serum 10% and alkaline buffer (1:1), all glutamate concentrations induced cell death (IC₅₀=50 mM for 4h and IC₅₀=31 mM for 24h), except the lowest one (8mM), compared to untreated PC12 cells. In contrast, when employed glutamate was a mix of DMEM/bovine fetal serum 10% and alkaline buffer (1:0.2) we did not observed significant cell death in treated cell cultures for 24h, respect to untreated ones. Probably, this is due to more favorable conditions for glutamate-receptors interactions when using a more alkaline glutamate solutions like the first mix mentioned. In case of hydrogen peroxide treatment, we observed cell death in all used concentrations (IC₅₀=315 μM for 4h and 24h), except the lowest one. Conclusions: We established glutamate excitotoxicity and hydrogen peroxide-induced PC12 cell death models, according with our environmental and laboratory conditions.</p>
<p>PFE 079</p>	<p>EFFECT OF A YEAR OF TREATMENT WITH NEURO-EPO FOR NASAL WAY IN THE HISTOLOGICAL STRUCTURE OF THE CEREBELLUM IN ATAXIA BIOMODEL SCA-2. García Barceló¹, Batista Castro Z¹, Rodríguez Cruz Y¹, García Rodríguez JC².</p> <p>1. Department of Histology ICBP "Victoria de Girón" Havana. Cuba. 2. Head of the Neurosciences. CENPALAB. Havana, Cuba. Email. neurotox@cenpalab.inf.cu</p> <p>Introduction: Ataxia type 2 (SCA-2) is an inherited, degenerative disease of the nervous system that affects several nervous system structures such as the cerebellum. Holguin is the province that has the highest prevalence of SCA-2 in the world, with about 440 patients, while in the country have been diagnosed a total of 552 people and 6000 are at risk. The use of molecules with therapeutic activity produced by the body itself is a recent proposal in neuroscience research. Recent studies have shown efficacy in neuroprotection of recombinant human erythropoietin low sialic acid content (Neuro-EPO), nasally applied in models of cerebral ischemia[1]. Our objective was determine the effect of the application of recombinant human erythropoietin low sialic acid content (Neuro-EPO) administered intranasally in the histological structure of the cerebellum of biomodel SCA-2. Material and Methods: We used transgenic</p>

	<p>mice with SCA-2 and identified two experimental groups, one control and one with application of Neuro-EPO intranasally at a dose of 10 micrograms / day three times a week for one year, after which, were sacrificed and evaluated macro and microscopic aspects of the cerebellum. The samples were processed by the technique of inclusion in paraffin, cut to 5 mm thick and stained with hematoxylin and eosin. Results: The histological study of the cerebellum in the group treated with Neuro-EPO, showed the preservation of the cytoarchitecture of the layers of the cerebellar cortex, as well as the quantity and histological structure of Purkinje cells compared with the control group. We discuss the therapeutic significance of the results in the treatment of chronic diseases [2]. Conclusions: The use of Neuro-EPO decreases intranasal cerebellar histological changes in transgenic mice with SCA-2, which could be an alternative chronic neuroprotective treatment for patients with this disease. New investigations are conducted to confirm or not this therapeutic possibility.</p> <p>Referencias:</p> <p>1. Sosa IT, JC, GR, JD, GS, J, S., N., S.M., C., G.T., Y., R.C., and J., C.R. (2006). Intranasal administration of recombinant human erythropoietin exerts neuroprotective effects on post-ischemic brain injury in Mongolian gerbils. <i>Pharmacologyonline</i> 1, 100-112</p> <p>2. Rodríguez, J.C.G., and Teste, I.S. (2009) The Nasal Route as a Potential Pathway for Delivery of Erythropoietin in the Treatment of Acute Ischemic Stroke in Humans. <i>TheScientificWorldJOURNAL</i> 9, 970-981.</p>
<p>PFE 080</p>	<p>BRAIN EXPRESSION OF EPO AFTER INTRANASAL APPLICATION OF NEURO-EPO IN A MODEL OF STROKE IN MONGOLIAN GERBIL</p> <p>Rodríguez-Cruz Y¹, Gao Y², Mengana-Támos Y³, Sosa-Teste I³, Zhang C², García-Rodríguez J C³.</p> <p>¹Institute of Medical Sciences of Havana. Faculty Playa "Victoria de Girón". Cuba. ²Department of Neurobiology. Institute of Radiation Medicine. Beijing China ³National Center for Laboratory Animals Breeding (CENPALAB). Cuba. email: neurotox@cenpalab.inf.cu</p> <p>Introduction: Recombinant human erythropoietin low sialic acid content (Neuro-EPO) intranasally (VIN) acts as a neuroprotectant in focal ischemia model in Mongolian gerbils [1]. The underlying mechanisms responsible for the neuroprotective functions of the Neuro-EPO in vivo are unknown, including how the brain modifies the expression by exogenous EPO. To evaluate the immunohistochemical expression of EPO in the hippocampus and cerebral cortex after application of Neuro-EPO VIN model of focal ischemia in Mongolian gerbils. Methods: Focal ischemia model in Mongolian gerbils 99 males who were administered EPO Neuro-VIN (30 micrograms / day) or vehicle at different times (0min, 10min, 1 hour, 12 hours, 24hours, 48hours, 72 hours and 5weeks. after ischemia. The brains were fixed for 7 days and embedded in paraffin, for qualitative assessment of hematoxylin and eosin staining. Immunohistochemistry detection levels of EPO in the cortex and hippocampus were done. Results: The pathology showed a significant reduction of neuronal death in the cerebral cortex and hippocampus in animals treated with Neuro-EPO when compared with untreated patients. The immunohistochemical expression of EPO in the lesioned hemisphere was lower in the treated group, in cingulum, cerebral, auditing and pear peel at 12 and 48 hours of injury. We discuss the Immunohistochemistry detection levels of EPO at different time and the possible mechanism of neuroprotection. Conclusions: These results support our previous reports [2] which suggest a VIN Neuro-EPO act as a neuroprotectant in acute stroke.</p> <p>References:</p> <p>1- Sosa, I., Mengana, Y., García, J.D., Subiros, N., Cruz, J., Muñoz, A., Nuñez, Y., and García, J. (2008) Recombinant human erythropoietin as a neuroprotective therapy in brain ischemia. <i>Biotechnología Aplicada</i> 25, 223-229.</p> <p>2- Rodríguez, J.C.G., and Teste, I.S. (2009) The Nasal Route as a Potential Pathway for Delivery of Erythropoietin in the Treatment of Acute Ischemic Stroke in Humans. <i>TheScientificWorldJOURNAL</i> 9, 970-981.</p>
<p>PFE 081</p>	<p>EFFECT OF A YEAR OF ZINC SUPPLEMENTATION IN THE DIET ON THE HISTOLOGICAL STRUCTURE OF THE CEREBELLUM IN GENETICALLY MODIFIED BIOMODEL ATAXIA SCA-2</p> <p>Batista Castro Z¹, Garcia Barceló¹ Rodríguez Cruz Y¹, Forte C² and García Rodríguez JC³.</p> <p>1. Department of Histology ICBP "Victoria de Girón" Habana. Cuba. 2. Department of Nutrition. CENPALAB. Havana. Cuba. 3. Head of the Neurosciences. CENPALAB. Havana, Cuba. email. neurotox@cenpalab.inf.cu</p> <p>Introduction: Ataxia type 2 (SCA-2) is the molecular form of autosomal dominant Heredodegenerative group of diseases, which especially Cuba and Holguin province, has the highest rate worldwide. Currently there are 125 affected families in Cuba, a total of 772 patients have the disease and 8 of 100,000 members of these families at risk for developing. This genetic disease is an orphan of treatment. Having a genetically</p>

	<p>modified animal (AGM) carrying the gene of SCA-2 [1], is a fundamental tool for identifying new therapeutic targets to enable at least in part to improve the quality of life of patients and divert the course of this disease. Previous studies have shown a deficiency of Zn²⁺ in the serum and cerebrospinal fluid (CSF) of patients ataxic (SCA-2) when compared with neurologically healthy controls. Our objective was to evaluate the neuromodulator action of Zn²⁺ supplementation in the diet in the development of type ataxia (SCA-2) in genetically modified animals (AGM) carrying the gene for human mutant ataxin 2. Material and methods: We established two experimental groups fed a normal diet and the other with a diet enriched with zinc supplements for at least 1 year, evaluating histological and morphometric aspects of the CNS, primarily the cerebellum as a target organ of this disease. Results: Shows the molecular layer recovery and preservation of a significant number of Purkinje neurons and improved the cytoarchitecture of three layers of the cortex of the cerebellum when compared groups of animals treated and not treated with zinc. Results are discussed in light of the satisfactory results obtained in recent clinical trial Phase I-II study and concluded, as well as the proposed new Phase III clinical trial. While therapy is not an alternative proposal specific therapy, they showed an improvement in the quality of life of patients. Conclusions: Our findings provide a full scientific innovation within the research group aimed at developing alternative therapies against the progression of the disease.</p> <p>References: Aguiar, J., Fernández, J., Aguilar, A., Mendoza, Y., Vázquez, M., Suárez, J., Berlanga, J., Cruz, S., Guillén, G., Herrera, L., Velázquez, L., Santos, N., and Merino, N. (2006) Ubiquitous expression of human SCA2 gene under the regulation of the SCA2 self promoter cause specific Purkinje cell degeneration in transgenic mice. <i>Neuroscience Letters</i> 392 202-206.</p>
<p>PFE 082</p>	<p>PREVENTIVE TREATMENT WITH THE MONOCLONAL CHIMERIC ANTI-PROTEOGLYCAN ANTIBODY S3Q (mAb S3Q) REDUCES OXIDATIVE STRESS AND ATHEROSCLEROTIC LESIONS IN A LIPOFUNDÍN MODEL IN RABBITS</p> <p>L. Delgado¹, Acosta E¹, Fraga A¹, Bécquer MA¹, Hernández Y¹, Soto Y², Vázquez AM², Fernández E¹</p> <p>¹Center of Studies for Research and Biological Evaluations, Pharmacy and Food Science College, University of Havana, Havana, Cuba. email: livan@cieb.sld.cu ²Antibody Engineering Department, Center of Molecular Immunology, Havana, Cuba.</p> <p>One of the most consistent hypotheses of atherosclerosis are the retention of low-density lipoproteins and the oxidative modification of these. In the Antibody Engineering Department of the Center of Molecular Immunology (Havana, Cuba) it was obtained a human IgG1 monoclonal chimeric antibody S3Q (mAb S3Q) that reacts with sulfatides. Due to the importance of sulphated molecules, as proteoglycans in atherosclerosis, the effect on systemic redox environment and atherosclerotic lesions development was evaluated in a Lipofundín-induced atherosclerosis model in rabbits. After prophylactic administration of 100 µg/doses in 500 µl of the mAb S3Q, animals were treated with 2 ml/kg of Lipofundín intravenously, during a period of 8 days. Using spectrophotometric assays, oxidative stress biomarkers were evaluated. The immunization with low doses of the mAb S3Q prevented the redox state disruption. Also, the histopathological analyses using eosin/hematoxylin technique, demonstrated that treatment with mAb S3Q prevented the formation of aortic atherosclerotic lesions induced in rabbits by the administration of Lipofundín.</p> <p>Key words: Atherosclerosis, oxidative stress, proteoglycans, lipofundín, monoclonal antibody.</p>
<p>PFE 083</p>	<p>LIPOFUNDÍN AT 20% INDUCES OXIDATIVE STRESS AND ATHEROSCLEROTIC LESIONS IN NEW ZEALAND WHITE RABBITS</p> <p>L. Delgado¹, Acosta E¹, Fraga A¹, Bécquer MA¹, Noa M², Vázquez AM³, Fernández E¹.</p> <p>¹ Center of Studies for Research and Biological Evaluations, Pharmacy and Food Science College, University of Havana, Cuba. email: livan@cieb.sld.cu ² Center of Natural Products, CPN-CNIC, Cuba. ²³ Antibody Engineering Department, Center of Molecular Immunology, Cuba.</p> <p>Atherosclerosis is considered as a major cause of death in the western world. Endothelial dysfunction represents an initial stage of atherogenesis and it is known that oxidative stress plays a central role in the process. The aim of this study was to investigate the status of redox biomarkers in a Lipofundín-induced atherosclerosis model in rabbits. Blood samples of 10 animals by group were tested by spectrophotometric techniques. All measured biomarkers were significantly modified in animals treated with 2 ml/kg of Lipofundín intravenously, during a period of 8 days compared to control group. An increase of biomolecules damage was noted. Antioxidant enzymes activity was activated in treated rabbits and also an increase in lipid peroxidation susceptibility was observed after treatment with Lipofundín. The evaluated</p>

	<p>biomarkers were correlated with histological modification in those animals who received Lipofundín. These indices offer an overview of redox balance disruption in this Lipofundín-induced atherosclerosis model in rabbits and they could also be used as index of atherogenic development. Key words: Atherosclerosis, lipofundín, oxidative stress.</p>
PFE 084	<p>SYNTHESIS OF NEW HEXAHYDROQUINOLINE DERIVATIVES AND PHARMACOLOGICAL EVALUATION OF THEIR CALCIUM ANTAGONIST PROPERTIES Galán L¹, Verdecia Y², Ochoa E², Salfrán E², Barriet B², Suárez M², Alvarez J³</p> <p>¹- Facultad de Ciencias Médicas “10 de Octubre”. Universidad de Ciencias Médicas de La Habana. Calzada 10 de Octubre No. 130. Cerro. Ciudad Habana, Cuba. email: logama@infomed.sld.cu. ²- Laboratorio de Síntesis Orgánica. Facultad de Química. Universidad de La Habana. ³- Laboratorio de Electrofisiología. Departamento de Investigaciones. Instituto de Cardiología y Cirugía Cardiovascular.</p> <p>Introduction: Nifedipine and 1,4-dihydropyridine derivatives are well known calcium channel blockers and are used in clinics since long for the treatment of several cardiovascular disorders. There is still, however, a need for more vascular selective compounds due to the potentially life-threatening effects of their cardiac depressant action (Edraki et al., 2009). The research for the development of new calcium antagonists has focused attention on their vascular selectivity. Recently, some new hexahydroquinoline derivatives with calcium antagonistic activities have been developed (Kismetli <i>et al.</i>, 2004). Their structure have the pharmacophoric ring of the 1,4- dihydropyridine. Thus, the present study was undertaken to investigate the synthesis and pharmacological evaluation of new five hexahydroquinolines. Material and Methods: Five hexahydroquinolines were prepared through one-step synthesis from an aromatic aldehyde called β- alkyl aminocrotonate (enamin) and dimedone in pure ethanol as solvent. The effects of the five hexahydroquinolines on contractility of rabbit’s aorta rings and on contractility of papillar muscles of rat’s right ventricle were characterized in a comparative way to classical nifedipine. Results and Discussion: All hexahydroquinolines inhibited the contractile activity of both vascular smooth muscle and cardiac muscle, and they showed effects that are characteristic of calcium antagonist compounds, although with less potent action than nifedipine. However, two of the studied hexahydroquinolines presented some mild vasoselectivity. Conclusions: Our results indicate that these hexahydroquinolines are attractive molecules since they retain the calcium antagonist properties of their congeners 1,4- dihydropyridine derivatives, and two of these hexahydroquinolines have vascular selective action.</p> <p>References: Edrak N, Mehdipour AR, Khoshneviszadeh M, Miri R. Dihydropyridines: evaluation of their current and future pharmacological applications. <i>Drug. Discov. Today</i> 2009;14(21-22):1058-66. Kismetli E, Safak C, Erol K, Sirmagul B, Linden A. Studies on 3-diethylaminocarbonyl-1,4,5,6,7,8-hexahydroquinoline derivatives and their calcium channel antagonistic activities in vitro. <i>Arzneimittelforschung</i>. 2004; 54(7):371-5.</p>
PFE 085	<p>ANTIANEMIC EFFECT, UTILIZATION AND BIOAVAILABILITY OF A NEW FORMULATION OF TROFIN WITH FERROUS SULPHATE ON ANEMIC RATS García Y¹, González R¹, Cárdenas R², Carmona A²</p> <p>¹.National Center of Biological Products (BIOCEN) Beltrán Mainroad, 1½ Km, Bejucal, Havana. Cuba. email:yenela@biocen.cu ². Facultad de Ciencias.Universidad Nacional Autónoma de México. México,D.F., México. rcv@fciencias.unam.mx</p> <p>Introduction: Trofin® is an antianemic and restorative natural product containing heme iron that had demonstrated high efficiency without adverse reactions. Iron salts have found wide use in the treatment of iron deficiency anemia, despite their adverse effects and low bioavailability. The incorporation of ferrous iron salt into the Trofin® formulation could improve the antianemic effect and bioavailability of this new formulation. The aim of this work was to evaluate the antianemic effect and bioavailability of a formulation of dry Trofin with Fe₂SO₄ in anemic Wistar rats. Materials and Methods: During the experimental design, rats were fed with a casein diet containing low content of proteins and iron. The first two weeks was to depleted Hemoglobin level to ≤ 90 g/L. The anemic rats were distributive in three groups of 6 animals each one. Anemic rats were treated with Trofin plus Fe₂SO₄ (4, 05mgFe/día), Trofin (0,1mgFe/día) or Fe₂SO₄ (8 mgFe/día), that were additioned daily in the casein diet during 10 days. The fourth group was non anemic rat that was fed with a casein diet containing protein and iron in normal level (control). During these period the weight and food intake of the rats were recorded daily. Results and</p>

	<p>discussion: Increase of Hemoglobin didn't shows difference between groups. Oxidative damage was measured as TBARS and carbonyls group in mucous scraped of duodenum and didn't show difference between groups too. Were compared the three group treated with antianemic formulation about iron utilization, efficiency of hemoglobin generation (EHG) and biological value relative (BVR) to Fe₂SO₄ or Trofin. The EGH and BVR to Fe₂SO₄ were higher in Trofin with Fe₂SO₄ than Fe₂SO₄ alone, and lower than Trofin alone. Conclusions: These results showed the efficiency of this new antianemic formulation with Trofin and ferrous iron salt in rats and it help us predict this effect in humans.</p>
<p>PFE 086</p>	<p>THE DERMAL RECONSTITUTION IN WOUND HEALING OF SKIN TREATMENT WITH HYALURONAN BIOCHEMICAL EVALUATION AS AN INDICATOR OF COLLAGEN SYNTHESIS L. Oruña^{1,2}, G. Coto³, G. Lago³, J. Maza^{2,4}, P. Barzaga⁵, N. Merino⁵</p> <p>Center State for Quality Control of Drug, Havana City, Cuba; ²Medicine Latinoamerican Faculty, Havana City, Cuba; ³Placental Histoterapy Center, Havana City, Cuba, ⁴Neurology Institute, Havana City, Cuba; ⁵Pharmaceutical Chemical Centre, Havana City, Cuba</p> <p>Hyaluronic acid plays an important role in dermal wound healing. Hence, biochemical indicators such as alpha amino nitrogen and total amino acid content were determined in dermis samples to asses dermal reconstitution in open wounds treated with Hyaluronan jelly (HA). The treatments were: jelly with HA at 2, 4, and 8%, a placebo and a control applied for 5 and 7 days. A similar dermal area was taken to study each treatment and acid hydrolysis was used to quantify the alpha amino acid groups as an indicator of total amino acid content in collagen synthesis. The values of alpha amino nitrogen were higher for the 4% jelly on the 7th day with 4.32 mg/area⁻¹ followed by the 8% concentration. Glycine was the most abundant amino acid on the 7th day with 310 and 402 µg/area⁻¹ in the 4 and 8% jelly respectively, while for the hydroproline it was of 10.3 and 13.3 µg/area⁻¹. This shows a direct relationship between the behavior of both treatments (4 and 8%) and the histological results, expressed as the reconstitution of collagen fibers that presents a 100% response with the 4% jelly. The quantitative values of alpha amino nitrogen and glycine indicate collagen synthesis and dermal reconstitution; the quantitative hydroxyproline values show an adequate response given that this amino acid is a biochemical marker for this. The correlation between the biochemical and histological results of the dermis with the 4% HA jelly showed better dermal reconstitution than other treatments.</p>
<p>PFE 087</p>	<p>EVALUATION OF THE REDOX STATE IN ALCOHOLIC RATS TREATED WITH OZONE MT Díaz, León OS, Fraga A., Casanova M, Arteaga M</p> <p>Institute Pharmacy and Food, 222 and 25 ave, La Coronela, Lisa, Havana City, Cuba.</p> <p>Introduction: Alcoholism is an addiction that affects not only the person who has it but has important consequences for the social environment where it grows. The metabolism and neuronal affectations caused by the alcohol generated radical reactions that result in quality of life of the alcoholic patient, however there is no activity in antioxidant therapy capable of controlling the addictive behavior. Considering these aspects of this study is to the overall objective. To determine the effects of ozone on behavioral parameters and related to oxidative stress in a model of alcoholism developed in male Lewis rats. Materials and methods:The study was conducted with male Lewis rats (n = 20), 10 control rats, 10 rats, the latter replaced the administration is increasing. At different stages were analyzed concentrations of CAT, SOD and MDA, were controlled body weight, food intake and fluid. When the ethanol that was administered 60ml per day as follows 10% ethanol, 20%, 30% to 40% two weeks each concentration. Then from the model of alcoholism should be raised to the application of ozone. They take four study groups: control, positive control alcoholic, alcoholic positive control treated with oxygen and positive control treated with ozone alcoholic. Results and Discussion: Weight control, fluid and food intake, suggest affects metabolism in rats treated with alcohol compared to control group. The administration of ethanol in increasing concentrations was able to develop addictive behavior in rats studied. There was presence of lipid peroxidation in the treated animals, as evidenced by increased MDA, CAT and SOD in serum. Ozone administration restored the redox balance. Conclusions: It is possible to establish animal model of alcoholism by administering increasing concentrations of ethanol, which leads to the development of addictive behavior in which oxidative stress is present which can be controlled ozonotherapy.</p>

<p>PFE 088</p>	<p>EFFECT OBSERVED AFTER ACUTE AND SUB-ACUTE NASAL DOSING OF ERYTHROPOIETIN WITH A LOW CONTENT OF SIALIC ACID <u>Lagarto A</u>, Bueno V, Couret M, Valdés O, Barzaga P, Sánchez J.A, Beausoleil I, López R, Guerra I, Gabilondo T, Vega Y</p> <p>Drug Research and Development Center. CIDEM. 17 No. 6208 e/ 62 y 64, Playa, código postal 11300, Ciudad Habana, Cuba. email: alicia@cidem.sld.cu</p> <p>The erythropoietin with a low content of sialic acid (rh-EPO_b) may be used as a neuroprotective agent without risk of thrombotic events. The objective of this investigation was to assess the toxicological potential of a nasal formulation with rh-EPO_b in acute, sub-acute and nasal irritation assays in rats besides evaluate the immunogenicity and erythropoietic effect of the test substance. In an irritation test, rats received 15 µl of rh-EPO_b, slides of the nasal mucosa tissues were examined 24 hours later. Control and treated groups showed signs of a minimal irritation. In the acute toxicity test, the dose of 47'143 UI/kg was administered by nasal route in rats. Haematological patterns, body weight, relative organ weight, and organ integrity were not affected. In the 14-days subacute toxicity test, both sexes rats received 6'600 UI/kg/day. An increase of lymphocytes was observed in males. Histopathological examination of organs and tissues did not reveal treatment induced changes. In the 28-days subacute toxicity test, animals received 2357, 4714 and 6600 UI/kg/day. We observed slight variations in hematocrit and total erythrocyte count in female treated groups. These effects did not modify the hemoglobin and blood clotting time results. A slight increase in glucose level of treated female animals within the normal range was observed. Both effects were not observed 14-days after treatment. Antibody formation was not observed in any of the test doses. Histopathological examination of organs and tissues did not reveal treatment induced changes. Female B6D2F1 mice were used for evaluated erythropoietic effect of the nasal formulation. Hematological endpoints were examined every week during 28 days of intra-nasal dosing of 6600 UI/kg/day. The administration of rhEPO_b in normocythaemic mice did not produce erythropoietic effect. These results suggest that rhEPO_b could be used as a neuroprotective agent, without significant haematological side effects.</p> <p>Keywords: erythropoietin, nasal administration, nasal irritation, subacute toxicity, immunogenicity.</p>
<p>PFE 089</p>	<p>PRECLINICAL EVALUATION ON TOXICITY, INMUNOGENICITY AND DELAYED TYPE HIPERSENSIBILITY OF DEC-HER 1 VACCINE WITH ANTICANCER EFFECTS <u>Bada AM</u>¹, Casacó A², Sánchez B², Arteaga ME¹, González B¹, León A¹, González C¹, Gómez D¹, Ocaña R¹, García A¹, Contreras F¹, Contreras B¹, Pérez B¹, Ballart N¹, Somoza N¹, Legró M¹, Blanco D¹, Peña A¹, Ronda M¹, Escalona MA¹, Lemus M¹, Hernández Y¹, Thomas A¹, Prida Y¹, Torres Y¹, Mesa M³</p> <p>¹Experimental Toxicology Center, National Center for Laboratory Animal Breeding, Bejucal, Havana, Cuba email: ambada@cenpalab.inf.cu ²Center of Molecular Immunology, P.O. Box 16040, Havana, 11600, Cuba ³Centro de Investigaciones Médico Quirúrgicas, Havana, Cuba</p> <p>Introduction: Active specific immunotherapy may be an alternative and complementary approach for the treatment of several cancer types. The Center of Molecular Immunology has developed several vaccines, including DEC-Her1, based in the extracellular domain of the epidermal growth factor receptor (EGFR). The objective of our study was to assess the toxicity, immunogenicity and Delayed Type Hypersensitivity (DTH) in non human primates immunized with DEC-Her1 vaccine in a 6 months period. Material and Methods: <i>Macaca fascicularis</i> monkeys were randomly distributed into two groups of 3 animals/sex: Control (Saline) and Treated (DEC-Her1 vaccine: DEC-Her 1 + NAcGM3/VSSP + Montanide ISA 51 VG). Immunizations were made on days 0, 14, 28, 42, 56, 84, 112, 140 and 168. Animals were inspected daily for clinical signs and body weight, rectal temperature, and cardiac and respiratory frequencies were measured along the study. Blood samples were collected at 5 sampling times for hematological, serum biochemical determinations and immune response evaluation. DTH was assessed four times during the study. At the end of the study, skin biopsy was performed in all animals. Results: Study survival was 100%. Local reactions were observed at the administration site of several Treated animals. Clinical pathology parameters were not affected and no DTH response was detected. Conclusions: The study showed that the immunization of <i>Macaca fascicularis</i> monkeys with DEC-Her1 vaccine was well tolerated, eliciting local reactions at the administration site.</p>

<p>PFE 090</p>	<p>SHELF-LIFE STABILITY STUDY OF A NOVEL ADJUVANTED AND ADSORBED HOUSE DUST MITE ALLERGEN VACCINE Más A, Ramírez W, Labrada A, Oliva Y, Mateo M, Bourg V, Torralba D, Huerdo L, Morales T, Llama J. Allergens Dept., National Center of Bioproducts, Havana, Cuba. email: arelis@biocen.cu</p> <p>Introduction: Evaluation of shelf-life stability of pharmaceutical products is required during the pharmaceutical development phase, prior to advancing to clinical trials. The objective of this work was to test the stability of a new experimental allergen vaccine of <i>Dermatophagoides siboney</i> adjuvanted with Outer Membrane Vesicles (OMV) of <i>Neisseria meningitidis</i> and adsorbed into Alum hydroxide. Methods: The ICH methodology established for stability studies for biological products was followed. Samples of three pilot scale GMP batches were stored at 4 °C and assayed at 0,3,6,9,12,18 and 24 months. Possible desorption from alum gel was monitored, testing the supernatant for allergenic activity (IgE-inhibition ELISA), Der s1 content (MAb-ELISA) and total protein content. Preservation of antigen's integrity was checked by SDS-PAGE and Western-Blotting after forced desorption. Other tests were applied for measuring preservative content, pH stability, and sterility. Acceptance limits matched those used for product release. Since, a potency test is not yet established for this new vaccine, allergen-specific immunogenicity in Balb/C mice was determined at the beginning and end of the study. Results: After 24 months no deviations of quality specifications were detected in any parameter. Although a slight tendency toward increasing the allergen activity and Der s 1 content in the supernatant was noted, it was not statistically significant (regression analysis, p<0.05). The immunogenicity test showed the expected outcome regarding induction of allergen-specific IgG, IgG1 and IgG2a antibodies (the later is dependent of the OMV adjuvant effect), similarly to initial results. Conclusion: This study proved the vaccine stability during 24 months as a basis for approval of a reliable expiration period.</p>
<p>PFE 091</p>	<p>RADIOSENSITIZATION OF U87MG BRAIN TUMORS BY ANTI-EPIDERMAL GROWTH FACTOR RECEPTOR MONOCLONAL ANTIBODIES Díaz Miqueli A¹, Rolff J², Lemm M², Fichtner I², Perez R¹ Leon K¹ and Montero E¹</p> <p>¹Centre of Molecular Immunology, P.O. Box 16040, 214 Street, Havana 11600, Cuba. email: arlhee@cim.sld.cu ²Max Delbrück Center for Molecular Medicine. Robert-Rossle-Strasse 10, Berlin-Buch 13125, Germany.</p> <p>Introduction: As epidermal growth factor receptor (EGFR) has been reported to be a radiation response modulator, HER inhibitors are regarded to act as potential radiosensitizers. Our study examined the role of nimotuzumab and cetuximab both, the two monoclonal antibodies (mAbs) to EGFR, as radiosensitizers. Materials and Methods: The human-mouse chimeric mAb cetuximab was provided by ImClone Systems. The humanized mAb Nimotuzumab was generated at the Centre of Molecular Immunology. U87MG is a human glioblastoma cell line. Cell proliferation was assessed by Ki-67; CD31/PECAM-1 and CD133 immunostaining was performed to visualize endothelial blood microvessels and identification of cancer stem cells (CSCs) population, respectively. Immunofluorescence TUNEL assay was used to evaluate apoptosis and immunoblotting assays to determining the inhibition of EGFR-related downstream signaling. Results and Discussion: Co-administration of both the antibodies with radiation increased the radiosensitivity of U87MG, resulting in a significant delay of subcutaneous (s.c.) tumor growth. Furthermore, the addition of antibodies to the radiation decreased brain tumor sizes and is inhibited by 40–80% the increased tumor cell invasion provoked by radiotherapy, although promoted tumor cell apoptosis. Whereas nimotuzumab led to a reduction in the size of tumor blood vessels and proliferating cells in s.c. tumors, cetuximab had no significant antiangiogenic nor antiproliferative activity. In contrast, cetuximab induced a more marked inhibition of EGFR downstream signaling compared with nimotuzumab. Moreover, both antibodies reduced the total number of radioresistant CD133⁺ CSCs. Conclusions: These results were encouraging, and showed the superiority of combined treatment of mAbs to EGFR and radiation over each single therapy against glioblastoma multiform (GBM), confirming the role of these drugs as radiosensitizers in human GBM. In addition, we first showed the ability of mAb specifics against EGFR to target radioresistant glioma CSC, supporting the potential use in patients.</p>

<p>PFE 092</p>	<p>MORPHOLOGICAL RESPONSE INDUCED BY DPPC LIPOSOMES ENCAPSULATING ALLERGENS FROM <i>Dermatophagoides siboney</i> <u>Bárbara Gonzalez Navarro</u>¹, Virgilio Bourg², Lesly Calderon³, Elisa Facenda², and Alexis Labrada²</p> <p>¹CETEX - CENPALAB, La Habana, Cuba. ² BIOSEN, La Habana, Cuba. ³ Centro de Estudios de Proteínas, Facultad de Biología, UH, C Habana, Cuba.</p> <p><u>Introduction:</u> Mites from the genus <i>Dermatophagoides</i> are the major source of allergen in house dust (maDer s) and play an important role in the pathogenesis of asthma and other atopic diseases. Liposomes (LD) are non toxic and biodegradable lipid vesicles, which are safe and effective adjuvants to induce Th1-skewed immune responses. We characterized of the morphological response against the major allergens from <i>D. siboney</i> encapsulated in to LD, using the same allergens adsorbed to Alum in BALB/c mice. <u>Material and Methods:</u> Four groups of female 6-8 weeks old mice were intraperitoneally immunized with maDer s dissolved in PBS, or encapsulated in DPPC DRV s, or adjuvanted with Alum. Each injection contained 5 µg of Der s 1. Alum and DPPC doses were 600 µg and 5.4 mg per injection. Immunizations were administrated on weeks 0 and 2. Control group was injected with sterile PBS. Ten days after the last immunization, five mice per group were placed in a chamber (18x12x21x) and exposed aerosolized <i>D. siboney</i> extrat during 1 hour. The output of the nebulizer was 0.3 mL/min and Der s 1 concentration in mite extract solution was 100 µg/mL. 24 hours after the aerosol exposure mice were sacrificed; their lungs fixed in 10% phosphate-buffered formalin and submitted to histological examination. Lungs sections were embedded in paraffin, sectioned and stained with haematoxylin-eosin. <u>Results and Discussion:</u> Mice receiving maDer s encapsulated into DPPC liposomes or dissolved in PBS had normal lung histology similar to control group and in contrast with those receiving maDer s adsorbed in Alum. In this group, extensive peribronchovascular inflammation was found. <u>Conclusions:</u> This vaccine formulation could be also considered as a promising alternative for prophylactic vaccination against allergy.</p>
<p>PFE 093</p>	<p>SEARCHING FOR MARKERS OF BIOLOGIC/ALLERGENIC ACTIVITY DURING HOUSE DUST. MITE CULTURE PROCESS FOR MANUFACTURING ALLERGEN VACCINES <u>Fernández BI</u>, Labrada A, Torralba D, Luis B, Ramírez W, Mas A</p> <p>Allergens Dept, National Center of Bioproducts, Havana, Cuba. email: baby1@biocen.cu</p> <p><u>Introduction:</u> Current standardization of allergen vaccines is based mostly on allergenic activity as measured by IgE competition immunoassays, using human sera from allergic patients. Alternative approaches comprising individual allergen content and enzymatic activity have been proposed. The aim of this work was to asses the relationship between the allergenic activity of the House Dust Mite <i>Dermatophagoides siboney</i>, enzymatic activity and content of its major allergen Der s1 (a cysteine-protease), during the mite culture process. <u>Methods:</u> For this purpose, samples of cultures, maintained in a hypoallergenic growth medium, were collected weekly during 10 weeks. Total allergenic activity was measured by IgE inhibition ELISA, protein composition by SDS-PAGE, Der s1 content by mab-ELISA and protease activity by a kinetic test using casein as substrate and by a gelatinolytic zymogram method. <u>Results:</u> Both, the allergenic potency and Der s1 content achieved peak values after 6 weeks of culture. Allergenic activity was significantly correlated to Der s1 content (r=0.84, p=0.005) and even to greater extent to enzymatic activity (r=0.95, p<0.0001). The zymogram showed that the enzymatic activity was focused in the 25kda band corresponding to Der s1, which showed a marked time-dependent increase by SDS-PAGE. The consistency of the Der s1 content was confirmed in 28 consecutive culture batches during a period of 4 years, with a mean geometric value of 3.91 mg/g (Geometric CV: 2.42). <u>Conclusions:</u> These results support the introduction of Der s1 content and enzymatic activity as surrogate markers of biological potency during mite culture process.</p>
<p>PFE 094</p>	<p>A NOVEL CELL PENETRATING PEPTIDE THAT REDUCES TUMOR GROWTH AND MODIFIES THE EXPRESSION OF GENES IN HUMAN CANCER CELL LINES Guerra M¹, Fernández J², <u>Oliva B</u>¹, Torrens I¹, Garcia I³, Falcon V¹, Garay H¹, Mendoza O¹, Granadillo M¹, Reyes O¹</p> <p>¹Division of Pharmaceuticals, Center for Genetic Engineering and Biotechnology, Havana, Cuba; ²Division of Genomics and Immunodiagnostic, Center for Genetic Engineering and Biotechnology,</p>

	<p>Havana, Cuba; ³ Basic Studies Department, Institute of Oncology and Radiobiology. F and 29, Vedado, Havana, Cuba. email: brizaida.oliva@cigb.edu.cu</p> <p>Introduction: In the context of cancer therapy, cell-penetrating peptides (CPPs) overcome the problem encountered using standard techniques, which has low specificity of target that affect normal cells as well as tumor. The CCPs, as a delivery modality, allows the development of novel agents which specifically target cancer cells. The peptide LALF31-52 is a small cationic and amphipatic peptide from the <i>Limulus</i> anti-LPS factor (LALF). In this work, we documented that analogous peptides from region 32-51 of the <i>Limulus</i> anti-LPS factor possess the ability to inhibit tumor cell proliferation by a mechanism that doesn't imply to bind LPS. Materials and Methods: The cytotoxicity of peptide was monitored in several tumor cells line by SRB [Sulforhodamine B, sodium salt] assay. <i>In vivo</i> therapy of tumor solid was evaluated in both immunocompetent and nude mice. To isolate the gene transcripts specifically regulated by L-2 in tumor cells, we conducted suppressive subtractive hybridization (SSH) analysis. Results and Discussion: We identified the peptide L-2 and L-20 diminished capacity to bind LPS and the cytotoxic activity of L-2 was higher than L-20 on various tumor cell line. Our findings demonstrated the alanine substitution in the non-cyclin LALF₃₂₋₅₁ sequence, abolished its ability to bind LPS and an effective cytotoxic activity. These peptides demonstrated the cell-penetrating capacity in cells lines. Furthermore, the peptide L-2 showed a potent antitumor effect compared to L-20 when is systemically injected in murine tumors implanted in the TC-1 model and in a human colon tumor xenograft in nude mice. The differential expression of a unique set of differentially expressed genes in tumor cells treated with L-2 may be one of the mechanisms through which it carries out its antitumor activity. Conclusions: We have provided a proof-of-concept that L-2 peptide is a novel cell-penetrating peptide with antineoplastic activity.</p>
PFE 095	<p>ALUMINUM PHOSPHATE AS ADJUVANT IMPROVES THE IMMUNOGENICITY OF MONOVALENT CONJUGATES AGAINST SEROTYPES 1 AND 14 OF <i>STREPTOCOCCUS PNEUMONIAE</i></p> <p>García-Rivera D¹, Ney G², Rodríguez L¹, Pérez A¹, Nadal L², Martín Y¹, Amador A¹, Pedroso J³, Santana D⁴, Serrano Y⁴, Chang J⁵, Valdés Y⁶, Fernández V⁶, Vérez V⁶.</p> <p>Center for Biomolecular Chemistry. 200 and 21th, Atabey, Playa. Havana. Cuba. Department of: 1) Immunology 2) Formulations 3) Chemical Analysis 4) Glycoconjugation 5) Glycotechnology. 6) Head of Research Project. email:dagmar.garcia@cqb.cu</p> <p>Introduction: <i>Streptococcus pneumoniae</i> (Neumococco) is an encapsulated pathogen that can cause bacterial pneumonia, bacteremia, meningitis and otitis media. The vaccination with capsular polysaccharides (PS) is ineffective in toddlers and young infants, due to the T-independent nature of these antigens. The success of conjugated vaccines against Neumococco is due to PS are become immunogenic for these groups of risk, because they are processed as T-dependent antigen by immune system. Currently, the Center for Biomolecular Chemistry is working on develops an heptavalent conjugated vaccine against Neumococco. Frequently, aluminum adjuvants are included on vaccine formulations to improve the immunogenicity of antigens. Herein, the effects of aluminum phosphate (AlPO₄) adjuvant on the immunogenicity of two monovalent conjugates against serotypes 1 and 14 were evaluated. Materials and Methods: Balb/c mice were immunized with three doses s.c of conjugates 1-TT or 14-TT (2 □g PS/dose) with and without AlPO₄ adjuvant. The serum and mucosal antibody response and the antibody avidity were evaluated by ELISA. Results and Discussion: An improvement of the immunogenicity was found when both conjugates were adjuvated, and the effects were better for serotype 14 than 1. The conjugate 1-TT adjuvated induces antibodies IgG with higher avidity and promote affinity maturation compare with non-adjuvated, but the adjuvant doesn't improve the levels of antibodies IgM or IgG anti-PS in serum or mucosa. For conjugate 14-TT, adjuvant induces higher levels of IgG anti-PS after second dose and marked enhance of IgG1 in serum and IgG in respiratory mucosa compare with the same conjugate without adjuvant. Conclusions: AlPO₄ as adjuvant improve the immunogenicity of monovalent conjugates 1-TT and 14-TT. These evidences for serotypes 1 and 14, together with the results for the other serotypes, could be the major reason for the use of AlPO₄ as adjuvant in heptavalent conjugated vaccines against Neumococco.</p>

<p>PFE 096</p>	<p>PROTEASE AND ALLERGENIC ACTIVITY OF ALLERGEN EXTRACTS OF <i>BLOMIA TROPICALIS</i>, <i>DERMATOPHAGOIDES PTERONYSSINUS</i> AND <i>DERMATOPHAGOIDES SIBONEY</i></p> <p>Pérez M¹, Torralba D¹, Labrada A¹, Fraga R².</p> <p>¹ National Center of Bioproducts, PO Box 6048, Havana 10600, Cuba. ² ICIDCA, Havana, Cuba. email: damari.torralba@biocen.cu</p> <p>Introduction: Molecular characterization of several mite allergens has elucidated their enzymatic proteolytic properties, which can be linked to allergenicity. On the other hand, the presence of active proteases in biopharmaceutical products could lead to protein degradation affecting product stability. The objective of this work was to study the gelatinolytic protease profile of allergen extracts of <i>Dermatophagoides siboney</i> (Ds), <i>D. Pteronyssinus</i> (Dp) and <i>Blomia tropicalis</i> (Bt) and its relation to IgE binding-activity. Methods: Zymogram using gelatin as substrate and SDS-PAGE followed by IgE Western Blotting (WB). Results: The gelatinolytic profile of Bt consisted of 8 separate bands. Only the 30 kd band was resistant to incubation in denaturing conditions at 100°C, during 5 min. In the Dp extract, 4 gelatinolytic bands were detected, 2 of them thermo-resistant, including the most intense, which corresponds to the major allergen Der p 1. In spite of the taxonomic and allergenic similarity between Dp and Ds, in the last specie, it was detected up to 6 enzymatically active bands, whereas only Der s 1 was thermoresistant. Oxidation of Ds extracts using metal ions (Zn⁺, Cu²⁺) showed inhibition of some bands. The overall comparison of zymograms with the allergenic profiles, as measured by WB, suggests that most allergenic components have enzymatic activity in the case of Bt, in contrast to Dp or Ds. The incubation at high temperatures removed most of the enzymatic bands, not affecting IgE-binding bands, i.e. allergenic activity. Conclusions: These results suggest that inactivation at high temperature could be used for the development of allergen vaccines with reduced enzymatic activity.</p>
<p>PFE 097</p>	<p>IMPACT OF CHANGES IN THE CELL DIVISION STAGE DURING THE OBTENTION OF THE ERYTHROCYTES SENSITIZE SUBSTANCE (ESS) FOR THE LEPTOSPIROSIS DIAGNOSIS</p> <p>Arencibia DF¹, Batista N¹, Blaín K¹, Solís RL¹, Rosario LA², García L¹</p> <p>¹Researches Vicepresidency (Finlay Institute), 17 avenue between 198 and 200 street. Playa Municipality. Havana City. Cuba. email: darencibia@finlay.edu.cu ²Institute of Pharmacy and Food Science (IFAL, U.H), 27 avenue and 222 street. Lisa Municipality. Havana City. Cuba.</p> <p>Introduction: In Cuba since 1981 has implemented the passive hemagglutination (HA) as an alternative technique of Leptospirosis diagnosed, in the absence of others that may be more costly but effective at different stages of the disease. This method is used with varying degrees of success in the Provincial Centers of Hygiene and Epidemiology. For the development of the technique requires the erythrocytes sensitize substance (ESS), assuming the production Finlay Institute in 2009, from obsolete technology in the process of cell multiplication. The aim of this study was to make changes at this stage to obtain the ESS with the culture media that exist today and available at the plant for optimum product performance, without affecting the biological activity as the basic parameter of quality. Material and Methods: Eight experimental groups were formed according to multifactorial design, taking into account: production strain (LABIOFAM or Finlay strain of <i>L. biflexa</i> Patoc I), culture medium (MK and MEJH) and culture conditions (static or agitated at 130 r.p.m). Results and Discussion: We obtained as a result that the best variant was the combination (LABIOFAM strain, growth in MEJH and agitated). This variant had a duplication time of 2 days, being smaller with regard to the variant 1 (control) that was of 4,15 days. The ESS was obtained in 15 days less than in the control that is of 30 days. It had a 1/64 title, consistent with the demands of quality; with more biological activity than the other variants and with regard to the control that was 1/16. This variant will allow to give bigger quantity of flasks to the National Program of Leptospirosis when producing a single lot. Conclusion: This work allowed to use the best variant to begin the different designs of studies of stability of the product.</p>

<p>PFE 098</p>	<p>STABILITY OF REFERENCE MATERIALS USED FOR DETERMINING ANTIGEN CONTENT BY FLOCCULATION METHOD IN TETANUS VACCINES Cisneros D¹, Mahy T², Herrera L, Ontivero I, Landys M</p> <p>Reference Materials Department, Finlay Institute, 27 Ave No. 19805, P.O. Box 16017, Havana, Cuba. email: dcisneros@finlay.edu.cu</p> <p>Introduction: As part of the quality control of tetanus toxoid vaccines, it is needed to determine the antigen content. For that, stable working reference tetanus antitoxin and toxoid standards, which must comply with requirements, such as the stability of the property of interest in shelf life and stress conditions, whose study was the aim of our work. Materials and Methods: The test method is the Ramon's Flocculation Test based on an immunoprecipitation reaction, for which use work reference materials and International Not Adsorbed Toxoids. Three batches of lyophilized tetanus antitoxin and one batch of liquid tetanus toxoid were evaluated on shelf life stability study, kept at 2-8 ° C, sampled annually over a period of 5 years from the date of manufacture. Only the batch of toxoid was studied in temperature stress conditions, kept at 25 ° C and sampled on 30th, 60th and 90th day; also kept at 40 ° C and sampled on 15th, 30th, 60th and 90th day. Results: The reference materials remain the property of interest stable at all studied times under conditions of shelf life. The tetanus toxoid retains its activity value at 25 for 90 days and 40 for 15 days, Conclusions: The antitoxin and tetanus toxoid are stable, preserved at 2-8 ° C for 5 years. The tetanus toxoid is stable under temperature stress at 25 ° C for 90 days and at 40 ° C for 15 días.</p>
<p>PFE 099</p>	<p>PROCESS DEVELOPMENT OF PURIFIED PROTEIN ALLERGENS AS THE ACTIVE PHARMACEUTICAL INGREDIENT FOR AN ADJUVANTED THERAPEUTIC ALLERGY VACCINE Martínez D, Labrada A, Más A, Torralba D.</p> <p>Allergens Dept, National Center of Bioproducts, Havana, Cuba. email: deibbys.martinez@biocen.cu</p> <p>Introduction: Novel allergen vaccines intended for allergy immunotherapy are based on recombinant or purified natural allergen proteins and adjuvants. The allergens are regarded the active ingredients since they induce an adaptive immune response. Objective: To assess the process consistency and effectiveness of the purification steps of Dermatophagoides major allergens. Materials and methods: A purification process in GMP conditions was followed starting from a freeze-dried allergen extract of D. siboney (VALERGEN-DS, BIOECEN) comprising salting-out steps and chromatography in SUPERDEX-200. The major allergen content (Der s 1) was assessed by ELISA and the allergenic activity was measured using IgE competition assay with human sera. Purity was determined by SDS-PAGE. Results: The purification process showed consistent results after 15 consecutive batches. The average concentration of Der s 1 was 154 µg/mL, with a CV of 8.4%. Main total protein content was 254µg with a CV of 15%. Purity of Der s 1 (25KDa) and Der s 2 (15Kda) components was higher than 90 % for all the batches. Overall Der s 1 recovery was above 60% during the process and batch yield was 4.3 ± 0,6 mg. No batches were found out of the specification or ±3σ limits. The maximum failure probability according to Process capability Analysis was 3 % for the Der s 1 content and allergenic activity. These values are regarded as satisfactory considering the high variability of the analytical methods (which is estimated to be much greater than the intrinsic process variability). Conclusion: it was demonstrated the consistency of the main quality parameters of the active ingredient for a novel allergen vaccine, which is very relevant to clinical development of the product.</p>
<p>PFE 100</p>	<p>EVALUATION OF A NEW CULTURE MEDIA USED TO OBTAIN PURIFIED NEISSERIA MENINGITIDIS SEROGROUP C POLISACCHARIDE Humberto González¹, Domingo González¹, Luis Manuel Rodríguez¹, Marixa Hernández, Ricardo Carmona, René González, Juan Carlos Martínez, Dorian Armenteros, Kirenia Rivero, Dairon Arjona, Marylin Pérez, Rene Tejedor, Adrián Reyes, Fara Primelles, Greter Jordán, Lianelis Pellicer, Naylet Marrero, Odalis Guerra, Maricel Guerra, Magda Pampin, Maricel Rosabal.</p> <p>Pharmaceutical Development Direction. Finlay Institute. email: hgonzalez@finlay.edu.cu</p> <p>Introduction: Now days, meningococcal disease is still being a threat for humanity, no matter all efforts made by investigators. <i>Neisseria meningitidis</i> serogroup A, B and C are the main responsables for more than 90 % of the disease around the world. The disease is present in different groups with a high rate in</p>

	<p>early aged children and its clinical manifestations may include even death. On the other side, there is an upraising need of finding stronger culture media guarantying high cell biomass and an increasing of polysaccharide production, without compromising their structural integrity. In this work it was evaluated the liquid culture media used for <i>Neisseria meningitidis</i> (LMNM) and compared to traditional Frantz modified culture media. Materials and Methods: This comparison was established on the basis of sialic acid production in each media. RMN¹H analysis was performed to demonstrate modification in the polysaccharide structure Results and Discussion The sialic content values were five times higher for LMNM in relation with Frantz modified media. Consistency process allowed corroborating the huge impact of the new culture media on the purified polisaccharide, with an increasing of five times regarding the historical values. Besides, it was obtained a polysaccharide that meets WHO regulation requirements for this kind of products. Analysis using RMN¹H showed that there was no change in the purified polysaccharide structure. Conclusions: It was demonstrated it's possible to use the LMNM as a suitable alternative for the manufacturing of purified C Polysaccharide, adding to this the economical impact on the reduction of costs compared to the use of the traditional media.</p>
<p>PFE 101</p>	<p>STANDARDIZATION AND VALIDATION OF THE FORMALDEHYDE RESIDUAL PRESENT IN PHARMACEUTICAL ACTIVE AND BOVINE INGREDIENTS Delgado I, Miranda G, Abreu J, Merchan Y, Mandariote A.</p> <p>Finlay Institute. 27 Ave # 19805 e/ 198 and 202. La Lisa. Havana City. Cuba. email idelgado@finlay.edu.cu</p> <p>Introduction: Formaldehyde is found in some drugs, either as a preservative or as an impurity from the production of them. Their determination is of vital importance. The residual formaldehyde test described in the European Pharmacopoeia was amended to ensure proper quantification. standardization and validation of the method was performed in products such as Active Pharmaceutical Ingredients (tetanus and diphtheria toxoid, packed cells of Bordetella pertussis) and antigens of Leptospira and the finished product (typhoid vaccine: vax-TyVi). Material and Methods: Validation was determined through the parameters of Precision, Accuracy and Specificity. Accuracy was analyzed in terms of Repeatability and Intermediate Precision at a single level of concentration. To estimate the Accuracy, samples were spiked with formaldehyde solution and placebo was used in Specificity, Limit of quantification and linearity of the calibration curve was carried out with concentrations 0024, 0020, 0.016 mg / mL . Statistical test such as t test, Fischer's F, ANOVA for the lack of fit of the calibration curve and the estimation of confidence intervals of the intercept was used for comparison an estimation. On the active ingredients, precision VC were at most 9.5% and in final products up to 2.5% . Accuracy: The recovery ranged from 100.1-100.8%.. The specificity was satisfactory, the limit of quantification was 0.003 mg / mL and the linear correlation coefficient r = 0.99. In general, the levels of all parameters were satisfactory. Conclusions: These results show a method of reliable quantification, that which is translated in a security of the medications</p>
<p>PFE 102</p>	<p>ADJUVANT EFFECT OF IMS 4112 OVER A MULTIEPITOPIC PROTEIN OF HIV-1 AND COMPARISON WITH A MULTIANTIGENIC FORMULATION USING VLP FROM HBV Rodríguez-Alonso I¹, Soria Y², García D¹, García-Díaz D¹, Santisteban Y¹ and Iglesias E¹.</p> <p>¹ Vaccine Department. Center for Genetic Engineering and Biotechnology, Cuba. ² Animal Care Facilities. Center for Genetic Engineering and Biotechnology, Cuba. email: ingrid.rodriguez@cigb.edu.cu</p> <p>Introduction: An increase in the humoral and cellular responses is reported in schedules combining mucosal and parenteral immunizations. Using such schedules, we developed a multiantigenic formulation including a recombinant multiepitopic protein (CR3) and the surface (HBsAg) and core (HBcAg) virus like particles (VLP) of HBV for promoting a Th1 immune response to obtain a vaccine candidate against HIV-1. On the other side, new adjuvants are been developed like the experimental IMS 4112 produced by SEPPIC, which is a nanoparticle aqueous formulation for eliciting Th1 immune responses. The aim of the present work is to compare the adjuvant effect of IMS 4112 with VLP of HBV over the CR3-specific immune response in Balb/c mice using a schedule that combine nasal (i.n) and subcutaneous (s.c) inoculations. Materials and Methods: Fifteen female Balb/c mice per group were immunized with 10 µg of each antigen. CR3-specific cellular immune response was assessed by IFN-γ ELISPOT assay and CD4+/CD8+ T cell proliferation. Antibody levels were measured by ELISA in sera and vaginal washes. Results: After five doses we observed the induction of CR3-specific CD4 and CD8 cells and IFN-γ</p>

	<p>secreting cells in mice's spleen only in the group immunized with CR3 and the VLP of HBV; but not in the group using IMS 4112. However, similar levels of CR3-specific antibodies were detected in vagina and sera of animals in all groups. Overall these results suggest the induction of a very low CR3-specific cellular response in mice immunized with IMS4112. Additionally, anti-HBsAg and anti-HBcAg antibodies were elicited in sera of animals. Conclusion: These results suggest the use of the multiantigenic formulation comprising CR3 and VLP of HBV in a future phase-1 clinical trial in HIV infected individuals.</p>
PFE 103	<p>EVALUATION OF TETANUS POTENCY IN VACCINES BY USING A GUINEA-PIG SEROLOGY METHOD Ontivero I, Adames Y, Gutiérrez N, Lara M, Izquierdo L, Chovel ML, Mandiarote A, Barrios T</p> <p>Introduction: The potency of Tetanus vaccines is determined by using recognized <i>in vivo</i> potency tests as the WHO challenge tests and the neutralization tests (TN) recommended by FDA. Recently, new approaches have been established focused on the possibility to replace the <i>in vivo</i> methods by relevant <i>in vitro</i> alternatives. The aim of this Paper is to describe the behaviour of a guinea-pig serology method (ELISA) developed at Institute Finlay for determining Tetanus Potency in vaccines as an alternative to the traditional TN. Materials and Methods: A guinea-pig serum was used as calibration curve after its own calibration against the international standard of Diphtheria and Tetanus antitoxin Guinea Pig serum (98/572). Once calibrated the standard, 44 guinea pig sera from Tetanus Toxoid, DT and DwPT vaccines were analysed by <i>in vivo</i> and ELISA methods in parallel and the results were compared by linear regression analysis. Results and Discussion: Tetanus potency estimates obtained by <i>in vitro</i> and TN tests were in good agreement for the different vaccines tested. Conclusion: It was demonstrated that the serological alternative (ELISA test) is a suitable <i>in vitro</i> assay for assessing the potency of tetanus toxoid component in single and combined vaccine batches for human use.</p>
PFE 104	<p>INTERNATIONAL TRENDS IN THE FIELD OF VACCINES Hernández-Roche Jonatan, Talavera Coronel Arturo, Solis Rodriguez Rosa Lydia, Pérez Martin Oliver.</p> <p>Finlay Institute. Centre of Research, Development and Manufacturing of Vaccines. 27th Ave No. 19805, Lisa, Havana City. A.P 11600. email: jhernandez@finlay.edu.cu</p> <p>Introduction. According to the World Health Organization (WHO), along the lines of the first order, in Research and Development Vaccines are getting candidates against rotavirus, pneumococcal, meningococcal, Influenza, Tuberculosis, Malaria and AIDS, among others diseases. They are also prioritized within these lines cervical cancer, HPV, among others. In second line of priority is the development of candidates against dengue, leishmaniasis, enteric diseases, among others, and adapt new technologies to the formulation and controlled release. This paper aims to analyze international trends in the field of vaccines and their applicability to the institutional environment. Material and Methods: The methods used were analysis of bibliometric indicators and processing of information in scientific papers and patent information from database as PubMed, WIPO and EPO USPSTO. Results and Discussion: These studies allowed the identification of: 1.- there is a change in trends of development of vaccines against infectious diseases non-infectious. 2.- the great vaccine market is approaching a high level of consolidation and low competition ($HI^* = 0.18$), given that a small number of companies dominate over 81% of the global market. 3.- new lines of research projects, use of technologies and the possible trend in the field of vaccines. Conclusions: In general, large companies are focusing their strategy on chronic diseases such as cancer and diabetes. However, there continue to develop strategies for infectious diseases such as HIV / AIDS, rotavirus, pneumococcal disease. References: WHO. http://www.who.int/vacines; Report the Vaccines Market Outlook To 2014, 2009. Business Insights Ltd, 2009.</p>
PFE 105	<p>VALIDACION DEL ENSAYO DE TOXICIDAD ESPECIFICA DE DIFTERIA EN EL INSTITUTO FINLAY Juan F. Núñez, Oriallys Valle, Ileana Delgado, Irma Labrador, Regla Sosa, Nayla Salazar, Eduardo Cajuzo, José Dupuig, Aleida Mandiarote</p> <p>Instituto Finlay. Ave 27. No 19805. La Lisa. AP 16017. CP 11600. Ciudad Havana. Cuba.</p> <p>At present, vaccines with the component Diphtheria Toxoid are widely used, so it is vitally important to establish the non-toxicity of this product, which is made using the specified toxicity test for this component. The test uses the toxic effect that produce the diphtheria toxin in the skin of guinea pigs when are inoculated by intradermal way. This effect is characterized by the formation of a red granuloma after</p>

	<p>48 to 72 hours of the inoculated animal due to the effect dermonecrotizante that produces the diphtheria toxin. Materials and methods: Specifies toxicity testing of vaccines for diphtheria component was done, by WHO procedures description, the samples of diphtheria toxoid and the same sample loaded with diphtheria toxin were evaluated. The reference materials used were diphtheria toxin of reference (TDR 3 / 04) and antitoxin reference produced by Finlay Institute. Duncan Hartley guinea pigs with a weight between 600-700 gr. were used. The results obtained in the parameters tested during the validation were satisfactory, so we can use the method with reliable results.</p>
<p>PFE 106</p>	<p>TRANSCRIPTIONAL CHANGES OF TUMORAL CELL LINES TREATED WITH THE ANTITUMORAL PEPTIDE L-2. Fernández J¹, Palenzuela D¹, Guillen I¹, Vazquez D¹, Oliva B², Novoa L¹, Guerra M²</p> <p>¹Division of Genomics and Immunodiagnostic, CIGB, Havana, Cuba. ²Division of Pharmaceuticals, CIGB, Havana, Cuba. email:julio.fernandez@cigb.edu.cu</p> <p>Introduction: The peptide L-2 is a novel molecule with antineoplastic and cell-penetrating capacity in several tumor cell lines. Systemic injection of immunocompetent and nude mice with established solid tumor, resulted in regression of tumor mass and apoptosis¹. Oligonucleotide arrays were employed to identify a set of genes that are differentially expressed in tumor cells following treatment with the peptide. The results shown in this study suggest that peptide L-2 may be a potential agent in the treatment of solid tumors. Materials and Methods: We used a microarray based approach to analyze Hep-2 and H125 cells lines treated with 150 μM of L-2 for 2 hours. The differential expression analysis was conducted using Bioconductor². For gene annotation, classification and pathway analysis we used DAVID³. Results and Discussion: We identified a set of 341 genes differentially expressed when compared treated vs untreated cells. As defined by gene ontology the enriched categories were regulation of cell death, negative regulation of biological process, response to protein stimulus, establishment of protein localization, negative regulation of cell proliferation and mitotic cell cycle. Pathway analysis enrichment reveals that genes belong to p53 signaling pathway and cell cycle. Conclusions: Our findings provide a good indication for understanding the mechanisms by which L-2 peptide acts and provide good theoretical support for clinical applications.</p> <p>References: 1 Vallespi, M. G. et al., J. Pept. Sci. 16 (June 2009), 40 (2010). 2 Gentleman, R. et al., Genome Biology 5 (10), R80 (2004). 3 Huang, D. W., Sherman, B. T., and Lempicki, R. A., Nat. Protocols 4 (1), 44 (2008).</p>
<p>PFE 107</p>	<p>USING QUALITY RISK MANAGEMENT IN THE DESIGN OF PLANTIBODY HB-01 MANUFACTURING BY TRANSGENIC TOBACCO PLANTS FOR VACCINE PRODUCTION Milá L¹, Valdés R¹, Padilla S¹, Mendoza O¹, Gómez L¹, García C¹, Geadá D², Ferro W¹, Pujol M¹, Tamayo A¹, Enríquez G¹, Álvarez T¹, Sánchez R¹ & Brito J¹</p> <p>¹ Center for Genetic Engineering and Biotechnology. Ave 31/ 158 and 190, POBox. 6162. Havana 10600, Cuba. email: lorely.mila@cigb.edu.cu ²Tobacco Research Institute. Tumbadero Road 8^{1/2} km. San Antonio de los Baños. Havana 3500. Cuba.</p> <p>Introduction. The production of biopharmaceuticals by transgenic plants is a promising choice to achieve the multi-kilogram amount of products needed to treat many human diseases. However, this scientific field is still lacking of approved specific guidelines regarding points to consider for manufacturing and application of these products. In such sense, the implementation of new manufacturing processes and quality systems using the <i>Quality Risks Management</i> is recognized as something of prime importance in the current pharmaceutical industry. In this work, we summarize the application of the FMEA method to design the manufacturing process of a plantibody, employed in the hepatitis B vaccine production to ensure the vaccine high quality.</p> <p>Material and Methods: The application of the FMEA method started with the analysis of the type and occurrence of failures and the analysis of their consequences on the plantibody quality and manufacturing process. Subsequently, ten-point scales of severity, occurrence and probability of detection of failures were defined to determine the risk priority number (RPN). Results and Discussion: The list of causes of potential failures was grouped within several groups: personnel (36.6%), procedures (23.3%), equipments (13.3%), materials (16.6%), and environment (10%). In the biomass production step were identified 14 causes. In the plantibody downstream process the risks with the highest RPNs were: mistakes in sterile</p>

	<p>filtration procedures, and incorrect packing of the chromatographic columns. The analysis of the main potential failures in the immobilization step demonstrated the safety of the process because the huge majority (91,6%) of potential failures don't have impact on the manufacturing process and therefore don't require validation.</p> <p>Conclusion: The FMEA allowed an objective assessment of the type and frequency of occurrence of potential failures in the PHB-01 manufacturing process and the consequences of these failures on the quality of plantibody and manufacturing process.</p>
PFE 108	<p>SHELF LIFE STABILITY OF PERTUSSIS VACCINE USED AS WORKING REFERENCE FOR POTENCY TEST Herrera L, Mahy T, Cisneros D, Valle O, Nuñez F, Labrador I, Ontivero I.</p> <p>Finlay Institute, Center for Research Development and Production of Vaccines 27 Ave No. 19805, P.O. Box 16017, Havana, Cuba. email: lherrera@finlay.edu.cu</p> <p>Introduction: Diphtheria, Tetanus and Pertussis (DPT) vaccine is one of the products manufactured at Finlay Institute. In order to determine the biological activity of the Pertussis component, it's necessary a Reference Material for assigning values expressed in international units to the evaluated vaccine batches. For this purpose a working standard of whole cell Pertussis Vaccine (VPR(1)/99) was produced with an activity value of 40 UI / mL, stored at 2 - 8 °C in lyophilized form and used since 1999 in laboratory routine assays. The aim of this work was evaluate the shelf life stability of this working vaccine standard.</p> <p>Materials and methods: The stability assessment was based on potency values obtained by using the intracerebral mouse protection test (Kendrick test) described by WHO every two years for 6 years. As references we used the International and Regional Standards (OMS 66/303, PER 01 and PER 02) Results and Discussion: The working standard maintained the activity value of 40 UI / mL for 4 years. This batch was characterized again 5 years after its certification with a potency value of 30 UI/mL, kept even one-year later demonstrating the stability of the certified value. Conclusions: The working vaccine reference was stable at 2-8 °C for 6 years, demonstrating its suitability for the routine vaccine quality control.</p>
PFE 109	<p>ABSORBANCE AND CFU CALIBRATION IN TWO STAGES Izquierdo Luis A</p> <p>Instituto Finlay, Ciudad de La Habana, Cuba. email: lizquierdo@ finlay.edu.cu</p> <p>Introduction: It is well known the positive association of CFUs (colony forming unit) and Absorbance in dilution samples of any bacteria, both increase in the same direction. In this work it is shown how it was obtained an accurate set of calibration curves combining a few really counting data and a lot of routine laboratory determinations. All data came from the production process of VaxSpiral which includes cells from three serovars of Leptospira.</p> <p>Materials and Methods</p> <ul style="list-style-type: none"> • Main data analysis and evaluation of fitted relation was carry out with data from 156 culture production batch of Leptospira (Canicola serovar:56; Ictero serovar:46 ; Pomona Serovar: 54). At this stage it was made the choice of the best model to fit the calibration and the estimation of one the parameters • Using data from 15 culture production batch of Leptospira (Canicola serovar: 6 ; Ictero serovar: 5 ; Pomona Serovar: 4) it was made the other parameter of the model. • Exploratory Graphical and Analytical Data Analysis, and Regression Analysis (unweighted and weighted) were main statistical techniques used <p>Results and Discussion: Relation log/log with between CFU and Absorbance with common slope for the three serovars was enough good (r=0.998) to accurately quantify CFU of this Leptospira serovars.</p> <p>Conclusions: Applying some standard statistical tools it is possible, with minimal additional lab data, improve the accuracy and precision of the daily UCF counting procedure.</p>
PFE 110	<p>IMPROVEMENT OF HEMODERIVATES QUALITY CONTROL IN CUBA. Blanco M, Pérez MT, Valdés N, Romero K, Machado L, Ruíz N, Izquierdo M.</p> <p>AIDS Research Laboratory (LISIDA). Carretera de Tapaste y Autopista Nacional. San José de las Lajas, La Habana. email:lisida@infomed.sld.cu.</p>

	<p>Introduction: Viruses transmitted by blood, constitute a challenge to the security in the production of blood products. In Cuba, the company of serums and blood products Adalberto Pessant, use certified plasma as raw material from the national network of blood banks for the production of these hemoderivates. Since 1989 the LISIDA was designated for the study of viral markers (HIV-1, HCV and HBV) serological and molecular techniques to the end blood products, this diagnosis was upgraded in 2003 introducing the screening of the active pharmaceutical ingredient (API) and since 2005, the study of frozen plasma by nucleic acid technology (NAT), which decreases the risk of transmission by reducing the window period of viral agents, raising the quality and safety Cuban blood products. To show the development of the certification process and diagnostic algorithm for releasing of raw materials, API and final product of blood products. Materials and Methods: We established the documental system and diagnostic algorithms for certification of hemoderivates. We validated the techniques for serological analysis using different commercial kits specific to each viral marker. For molecular studies was used NAT technology AmpliScreen Roche. Results and Discussion: The enhancement of viral diagnosis has raised the quality and safety of blood products and losses are eliminated in the production process by introducing only certified raw material. Today, with the selected algorithm 910 030 units of frozen plasma for HCV and 888 558 HIV-1, has been processed by NAT. 48 positive donations have been eliminated from the production process, they have been reported to health authorities in order to feedback to the network of blood banks on the quality of their performance. In the past five years have been studied 435 API and 639 end products found negative for these viral markers. Conclusions: We are demonstrating the effectiveness of the algorithm used.</p>
PFE 111	<p>CIGB-370: A NOVEL ANTINEOPLASTIC AGENT DERIVED FROM INFECTION-MEDIATED TUMOR REGRESSION Abrahantes-Pérez, Martínez E, Bequet M, Velíz G, Alemán MR, González LJ, Valdés J, González D, Gavilondo-Cowley JV, García J, Mendosa O, Márquez G, Selman-Housein M, Claro Y, Castellano L, Paez R, Reyes-González J.</p> <p>Center for Genetic Engineering and Biotechnology, Ave 31/ 158 and 190, Cubanacán, Playa, Havana City, Havana 10600, P.O.Box 6162, Cuba. email: mc.abrahantes@cigb.edu.cu</p> <p>Introduction: Traditionally, infection-induced tumor resistance has been explained by stimulation of anti-tumor immunity. However, therapies based on it have not materialized. In our laboratory, we detected that tumor cells growing in the peritoneal cavity with <i>Serratia marcescens</i>, correlated with the impairment of efficient hybridoma growth as an ascitis tumor in some BALB/c mice. In this study, we identified a new polypeptide with potent antitumor activity derived from <i>S. marcescens</i>-induced tumor regression. Materials and Methods: Wild type <i>S. marcescens</i> SM2327 strain and tumor cells were co-inoculated intraperitoneally in BALB/c mice. <i>S. marcescens</i> CMIB4202 strain was isolated from animals with impaired tumor growth. A overexpressed polypeptide in the culture supernatant of strain CMIB4202 was detected, isolated and produced in <i>E. coli</i>. This recombinant molecule was evaluated as anti-cancer drug in five experimental systems. Results and Discussion: The recombinant polypeptide of 26 kDa encoded as CIGB-370, that belongs to Serralisin family showed a marked cytotoxic effect on the growth of tumor cell lines (i.e., lung, colon, melanoma, breast, prostate, glioma), with GI50 in the nM range. A single dose of CIGB-370 inhibited the TC-1 lung tumor growth and the A549 human lung carcinoma xenograft tumor (T/C<10%), with increased survival (T/C>160%) and inhibition of lung metastasis in the spontaneous metastasis model of Lewis lung cancer. CIGB-370 inhibited the endothelial cord formation on matrigel by human endothelial cells. The results of this work suggested that infections also inhibit tumors by a surprisingly different mechanism: overexpression of antiproliferative factors produced microorganism such as <i>S. marcescens</i> in tumor-bearing mice. Conclusions: CIGB-370 belong to a new class of tumor vasculature and cells-directed anti-cancer therapies, derived from tumor-regression. This polypeptide may be exploited to develop novel and more effective treatments for solid malignant tumors.</p>
PFE 112	<p>PLACENTAL AND MILK TRANSFER OF ENTEPIDERMAL GROW FACTOR RECEPTOR MONOCLONAL ANTIBODY ¹²⁵I-7A7 (IgG1) IN MICE. León M¹, González JE^{2,*}, Hernández I¹, García D¹, Garrido G³, Casacó A⁴.</p> <p>¹ Departamento de Desarrollo, Centro de Isótopos (CENTIS), La Habana, Cuba ² Laboratorio de Radiobiología, Centro de Protección e Higiene de las Radiaciones, La Habana, Cuba ³ Biotecnology Division, Centro de Inmunología Molecular, Habana 11600, Cuba.</p>

	<p>⁴ Clinical Trial Division, Centro de Inmunología Molecular, Habana 11600, Cuba. email: mariela@centis.edu.cu</p> <p>Introduction: The murine 7A7 monoclonal antibody (MAb) was generated as a new tool for the preclinical evaluation of Epidermal Growth Factor Receptor (EGFR) based therapies. The placental and milk transfer of anti-EGFR MAb ¹²⁵I-7A7 (IgG1) were studied in OF-1 mice. Material and methods: For placental transfer the MAb 7A7 labelled with ¹²⁵I was injected by tail vein on gestation day (GD) 14. The percentage of radioactivity in each organ was calculated. The placental transfer of ¹²⁵I-7A7 antibody on GD 15 was 4 ± 1% (mean ± SD). For milk transfer study the 7A7 MAb labelled with ¹²⁵I were injected by tail vein on lactation day 2 to dams. The blood of lactating dams and pups and gastric milk were sampled and radioactivity assayed in the precipitated protein fraction. Results: The percent of protein precipitated radioactivity increased in a time dependent manner in milk and plasma from pups while a decrease was seen in the lactating dams plasma.</p> <p>Conclusion: The data suggests that 7A7 MAb crosses the placenta and is transferred as expected in a superior quantity through the milk to pups.</p>
PFE 113	<p>ALTERNATIVE PROCEDURE FOR OBTAINING VACCINE INOCULUM OF <i>SALMONELLA TYPHI</i> POLYSACCHARIDE VI</p> <p>Hernández Fundora Marixa, González Díaz Domingo, González Rene Rivero Plasencia Kirenia, Martínez Juan Carlos, González Humberto, Carmona Ricardo, Arjona Dairon, Jordan Gretel, Armenteros Dorian,</p> <p>Direction of Pharmaceutical Development. Production Vice-presidency. Finlay Institute , Center for Research Development and Production of Vaccines. Havana City, Cuba. Calle 27, No 19805 e/198 y 200 la Lisa CP.11600 AP 16017. email: mhernandez@finlay.edu.cu</p> <p>Introduction: Having robust technologies ensuring high standard quality products is a main goal for the manufacturers of biotechnological products. There is an international trend focused on the use of free animal origin components media guarantying high levels of cell biomass and increasing the polysaccharides expression. The aim of this study was to evaluate formulations of free animal origin to obtain inoculum of Salmonella typhi. Materials and Methods: It was taken into consideration two key variables, one using vegetable peptone and another one using yeast extract. The evaluation was performed by the microorganism growth kinetics expressed by turbidimetry (absorbance) at a wavelength of 630 nm until an OD > 1.0. Samples were taken at intervals of 1 hour and viable counts were carried out at the beginning and the end of the experiment to monitor maximum viability. Results and Discussion: OD values reached in the variants tested were higher than those obtained with the use of modified Frantz medium, traditionally used to obtain vaccine polysaccharide. Microorganism growth kinetics in both media were similar, indicating a great similarity in at least the key components of the tested culture media, not showing significant differences between the optical densities of both cultures as an evidence of the impact on cell growth. Conclusions: Both culture media enhance Salmonella typhi growth. They are media of easy preparation that reduce processing time and allow a higher productive consistency. That's why they can be innovative choices for the manufacturing of Salmonella typhi polysaccharide Vi.</p>
PFE 114	<p>IGE/IGG4 RATIO AS A POSSIBLE SURROGATE MARKER OF CLINICAL EFFICACY DURING ALLERGEN IMMUNOTHERAPY</p> <p>Mateo M¹, Labrada A¹, Naranjo R², Olivares M², Artilés J², Navarro BI¹, Castro RL¹</p> <p>¹ Allergen Dept., National Center of Bioproducts, Havana, Cuba ² "Joaquín Albarrán" Hospital, Havana, Cuba email: mayteemm@biocen.cu</p> <p>Introduction: Allergen immunotherapy induces IgG4 antibodies with blocking effect, and in the long-terms reduces or prevents the seasonal raising of IgE antibodies. The problem of finding immunological suitable surrogate markers of clinical efficacy during IT is currently very pertinent. The aim of this work was to evaluate the allergen-specific IgE/IgG4 ratio as a paraclinical efficacy marker. Methods: IgE and IgG4 antibodies to <i>Dermatophagoides pteronyssinus</i>, <i>D. siboney</i> and <i>Blomia tropicalis</i> were measured by in-house ELISA in 120 asthmatic patients subjected to SCIT with standardized allergen vaccines (VALERGEN, BIOGEN) of each mite in three separate DBPC clinical trials (40 patients in each trial, half receiving placebo). Antibody titres were expressed in relative units, normalized and averaged between the three trials. Size effect was calculated as the Standard Mean Difference (SMD) between the active and</p>

	<p>placebo groups, and averaged using meta-analysis tools. Results: After 6 months there was a significant increase of IgG4 antibodies ($p < 0.05$), whereas no significant change was noted for IgE. At 12 months the IgG4 increase was even greater and the reduction of IgE achieved significance. The IgE/IgG4 ratio was the immunological variable with the greatest size effect value (SMD=0.81 CI95%:0.71-0.91) since it combined the IgG4 increase and IgE decrease, showing a figure close to the clinical effect (symptom-medication SMD = 1.2 CI95%:0.7-1.7). IgE/IgG4 ratio was significantly correlated to the clinical variable ($r=0.23$, $p=0.04$) and to the reduction of skin reactivity on a per patient basis. Conclusion: These results support the use of this serological marker for evidencing the immunological changes during IT and possibly, for predicting patient's clinical improvement.</p>
PFE 115	<p>PASSIVE ADMINISTRATION OF SECRETORY IGA FROM HUMAN COLOSTRUM INDUCES PROTECTION AGAINST MYCOBACTERIUM TUBERCULOSIS IN A MURINE MODEL OF PROGRESSIVE PULMONARY INFECTION</p> <p><u>Álvarez N</u>¹, Otero O¹, Aguilar D², Rivas CE², Cervantes A², Falero-Díaz G¹, Orozco H², Cádiz A³, Marcet R⁴, Molina C², Sarmiento ME¹, Mohd N⁵, Hernández-Pando R², Acosta A¹.</p> <p>¹ Department of Molecular Biology. Finlay Institute. Center of Research – Production of Vaccines. Ave. 27 No. 19805, La Lisa. Ciudad de la Habana, Cuba. AP. 16017, CP11600. email: nalvarez@finlay.edu.cu</p> <p>² Experimental Pathology Section, Department of Pathology, National Institute of Medical Sciences and Nutrition “Salvador Zubirán”, Mexico.</p> <p>³ Company Productor of Serums and Hemoderivates “Adalberto Pesant González”. Ave 51 No.33 235 km 19 medio ½. Arroyo Arenas, La Lisa. Ciudad de la Habana, Cuba. CP 13400.</p> <p>⁴ Institute of Tropical Medicine “Pedro Kouri”.</p> <p>⁵ School of Health Sciences, University Sains Malaysia, 16150 Kubang Kerian, Malaysia.</p> <p>Introduction: Human secretory immunoglobulin A is the major class of antibody that is produced, associated with the immune protection of the mucosal surfaces. Human colostrum contains a high concentration of this immunoglobulin, which is transferred to newborn, as a passive protection mechanism against bacterial diseases. Material and Methods: In the present work, human secretory immunoglobulin A was obtained from human colostrum by chromatographic techniques. The quality of purified human secretory immunoglobulin A was confirmed by acrylamide electrophoresis gel 12.5 %, showing only the presence of the secretory component, heavy chain and light chain. Since immunoglobulin A is the principal antibody class in the secretions protecting the mucosa surfaces from pathogens invading the respiratory tract surfaces, also their reactivity against mycobacterial antigens was tested. Results and Discussion: Western blot analysis revealed the specific recognition of mycobacterial proteins by human secretory immunoglobulin A, being higher against <i>Mycobacterium tuberculosis</i>. Furthermore, passive treatment with human secretory immunoglobulin A reduced the bacterial load in the lungs, diminished tissue injury, and prolonged survival of mice following experimental infection with virulent <i>M. tuberculosis</i>. Conclusions: Our results demonstrated for the first time the prophylactic effect of mucosal administration of sIgA obtained from human colostrum in a model of infection with <i>M. tuberculosis</i> in mice. In addition, we demonstrated that, incubation of <i>M. tuberculosis</i> with hsIgA could inhibit the bacteria's infective potential.</p>
PFE 116	<p>TRANSFECTION AS METHOD FOR “IN VITRO” CONTROL OF THERAPEUTIC GENES EXPRESSION</p> <p><u>Amin N</u>¹, Camacho F¹, Vila A¹, Acosta A¹, Aguilar A¹</p> <p>¹ Virología Molecular. Vicepresidencia de Investigaciones. Instituto FINLAY. Ave 27, No 19805, La Lisa, Ciudad Habana, Cuba. e-mail: namin@finlay.edu.cu</p> <p>Introduction: Gene therapy for infectious diseases requires the introduction of gene designed to specifically block or inhibit the gene expression or function of gene products. Transfection is an essential tool to study gene expression, DNA replication, genetic recombination, and consist on introduction of exogenous DNA inside eukaryotic cells. In this study Vero and BHK-21 cells were transfected with the plasmid CMVsn EGFP using the cationic polyethylene imine (PEI) to establish a work model in our laboratory to future assays of transient expression of genes in mammalian cells as gene therapy for dengue infections.</p> <p>Materials and method: Different concentration of Vero and BHK21 cell were seeded into 24 wells plates and were grown at 37⁰ C overnight. When the growth of cells reached 70-80% confluence, 1, 2, 3 μg of</p>

	<p>DNA were mixed with 1 and 3,3 μl of PEI and then the mixture was added to the cells. After incubation for 4 hour at 37^o C, the cells were washed and fresh medium with 20% fetal bovine serum was added. The expression of reporter gene in both cells was observed under fluorescence microscope to 24, 48 and 72 hours post-transfection. Results: BHK -21 had better results than Vero cells to the transfection of EGFP plasmid. We observed fluorescence only in cytoplasm and nucleus of transfected cells. The optimal concentration of ADN was 1 μg for both cells line. We obtained similar results for 1 and 3,3 μl of PEI. The highest percentage of fluorescent cells were gotten at 72 hours post infection. Conclusions: Our results indicate that transfection represent an useful assay for control of therapeutic genes expression.</p>
PFE 117	<p>VAX-SPIRAL®, ANTILEPTOSPIROSIC CUBAN VACCINE: HETEROLOGOUS PROTECTION AGAINST STRAINS OF CLINICALS CASE IN NICARAGUA, EVALUATED IN THE HAMSTER SIRIO AS BIOMODEL Batista N¹, Arencibia DF¹, Blain K¹, Solís RL¹, Rosario LA², García L¹.</p> <p>¹Researches Vicepresidency (Finlay Institute), 17 avenue between 198 and 200 street. Playa Municipality. Havana City. Cuba. email: nbatista@finlay.edu.cu ²Institute of Pharmacy and Food Science (IFAL, U.H), 27 avenue and 222 street. Lisa Municipality. Havana City. Cuba.</p> <p>Introduction: In 2007, Felix hurricane affected Nicaragua and were produced outbreaks of leptospirosis. Sixteen strains were isolated from patients with epidemiologic and serologic evidence and typical symptoms of the disease. The aim of this work was determined the heterologous protective capacity of vax-SPIRAL® against strains isolated from clinical cases in Nicaragua using challenge experimental in hamster sirio biomodel. Material and Methods: Sixteen strains isolated from patients and previously serogrouped were cultured in liquid medium EMJH. Hamster sirio biomodel was employed in all experiments. Virulence was evaluated as selection criterion in the protection assay and was determined LD50. Active and passive protection confer for vax-SPIRAL® against challenge with 10,000 LD50 of each selected strain. Prevalence of leptospira in kidneys and liver was verified in survival animals. Results and Discussion: Five strains resulted highly virulent; the other ones did not cause lethal infection. LD50 of 7407 (Sejroe), 6307 (Pomona) and 8807 (Ballum) strains ranged 30-35 leptospiras, and for 4207 (Sejroe) and 3507 (Icterohaemorrhagiae) strains was lower to 7 leptospiras. Clinical signs were observed in animals between 5 and 10 days post-inoculation and they died 9 days after. 100% of protection was evident in the immunized in both protection assays (active and passive), and 100% of mortality in control groups. No significant difference between the level of protection conferred for vax-SPIRAL® in the two assays. The macroscopic analysis of the organs in the survival animals showed lack of characteristics signs of infection and microbial growth in several section of the organs. Nevertheless, controls showed all characteristics signs of this infection and leptospiras were isolated from liver and kidneys and macroscopic signs of the lesions caused by the bacterium. Conclusions: The results of this study showed that vax-SPIRAL® confers heterologous protection experimentally and it could be considered as prophylactic way in disasters situations such as happened in Nicaragua and in risk populations.</p>
PFE 118	<p>IN VITRO ACTIVITY OF SURFACEN® AGAINST LEISHMANIA AMAZONENSIS Blanco O¹, Lugones Y¹, Díaz E¹, García M², Faure R¹, Monzote L²</p> <p>¹Centro Nacional de Sanidad Agropecuaria, CENSA, San José de Las Lajas, CP 32700, La Habana, Cuba email: odalysbh@infomed.sld.cu ²Departamento de Parasitología, Instituto de Medicina Tropical “Pedro Kouri”, Apartado Postal 601, Marianao 13, Ciudad de la Habana, Cuba</p> <p>Introduction: Leishmaniasis refers to a spectrum of diseases ranging from self-healing cutaneous lesion to debilitating mucocutaneous and lethal visceral infections. In recent years, there has been growing interest in alternatives therapies the use of natural products. SURFACEN® is an exogenous natural lung surfactant and which is applied with successful in Respiratory Distress Syndrome in Newborn since 1990, recently their antibacterial effect has been demonstrated. The aim of the present study was to assess the potential antileishmanial activity of Surfacen®. Material and Methods: Macrophages were harvested from peritoneal cavities of normal BALB/c mice in RPMI medium, <i>amazonensis</i> promastigotes were added at a 4:1 parasite/macrophage ratio The cultures were incubated for 4 h, washed to remove free parasites and Surfacen concentrations were added between 12,5 and 100 μg/mL for 48 h The results were expressed as percent of reduction of the infection rate (%IR). Results and Discussion: The product showed activity against the amastigote form of the parasite, with an IC50 value of 18 \pm 3 μg/mL; while no toxic effect on</p>

	<p>host cell was observed until 200 µg/mL. Conclusions: This is the first report about the antileishmanial activity of SURFACEN®. Its effect and low toxicity suggests that this product could be explored in the design of new molecules against <i>Leishmania</i> parasite.</p>
PFE 119	<p>DEVELOPMENT OF AN ALLERGY VACCINE FORMULATION ADSORBED INTO ALUMINUM – CONTAINING ADJUVANTS Nguyen Phuoc CA¹, Mayo Abad O², Labrada Rosado A³, Alonso Oramas Y³, Oliva Díaz Y³</p> <p>¹ Medical Biology Department, Biotechnology Centre of Ho Chi Minh City, Vietnam. ² Development Department, National Center for Bioproducts, Havana, Cuba, omayo@biocen.cu ³ Allergens Department, National Center for Bioproducts, Havana, Cuba.</p> <p><i>Dermatophagoides siboney</i> has been commonly found in house dust in the Caribbean and it is associated to allergic asthma. In order to obtain a house dust mite allergen vaccine containing aluminum adjuvant that can satisfy the requirements of consistency and immunological potency, the mixture of lyophilized major allergens extract of <i>D. siboney</i> was adsorbed into aluminum adjuvants (aluminum hydroxide and aluminum phosphate), aiming to establish the parameters that determine the highest adsorption capacity. Analytical techniques including immuno - analytical methods were carried out in order to study the adsorption process and immunological potency of the formulated product. The results of this research showed that aluminum hydroxide was a better adjuvant when compared to aluminum phosphate. The best adsorption condition using aluminum hydroxide was obtained with 0,9 % NaCl at pH 8 in 0,5 hour. Sodium phosphate - buffered saline (sPBS) had a negative effect to the adsorption process using aluminum hydroxide and sodium acetate could be an alternative buffer for sPBS. The consistency of the adsorption process in the absence of buffer was demonstrated as well as the immunogenicity of the formulation.</p>
PFE 120	<p>VALIDATION OF THE ESSAY OF REVERSION TO THE TOXIN OF THE ANATOXIN STERILE AND PURIFIED Orialys Valle, Juan F Núñez, Regla Sosa, Irma Labrador, Nayla Salazar, Ileana Delgado, Eduardo Cajuso, José Dupuig, Aleida Mandiaroti, Pedro Muñoz. Finlay Institute, Havana, Cuba.</p> <p>Vaccines with diphtheria component are widely used today, such vaccines are made from Diphtheria toxin obtained by fermentation of <i>Corynebacterium diphtheriae</i>, which is detoxified in the production process with chemist agents like formaldehyde. The World Organization Health sets the toxicity reverse test of purified diphtheria toxoid (ADPE) as obligatory controls. Quality Control of pharmaceutical products must show their safety, that goal is realized with the validation of reverse test to ADPE. The test uses the toxic effect that produce the diphtheria toxin in the skin of guinea pigs when are inoculated by intradermal way. This effect is characterized by the formation of a red granuloma after 48 to 72 hours of the inoculated animal due to the effect dermonecrotizante that produces the diphtheria toxin.</p> <p>The samples evaluated were: ADPE (Lot 8010). ADPE (Lot 8010), loaded with diphtheria toxin.</p> <p>The references used were: Diphtheria toxin Working Reference Material (lot TDR 3 / 04) Antitoxin diphtheria Working Reference Material (lot ADRN 3 / 05)</p> <p>The results obtained during the validation were satisfactory, so we can use the method with reliable results.</p>
PFE 121	<p>PRESERVATION OF REFERENCE STRAINS TO BE USED FOR THE STERILITY TEST OF VACCINES Morales Valdés R, Avilés Boza AR, Perdomo Dimas AR</p> <p>Centre for the State Quality Control of Drugs (CECMED). Calle 200, No. 1706, Entre 17 y 19, Siboney, Playa, La Habana, Cuba.</p> <p>Introduction: Sterility test is one of the compendial quality control test for lot release for vaccines, parenteral and some other sterile pharmaceutical products. In this assay, some reference strains are used for the growth promotion test performed to the culture media and for its validation. These reference strains must be kept by proper methods assuring their purity, viability and genetic stability. Materials y methods: The strains are preserved by using the following two methods: freezing the test microorganism at - 70 °C using skim milk and glycerol as cryoprotectans and the freezing at - 70 °C in Porcelain beads using glycerol as cryoprotectan agent. Controls of purity, viability and stability with a frequency of a week, 6</p>

	<p>months and once a year were performed. Lost of viability and survival curves were used as control parameters. Results and Discussion: <i>Candida albicans</i> ATCC 10231 showed the best results reached with preservation using Porcelain beads. On the other side, <i>Bacillus subtilis</i> ATCC 6633 preserved in beads had a reduction in its viability under accepted limits (10^5-10^6 UFC/mL). <i>Staphylococcus aureus</i> ATCC 6538 was the only strain preserved in skim milk keeping an acceptable viability. <i>Escherichia coli</i> ATCC 8739 showed good viability in the two conditions of preservation. Nevertheless, <i>Pseudomonas aeruginosa</i> ATCC 9027 had a non significant lost of viability in both conditions. Conclusions: After 5 years all the reference strains kept their characteristics of viability, purity and stability preserved by the two methods used. It was a good result taking into consideration that the preservation at - 70 °C is recommended for two years and could be used during longer periods depending on the type of the strain and the formulation used. It was demonstrated that there is not a general method for the preservation of all microorganisms and it's needed to determine the most suitable one on a case-by-case basis. Hence, it's possible to have stable and reliable reference strains to be used in sterility tests for vaccines.</p>
<p>PFE 122</p>	<p>ADJUVANT AND VACCINE POTENTIAL OF NANO AND MICROPARTICLES DERIVED FROM <i>VIBRIO CHOLERAE</i> O1 EXTRACTS Reinaldo Acevedo¹, Adriana Callicó¹, Judith del Campo¹, Caridad Zayas¹, Elizabeth González¹, Gisselle Reyes¹, Yisabel Aranguren, Valerie A Ferro², Luis Garcia, José Luis Pérez¹ and Oliver Pérez¹.</p> <p>Finlay Institute¹ of Havana City, Cuba and ²Strathclyde University of Glasgow, Scotland. email: racevedo@finlay.edu.cu</p> <p>The role of nano- and micro-particles as delivery systems with adjuvant potential has been already revisited elsewhere. “Natural” purified or synthetic materials like phospholipids and cholesterol are used in their preparation and known antigens or immunostimulator molecules may be included in formulations. Several techniques have been developed to characterize the final product, stability, etc. However, nano-/microparticles derived from bacterial source may contain these molecules but must be downstream analysed to determine their physical and chemical properties. Several proteins and immunogenic lipopolysaccharide were identified in proteoliposome extracted from <i>V. cholerae</i> O1 strain (AFPL2) and the adjuvant effect of their transformation into cochleate structure (AFCo2) was evaluated in mice model mucosally immunized. Intranasal vs. intragastric administrations elicited different mucosal (specific IgA in saliva and feces) and systemic (specific IgG in sera and vibriocidal activity) immune response against <i>V. cholerae</i> antigens. Results show that AFCo2 was more stable at low pH <i>in vitro</i> than AFPL2 and more immunogenic <i>in vivo</i> whatever the route used, particularly by nasal route. Finally, polysaccharide Vi (Poly Vi) from <i>Salmonella</i> Typhi was admixed and administered with AFCo2 by intranasal route. Mucosal and systemic immune response elicited against adjuvanted Poli Vi was higher than induced by non adjuvanted antigen. Overall, AFCo2 is a very immunogenic structure with adjuvant potential to raise immune responses against <i>V. cholerae</i> and <i>S. Typhi</i>.</p>
<p>PFE 123</p>	<p>EVALUATION OF THE HUMORAL IMMUNE RESPONSE AND CROSS REACTIVITY AGAINST <i>MYCOBACTERIUM TUBERCULOSIS</i> OF LIPOSOMES CONTAINING TOTAL LIPIDS OF <i>MYCOBACTERIUM SMEGMATIS</i> Borrero R¹, García MA¹, Canet L², Zayas C¹, Reyes F¹, Prieto JL¹, Infante J F.¹, Lanio ME.², Sarmiento M E¹, Mohd N³ and Acosta A¹</p> <p>¹ Finlay Institute. Ave. 27 No. 19805, La Lisa. Ciudad de la Habana, Cuba. AP. 16017, CP11600. ² Biology Faculty, Havana University, Calle 25 No. 455 Vedado, Havana city, Cuba. ³ School of Health Sciences, University Sains Malaysia, 16150 Kubang Kerian, Malaysia email: rborrero@finlay.edu.cu</p> <p>Introduction. The fast-growing nonpathogenic bacterium <i>Mycobacterium smegmatis</i> shares many features with the pathogenic <i>Mycobacterium tuberculosis</i>, the causative agent of tuberculosis. <i>M. smegmatis</i> has several cell wall glycolipids in common with <i>M. tuberculosis</i>, which play an important role in the pathogenesis of tuberculosis and the induction of a protective immune response against <i>M. tuberculosis</i> infection in some animal models. In this study, we evaluated the humoral immune response and cross reactivity against <i>M. tuberculosis</i> of liposomes containing cell wall glycolipids of <i>M. smegmatis</i>, in order to study its possible use as a component of a vaccinal candidate against tuberculosis. Materials and Methods. Total lipid extracts were obtained from <i>M. smegmatis</i> and analyzed by unidimensional TLC. Liposomes containing total lipids from <i>M. smegmatis</i> were prepared by the dehydration-rehydration</p>

	<p>technique and subjected to electron microscopic analysis. BALB/c mice were immunized with the liposomes obtained and the antibody response and cross reactivity against <i>M. tuberculosis</i> were tested by ELISA. Results. Total lipid extract from <i>M. smegmatis</i> showed the presence of several polar lipids in common with <i>M. tuberculosis</i> as phosphatidylinositol mannosides. Liposomes that contained lipids of <i>M. smegmatis</i> were capable of inducing a specific IgG antibody response that allowed the recognition of surface antigens of <i>M. tuberculosis</i>. Conclusions. The results of this study showed the presence of immunogenic glycolipids in <i>M. smegmatis</i>, which could be included to enhance the protective effects of subunit vaccine formulations against tuberculosis. Key words: Glycolipids, <i>Mycobacterium tuberculosis</i>, Immunity.</p>
PFE 124	<p>DEVELOPMENT OF A NEW THERAPEUTIC RADIOPHARMACEUTICAL, ¹⁷⁷Lu-NIMOTUZUMAB® FOR RADIONUCLIDE THERAPY Leyva Montana R¹, Hernández González I¹, Zamora Barrabí M¹, León Pérez M¹, Bortoleti de Araújo E², Brunelli Pujatti P², Chinol M³, Papi S³, Melichar F⁴, Beckford D⁴.</p> <p>¹Isotope Center, Ave. Monumental y Carr. La Rada km 3½, Guanabacoa, Havana City, Cuba email: rene@centis.edu.cu ²Instituto de Pesquisas Energeticas e Nucleares, Departamento de Processamento de Material Radioativo.Travessa R. 400, Cidade Universitaria 05508-900 Sao Paulo, Brazil. ³European Institute of Oncology, via Ripamonti, 435. I-20141 Milano, Italy. ⁴Nuclear Research Institute Řež, Husinec-Rez 130, CZ-25068 Rez. Czech Republic</p> <p>Introduction: Despite more than 20 years since the introduction of radioimmunodetection (RID) and radioimmunotherapy (RIT), representing the use of isotopes conjugated to monoclonal antibodies (mAbs) for imaging and therapy, respectively, only in the last few years has this technology attracted the increasing interest of clinical oncologists. This new interest may be attributed to the encouraging results achieved with RIT in the management of hematopoietic neoplasm, especially non-Hodgkin's lymphoma (NHL). Now, many other radioimmunoconjugates are in preclinical and clinical evaluation. Several radionuclides have been applied to label proteins for radionuclide therapy and ¹⁷⁷Lu has emerged as a promising short-range β emitter for this purpose. Material and methods: Nimotuzumab, hR3 is a monoclonal antibody that recognizes receptors of epidermic growth factor was supplied by CIMAB (Cuba), 50mg/10mL, pH 7.0 buffer. Chelating agents DOTA-NHS and DOTA-SCN from Macrocylics were used for protein conjugation to radionuclide. <i>Radioisotope</i> ¹⁷⁷LuCl₃, high specific activity was obtained from IDB (Netherlands) and low specific activity from UJF (Czech Republic). Na¹³¹I was obtained from Nordion (Canada). All other chemicals and reagents required for experiments were of analytical grade and purchased from Sigma Aldrich. Different analytical methods were used for immunoconjugates characterization and radiochemical quality control. Results and discussion: The stable hR3-DOTA immunoconjugates were synthesized and were labeled with ¹⁷⁷Lu high efficiency and specific activity of ¹⁷⁷Lu of about 400 MBq/mg hR3. Radiochemical purity of the products was found to be > 95 %. Normal Biodistribution studies were provided and immunoconjugates characterization was completed by HPLC, electrophoresis and ITLC. The number of chelate groups per protein was achieved (10-14 DOTA groups). Conclusions: The methods for synthesis of hR3-DOTA bioconjugates and their labeling with ¹⁷⁷Lu have been successfully developed. The promising results for further preclinical experiments in animal models constitutes a premonition, that this radiopharmaceutical will be a good agent for the radionuclide therapy.</p>
PFE 125	<p>DEVELOP OF WESTERN BLOTT TECHNIQUE IN VA MENGOC BC VACCINE WITH MONOCLONALS ANTIBODIES EMPLOYMENT Quintero Pérez R, Diéguez Castro R, Otero Alfaro O, Pérez ME, Falero Díaz G, Landys Chovel M Finlay Institute, Havana, Cuba</p> <p>Introduction: The scientific development reached at this moment in the World, has increased the demand and the rigor as for the requirements settled down in the productive process and the control of the biofarmaceutics products dedicated to its certification and approval for its commercialization in the market. An example of that expressed is in the production and control of the Cuban antimeningocóccicas vaccines. The antimeningocóccica Cuban vaccine, VA MENGOC BC® The importance of the approach of identity in the identification of the main antigénics proteins present in the Vesicle of External Membrane of <i>Neisseria meningitidis</i> serogroup B like main component of the vaccines and in the own vaccine as final product. The employment of monoclonales antibodies in the specific identification of the proteics bands in Western Blot technics, offers a bigger security and dependability to the results. Materials and methods: The proteins component desadsorption of the aluminum gel, as adyuvant employed in the vaccine, the</p>

	<p>phosphate method was used. The electroforesis was carried out under the same conditions described in the Normalized Procedure of Operation (PNO 12-114). A discontinuous system of gels was used with a gel separator of 12.5 % and the established steps for the development of Western Blot technique was continued according to that settled down in PNO 12-149. One of the membranes was incubated with the monoclonal antibody anti P1, the other one with the monoclonal antibody P2 and the third membrane with monoclonal antibody 70 K . This incubation was carried out during the overnight at the laboratory temperature with soft agitation in the revoluble zaranda. Results and discussions: As much in the vesicles and the vaccine lots studied, the presence of the antigénic proteins was observed P1, P3 and 70 K responsible for the immune answer of the vaccine in human. This results were compared with those that were possible when studying the vaccine with the gamma antimeningocócica, in the same one they were obtained a high number of bands corresponding to proteins, possible degradation bands (some of them with antigénic properties) products besides possible overlamping bands for its proximity in molecular weighth offer doubts. Conclusions: The presence of majority antigénic proteins bands corresponding to the P1,P3 and 70 K were identified in the VA MENGOC BC vaccine. References: 6. Puido A, Ruisanchez I, Boqué R, Ruis FX. Western Blot como método analítico de control. <i>Analytical Chim Acta.</i> 455, 267(2002).</p>
<p>PFE 126</p>	<p>IMMUNOGENICITY OF A <i>Dermatophagoides siboney</i> ALLERGEN VACCINE ADSORBED ON ALUMINUM HYDROXIDE FORMULATED WITH DIFFERENT BUFFERS Samalea R, Alonso Y, Labrada A, Oliva Y, Torralba D, Cruz R, Mateo M</p> <p>National Center Bioproducts (BioCen). email: roxana.samalea@biocen.cu</p> <p>Introduction: Phosphate ions may interfere with the adsorption of the major allergen Der s 1 to alum. This study was conducted to assess the immunogenicity of different formulations of a vaccine composition of the house dust mite <i>Dermatophagoides siboney</i>, adsorbed on alum hydroxide gel, using buffers not containing phosphate salts. Methods: GMP scale batches were formulated with different buffers: PBS, TRIS, and sodium acetate at a physiological pH value. Der s1 adsorption was measured by ELISA. The immunogenicity was assessed in Balb/c mice, administering two injections subcutaneously of each formulation at 0 and 10 days, with a dose of 5 µg Der s 1 per injection. Blood samples were taken at 0 and 17 days. Serum was analyzed for IgG antibodies, specific to D. siboney, by indirect ELISA. Statistical analysis was accomplished by ANOVA.</p> <p>Results and discussion: The adsorption of Der s1 was higher in presence of Sodium Acetate or TRIS (99.9%) as compared to PBS (89.6%), which agrees with previous findings. However the IgG levels were statistically not different (p <0.05).between the different buffer variants, suggesting that the adsorption to alum of this major allergen may not be as relevant as thought for inducing antibodies. Conclusions: The use of alternative buffers (TRIS, Sodium Acetate) is feasible, as they show high adsorption of Der s 1 and suitable immunogenicity, not inferior to phosphate buffers.</p>
<p>PFE 127</p>	<p>STABILITY OF WORKING STANDARDS USED IN THE TETANUS VACCINES POTENCY TEST Mahy T, Cisneros D, Ontivero I, Herrera L Finlay Institute. Ave. 27, No. 19805, CP 11600, La Lisa, Ciudad de La Habana, Cuba. E-mail: tmahy@finlay.edu.cu</p> <p>Introduction: The in vivo seroneutralization test (TNT), introduced as recommended by FDA for evaluating the potency of Tetanus Toxoid vaccines at Finlay Institute, requires the use of well characterized and stable standards like Tetanus Antitoxin and Toxin reference materials guarantying the trazability and reliability of the vaccine batches production. The aim of this work was to demonstrate the relationship existing between the conservation procedure and the stability of these products. Materials and methods: The Working Reference batches of Tetanus Antitoxin were prepared from equine purified serum from Pasteur Merieux Institute. They were stored at 2-8 °C in lyophilized form. The characterization consisted on evaluating the biological activity comparing them with the Tetanus Antitoxin International Standard (lot 60/013). The stability was verified once a year. Tetanus Toxin batches with different grades of purity were distributed. They were conserved in liquid and lyophilized form at (2 at 8) °C. They were characterized by a L+/10/50 method against Tetanus Antitoxin Standards (International and Regional) and the stability in the time was verified using the same procedure. Results and Discussion: The lyophilized Tetanus Antitoxin and Toxin stored at 2- 8°C demonstrated to be very stable. However, the Tetanus Toxin liquid was much less stable, with the exception of a liquid Tetanus Toxin batch purified by chromatography that was stable during 10 years. Conclusions: The Tetanus Antitoxin and Toxin can be stored lyophilized at 2-8 °C for a period of 2-3 years. It was also demonstrated that a higher level of</p>

	<p>purification of liquid forms guarantees a higher stability of Tetanus Toxin working standards.</p>
PFE 128	<p>INFLUENCE OF A PROTEOLIPOSOME ADJUVANTED ALLERGEN VACCINE ON TO AN EARLIER RESPONSE AGAINST NEISSERIA MENINGITIDIS Ramírez W, Labrada A, Bourg V, Torralba D, Más A, Huergo L</p> <p>Allergens Department, National Center of Bioproducts, Havana. email: wendy@biocen.cu</p> <p>Introduction: A novel anti-allergic therapeutic vaccine candidate is based on purified allergens of <i>Dermatophagoides siboney</i> House Dust Mite and proteoliposome (PL) of <i>Neisseria meningitidis</i> as immuno-stimulatory adjuvant. A major potential benefit provided by this vaccine would be enhancement of efficacy of allergen vaccination, reducing the number of injections required for that treatment. The PL is a component of the anti-meningococcal vaccine (VAMENGOC-BC, Finlay Institute, Havana), therefore, this study aimed at assessment of the influence of the antiallergic vaccine on to an earlier response against <i>N. Meningitidis</i> induced by prophylactic vaccination. Methods: It was measured the PL-specific IgG antibody response, including IgG1 and IgG2a subclasses, before and after the administration of three doses of the allergen vaccine (2 µg Der s 1, each) in Balb/C mice vaccinated previously with two doses of VAMENGOC-BC. The allergen specific IgG and subclass antibody response was also evaluated. Results: The administration of the PL-containing allergen vaccine in these mice showed only a slight dose-dependent increase on PL-specific IgG, IgG1 and IgG2a antibodies. Unexpectedly, previous immunization with VAMENGOC was associated to a significant increase of the allergenspecific IgG, IgG1 and IgG2a antibody response induced by the later administration of the allergen vaccine (ANOVA, p<0.05). Current results confirmed that the highest IgG2a and IgG1 response to the allergen vaccine was obtained after the third dose. Conclusion: These results sustain the safety of this novel anti-allergic vaccine with regard to its lack of negative influence to anti-meningococcal response.</p>
PFE 129	<p>VALIDATION OF DIAFILTRATION PROCESSES OF HOUSE DUST MITE ALLERGEN VACCINES Castillo Y¹, Perea Y¹, González G¹, Seuret N¹, Labrada A²</p> <p>¹ Active Ingredients Plant, National Center of Bioproducts, Ave, Beltran Km 1 ½, Bejucal, Havana, Cuba. email:yainelysc@biocen.cu ² Allergens Department, National Center of Bioproducts, Ave, Beltran Km 1 ½, Bejucal, Havana, Cuba.</p> <p>Process validation is a requirement of pharmaceutical industry. Validations studies are designed to demonstrate the expected results of each process. Ultrafiltration is used in the manufacturing process of allergen extracts as a purification step after a prior clarification, intending to remove low molecular weight irrelevant components. The aim of this work was to validate the diafiltration process, using Hollow Fibber cartridges with a cutt-off of 10 kDa, for allergen extracts obtained from the whole culture of <i>Dermatophagoides pteronyssinus</i>, <i>D. siboney</i> and <i>Blomia tropicalis</i>. The following studies were performed: Operational Qualification of the DC-10 Amicon equipment; Validation of the Cleaning In Place (CIP) cycle, regarding the removal of cleaning agents, and Performance Qualification. Washing with Sodium Hydroxide 0.2 mol/L and Formaldehyde 0.5% followed by 3 rinsing cycles with purified water, was able to remove completely the remains of cleaning agents and allergen products, as measured by Total Organic Carbon test (<500 ppb), pH and conductivity, maintaining the microbiological counts within the specification limits. Cartridge performance and integrity assessment demonstrated to retain more than 99% of Human Albumin 1% solution, after a full diafiltration-concentration cycle. The performance qualification using four batches of allergen products showed the expected values regarding recovery of Group 1 Major allergens and other allergenic proteins, and the corresponding shift in conductivity and absorbance. In conclusion, this validation work demonstrated the proper performance of this important step in the context of the manufacturing process, contributing to guarantee the quality of the final product.</p>
PFE 130	<p>ACTORS INFLUENCING THE ADSORPTION OF <i>Dermatophagoides siboney</i> ALLERGEN EXTRACT INTO ALUMINUM ADJUVANTS Nguyen Phuoc CA¹, Alonso Y², Oliva Y², Mayo O³, Labrada A²</p> <p>¹ Division of Medical Biotechnology, Centre of Ho Chi Minh City, Vietnam. ² Allergens Department, National Center of Bioproducts, Havana, Cuba. ³ Development Department, National Center of Bioproducts, Havana, Cuba. email: yarima@biocen.cu</p>

	<p>Introduction: Allergen-specific immunotherapy consists of periodic administration of allergen vaccines, particularly from House Dust Mites (HDM), for desensitization and amelioration of allergic symptoms. The mite <i>Dermatophagoides siboney</i> has been commonly found in house dust in the Caribbean and it is associated to allergic asthma. In order to obtain a depot HDM vaccine containing aluminum adjuvant, a lyophilized allergen extract of <i>D. siboney</i> was adsorbed into aluminum hydroxide (AH) and aluminum phosphate (AP) gels, aiming to establish the parameters that determine the highest adsorption capacity.</p> <p>Methods: Allergen adsorption was measured by Lowry total protein assays and by Der s 1 allergen-specific MAb-ELISA. Immunogenicity was assessed in Balb/C mice using two doses of 5 ug Der s 1, by subcutaneous route.</p> <p>Results: AH showed better adsorption capacity when compared to AP. The best adsorption conditions using AH were: 0.9 % NaCl at pH 8 in 30 min. Sodium phosphate buffered solution showed a negative effect on the allergen adsorption into AH, both, when used during the mixing process or added later. The within-batch consistency of the adsorption process in absence of phosphate buffer was demonstrated, as well as the immunogenicity of this formulation, regarding induction of allergen-specific IgG antibodies in mice.</p> <p>Conclusion: The immunogenicity and quality consistency of this optimized formulation can be relevant for the development of improved adsorbed allergen vaccines.</p>
PFE 131	<p>ASSESSMENT OF CONSISTENCY OF THE MANUFACTURING PROCESS OF HOUSE DUST MITE ALLERGEN VACCINES <u>Perea Y¹</u>, Castillo Y¹, González G¹, Seuret N¹, Labrada A²</p> <p>¹ Active Ingredients Plant, National Center of Bioproducts, Ave, Beltran Km 1 ½, Bejucal, Havana, Cuba. yperea@biocen.cu ² Allergens Department, National Center of Bioproducts, Ave, Beltran Km 1 ½, Bejucal, Havana, Cuba.</p> <p>Consistency of quality parameters of the final and intermediate products is a requirement of the pharmaceutical processes, and it is of special concern for biological complex products, such as allergen extracts. The objective of this work was to evaluate the consistency of consecutive batches of allergen extracts of <i>Dermatophagoides pteronyssinus</i>, <i>D. siboney</i> and <i>Blomia tropicalis</i>. The following specific tests were used: allergenic potency, as measured by IgE-inhibition ELISA, allergen profile by Western Blotting, SDS-PAGE. Major allergen (Der p1 and Der s1, as measured by ELISA) and total protein content were monitored during the whole manufacturing process. A total of 32 batches were monitored over a period of 6 years and process capability index was calculated. No batches were found out of the specification or $\pm 3\sigma$ limits. The maximum failure probability was estimated to be 6% for the allergenic potency. A similar value was observed for allergen composition parameters (intensity of the bands corresponding to major allergens). Lower failure probabilities were found for protein composition (0.2%) and Der p1/Der s1 allergen content (3%), both at the finished product or the active substance stage. These values are regarded as satisfactory considering the high variability of these analytical methods (which is estimated to be much greater than the intrinsic process variability) and are found to be similar to the rejection rate of standardized allergen extracts in USA. In conclusion, it was demonstrated the consistency of the main quality parameters of standardized allergen vaccines, which is very relevant to clinical safety and efficacy.</p>
	CLINICAL PHARMACOLOGY AND TEACHING/ FARMACOLOGIA CLINICA Y ENSEÑANZA
	<i>Clinical Pharmacology, Pharmacology Teaching and Drugs Design. / Farmacología Clínica, enseñanza de la Farmacología y diseño de fármacos</i>
<i>Chairs</i>	<i>María Acelia Marrero, Alberto Hernández, Doris Perdomo, Lianne Pajarin, Ernesto Groning, Tamara Vilches</i>
PFC 01-54	FARMACOLOGIA CLÍNICA / CLINICAL PHARMACOLOGY
PFC 01	<p>EFFICACY AND SAFETY OF SUBCUTANEOUS IMMUNOTHERAPY USING STANDARDIZED HOUSE DUST MITE VACCINES IN THE TREATMENT OF ALLERGIC ASTHMA IN A CUBAN POPULATION. RESULTS FROM DOUBLE-BLIND PLACEBO CONTROLLED CLINICAL TRIALS <u>Castro RL¹</u>, Ronquillo M², Rodríguez-Canosa J², Álvarez M², Oliva Y¹, Labrada A¹</p> <p>¹ National Center of Bioproducts, Havana, Cuba.</p>

	<p>² "Calixto García" University Hospital, Havana, Cuba. email: rcaastro@biocen.cu</p> <p>Introduction: Specific Immunotherapy is an effective treatment for rhinitis and mild to moderate asthma. Allergic sensitization to House Dust Mites <i>Dermatophagoides pteronyssinus</i>, <i>D. siboney</i> and <i>Blomia tropicalis</i> has been described before in Cuba, as strongly linked to asthma. The aim of this work was to evaluate the efficacy and safety of standardized allergen vaccines of these 3 mite species (VALERGEN, BIOGEN, Cuba), in asthmatic patients. Methods: Three separate DBPC clinical trials were performed in 40 asthmatic patients each, with variable polysensitization, but positive predominant Skin Prick Test (SPT) to the vaccine allergen, respectively. Half of patients received the active treatment consisting of subcutaneous injections with increasing doses. The total one year cumulative dose was 63035 BU, in an average of 20.5 injections. Results: The treatment was effective in the reduction of clinical symptoms (up to 32%, CI95%: 28-36%; p=0.0006) and medication intake (23%, CI: 18-28%), as compared to control treatment. The skin sensitivity to the allergens decreased significantly (p=0.0001), with regard to the beginning of the treatment. Immunotherapy with Dp induced also desensitization to Ds, and vice versa, while no cross-effect was observed to Bt. The reduction of skin sensitivity was correlated (p<0.05) to clinical outcome. Improvement of the lung function was observed, as a modest PEF increase and reduction of PEF daily variability (p<0.05). SIT was effective in 71% of patients. The frequency of local adverse reactions was 2.4 % of injections.</p> <p>Conclusions: The overall results indicate that immunotherapy using VALERGEN standardized vaccines is effective for the control and amelioration of the allergic asthma in our population.</p>
PFC 02	<p>THERAPEUTIC EFFECT IN ASTHMATIC ADULTS TREATED WITH SUBLINGUAL IMMUNOTHERAPY WITH A STANDARDIZED ALLERGEN VACCINE OF <i>Dermatophagoides pteronyssinus</i></p> <p>Rodríguez J,¹ Castro RL,² Ronquillo M,¹ Álvarez M,¹ González M,³ Navarro BI,⁴ M Quiza¹, Mateo M,² Oliva Y,² García I,¹ Enriquez I,¹ Labrada A²</p> <p>¹ University Hospital "Calixto García", Havana, Cuba. ² National Center of Bioproducts (BioCen), Havana, Cuba. ³ Docent Polyclinic "Pedro Fonseca", Punta Brava, Havana, Cuba. ⁴ Polyclinic Capdevila, Havana, Cuba. email: rcaastro@biocen.cu</p> <p>Introduction: Sublingual immunotherapy (SLIT) has been regarded as a practical alternative to subcutaneous immunotherapy (SCIT). During the last 20 years, increasing evidence on the clinical efficacy and safety of SLIT in rhinitis and asthma has been provided. Objective: To evaluate the therapeutic effect and safety of a <i>Dermatophagoides pteronyssinus</i> (Dp) standardized allergen vaccine (VALERGEN-DP, BIOGEN) for SLIT in asthmatic patients. Methods: A DBPC clinical trial was performed in 40 adults with mild to moderate asthma. After a 4-week baseline phase, patients were randomized to placebo or active treatment, consisting on sublingual drops with increasing daily doses for 3 weeks and maintenance doses twice a week for 12 months. Maximum dose was 2000BU. The effect was evaluated with symptom/medication diary cards, peak expiratory flow (PEF) measures and skin reactivity. Adverse reactions were classified according to WAO. Results: After 12 months, SLIT significantly reduced clinical symptoms (up to 35%) and medication (30%), with respect to the placebo group. Allergen-specific skin sensitivity was also reduced significantly (p<0.05). Similarly to SCIT, SLIT with Dp was able to induce desensitization towards <i>D. siboney</i>. A slight improvement of the respiratory function with reduction (p<0.005) of PEF variability was noted. Overall, 75% of patients reported clinical improvement. These figures are similar to those reported by SCIT with the same vaccine. Moreover, safety was clearly superior. No specific systemic reactions were reported. Local reactions were described only in 0.58% of administrations. Conclusion: These results support the efficacy and safety of SLIT with VALERGEN-DP for asthma treatment in our population and endorse its large-scale introduction in our healthcare system.</p>
PFC 03	<p>CLINICAL TRIAL OF SUBLINGUAL IMMUNOTHERAPY IN ASTHMATIC CUBAN PATIENTS USING A STANDARDIZED ALLERGEN VACCINE OF <i>Dermatophagoides siboney</i></p> <p>Álvarez M,¹ Castro RL,² Ronquillo M,¹ Rodríguez-Canosa J,¹ González M,³ Navarro BI,⁴ Mateo, M,² Oliva Y,² García I,¹ Enriquez I,¹ Labrada A²</p> <p>¹ University Hospital "Calixto García", Havana, Cuba. ² National Center of Bioproducts (BioCen), Havana, Cuba. ³ Docent Polyclinic "Pedro Fonseca", Punta Brava, Havana, Cuba. ⁴ Polyclinic Capdevila, Havana, Cuba. email: rcaastro@biocen.cu</p>

	<p>Introduction: Specific immunotherapy using mite allergen vaccines is considered an effective treatment for allergic asthma. Sublingual route has the potential for decreasing the risk of systemic reactions and improving compliance. The objective was to determine the therapeutic effect and safety of sublingual immunotherapy using a standardized vaccine of <i>Dermatophagoides siboney</i> (VALERGEN-DS, BIOCEN, Cuba) in Cuban asthmatic patients. Methods: A Double-Blind Placebo-Controlled study included 40 adult patients, with mild to moderate asthma and allergic sensitization to <i>Ds</i>. Half of patients were randomized to placebo. Treatment consisted of sublingual drops with escalating dosage up to 2000 BU; 107 applications were administered in each patient, 21 of them corresponding to the increment phase with a daily frequency. In the maintenance phase the vaccine was administered twice per week during 12 months. Results: The treatment was very effective in decreasing clinical symptoms (up to 37%) and medication (29%), compared to conventional medication in the control group. Allergen-specific skin reactivity, as measured by the wheal diameter, and PEF variability decreased significantly ($p < 0.05$). Clinical outcome was correlated with reduction of skin reactivity. Overall, the treatment was considered effective in 70% of patients. Efficacy of the sublingual treatment was similar to a previous trial with subcutaneous route. However, safety was clearly superior: no product-related systemic reactions were reported. Local reactions were reported in only 0.36% of administered doses. Conclusion: This study indicates that sublingual immunotherapy with VALERGEN-DS is an effective and safe treatment for allergic asthma in Cuba and support its introduction in Allergy Services in our Healthcare System.</p>
<p>PFC 04</p>	<p>EFFECT OF THE TREATMENT WITH LEUKAST IN ASTHMATIC PATIENT <u>Águila de la Coba</u>¹, Castillo Méndez AC²</p> <p>¹Cerro Pediatric Hospital, Cerro, Havana City, Cuba. rac@infomed.sld.cu ²Salvador Allende Hospital, Cerro, Havana City, Cuba. ada.mendez@infomed.sld.cu</p> <p>Introduction: Asthma is cronic inflammatory illness of the air roads in which several cells playing an important rol in the development of the bronchial hiperreactivity. The leukotriens are mediators that participate in the inflammatory process being involved in the bronchoconstriction. Objectives: To evaluate the effectiveness of the Montelukast (Leukast) in patient pediatic and adults with Moderate-Severe Persistent Asthma. Material and methods: 201 patients were studied, 101 of 6 to 16 years of age and 100 of 17 or more years old with persistent moderate and severe asthma, without antecedents of illnesses hematológic, hepatic or renal, to those that were administered montelukast in dose from 5mg of 6 to 14 years and 10 mg to those bigger than this age, once a day during 6 months. A monthly pursuit of its clinical evolution was taken, with control of the renal function and liverwort to the beginning, to the three months and when concluding the study; tests of breathing function were also made to the beginning and when finishing the treatment.</p> <p>Results: neither of the patients worsened, 81% of them passed to stay asymptomatics in this period and 18.9% they happened to fast. In six cases it was necessary to move away the treatment for different reasons for causes unaware to the medication. Conclusions: the effectiveness of this medication was demonstrated and they were not problems of intolerance or important adverse effects.</p>
<p>PFC 05</p>	<p>NEOADYUVANT CHEMOTHERAPY IN BREAST CANCER PATIENTS O'Farril MA¹, <u>Morales M</u>², Puebla Y², Segura D¹, Suarez F¹, Rodríguez I¹</p> <p>¹ Oncology Hospital "Conrado Benítez". Santiago de Cuba, Cuba. ² Department of Pharmacy, Faculty of Natural Sciences, University of Oriente. Patricio Lumumba y Avenida de Las Américas. Santiago de Cuba, Cuba. CP 90 500. email: maramg@cnt.uo.edu.cu</p> <p>Introduction: Breast cancer is the most frequent malignant tumor on women. Standard treatment modalities have improved the overall outlook and quality of women life with breast cancer; however, the fact that 40% still succumb to the diseases highlights that needs new therapeutic approaches. The locally advanced breast cancer has an incidence of 30-50% of all in developing countries. The response to neoadjuvant chemotherapy is an important prognostic factor in this group. The aim was to evaluate tumor respose to neoadjuvant chemotherapy treatment in patient with breast cancer at stage III. Methods: A pharmacotherapy follow-up was carried out during January 2004 to December 2009 in the Oncology Hospital "Conrado Benítez García" in Santiago de Cuba. All the women with locally advanced breast cancer and treated with neoadjuvant chemotherapy were analyzed. The adjustment of prescription was determined as well as the treatment compliance, histopathology and clinic response of the neoadjuvant chemotherapy. Results: The ductal cancer was histological diagnostic more prevalence. The chemotherapy outlines more employees were Cyclophosphamide-Adriamycin and Cyclophosphamide-</p>

	<p>Methotrexate-5-Fluorouracil. The 67.5% patients with non appropriate treatment compliance of the neoadjuvant chemotherapeutic prescribed, due to fundamentally that didn't complete with the suitable interval among cycles. The 69.76% of the patients had histopathology non favourable response and 65.11% patients with partial remission as clinical response to the treatment influencing in these responses the great tumoral size that the patients presented. From the statistical point of view relationships could not settle down between the adaptation of the execution and the histopathology and clinic response. Conclusions: Patients who complied fully with the therapy, associated with remission axillary tumor and small tumor size, had complete response to the treatment.</p> <p>References: Sellaheva Ch, Nightingale P, Carmichael AR, Women with large breasts are at an increased risk of advanced breast cancer. International Seminars in Surgical Oncology 2008, 5:116.</p>
<p>PFC 06</p>	<p>A COMPARATIVE STUDY ON THE EFFECTS OF NIACIN PLUS ATORVASTATIN WITH THAT OF FENOFIBRATE PLUS ATORVASTATIN IN DYSLIPIDAEMIA Salim Ahmed, AKM Mosharrof Hossain, Sudhangshu Ranjan Dey, AKM Akhtaruzzaman, Musammath Moriom Siddika</p> <p>¹ Department of Pharmacology, Jalalabad Ragib-Rabeya Medical College & Hospital, Sylhet. email Address: dr.salimahm@yahoo.com ² Department of Pharmacology, Sylhet M.A.G. Osmani Medical College, Sylhet ^{3,4} Department of Cardiology, Sylhet M.A.G. Osmani Medical College, Sylhet ⁵ Department of Pediatrics, Jalalabad Ragib-Rabeya Medical College & Hospital, Sylhet, 3100, Bangladesh.</p> <p>Introduction: Coronary heart disease (CHD) patients usually associated with low HDL-cholesterol, high triglycerides as well as elevated LDL-cholesterol. Low HDL-cholesterol predicts CHD risk independently even when LDL-cholesterol is low. Previous studies suggest that statin combined with either niacin or fibrate significantly modify lipid profile in patients with CHD. The present study was designed to evaluate and compare the effects of co-administration of atorvastatin either with niacin or fenofibrate in dyslipidaemia.</p> <p>Materials and Methods: This prospective consecutive interventional study was conducted on a total number of 108 CHD patients with evidence of dyslipidaemia in the Department of Pharmacology and Therapeutics in active collaboration with Department of Cardiology of Sylhet MAG Osmani Medical College Hospital (SOMCH) during the period of July 2006 to June 2007. Niacin 1000 mg plus atorvastatin 10 mg was administered to 64 patients (Group I) while 44 patients were (Group II) treated with fenofibrate 200 mg plus atorvastatin 10 mg daily for 12 weeks. Of them, a total 67 patients (35 patients in Group I and 32 patients in Group II) completed the study. Their fasting lipid profiles, SGPT, serum creatinine and fasting blood glucose levels were estimated before and 12 weeks after initiation of treatment. Predisposing risk factors such as age, sex, obesity, history of diabetes mellitus (DM), hypertension (HTN), smoking and family history of coronary heart disease (CHD) were also analyzed. Adverse events were also recorded to assess the safety and tolerability. Obtained data were analyzed using by paired 't' and 'Z'-test at 95% confidence interval.</p> <p>Results: The niacin-atorvastatin combination significantly reduced TC by 25.73%, TG by 14.03%, LDL-C by 38.41% and increased HDL-C by 10.04% (p<0.001 for all). Another combination of fenofibrate-atorvastatin significantly reduced TC by 30.22%, TG by 35.03%, LDL-C by 38.58%, whereas it increased HDL-C by 7.22% (p<0.001 for all). In comparison between two groups, there were no significant difference in serum lipid profile except in level of TG reduction where fenofibrate-atorvastatin combination yielded significant (p<0.001) results. In this study, SGPT level significantly raised and fasting blood glucose level decreased in fenofibrate-atorvastatin treated group than niacin-atorvastatin combination. Serum creatinine level decreased in niacin-atorvastatin treated group compared to fenofibrate-atorvastatin, but the changes was within normal limit. Conclusion: This study showed that both combinations are equally effective in dyslipidaemia. Although, fenofibrate-atorvastatin combination decreased more TG and niacin-atorvastatin combination appeared safer considering some adverse effects. Further studies including randomized, double blind, multi-center trials with different dose schedule and different combination have been suggested.</p>
<p>PFC 07</p>	<p>CLINICAL COMPARISON BETWEEN IMMUNOSUPPRESSIVE REGIMENS USED FOR KIDNEY TRANSPLANTATION IN THE INSTITUTE OF NEPHROLOGY, 2000-2007. Pérez Rodríguez A¹, Marmol Soñora A¹, Perez de Prado Valdivia JC¹, García Gutiérrez F¹.</p> <p>¹Institute of Nephrology. Avenida 26 and Boyeros. Havana. Cuba. Email: alex.perez@infomed.sld.cu</p>

	<p>Introduction: Advances in maintenance immunosuppression over the last decade led to a significant reduction in the incidence of acute rejection (AR) and best long-term results for renal transplantation. But new drugs continue to lack sufficient specificity, many of them require continuous monitoring and also can produce virtually all acute or chronic nephrotoxicity in addition to irrigation with infections and tumors. The long-term success of the TR is still a challenge and it is known that the delay of renal function and RA represent a negative influence on graft survival. The introduction of Cyclosporine (CyA) in the early 80s and biological agents in the 90s enabled a dramatic reduction in RA with significant impact on graft survival.</p> <p>At present there are differences in the results obtained with different immunosuppressive regimens as preferred use according to the characteristics of the patient to be transplanted, and this makes it necessary to know in depth the advantages and disadvantages of each. Design & Aims: Observational descriptive retrospective cohort, to compare the incidence of acute rejection, their classification (Banft 1997) and causes loss of the grafts, three protocols of immunosuppression. Methods: We studied all kidney transplants, cadavers (116), conducted at the Institute of Nephrology "Dr. Abelardo Buch López", from 2000 to 2007. Patients were excluded who lost their function or died of causes unrelated to the immunosuppressive protocol employed. The protocols compared were: I-) Quadruple sequential polyclonal antibodies (AcP, Thymogam), II-) Quadruple sequential Monoclonal antibodies (mAb, IOR-T3) and III-) Triple. Immunological variables were analyzed as HLA compatibility and the percentage of HLA antibodies and the immune system like number of TR, donor age, cause of death, cold ischemia, acute tubular necrosis post-TR, days of treatment with biologic therapies and side reactions. We used the statistical technique of analysis of frequency distribution and the homogeneity test, the analysis of qualitative variables. Was calculated for quantitative arithmetic mean and standard deviation, and used the Kruskal Wallis test. Results: The protocol I showed lower incidence of the first crisis of RA (18.5% v / s 33.3% and 43.2 % for protocols II and III), with no loss of RA grafts in the first year, despite having been used in patients with high immunological risk, unlike the protocols II and III where if losses were found in transplants 22.2% and 20.5% respectively. When presented with the RA, the severity was much lower in the protocol I (25.0% RA and suspected RA IA 75.0%, in contrast to RA in protocols II and III where there is also RA IIA and IIB. Conclusions: The use of quadruple sequential protocol AcP, Thymogam has better results in our environment and is ideal for high immunological risk patients.</p>
PFC 08	<p>EFFICACY AND SAFETY OF IOR®EPOCIM FOR CORRECTION OF ANEMIA IN CHRONIC KIDNEY DISEASE IN DIALYSIS PATIENTS Vargas A¹, Mendoza I¹, Pérez-Oliva JF², Piedra P³, Saurez G³, Robaina M¹</p> <p>¹National Center Coordinating of Clinical Trials, 200 at 21 Ave, Atabey, Playa, Havana City, Cuba. email: alicia@cencec.sld.cu</p> <p>²National Institute of Nephrology "Dr. Abelardo Buch López". Avenida 26 y Boyeros. Plaza de la Revolución, Havana City, Cuba.</p> <p>³Center of Molecular Immunology, CIMAB S.A. Calle 206 No. 1226 esq.21, Atabey, Playa, Havana City, Cuba.</p> <p>Introduction: Anemia is a common complication of chronic kidney disease (CKD). Treatment with Recombinant human erythropoietin (RHuEPO) has been shown to enhance quality of life, benefits of anemia correction and reduce the need for blood transfusions. Materials and Methods: A fase IV, multicenter, open-label trial, in dialysis patients with anaemia with chronic kidney disease was conducted. The objective of this study was evaluate the efficacy and safety of ior®EPOCIM, (RHuEPO) produced by the Center of Molecular Immunology. Subcutaneous erythropoietin (epoetin alfa) was administrated at the doses and frequencies used in the habitual medical practice. Eligible patients were included if they have stable dialytic therapy for a period superior to 3 month. The working hypothesis was the maintaining to hematocrit ≥ 30 % during the period treatment (12 months). The primary end point was the hematopoietic response and identify the adverse events evaluated every month. The quality of life was evaluate at the beginning and the end of the treatment. Laboratory data including: haemoglobin, hematocrit, leucocytes, erythrocytes, platelets, reticulocytes count and serum iron. Results and Discusión: Were analyzed 616 patients The initial mean hematocrit was 35.21%, reporting at the end of the study the mean hematocrit was 36.68%. The safety assessment is not reported changes in laboratory parameters in final assessment in relation to the initial. Events were reported in 55.5% of patients. Fever, hypertension and pain in the injection site were the most frequent adverse events, reported in 10.7%, 7.0% and 5.3% of all reported</p>

	<p>events. Regarding the quality of life, there was an increase in the mean scores of the scales but this increase was not statistically significant. Conclusions: ior® EPOCIM proved to be safe and effective at the doses and frequencies used in the habitual medical practice in anaemic patient in dialysis with chronic kidney disease.</p>
<p>PFC 09</p>	<p>CERTIFICATION OF GOOD CLINICAL PRACTICE AT THE CLINICAL TRIAL UNIT OF THE NATIONAL CENTER OF TOXICOLOGY González Delgado CA¹, Díaz Machado A¹, Pérez Rodríguez S¹, David Valdo M¹, Barrero Viera L¹, Alvarez Delgado M¹, Tamayo Rodríguez M¹, Rivero Vásquez I¹, Ravelo Castro MV¹, Pérez Pérez O¹, Frias Ledesma E¹, Rodríguez Gener G¹, Montoya Calas N¹</p> <p>¹National Center of Toxicology, Ave 31 y Calle 114, Marianao, Ciudad de la Habana. email: eclinicos@infomed.sld.cu</p> <p>Background: The development of the Biopharmaceutical Industry has encouraged the increase of clinical studies together with the compliance of Good Clinical Practice (GCP) at the Clinical Sites of Research. The Center for the National Quality Control of Drugs (CECMED) as the National Drug Regulatory Authority has put into practice a program for the Certification of GCP at the Clinical sites and Services involved in Clinical trials so as to guarantee reliability and credibility of results obtained in the clinical trials conducted in such places. Since 1992, bioequivalence studies to generic drugs and Phase I-II studies are carried out in the National Center of Toxicology (CENATOX). The results achieved in the compliance of GCP during the inspection executed by CECMED paved the way for starting the certification of GCP at CENATOX. Objective: To elaborate an action plan aimed at certifying the Clinical Trials Unit at CENATOX as a Research Clinical Site. Materials and Methods: A self-evaluation was carried out according to the Clinical Site Accreditation Manual for the conduction of Clinical Trials established by CECMED and the National Coordinator Center of Clinical Trials (CENCEC), the corresponding regulatory document and the Regulation No. 52-2008, Requirements for the certification of GCP issued by CECMED. A plan for correcting non-conformities was established. The corresponding inspections were received and correcting actions for the non conformities were taken. Results and Discussion: Eighteen non conformities were detected, suggesting the need of training the staff involved in the clinical trials. The revision, updating and completion of technical and regulatory documents. The facility was repaired. Three inspections visited the site : A preevaluation by CENCEC and two by CECMED with a total of 15, 14 and 7 non conformities respectively, which were totally corrected. The compliance of GCP in the inspected services was evidenced, that is in the hospitalization ward, pharmacy, archives and ethical committee. The services of laboratory and imagenology were convened with CIMEQ hospital, previously certified. Conclusion: The Clinical Trials Unit of CENATOX attained the certification of compliance with GCP and became in the second clinical site of the country that achieved such condition.</p>
<p>PFC 10</p>	<p>DEVELOPMENT AND IMPLEMENTATION OF A QUALITY ASSURANCE SYSTEM COMPLYING WITH ISO 9001-2008 AIMED AT CONDUCTING CLINICAL TRIALS AT THE NATIONAL CENTER OF TOXICOLOGY. González Delgado CA¹, Díaz Machado A¹, Ravelo Castro MV¹.</p> <p>¹National Center of Toxicology, Ave 31 y Calle 114, Marianao, Ciudad de la Habana Email: eclinicos@infomed.sld.cu</p> <p>Background: The quality of Clinical Trials (CT) depends on the accomplishment of Good Clinical Practice (GCP), thus, for assuring reliability and credibility of results. However, its combination with ISO 9001-2008, an international quality standard, is not generalized. In Cuba, there are institutions and health services with a certified Quality Assurance System (QAS), but none of them performs Clinical Trials. Recently, the Clinical Trials Unit of the National Center of Toxicology (CENATOX) attained such certification for complying with the GCP. Objective: To develop and implement a QAS complying with ISO 9001-2008 aimed at improving the quality and control of the processes within Clinical Trials combined with GCP. Materials and Methods: A schedule for planning the system was elaborated, it included: Compilation, reviewing, updating and study of technical, legal and regulatory documentation of Clinical Trials. Processes and their interrelationships were identified. Diagnosis and adaptation of the requirements of the standards of the already existing GCP documents. Implementation of the system. Writing of Technical documents and taking of actions. Results: A QAS was developed and implemented at CENATOX. Three processes were identified within the Clinical Trial macro process: Design and Planning, Selection and Hospitalization. Their sequence and interrelationship were defined. The documents</p>

	<p>of the system were elaborated including the procedures and registry manual. Similarly, the indicators for guaranteeing the follow up and control of processes were established. The Quality Manual as a guidance document was elaborated; it describes the four basic elements of the system: responsibility of the direction, resources management, conduction, measurement, analysis and improvement of the final product.</p> <p>Conclusion: The development and implementation of the Assurance System has improved the rigor and quality of the services offered by the CT Unit for, it involves all the activities and staff linked with the clinical trials. The identification and documentation of the processes, and the control and follow up by indicators assures the evaluation and continuous improvement. The QAS developed at CENATOX renders a superior competitive position and self identity within the field of clinical trials of the country, thus, originating a greater interest in the promoters, our clients.</p>
PFC 11	<p>RENIN ANGIOTENSIN SYSTEM BLOCKING IN PATIENTS WITH IgA NEPHROPATHY: META-ANALYSIS OF CONTROLLED CLINICAL TRIALS Leyva C¹, Furonés JA², Pérez A¹, Pérez de Prado JC¹, Heras A¹, Dávalos JM¹</p> <p>¹Nephrology Institute, 26 at Boyeros Ave, Plaza, Havana City, Cuba. email:leyvachr@infomed.sld.cu ²Center for the Development of Pharmacoepidemiology, National Pharmacovigilance Unit, 5ta Ave and 44 St, Miramar, Playa, Havana City, Cuba.</p> <p>Introduction: There is no solid evidence on the effectiveness of the blockade of the renin angiotensin system in preserving renal function and decreasing proteinuria and IgA nephropathy. Material and Method: A meta-analysis of controlled clinical trials present at the bases of MEDLINE and Cochrane data designed to demonstrate the efficacy of inhibitors of angiotensin converting enzyme (ACE) and / or antagonists receptor type 1 angiotensin II (ARB) in preserving renal function and reducing proteinuria in patients with IgA nephropathy. Trials with immunosuppressants were excluded. We applied the Jadad index. Results and Discussion: We selected nine clinical trials; five with Jadad's rate 3 or more. They demonstrated no reduction in glomerular filtration rate decline with ACEI / ARB when all trials were analyzed (DEM = -0.5415, 95% CI: -1.6057 to 0.5227), however, by repeating the analysis with better quality clinical trial it showed decrease in the decline of glomerular filtration rate with these drugs (DEM = -1.1459, 95% CI: -2.2125 to -0.0794). The risk of progression of renal damage was lower in the ACE inhibitor / ARB using the criterion of 50% increase in creatinine (RR = 0.28, 95% CI 0.16 to 0.48) and arrival terminal chronic renal disease (RR = 0.44, 95% CI 0.26 to 0.73). It was observed reduction of proteinuria in favor of treatment with ACEI / ARB (DEM = -2.94, 95% CI: -4.00 to -1.88). Few adverse events were reported in relation to different therapeutic options. Conclusions: ACE inhibitors / ARBs alone or in combination, appear to be effective in preserving renal function and in reducing proteinuria in patients with IgA nephropathy, although there is heterogeneity between clinical trials and publication bias.</p>
PFC 12	<p>CLINICAL EVALUATION OF CIMAVAX EGF IN SCHEDULE VACCINE-CHEMOTHERAPY-VACCINE IN THE TREATMENT OF PATIENTS WITH HORMONE-REFRACTORY PROSTATE TUMOURS." PRELIMINARY RESULTS Ills D, Mendoza I, Guerra PP, González J, Amador R, Santiesteban E, Crombet T, Rodríguez C, Viada C.</p> <p>Introduction: The prostate cancer is the second cause of death for cancer in Cuba, in the last decade the incidence has increased in a 12% for 75-84 range of age and in a 42% for male over 85 years old. OBJECTIVE: To evaluate the effect and safety of the therapeutic vaccine CIMAvax EGF in patients with hormone-refractory prostate cancer. Materials and methods: A phase II, controlled, multicentric and open label study was designed. Patients were randomized into two groups: I) CIMAvax EGF in schedule vaccine-chemotherapy-vaccine and II) standard chemotherapy (QT). The QT (mitoxantrone, 12 mg/m², every 21 days during 10 cycles and prednisone 10 mg daily during the 10 cycles of QT) started when the symptoms appeared. Global survival was the main end point and adverse events identified during the treatment, were also analyzed. Results: The intention to treat analysis for survival showed rates of 26.59% vs. 17.44% (for 24 months) and 22.79% and 13.95 (for 36 months), in behalf of the vaccinated group. Medians of survival were 17.10 vs. 10.73 months, for vaccinated and control group, respectively. The survival, for patients with at least 6 doses of CIMAvax EGF (group I) and 4 months of survival (group II), showed a tendency to a differ separation starting from 12 months, with rates of 81.99% vs. 57.04% (12 months), 38.77% and 17.94% (24 months) and 38.77% vs 17.94% (36 months) in behalf of the vaccinated group, and medians of 19.37 vs. 13.5 months, for vaccinated and control groups, respectively. Bone pain was the most frequent adverse event (AE) (26.8% vs 47.9%) for vaccinated and control patients. Other frequent AE were vomiting, fever and headache. Conclusions: The vaccine showed to be safe with a tendency of benefit in the rates of survival in behalf of vaccinated patients.</p>

<p>PFC 13</p>	<p>EVALUATION OF THE METHODOLOGY FOR THE TRAINING OF HUMAN RESOURCES NATIONAL HEALTH SYSTEM IN CLINICAL TRIALS. GUANTANAMO. 2009. Silva Valido J¹, Soler Cano D¹, Hernández Martínez R, Elias Oquendo Y², Franco Bonal A²</p> <p>¹University Medical Sciences Guantánamo, 5 oeste% 6 y 7 Norte. Guantánamo email:dayamisc@infosol.gtm.sld.cu ²Agosthino Neto Hospital 5 oeste% 12 y 13 Norte. Guantánamo</p> <p>Quasi-experimental research was conducted to evaluate the methods of training and human resource development in the subject of clinical trials. There were 3 courses and workshop aimed at clinical researchers, nurses and hospital ethics committee "A. Net "in the first half of 2009. Statistical techniques were used descriptive research level. Data processing was performed using SPSS v.13. Initially it was determined a low percentage of knowledge about clinical trials (38%) for researchers and identified learning needs. After the training, 98.6% of researchers overcame their cognitive deficits. 100 percent of the researchers met their initial expectations and reached its objectives with a high score in relation to the appropriation of knowledge related to clinical trials. The methodology is feasible for the training of professionals linked to the activity.</p>
<p>PFC 14</p>	<p>USE OF IMMUNOTHERAPEUTIC PRODUCTS IN CLINICAL ASSAYS PERFORMED IN SANTIAGO DE CUBA. AN OVERVIEW. Griñán D¹ Perdomo D¹, Landazuri S¹, Saumell Y², Peacock S²</p> <p>Clinical Trials Subcenter of Santiago de Cuba. Américas Avenue between E and I streets. "Sueño" District. Santiago of Cuba CP 90400. Cuba. email: dianne.yurien@medired.scu.sld.cu</p> <p>During last three decades the therapeutic treatment of patients with cancer has enhanced its possibilities with the incorporation of a fourth modality denominated Immunotherapy. This therapy can be used to complement some of conventional oncospecific treatments, and it is based on focusing the immune response against tumour cells to obtain a repair, stimulation or amplification of responsible immune mechanisms involved in tumour's growth and dissemination. The therapeutic vaccines against cancer constitute a new immunotherapeutic strategy that stimulates in the patient the immune response against tumour antigens. So far, many vaccines types exist and they are tested in different locations. . The subcentre of clinical trials of Santiago de Cuba has a vast experience in the management of these studies; that's why in the present work we will offer a panoramic of these investigations in patients cancer. Additionally, the quality of trials related to Good Clinical Practices fulfilment will be evaluated. This work summarizes the results obtained during 17 years in the management of clinical trials performed with immunotherapeutic products in Santiago de Cuba. In these years, more than 100 investigators of 22 medical specialities and 4 of our institutions (Hospital Oncológico Conrado Benítez, Saturnino Lora, Juan Bruno Zayas and Infantil Sur) have participated in clinical trials. Additionally, we have executed 18 protocols in 15 localizations such as breast, prostate, glyoma, lung, esophagus, colon, ovary, skin by using 8 immunotherapeutic products from the Molecular Immunology and Genetic Engineering Centres, so around 170 patients have been beneficiated. Overall, all investigations have been performed respecting the ethical principles and good clinical practices.</p>
<p>PFC 15</p>	<p>EFFICACY AND SAFETY OF RECOMBINANT STREPTOKINASE SUPPOSITORIES IN THE THROMBOSIS AND HEMORRHOIDAL FLUXION. Hernández-Bernal F¹, Valenzuela C¹, Quintero L², López M², Aguilera A¹, Páez R¹, Martínez E¹, Castellanos G², Domínguez J², Rodríguez H², Catasús K², Silva J², Ruiz J², Monterrey D², Peláez Y¹, Bermúdez Y¹, Bermúdez CH¹, Melo G¹, Álvarez L¹, Bobillo H¹, Poch E², Pupo A², Ramírez L², Fernández M², Fernández R², Rojas I², Martínez H², Herrera L¹, López-Saura P¹, on the behalf of the THERESA-2 (<i>Treatment of Hemorrhoid with Recombinant Streptokinase Application</i>) Group, Cuba.</p> <p>¹. Center for Genetic Engineering and Biotechnology (CIGB), Havana, Cuba. email: hernandez.bernal@cigb.edu.cu;². Ministry of Public Health (MINSAP), Cuba.</p> <p>Background/Aims: The hemorrhoidal disease constitutes a health problem, where a medical treatment could be beneficial before resorting to aggressive procedures. The recombinant streptokinase (SK) has shown favorable results in animal models of rectal inflammation and in humans. A phase II-III, multicenter, randomized, double blind, placebo controlled clinical trial was carried out to determine the efficacy and safety</p>

	<p>of SKr suppositories in the treatment of patients with hemorrhoidal fluxion and thrombosis. Materials and Methods: Eighty patients over 18 years-old that gave their consent to participate were included. They were randomly distributed in 4 treatment groups: I-Placebo, II-Sodium salicylate, III-SK 100 000 IU and IV-SK 200 000 IU per suppository. The corresponding product was administrated by the rectal route in every 6 hours up to 4 administrations. The patients were hospitalized for 24 hours and the evaluations were carried out at 24 hours and at 3, 5 and 20 days after the inclusion. An adaptive design using a Bayesian sequential analysis was performed.</p> <p>Results and Discussion: The efficacy of the SK suppository (200 000 IU) was demonstrated for healing of the haemorrhoidal fluxion and thrombosis at the 5th day (37% significant difference with respect to placebo); time for healing was significantly shorter in this group IV (SK–200 000 IU) with respect to the rest of the groups. Likewise, response evaluation at the 5th day showed the superiority of the SK suppository (200 000 IU) with statistically significant differences with respect to the placebo, salicylate and SK–100 000 IU groups. In the internal and mixed haemorrhoids grades III and IV, the higher SK dose showed advantage of healing with respect to placebo (68% difference) and superiority with respect to placebo and to salicylate groups concerning total response (52 and 40% differences, respectively). Conclusions: The Recombinant Streptokinase suppository was effective, safe and tolerable for healing of the haemorrhoidal crisis.</p>
<p>PFC 16</p>	<p>IMMUNOLOGICAL PERSISTENCE IN 18 MONTHS CHILDREN PREVIOUSLY VACCINATED IN INFANCY WITH THE CUBAN PENTAVALENT VACCINE HEBERPENTA. Véliz G, Aguilar A, Muzio V¹, Torraño H², García E¹, Trujillo J³</p> <p>¹ Biotechnology and Genetic Engineering Center. ² Lab. Pedro Kuri, Tropical Medicine Institute, Havana City Cuba. ³ Lab. National Center for Immunoassay Havana City Cuba. email: gloria.veliz@cigb.edu.cu</p> <p>Background: The combined diphtheria-tetanus-whole cell pertussis-hepatitis B + Haemophilus influenzae type b conjugate vaccine (DTPw-HBV+Hib) Heberpenta™ (HeberBiotec S.A, Havana, Cuba) is the only pentavalent vaccine currently manufactured in a third world country licensed for primary vaccination of infants and providing simultaneous protection against five major diseases of childhood. The persistence of the immune response against Hepatitis B virus and Hib in children aged 18 months previously vaccinated with three doses of DTPa-HBV+Hib vaccine was assessed in Cardenas, Matanzas province. Methods: A blood sample was collected from 178 children aged 18-20 months, all of whom had received 3-dose primary vaccination series with Heberpenta™ on field conditions (2-4-6 months) according to Cuban National Immunization Program. Antibodies against HBV (antiHBs) and Hib (antiPRP) were measured using commercial enzyme-linked immunoassay kits. Results: After the 3rd DTPw-HBV+Hib Heberpenta™ dose, seroprotective antibody levels persisted up to 18 months of age in =99.4 % and 99.5% of subjects for Hepatitis B and Hib, respectively; this is 12 months after completion of full primary vaccination series. Conclusion: The combined vaccine Heberpenta™ elicits long lasting immune response at least against hepatitis B virus and Hib antigens. This is the first demonstration of persistent immunological protection against HBV and Hib induced by Heberpenta™ administered on field conditions.</p>
<p>PFC 17</p>	<p>ASSESSING MEPERIDINE 5% IN SPINAL ANESTHESIA IN PATIENTS WITH GYNECOLOGICAL EMERGENCY SURGERY Ruíz H¹, Fernández Y², Ramos L¹, Quesada G², León O¹</p> <p>¹Departamento Coordinador de Ensayos Clínicos. Univ. de Ciencias Medicas. ² Hospital General "Camilo Cienfuegos" Circunvalante Norte. S/N. Olivos 3. Sancti Spiritus .Cuba. PC 60100. email: hector.ruiz@ucm.ssp.sld.cu</p> <p>Introduction: A controlled randomized single blind clinical trial was made with the objectives of evaluating the effectiveness and safety of meperidine 5%. Patients from the gynaecological emergency consultation of the "Camilo Cienfuegos" General Hospital of Sancti Spiritus were selected in the period from January to December of 2008. Material and Methods: 70 patients were included divided at random into two treatment groups: group I (Control) used lidocaine 5% and group II (Study) used Meperidine 5%, in both cases through the spinal route, at a dose of 1 mg/kg of weight. In the study, the following inclusion criteria were established: age over 18 years, with a surgical time shorter than 70 minutes and that gave their informed consent. Patients with allergy antecedents to medications, with mental disorders and with contraindications for the use of spinal anesthesia were excluded. Results: Variables such as the beginning</p>

	<p>time of action of each drug were used, where we observed that there were significant differences, and it was higher with the use of meperidine. The degree of sensitive and motor block was evaluated, and it was found to be higher than 50% for both medications. Haemodynamic parameters were analyzed such as arterial pressure and heart rate, where it was observed that there was a decrease in both groups, but in a slow and gradual way in group II. Adverse events occurred such as drowsiness (48, 57%) and pruritus (14%) with the use of meperidine, and hypotension (68, 57%) and tremors (54, 29%) with lidocaine. Other events were reported. Conclusions: Meperidine 5% is an effective and safe drug at the dose and route of administration used. It is an alternative for the treatment of these patients.</p>
PFC 18	<p>PHARMACOLOGICAL AND SAFETY EVALUATION OF A NOVEL CASEIN KINASE 2 (CK2) PEPTIDE INHIBITOR ADMINISTERED INTRALESIONALLY IN PATIENTS WITH STAGE IB2/II CERVICAL CANCER</p> <p>García I¹, Baladrón I¹, González L¹, Soriano JL², López A³, Batista N², Solares AM⁴, Valenzuela CM¹, Perea S⁵, Palau A³, Perera Y⁵, Acevedo BE⁶, Hernández I⁷, Vaillant A⁸, Quevedo LS⁸, López PA¹</p> <p>¹. Center for Genetic Engineering and Biotechnology (CIGB), Clinical Trials Division, Ave 134 e/23 and 25, Cubanacán, Playa, P.O. Box 6332, Havana 10600, Cuba. Telephone: +53 (7) 2087379; 2087465; Fax: +53 (7) 2736008. email: idrian.garcia@cigb.edu.cu.</p> <p>². Oncology Department, “Hermanos Ameijeiras” Hospital, San Lázaro No. 701 e/ Belascoáin and Marqués González, Havana 10300, Cuba.</p> <p>³. Nuclear Medicine Department, “Hermanos Ameijeiras” Hospital, San Lázaro No. 701 e/ Belascoáin and Marqués González, Havana 10300, Cuba.</p> <p>⁴. National Reference Center for Cervical Cancer Research, Gyneco-obstetric Hospital “Ramón González Coro”, Vedado, Havana 10400, Cuba.</p> <p>⁵. Laboratory of Molecular Oncology, Division of Pharmaceuticals, CIGB, Ave. 31 e/158 and 190, Cubanacán, Playa, P.O Box 6162, Havana 10600, Cuba.</p> <p>⁶. Business Development Group, CIGB, Ave 31 e/158 and 190, Cubanacán, Playa, P.O Box 6162, Havana 10600, Cuba.</p> <p>⁷. Isotope Center (CENTIS), Ave. Monumental and Carretera La Rada km 3. Guanabacoa, Havana, Cuba.</p> <p>⁸. Central Clinic “Cira García”, Ave. 41 and 20, No. 4101, Miramar, Playa, Havana 11300, Cuba.</p> <p>Introduction: Cervical cancer is now considered the second leading cause of death among women worldwide. CIGB-300 is a novel cyclic synthetic peptide that induces apoptosis in malignant cells and elicits antitumor activity in cancer animal models. Based on the perspectives of CIGB-300 to treat cancer, this study investigated its pharmacological properties and tolerability in patients with cervical cancer.</p> <p>Material and Methods: An open-label, non-controlled, sequential dose Phase I clinical trial was carried out, where 14 patients were included (6 both in 35 and 70 mg groups and other 2 in the 245 mg group). The treatment was applied intratumorally, once per day, during 5 days. The peptide was radiolabelled with ⁹⁹Tc in the first administration, when whole body gammagraphies and blood samples were taken during 48h for biodistribution/pharmacokinetic studies. Clinical-colposcopic and imagenological evaluations (CT scans, MRI) were used as measures of therapeutic action. Results and Discussion: The peptide presented a high tumoral retention, but higher percentage incorporation was evidenced with the lowest dose. However, in those patients that received 70 mg a higher reduction in the major diameter of the lesions and a major surrogate antitumoral effect (B23/NPM marker) was observed. The product was also mainly located in kidneys (main organ source), liver and spleen. CIGB-300 reached its maximum blood levels 5-15 minutes after the injection. The more frequent adverse reactions were those related with the syndrome of allergic reaction (100% of the patients), which had a significant correlation with the histamine levels and serum concentration. The intensity of these events had a direct relation with the magnitude of the administered dose. Conclusions: The CIGB 300 peptide had acceptable tolerability after intratumoral injection in patients with stage IB2/II cervical carcinoma (MTD: 70 mg). Certain findings shown reduction of the tumor volume that was correlated with the administered dose and also with surrogated biological variables of the peptide effect.</p>
PFC 19	<p>PHARMACOKINETIC AND PHARMACODYNAMIC COMPARISON OF TWO PEGYLATED INTERFERON ALPHA-2 FORMULATIONS IN HEALTHY MALE VOLUNTEERS</p> <p>García I¹, González CA², Valenzuela CM¹, Díaz A², Cruz M¹, Nodarse H¹, Pérez O², Bermúdez CH¹, Ferrero J³, Páez R⁴, Bello I¹, Castro FR⁴, López PA¹.</p>

	<p>¹.Center for Genetic Engineering and Biotechnology (CIGB), Clinical Trials Division, Ave 134 e/23 and 25, Cubanacán, Playa, P.O. Box 6332, Havana 10600, Cuba. Telephone: +53 (7) 2087379; 2087465; Fax: +53 (7) 2736008. email: idrian.garcia@cigb.edu.cu.</p> <p>².National Center for Toxicology, “Carlos J. Finlay” University Hospital, Ave. 31 and 114, Marianao, Havana 11400, Cuba</p> <p>³.Quality Control Direction, CIGB, Ave 31 e/158 and 190, Cubanacán, Playa, P.O Box 6162, Havana 10600, Cuba.</p> <p>⁴.Development Direction, CIGB, Ave 31 e/158 and 190, Cubanacán, Playa, P.O Box 6162, Havana 10600, Cuba.</p> <p>Introduction: Interferon (IFN) alpha conjugation of to polyethylene glycol (PEG) results in a better pharmacokinetic profile and efficacy. The aim of this study was to compare the pharmacokinetic, pharmacodynamic and safety properties of a new 40-kDa PEG-IFN alpha-2b preparation with a reference, commercially available PEG-IFN alpha-2a in healthy male volunteers. Material and Methods: A randomized, crossover, double-blind study with a 3-weeks washout period, was done. A single 180 µg PEG-IFN alpha-2 dose was administered subcutaneously. Sixteen apparently healthy male subjects were included. Serum PEG-IFN concentration was measured during 336 hours by an enzyme immunoassay (EIA). Other clinical and laboratory variables were used as pharmacodynamic and safety criteria. Results and Discussion: The pharmacokinetic comparison by EIA yielded a high similitude between the formulations. In spite of a high subject variability, the parameters were very close: AUC: 53623 vs. 44311 pg.h/mL; Cmax: 333 vs. 271 pg/mL; Tmax: 54 vs. 55 h; half-life (t1/2): 72.4 vs. 64.8 h; terminal elimination rate: 0.011 vs. 0.014 h⁻¹; mean residence time (MRT): 135 vs. 123 h for reference and study preparations, respectively. There were no differences with respect to the pharmacodynamic variables: serum neopterin and beta-2 microglobulin levels, stimulation of 2’5’ oligoadenylate synthetase expression, and serum IFN antiviral activity. A strong correlation between the pharmacokinetic and pharmacodynamic concentration-time curves was observed. Both products caused similar leukocyte counts diminution and had similar safety profiles. The most frequent adverse reactions were leukopenia, fever, thrombocytopenia, transaminases increase and asthenia, mostly mild. Conclusions: Both formulations are fully comparable from the pharmacokinetic, pharmacodynamic, and safety profiles. Efficacy trials can be carried out to confirm clinical similarity.</p>
PFC 20	<p>NURSING ROLE IN ADVERSE EVENTS FOR PATIENTS IN CLINICAL TRIALS Torres I¹, Rodríguez B¹, Cahimalle Y¹, Jiménez AI² email: imilla.torres@infomed.sld.cu, imilla@cencec.sld.cu</p> <p>¹National Center Coordinating of Clinical Trials, 200 at 21 Ave, Atabey, Playa, Havana City, Cuba. ²National Institute of Oncology. F street and 29. Plaza de la Revolucion. Havana City, Cuba.</p> <p>Introduction: The clinical trials are experimental evaluation of a substance or medicine through his administration or application to humans, with the aim of establishing effectiveness, adverse event profile or meet its pharmacodynamics or pharmacokinetic effects. The safety of patients in a clinical trial is one of the great importances and therefore should be approached from all angles to provide for an effective health intervention team, where the nurse is involved. Material and Methods: With the aim of defining the role of nurses in the prevention and management of adverse events of patients in clinical trials, it was conducted a literature review where theoretical methods were applied on the subject. Conclusions: Among the main issues identified were: to the nurse to intervene appropriately, you must perform independent and collaborative actions of nursing before, during and after the occurrence of adverse events. The ability of such personnel to minimize risks is an advantage of monitoring by nurses.</p>
PFC 21	<p>THALIDOMIDE IN THE TREATMENT OF THE PATIENTS WITH REFRACTORY OR IN RELAPSE MULTIPLE MYELOMA. Dita LM¹, Ramón LG², Hernández CR² ¹Gustavo Aldereguía Lima Hospital (GAL). Cienfuegos City, Cuba. ²Hematology and Immunology Institute (IHI). Havana City, Cuba. email: liermis.dita@gal.sld.cu</p> <p>Introduction: The use of the thalidomide in the treatment of patients with Multiple Myeloma (MM) it is based on their antiangiogenic, immunomodulatory and antitumoral activity. Several studies have demonstrated improvement in the quality of life and the survival. Purpose: With this clinical trial not randomized we intended to evaluate the effect and security of the rescue therapy with thalidomide, in</p>

	<p>patient with refractory or in relapse MM. Patients and Methods: Twenty patients received treatment with 200 mg thalidomide during the first 15 days, with increase the doses to 400 mg daily, according to tolerance. The duration of the treatment depended on the patient's response, with a maximum time to treat of 12 months. Response was evaluated after 6 months of the beginning of the treatment as: Complete Response (CR), Partial Response (PR), Minimum Response (MR), Stable Disease (SD) or Therapeutic Failure (TF). Continuity of the treatment up to 12 months was considered, according to the response. It was also determined one year-survival after treatment and the incidence of adverse events. Results: Results of the study showed 70 % of response (10 CR, 3 PR and 1MR). The media to reach the response (CR, PR or MR) was of 4. 8 months, with 79.69% of one-year survival. There were differences statistically significant in the response to treatment according to the dose administered (p=0. 04). The biggest percentage of response was reached at 200 mg. The patients in 2nd relapse had worse response that those that were in 3rd relapse (p=0. 004). The response didn't depend of the kind of monoclonal component (p=0. 781). The most frequent adverse events were: neuropathies (13. 6%), constipation (17. 3%), dermatitis (9. 9%) and drowsiness (14. 9%). Conclusions: The thalidomide showed effect and safety in the treatment of patients with refractory or in relapse Multiple Myeloma.</p>
<p>PFC 22</p>	<p>NGCGM3/VSSP VACCINE AND RACOTUMOMAB IN THE TREATMENT OF ADVANCED BREAST CANCER PATIENTS <u>Pérez L</u>, Pascau LJ, Macías A, Lorenzo-Luaces P, Estévez, Moreno Y, Hernández LE</p> <p>Center of Molecular Immunology (CIM) calle 216 esq. 15, Atabey, Playa. Ciudad Habana, Cuba. CP email: leslie@cim.sld.cu & liesel@jagua.cfg.sld.cu</p> <p>Introduction: The potent immunosuppressive capacity of NGcGM3 and the immunogenic characteristic of Racotumomab (1E10) make them interesting to conduct clinical trials in patients with advanced breast cancer. An expanded used program with NGcGM3/VSSP vaccine and Racotumomab in the treatment of advanced breast cancer patients were carried out to evaluate their safety and effect on survival. Materials and Methods: One hundred and twenty three patients with advanced breast cancer were enrolled in the expanded used program used NGcGM3/VSSP, Racotumomab and their combination. Both vaccines were administrated one dose every 14 days (induction period) and later every 28 days (consolidation period). Both vaccines should be administrated one week delay in order to decrease toxicity because of them. Overall survival (OS) was the main response variable and the appearance of adverse events was analyzed according to CTCAEv4.02 (Common Terminology Criteria for Adverse Events). The data were analyzed by SPSS version 16.0 for Windows. Kaplan-Meier test were used in order to establish the different among OS curves. Results: There was not significative difference among evaluated groups (p=0.77), but the OS with Racotumomab was highest (12.4 months). Seventy three patients (59.3%) had adverse events. The more frequent were: injection site pain, eritema, headache and arthralgia. The majority of them were classified as mild intensity. Conclusions: There was a tendency to an increased in survival for vaccinated patients and vaccines proved to be safe and exhibited a good level of immunogenicity.</p>
<p>PFC 23</p>	<p>CANCER RESEARCH AND PHASE 0 CLINICAL TRIALS <u>Fors López M</u> _National Center of Clinical Trials. Havana, Cuba. email: martaf@cencec.sld.cu Calle 200 esquina 21, Atabey, Playa, Ciudad de la Habana, Cuba</p> <p>Introduction: Phase 0 clinical trials, are intended to expedite the clinical evaluation of new molecular entities without having any therapeutic intent. The objectives of a phase 0 cancer clinical trial are to establish at the very earliest time, -before large numbers of patients have been accrued and exposed to potential drug-associated toxicity whether an agent is modulating its target in a tumor. The scientific justification for phase 0 trials includes determining sooner whether a new drug is capable of modulating its intended target in humans, and/or generating important information to go further. An estimated 40% of drugs fail in phase I trials because of unsuitable pharmacokinetics. Clearly, earlier identification of these drugs would increase the efficiency of drug development, allowing researchers to prioritise successful drugs, not only making effective drugs available to patients sooner, but also saving money. Methodology: A methodological review of fundamental requirements of clinical studies was performed and some common misconceptions regarding phase 0 trials in cancer have been addressed. Food and Drug Administration's guidance document on phase 0 trials was reviewed. Main particularities of this kind of studies were outlined. Some ethical concerns are arisen Results: it was found that these studies should precede traditional dose escalation and other pharmacokinetic-pharmacodynamic (Pk/Pd) relationships studies that ordinarily are performed in early drug development program. The number of subjects is</p>

	<p>smaller, 10 or less and the studies involve administration of small doses (subtherapeutic doses,) of an experimental drug over a shorter period of time. The risk of harm is much less than in a conventional phase I trial but still there is ethical concerns for using the human body as a Pk/Pd laboratory. Limitations of the use of these studies are shown in this paper. Conclusions: Even the scope of application for phase 0 trials is limited; these studies could be an option to use early data to guide further development of new drugs.</p>
PFC 24	<p>SOME STRATEGIES IN ANALYSIS OF INCOMPLETE LONGITUDINAL DATA IN CLINICAL TRIALS Robaina García Maytec¹, Uranga Piña Rolando¹</p> <p>¹Centro Coordinador Nacional de Ensayos Clínicos (CENCEC). Calle 200 esquina 21, Atabey. Ciudad de la Habana. Cuba. email. mrobaina@cencec.sld.cu</p> <p>Introduction: Longitudinal studies are used in research to assess outcome changes over time within and between individuals. In clinical trials the participants may drop out of a study prematurely, ignoring the nature of dropouts often leads to biased inferences and wrong conclusions of the study. The purpose of the present study is to illustrate the use of different methods to deal with incomplete longitudinal in clinical trials. Material y methods: “Complete-case analysis”, likelihood-based longitudinal analysis, and several imputation methods were applied, including “last observation carried forward” (LOCF) and multiple imputation. The concepts developed here are illustrated using data from one psychiatric clinical trial. Results: Although there were no striking differences in parameter estimates, all methods performed better than complete-case analysis and LOCF; the analysis method may have an impact on the conclusions of the study. Conclusions: Establishing the causes of dropouts should be an integral part of any statistical analysis with longitudinal data, and recommend to perform a sensitivity analysis when the pattern of missing data cannot be discerned.</p>
PFC 25	<p>QUALITY OF LIFE OF INCLUDED PATIENTS IN ONCOLOGICAL CLINICAL TRIALS IN VILLA CLARA, CUBA Pérez K¹, Arbolaéz M², Cárdenas P³</p> <p>¹Centro de Inmunología Molecular. Calle 216 Esq. 15. Atabey. Playa. Ciudad Habana ²Universidad de Ciencias Médicas “Dr. Serafín Ruíz de Zárate Ruíz”. Carretera Acueducto y Circunvalación. Santa Clara. Villa Clara. migdacelysae@ucm.vcl.sld.cu ³Hospital Universitario “Celestino Hernández Robau”. Paseo de la Paz. Santa Clara. Villa Clara.</p> <p>Introduction: In Villa Clara, several clinical trials have been developed sponsored by the Center of Molecular Immunology for the treatment of the cancer in different localizations. The patients included in general in clinical trials show values of survival and quality of life superiors to the rest, reason for which decided to carry out the present work with the objective of evaluating the survival and quality of the patients' life included in oncological clinical trials. Methods: For the execution of this objective the clinical histories of the total of patients were revised included in the clinical trials executed in the University Hospital "Dr. Celestino Hernández Robau" of Villa Clara, in the period 2002-2007. It was carried out an analysis of the time lapsed between the patient's diagnosis and the death to determine the time of survival. To evaluate the quality of life the surveys they were used in each investigation protocol. Results and Discussion: It was proven that the variables of the patients' treaties survival, showed superior values to those not reported for the patients with similar localizations of the tumor included in clinical trials. The localizations of more survival were: breast (54.3 months) and lung (60.3 months). In the case of the quality of life it was obtained that, in a global way, the patients maintained an excellent general state and in their majority they incorporated to the domestic and labor activities. Conclusions: The clinical trials showed an increment of the survival and quality of the patients' treaties life.</p>
PFC 26	<p>CLINICAL TRIALS VS. CANCER INCIDENCE. ANALYSYS OF ITS PERFORMANCE IN VILLA CLARA, CUBA. Rodríguez M¹, Méndez R¹, Sánchez P²</p> <p>¹Universidad de Ciencias Médicas- Villa Clara. Carretera Acueducto y Circunvalación. Santa Clara. Villa Clara. Cuba. e-mail: migdaliarr@ucm.vcl.sld.cu ²Policlínico Universitario “XX Aniversario”. Santa Clara. Villa Clara. Cuba.</p>

	<p>Introduction: In Cuba, cancer is the second leading cause of death and the first in years of potential life lost, in Villa Clara is the leading cause of death. Several biological products are in the stage of clinical trials and are targeted to increase survival and quality of life of cancer patients. It is important to analyze the correlation between the disease that are directed towards. research products and their impact on monthly, as well as patient access to these study protocols, in order to assess whether the strategies respond to real needs. Materials and methods: It was tabulated the monthly incidence of patients diagnosed with cancer, according to their location in the pathology department of the Hospital Universitario "Arnaldo Milian Castro" de Villa Clara in 2009. Locations were correlated with the predominant tumor offers existing clinical trial protocols in stage analyzed. We compared the inclusion of patients in the study protocols with the incidence of diagnosed cases. Results: In 2009 1466 cases of cancer were diagnosed in 32 locations, resulting in skin (575), head and neck (143), intestine (124), lung (109) the most common diagnoses. During this period, the province had 13 clinical trials (9 trials and 4 Clinical Expanded Use Programs) in the evaluation of the products promoted by the Center for Molecular Immunology looking for 8 tumor sites, where only 4 studies correspond to the locations higher incidence analysis. 229 patients were included in different protocols, representing 15.6% of cases diagnosed and 60.7% of them relate to the most frequent. Conclusions: The clinical trials offers products for cancer therapy during 2009 were inadequate to meet existing needs. A similar behavior presented the inclusion of patients in the protocols analyzed.</p>
<p>PFC 27</p>	<p>EFFECTIVENESS OF MONTELUKAST IN 60 CUBAN PATIENTS WITH MODERATE AND SEVERE ASTHMA AND RHINITIS. <u>Álvarez</u>¹, RL Castro², SD Orta³, M Ronquillo¹, I Enriquez¹, JS Rodríguez¹</p> <p>¹University Hospital Calixto García, Havana city, Cuba. ² National Center of Bioproducts, Havana city, Cuba ³ Center for the Quality Control of Drugs, Havana city, Cuba. email: mirtaac@infomed.sld.cu</p> <p>Introduction: The prevalence of Asthma and Allergic Rhinitis has increased worldwide during the last decades. Montelukast, a leukotriene receptor antagonist is used for treat asthma and it is administrated once a day. Methods: open clinical trial study was carried out to evaluate the therapeutic effect and safety of Montelukast in patients with rhinitis and persistent moderate and severe asthma, not controlled. Sixty asthmatic subjects were recruited and 56 completed the study that was conducted from October 2008 to June 2009. The evaluation included clinical symptoms and used medication at the beginning, 3 months and 6 months with treatment. The safety evaluation included control of renal and liver function, the appearing of adverse events. There were also carried out tests of breathing function at first month and 6 months of treatment. Results: There were differences respect to clinical improvement and decrease of use of concomitant medication (89% cases). We observed marked differences between the values of FEV1 before and after the treatment. Only 5 patients reported secondary effects (9%), in 2 of the cases was necessary to stop treatment. The headache was the most reported symptom (3 cases). Conclusions: Montelukast is a satisfactory treatment for patients with moderate and severe asthma and allergic rhinitis.</p>
<p>PFC 28</p>	<p>TWELVE WEEKLY MONOTHERAPY ADMINISTRATION OF HUMANIZED T1H (ANTI-CD6) MONOCLONAL ANTIBODY INDUCE CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS WITHOUT SERIOUS ADVERSE EVENTS <u>Hernández P</u>¹, Torres-Moya R², Molinero C², Prada D², Lopez AM², Hernández MV², Hernández IM², Martínez JP², Reyes Y², Milera YM², Gómez JA², Martínez O², Avila Y³, Rodríguez C¹, Montero E¹.</p> <p>¹ Center of Molecular Immunology, 216th & 15th Ave., Atabey, Playa, Havana City, Cuba email: patricia.hdez@infomed.sld.cu ² National Institute for Rheumatology, Havana City, Cuba. ³ National Center Coordinating of Clinical Trials, 200 at 21 Ave, Atabey, Playa, Havana City, Cuba.</p> <p>Introduction: Rheumatoid arthritis (RA) is a chronic inflammatory, autoimmune disorder of uncertain etiology, associated to a significant morbidity. T cells are involved in the pathogenesis of RA. The introduction of biologic agents as new disease-modifying anti-rheumatic drugs (DMARD) has improved the treatment of RA but still achieve incomplete patient's benefit. Hence, new therapeutic approaches based on novel targeted therapies are required. CD6 is a co-stimulatory molecule, predominantly expressed on lymphocytes, that has linked to the autoreactive response. Material and Methods: A Phase I, open-label, multidose, dose-finding study of T1h (anti-CD6) mAb to evaluate safety and preliminary clinical activity was conducted in 20 patients with active, DMARD-resistant RA. Four cohorts of five patients</p>

	<p>received monotherapy with T1h at doses of 0.1, 0.2, 0.4 or 0.8 mg/kg body weight. Results and Discussion: Evaluation of adverse events (AEs) over the entire study revealed that T1h had a good safety profile, with no severe or serious AEs reported so far. After a follow-up period of 10 weeks, more than 50% of patients achieve clinical response, according to American College of Rheumatology (ACR) response criteria. The optimal biological dose analysis shows that patients receiving T1h at 0.4 mg/kg body weight showed a rapid and sustained clinical response over the whole study period. Conclusions: T1h appears to be safe and well tolerated with preliminary evidence of sustained clinical improvements for patients with active RA. This results support the relevance of CD6 as a target for RA therapy.</p>
<p>PFC 29</p>	<p>CLINICAL DEVELOPMENT OF CIMAVAX EGF THERAPEUTIC VACCINE FOR NON-SMALL-CELL LUNG CANCER AND CASTRATION- RESISTANT PROSTATE CANCER. Pedro Camilo Rodríguez Clinical Researcher and Assistant Professor. Molecular Immunology Center. CUBA. email: camilo@cim.sld.cu</p> <p>Non-small-cell lung cancer (NSCLC) is one of the most common malignant diseases with a high mortality rate worldwide, while Castration- Resistant Prostate Cancer (CRPC) is a second leading cause of death among man worldwide. The epidermal growth factor receptor (EGFR) is overexpressed in 40% to 80% of advanced stage (IIIB/IV) NSCLC, and in 100% of CRPC. This overexpression is associated with a poor prognosis in both diseases. Nowadays five phase I/II and one phase II clinical trials have been concluded in Cuba with impact of the immunization on the survival (SV) of NSCLC patients (IIIB/IV stage). The safety profile of the vaccine, feasibility of inducing an immune response against autologous EGF, differentiation of immunized patients as poor antibody responders (PAR) or good antibody responders (GAR), according their anti-EGF antibody (Abs) response and correlation between Abs titers, serum EGF concentration and length of SV have been evidenced. Longer SV was observed in all vaccinated patients compared to controls, and interesting the difference was significant ($p < 0.05$) in the group aged < 60 years. At the moment a phase III study is ongoing with promising preliminary results. Evidences obtained from the above mentioned phase I/II clinical trials and the results of the phase II study led CECMED, the Cuban regulatory authority, to license CIMAvax EGF as a therapeutic vaccine indicated for adult advanced stage (IIIB/IV) NSCLC patients. Moreover, considering that EGFR has a central role in the resistance mechanisms to androgenic blocking and the previous evidences regarding the safety profile, a Phase II clinical trial is also ongoing using this therapeutic modality. The Clinical Development using CIMAvax EGF therapeutic vaccine for NSCLC and CRPC are presented.</p>
<p>PFC 30</p>	<p>EFFECTIVENESS AND SAFETY OF THE USE OF IOR[®] LEUKOCIM IN THE PROPHYLAXIS AND TREATMENT OF NEUTROPENIA IN HIV/AIDS PATIENTS Pedro Pablo Guerra Chaviano¹, Ivis Cristina Mendoza Hernández¹, Lilia Ortega², Giselle Sáurez³, Patricia Piedra³, Ventura Puente⁴, Maytè Robaina¹. ¹ Centro Nacional Coordinador de Ensayos Clínicos (CENCEC), Ciudad Habana, Cuba. Email: pedrop@cencec.sld.cu ² Instituto de Medicina tropical Pedro Kourí, Ciudad Habana Cuba ³ Centro de Inmunología Molecular, Ciudad Habana, Cuba ⁴ Hospital Clínico Quirúrgico Juan bruno Zayaz, Santiago de Cuba, Cuba.</p> <p>This study aimed to assess effectiveness and safety of ior[®]leukoCIM in prophylaxis and treatment of Neutropenia in HIV/AIDS patients who had associated or not malign opportunistic disease. An open, multicentric phase IV study was performed at the Institute Pedro Kourí and in Hospital Juan Bruno Zayas. The study included 60 episodes, 51 had available information. 25 episodes were treated under the stratum of prophylaxis (8 patients) and 26 under the stratum of treatment (22 patients). Patients received daily subcutaneously ior[®]LeukoCIM 5 µg/Kg/day regardless their body weight. In prophylaxis (25 episodes), the administration started at 24-72 h of concluded CT and/or RT continuing it during 5-8 days. The administration was extended in patients who developed neutropenia until CAN recovery at values $\geq 1.5 \times 10^9/L$. The treatment started in neutropenic episodes that appeared secondary to CT and/or RT cycles, once neutropenia was diagnosed and it continued daily until CAN recovery. The same was indicated for episodes that presented neutropenia associated to viral replication (HIV) or opportunistic infections. For cases of severe neutropenia, the recommended starting dose was 10 µg/Kg/day. Recovery and/or maintenance of CAN at $\geq 1.5 \times 10^9/L$ at 5th or 8th day of treatment were considered as main variables of response; administration of the next cycle of CT and /or RT, CAN recovery time and its figures at final</p>

	<p>evaluation were the secondary ones. LDH; FAL and UA values were monitored before and after the treatment to assess safety and adverse events. Results showed that in prophylaxis stratum 23 out of 25 episodes recovered CAN at levels higher than $1.5 \times 10^9/L$ 92% CI (78.9;99.9) and in the stratum of treatment 25 out of 26 recovered at values higher than $1.5 \times 10^9/L$ 96.2% CI (80.4;99.9). There were only 11 adverse events reported with slight, moderate and severe intensities. These results allowed the registry of the product in this indication by CECMED.</p>
PFC 31	<p>IMPACT OF PSYCHIATRY CLINICAL TRIALS OVER CLINICAL PRACTICE. THE CUBAN EXPERIENCE <u>Valle R¹</u>, Mendoza Y¹</p> <p>¹ National Coordinating Centre for Clinical Trials, 200 at 21 Ave, Atabey, Playa. Havana City, Cuba. email: roselin@cencec.sld.cu</p> <p>Introduction: Five of the 10 leading worldwide disability causes (major depression, schizophrenia, bipolar disorders, alcoholism and obsessive compulsive disorders) are mental problems. They are relevant as in poor as in rich countries, and all predictions indicate there will be a dramatic increase in the coming years. The National Coordinating Centre for Clinical Trials (CENCEC) is a Clinical Research Organization. Three clinical trials in psychiatry had been performed, since CENCEC's creation up to now. Objectives, Material and Methods: With the objective of evaluating the impact of psychiatry clinical trials over the clinical practice in Cuba, quality and efficiency indicators (structure, process) of the hospitality services were analysed. Results: The conduction of clinical trials in psychiatry had a positive impact over the clinical practice in Cuba. Those trials permitted the institutions to achieve the acquisition of material resources to better the infrastructure of the medical services needed to treat psychiatric patients. Besides that, vitally important was the training of a considerable number of specialists throughout the Island, which permitted the update of the national and international art of mental illness, the acquisition of skills and competence in the use of psychotherapy, how to handle placebo response and suicide risk, the acquisition of specific and updated bibliography, usually not available in the country, the introduction of diagnostic and assessment tools to clinical practice and the possibility of treatment for some patients with the first line of medications.</p> <p>Conclusions: Research practice offers numerous advantages for patients and investigators. After several years of intense work, CENCEC was able to establish a national net to conduct clinical trials with psychopharmacologic drugs according to international standards. However, new projects are needed to enhance and renew the acquired knowledge and the obtained experience.</p>
PFC 32	<p>HARMONIZATION OF QUALITY'S STANDARD FOR CLINICAL TRIALS. ISO 9001 STANDARD- GUIDELINES OF GOOD CLINICAL PRACTICE <u>Álvarez S</u></p> <p>National Center Coordinating of Clinical Trials, 200 at 21 Ave. Atabey. Playa. Havana City, Cuba. email: sandra@cencec.sld.cu</p> <p>Introduction: A clinical trial is an extensive, complex and necessary process to authorize the use of new medications in humans. To guarantee the quality and the standardization of this process the International Conference of Harmonization (ICH) and the national regulatory agencies have established the Guide of Good Clinical Practice (GCP). It also exist another standards that goes guided to guarantee the quality of the work in the organizations, the ISO 9001:2008 standards that it establishes requirements for Quality Management System. Objective: Establish elements that demonstrate the harmonization among the GCP of the ICH, the Cuban GCP and the ISO 9001:2008 for its use in the clinical trials. Material and Methods: In this work a study of GCP of the ICH, the Cuban BPC and the ISO 9001:2008 standards was carried out to analyze the aspects in common in their use for the clinical trials. Results and Discussion: It was observed that common points exists amount the three normative related with the requirements for the client, suppliers, process focus, documentation, management, revisions, realization of the investigation and improvement of the quality. For such a reason the combined use of the quality's standards studied elevates the quality of the clinical trials, independently of the application mark of each one of them. Conclusions: Considering all the above-mentioned we can affirm that doesn't exist any aspect contemplated in these standards that reflects contradiction for its use in the clinical trials but multiple common aspects that allow its harmonization. References: Guideline of Good Clinical Practice in Cuba. The Havana, 2000. ICH-E6</p>

	Guideline of Good Clinical Practice. 1997. ISO 9001:2008 standards. Quality Management System. 2008.
PFC 33	<p>APPLICATION OF CIGB-228 WITH ADJUVANT VSSP IN HIGH-GRADE CERVICAL LESIONS Ramos Gómez TI¹, Baladrón Castillo I¹, Solares Asteasuainzarra AM², Valenzuela Silva CM¹, García Iglesias E¹, Cintado Benítez A¹, Pereda Lamela L¹, Ale Martínez M¹, Nazabal Gálvez M, López Saura P¹, Torrens Madrazo I¹.</p> <p>¹ Center for Genetic Engineering and Biotechnology CIGB Ave 31 e/ 158 y 190, Playa, P.O. Box 6162, Habana 10600, Cuba Phone: 53-7-2718008, 53-7-2718466, Fax: 53-7-331779, 53-7-2718070. email: thelvia.ramos@cigb.edu.cu ² “Clodomira Acosta Ferrales” Hospital, Obstetrician-Gynecological Service Ave #8 e/17 y 19 Vedado Habana Phone 53-7- 8382611, 53-7-8382613.</p> <p>Introduction: An open-label, no-controlled clinical trial was carried out to evaluate primarily safety of the product CIGB-228 with adjuvant VSSP in patients affected of high-grade cervical lesions caused by HPV-16, HLA-A2 positive. Material and Methods: This product was injected subcutaneously each week during 4 weeks. Seven patients were included. Local and systemic adverse events were recorded over 24 hours after each administration. Laboratory tests were performed before inclusion, 24 hours after treatment and 2 weeks afterwards. The immunogenicity of the vaccine preparation (interferon gamma-producing cells) and first evidences of therapeutic effect (colposcopy and histology of the lesions) were also measured. Cervical cone was done to all patients, 3 months after the treatment. Results and Discussion: Local adverse events were burning, pain, redness, warmth, and edema, all of them typical of the expected inflammatory reaction. These events were mild and had spontaneous regression without any medication. None reported systemic events were related to the studied product. The obtained results were very consistent, since those patients with complete colposcopic and histological response had the highest values of IFN gamma-producing cells. They also didn't presented high degree lesions according to histology, three months after immunization. There are evidences of the safety of the tested new product leading to more probabilities of successful effects in the therapy of pre-invasive cervical lesions, preserving the integrity of the genital apparatus. Conclusions: We can conclude that application of CIGB-228 adjuvanted with VSSP demonstrated be safe in patients with high-grade cervical lesions. Also, the observed therapeutic findings suggest larger, randomized, controlled clinical trials.</p>
PFC 34	<p>COSTS AND CONSEQUENCES OF THE TREATMENT WITH EPOCIM OF THE ANEMIA POST CHEMOTHERAPY IN PATIENT WITH LUNG CANCER Saumell Y¹, Acosta S², Suárez G¹</p> <p>¹ Center of Molecular Immunology. email: yaima@cim.sld.cu ² Saturnino Lora Hospital. Santiago de Cuba</p> <p>Introduction: From an economic point of view the anemia in patients with lung cancer has a negative repercussion, because if it is not well treated it originates an increase of the costs for the high morbimortality, the decrease of the quality of life and the salary losses for the patients. The correction of the hemoglobin levels in this patients would improve the therapeutic results and the quality of life. Material and Methods: Was carried out a partial economic evaluation with the objective of determining the costs and the consequences of the treatment with EPOCIM in the anemia post chemotherapy in diagnosed patients of lung cancer in the Saturnino Lora Hospital in the year 2007. The direct, indirect, total and averages costs were analyzed, and they were evaluated as consequences of the anemia post chemotherapy the answer to the treatment given at least by the increment of 150 g/l from the hemoglobin at the 8 weeks and the appearance of adverse reactions, also the repercussion of the treatment in the requirements of transfusions and the adherence of the planned chemotherapy. The data were summarized in charts and graphics according to the variable type. Results and Discussion: The total cost of the treatment was of \$225195,63 and the cost average \$5492,57. The stocking of the hemoglobin had an increment of 22,8 g/l and the adverse reactions that appeared they were classified of probable and moderate, prevailing the pain in the injection place. The requirements of transfusions decreased in 56% regarding the beginning or pre-treatment, and alone they were interrupted due to the anemia post chemotherapy 6,7% of the planned chemotherapy cycles. Conclusions: The treatment with EPOCIM of the anemia post chemotherapy in patient with lung cancer is expensive, but it becomes better clinical results and it guarantees a bigger adherence from the patients to the chemotherapy.</p>

PFC 35	<p>ADVERSE EVENTS ASSOCIATED TO THE INTRATUMORAL APPLICATION OF CIGB/300 TO PATIENTS WITH CERVIX CANCER IN PHASES IB2-II Martín Y¹, Marrero R², Baladrón I³, González L³.</p> <p>¹Hospital Universitario “Celestino Hernández Robau” de Villa Clara. Cuba ²Universidad de Ciencias Médicas de Villa Clara. Dr. “Serafin Ruiz de Zárate Ruiz”. Vicerrectorado de Investigaciones. Subcentro de Ensayos Clínicos. ³Centro de Ingeniería Genética y Biotecnología. Cuba.</p> <p>Introduction: Cervical cancer is the malignant disease that most often affects women, followed only by breast cancer. Among the studies carried out by the Centre for Genetic Engineering and Biotechnology is the Evaluation of Safety and Therapeutic Effect of IGBC Intratumoral application 300 and conventional treatment with QRT to patients with cervix cancer in phases IB2-II, with the objective of evaluate the main adverse events related with this product. Materials and Methods: There were checked the clinical records of the two patients included in the clinical trial done in the Oncology Service of the University Hospital of Villa Clara province. There were collected the adverse events reported by the patients then classified according to the Common Terminology Criteria for Adverse Events (CTCAE) from the National Cancer Institute in USA, in terms of intensity and causality based on the algorithm of the FDA. Results and Discussion: A total of 29 adverse events were presented, according to the intensity degree the adverse events were classified as: mild (82,8%) and moderated (17,2%). Regarding causality the very probable ones predominated because all of them were formerly described. Must frequent presentation events were genital heat and face flushing and the most intense: rash and wheal (more than 50% of body surface). Conclusion: The group of adverse events was neither dose limiting nor constituted causes of treatment interruption.</p>
PFC 36	<p>MIGRAMENSTRUAL, PHASE III CLINICAL TRIAL IN THE MENSTRUAL MIGRAINE PREVENTION Avila Y¹, Reyes R², Olivera I³, Fernández O⁴, Marrero MA¹, Uranga R¹, Gil G¹, Barrese Y¹, Machado N³, González LE³, Cordero A⁴, Pérez K⁴, Sánchez A⁴, Ballagas C¹, et al.</p> <p>¹National Coordinating Center of Clinical Trials. 21 Ave and 200 St., Atabey, Playa, Havana City, Cuba. email: yisel@cencec.sld.cu ²International Center of Health “La pradera”. 222 Ave, Playa, Havana City, Cuba. ³“Hermanos Ameijeiras” Hospital. San Lázaro and Marquez González St., Centro Habana, Havana City, Cuba. ⁴National Institute of Neurology and Neurosurgery. 29 Ave and D St., Plaza de la Revolución, Havana City, Cuba.</p> <p>Introduction: Menstrual migraine (MM) is often prolonged and difficult to manage with conventional therapies. Migramenstrual is a phytfarm composed by a mixture of natural active principles developed for the prophylactic treatment of MM. Materials and Methods: A phase III, randomized, double-blind, placebo-controlled, two-period crossover trial was designed to examine the efficacy and safety of Migramenstrual 45 mg. A total of 75 women, aged 18 to 50 years, with regular menstrual cycles and at least one year history of MM with or without aura were studied. Efficacy was determined in terms of reduction in frequency and intensity of MM attacks. Results and Discussion: The mean age of women was 35.7 years. Use of Migramenstrual reduced the occurrence of MM in both treatment cycles. The attacks mean frequency reduced in the first cycle to 3.13 for Migramenstrual and to 11.92 for placebo, and in the second cycle to 2.00 for Migramenstrual and to 6.73 for placebo (p<0.0001). Migramenstrual provided a significant headache relief, a decrease in pain intensity to no pain, in comparison with placebo (p<0.0001), 72.41% vs. 3.70% in the first cycle and 73.91% vs. 21.05% in the second cycle. In these women the attacks mean duration reduced to less than 4 hours in the first cycle in 82.76% were using Migramenstrual and in 7.41% when using placebo, and in the second cycle in 86.96% and in 21.05%, respectively (p<0.0001). The quality of life increased significantly (p<0.0001) with the phytfarm. Conclusions: Migramenstrual reduces frequency, intensity and duration of MM; also is well tolerated in short-term migraine management.</p>
PFC 37	<p>PLACEBO RESPONSE IN DEPRESSION. RESULTS FROM TWO CLINICAL TRIALS IN CUBA. Mendoza Y¹, Valle R¹, Pascual MA¹</p> <p>¹National Coordinating Center of Clinical Trials, 200 at 21 Ave, Atabey, Playa, Havana City, Cuba.</p>

	<p>email: yudeximendoza@infomed.sld.cu, yudexi@cencec.sld.cu</p> <p>Some aspects related with depression and the use of placebo in clinical trials, were reviewed considering the Declaration of Helsinki and criteria exposed by the regulatory agencies from Europe and United States. The possible reasons that could have influenced the high placebo response (58% intention to treat analysis) observed in a clinical trial in depression coordinated by the National Coordinating Centre for Clinical Trials in Cuba (CENCEC) were also analyzed. Among then: spontaneous remission of symptoms, severity of depression, high expectancy from patients and raters, systematic evaluations, among others. We also present the different results obtained in a similar academic trial conducted after a training developed in the context of a collaborative research project “Psycho-pharmacological Training and Research Capacity in Cuba” with Dalhousie University, Canada. As part of it, clinical investigators were trained in different topics including strategies to diminish placebo response that is something that can reduce the power of clinical trials and might invalidate them. In this academic trial we had a significant reduction of placebo response (31.6% intention to treat analysis) compare with the previous trial, reinforcing the impact of the delivery training program that permitted to have better trained staff in the diagnosis, selection of patients, scales application and response evaluation.</p>
<p>PFC 38</p>	<p>CIGB500 ADMINISTRATION IN HEALTHY VOLUNTEERS. PHASE I STUDY DOSE ESCALATION</p> <p><u>Peláez Y</u>¹, Hernández F¹, Valenzuela C¹, López S¹, Cabrales A¹., Gil J¹, García E¹, Berlanga J¹, Abreu A², Selman-Housein K².</p> <p>¹Center for Genetic Engineering and Biotechnology, ave 31 e / 158 and 190 Cubanacan, beach. Havana. Cuba. email:Yurisbel.pelaez@Cigb.edu.cu; ²Research Medical Center - Surgical (CIMEQ), Havana</p> <p><u>Introduction:</u> CIGB500 (GHRP-6) is a peptide with stimulatory activity of growth hormone secretion. The administration of this product in an experimental model of myocardial infarction was found to be safe to reduce the extent of infarction. Has also been studied in preclinical studies of acute toxicity, repeated dose toxicity and local tolerance as part of the requirements for clinical trials. This study was carried out to determine the safety and tolerability and to assess the pharmacokinetics and pharmacodynamics of single dose intravenous administration of CIGB500. <u>Materials and methods:</u> We performed a phase I clinical trial, uncontrolled dose escalation in healthy volunteers. The product was administered single-dose intravenous doses in 6 scales: 1, 10, 50, 100, 200, 400 mg / kg. The sample consisted of 18 apparently healthy subjects, male gender, aged between 18 and 35 years with a body weight within normal limits and who agreed to participate voluntarily in the investigation. In each dose escalation level 3 subjects were discussed and progress to the next level depended on the absence of toxicity (severe adverse events). The primary endpoint assessment consisted of the safety and tolerability for which we collected clinical adverse events, vital signs, electrocardiogram and clinical laboratory data (hematology, biochemistry, plasma and urine). Secondary efficacy parameters were formed by the pharmacokinetic and pharmacodynamics of the product elements (hormones, markers of the redox system and echocardiogram). Subjects were followed for 10 days, including 72 hours of admission after the administration of the product under study. <u>Results:</u> The peptide CIGB500 had an acceptable safety profile, were completed six levels of dose escalation. No serious adverse events were reported, there were 6 different adverse events in 12 subjects (66.7%), and sweating (50%), bradycardia (44.4%) and somnolence (16.7%) the most common. All reported adverse events were mild or moderate, kept causal link with the peptide under study and failed spontaneously without therapy. In addition, the pharmacokinetic study of the peptide showed a biphasic profile of plasma concentration versus time, and the area under the curve increased with increasing dose. The cellular redox balance suggests that the administration of CIGB500 not generate damaging oxidative stress. Moreover, intravenous administration of single dose CIGB500 positive stimulated the GH / IGF-I / IGFBP3. In the evaluation of hormonal determinations we observed no overall dependence between the magnitude of the administered dose and increases in the hormones produced measures. The largest increases occurred with GH and prolactin. With other hormones increases were less impressive but stabilized during the period evaluated.</p>
<p>PFC 39</p>	<p>POSTOPERATIVE PAIN RELIEF WITH EPIDURAL KETAMINE IN LOW ABDOMINAL SURGERY</p> <p><u>González Pérez SF</u>¹</p>

	<p>¹General Hospital, Fomento, Sancti Spiritus, Cuba. email: sixto.ssp@infomed.sld.cu</p> <p>Introduction: Ketamine is a drug used for induction and maintenance of anesthesia, exists as a racemic mixture of R- and S+- enantiomers. Epidural ketamine starts to human administration about 80' years. After that, various studies have been published about the mechanism of analgesic action of ketamine: lamina-specific suppression of dorsal-horn unit activity, opiate agonist at the spinal level in the same way as opioids and non-competitive N-methyl-D-aspartate NMDA receptor antagonist. In this study, we evaluated the efficacy of epidural ketamine for postoperative pain relief in lower abdominal procedures.</p> <p>Materials and Methods: Fifty patients undergoing inguinal herniotomy were studied in a comparative prospective trial. They were divided into two groups: twenty-five patients in Group K received epidural ketamine 50 mg whereas twenty-five patients in Group M received epidural morphine 2 mg postoperatively. Vital signs (heart rate, blood pressure, respiratory rate and arterial oxygen saturation) were recorded continuously. Postoperative analgesia and side effects were compared between the two groups. Analgesia was assessed using a visual analog scale (VAS) pain every 1 hour for 24 h after surgery. Time of postoperative analgesia was defined as the time elapsed between epidural injection and first complaint of pain.</p> <p>Results and Discussion: There were no differences between the two groups with respect to age, weight and ASA physical status. No difference in cardiorespiratory variables was observed among groups. Epidural ketamine in doses to 50 mg provide adequate analgesia during 6 hours with episodes of drowsiness, nystagmus and excitement. Morphine administered epidurally obtained analgesia more than 18 hours with pruritus, urinary retention and vomiting.</p> <p>Conclusions: Epidurally administered ketamine is less effective than epidural morphine for postoperative analgesia, but it plays an important role in morphine-induced analgesia and during the combination with local anaesthetic.</p>
<p>PFC 40</p>	<p>USE OF THE SCALE ANALOGOUS OF THE PAIN IN PATIENT ONCOLOGICAL Montes de Oca N¹, Trista Y², León R³, Rúa M⁴</p> <p>¹ Medical Sciences University. Ave. De la juventud. Las tunas. ^{2,3,4} Ernesto Guevara Hospital. Ave 2 de Diciembre. Las Tunas. email:yusimit@cucalambe.ltu.sld.cu</p> <p>Introduction: The evaluation of the pain so much in the medical habitual practice since in the clinical tests, it turns out to be complex on having treated it self about a phenomenon sensory subjective whose intensity can change in the time and even to moment of the measurement, several capable scales of measurement exist of to detect the relief of the pain, inside them the second hand we find analogous scale of the pain.</p> <p>Material and methods: A descriptive, transversal study was carried out aimed at describing the evaluation of the pain for the scale analogous of the pain. The sample was formed by 42 patients treaties in the chemotherapy room to those that is applied the analogous scale to him of pain to evaluate the pain, characterizing them according to age, intensity of pain according to EVE and physical Examination.</p> <p>Results: Of the evaluated patients I predominate over the group of 60-70 years old, for 56 %, the intensity was classified between slightly and moderated by scale analogous of the pain in 78 % though to the physical examination 66 % not refer pain, in the pharmacological treatment 45 % was in the 2nd step of the analgesic stairs, the evolution of pain was favourable in 83 % of the patients evaluated by scale analogous of the pain.</p> <p>Conclusions: The evaluation of the pain across scale analogous of the pain is a method quantitative that allows the clinical one to take guidelines of treatment more rational</p>
<p>PFC 41</p>	<p>DRUG INTERACTIONS ON CYTOCHROME P- 450 METABOLISM, IN HOSPITALIZED PATIENTS WITH NEUROLOGICAL DISEASES Dupotey NM¹, Pupo M², Matos K³, Fernández Y⁴, Ramos B⁵, Veranes R⁶</p> <p>¹ Assistant Professor. Pharmacy Department. Universidad de Oriente. Santiago de Cuba. Patricio Lumumba Avenue SN. Santiago de Cuba. email: dupotey@cnt.uo.edu.cu ² Head of Pharmacy Service at General Hospital "Dr. Juan Bruno Zayas". Santiago de Cuba. ³ Pharmacist. Municipal Office of Health . Yara. Granma. ⁴ Pharmacist. Municipal Office of Health. III Frente. Santiago de Cuba ⁵ Pharmacist. ENCOMED. Santiago de Cuba ⁶ Pharmacist . Municipal Office of Health. Guamá. Santiago de Cuba</p> <p>Drug interactions involving the Cytochrome P-450 system are common, and generally result from either enzyme inhibition or induction. Hospitalized and polimedicated patients are more exposed to the drug interactions. It was performed a descriptive and prospective study to determine the incidence of drug interactions, with risky implications for the drugs metabolism in the Cytochrome P-450, given to patients</p>

	<p>with cerebrovascular disease and other neurological disorders, at General Hospital "Dr. Juan Bruno Zayas" of Santiago de Cuba. The study sample was 531 patients. Risky drug interactions were identified in prescriptions, with an emphasis on those with modification of the drugs metabolism in the Cytochrome P-450. Real and potential interactions were detected, and the drugs more interacting were identified. Patients with ischemic cerebrovascular disease, were predominant in the sample (73.8%). 1802 prescriptions were analyzed, and 57 types of risky drug interactions were detected in 313 patients (59%), of which 38.6% were interactions on the metabolism of drugs in 108 patients (35%). Of the total interactions detected, 77.8% were considered potential, because they were no clinical evidence in patients, 22.2% were real, which were related to failures pharmacotherapy by enzyme induction. Phenytoin and Carbamazepine, were the drugs more interacting, as enzyme inducers with a 79.6% and 42.6% respectively, and Cimetidine as enzyme inhibitor (24.1%). All detected interactions were analyzed with health team and pharmacotherapy recommendations were proposed to prevent and /or resolve them. It demonstrates the need to implement health education activities with health professionals related to these interactions so common in the prescriptions, to optimize the pharmacotherapy given to the patients with neurological disorders, one of the most frequent causes of death in Cuba.</p>
<p>PFC 42</p>	<p>EFFECT OF D-003, A MIXTURE OF HIGH MOLECULAR WEIGHT SUGARCANE WAX ACIDS, ON LIPID PEROXIDATION (LP) MARKERS OF OLDER INDIVIDUALS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY Yohani Pérez¹, Roberto Menéndez², José I. Ferrer¹, Ernesto Alvarez³, Gladys Castaño^{3†}, Julio Fernández¹, Rosa Más¹, Lilia Fernández¹, Sarahí Mendoza¹, Rosa M González⁴, Sonia Jiménez¹ and Melbis Mesa³</p> <p>¹Center of Natural Product, CNIC, Cuba. email: yohani.perez@cnic.edu.cu ²Center of Marine Bioproducts. ³Medical Surgical Research Center. ⁴Center of Neurosciences</p> <p>Introduction: Aging is associated with increased lipid peroxidation (LP). D-003, a mixture of long-chain aliphatic primary acids purified from sugarcane wax, has been found to inhibit LP in experimental models and healthy volunteers. The aim of study was to assess the effects of D-003 on LP markers and the lipid profile of older individuals. Material and Methods: This randomized, double-blinded, placebo-controlled study enrolled male and female patients age > 60 year. After a 3 week lead in and baseline assessment period, eligible patients were randomized to receive D-003 (5 or 10 mg/day) for 8 weeks. The effect on LP of LDL was the primary variable, whereas the effects on plasma total antioxidant status (TAS), malondialdehyde (MDA), antioxidant enzyme activities and lipid profile were secondary variables. A clinical examination, oxidative variables, and the blood tests (lipid profile, hematologic and blood biochemistry safety indicator) were performed at baseline and 8 weeks of treatment. Compliance and adverse events (AE) were assessed at weeks 4 and 8. Results: No variable changed significantly in the placebo group compared with baseline. D-003 (5 and 10 mg/day) significantly increased, in a dose-dependent manner, the lag phase of conjugated diene formation and decreased the maximal rate (Vmax) of conjugated diene propagation. D-003 (5 and 10 mg/day) increased TAS. All these changes were significant compared with baseline and placebo. At 10 mg/day, not at 5 mg/day, D-003 lowered plasma MDA levels. Antioxidant enzymes unchanged with treatment. D-003 (5 and 10 mg/day) also reduced low-density lipoprotein (LDL-C), total cholesterol (TC) and raised high-density lipoprotein-cholesterol (HDL-C). The treatment was well tolerated. No subject withdrew from the trial and three individuals (2 placebo, 1 D-003) referred mild adverse experiences. Conclusions: D-003 (5 and 10 mg/day) administered for 8 weeks inhibited LP of LDL and increased TAS. The dose of 10 mg/day also reduced plasma MDA, in older subjects. D-003 was well tolerated at both doses. [†]<i>Difunto</i></p>
<p>PFC 43</p>	<p>REVERSIBLE ENCEPHALOPATHY INDUCED BY CYCLOPHOSPHAMIDE. CASE REPORT AND REVIEW OF THE LITERATURE Arencibia A¹, Domínguez M¹, Gutiérrez A¹, Serrano J¹, Machín S¹, Otero A¹, Menéndez A¹, Jaime JC¹</p> <p>¹Paediatrics Clinic. Institute of Haematology and Immunology. Calzada of Aldabo and 100 St. . Habana City. Cuba. email: alberto.arencibia@infomed.sld.cu</p> <p>Introduction: Cyclophosphamide is an alkylating agent used in post remission treatment of childhood acute lymphoblastic leukaemia. Its most relevant side effects include myelosuppression, haemorrhagic cystitis and myocardial depression. Although encephalopathy is usually associated to ifosfamide, there have been only few reports concerning a possible association between this toxic effect and</p>

	<p>cyclophosphamide. Case report: We present a 16 year old male teenager, diagnosed as pre B acute lymphoblastic leukaemia and treated in the Paediatrics Clinic of the Institute of Haematology and Immunology. He underwent therapy according to the Acute Lymphoblastic Leukaemia Inter Continental 2002 protocol from Berlin-Frankfurt-Munster cooperative group. The patient has a sustained haematological remission and was on consolidation therapy. Immediately after completing infusion of cyclophosphamide and mesna, the patient suffered from hemiparesis and disartia associated to seizures that progressed to coma. After a period of three days the patient gradually improved his cognitive and motor functions until complete recovery. Infectious, metabolic and infiltrative causes were ruled out. Five months after that, the patient remains without neurological symptoms. Conclusions: To our knowledge, cyclophosphamide has only previously been implicated as a cause of encephalopathy in few patients; however in all of them it was in the context of cyclophosphamide-containing poly chemotherapy regimens. Our case is the first report in which encephalopathy is associated with cyclophosphamide alone. Physiopathology and its therapeutical implications will be discussed.</p>
<p>PFC 44</p>	<p>EFFECT OF ANTIHYPERTENSIVE TREATMENTS ON SERUM LEVELS OF S-100B AND NEURON SPECIFIC ENOLASE (NSE) IN HYPERTENSIVE PATIENTS. González-Quevedo A¹, González García S¹, Fernández Concepción O¹, Fernández I¹, Quevedo Sotolongo L², Menéndez MC¹, Peña Sánchez M¹, Fernández Carriera R¹</p> <p>¹Instituto de Neurología y Neurocirugía. Calle 29 y D, Vedado. La Habana, Cuba. email: aglez@infomed.sld.cu ²Clínica Central Cira García. 18 # 4304, Alt de Miramar, Playa. La Habana, Cuba.</p> <p>Introduction: In a previous investigation we found increased levels of serum S-100B and NSE in a group of patients with essential hypertension, and we suggested that this could be an expression of early brain damage in essential hypertension. As the majority of the patients were receiving antihypertensive drugs, we decided to investigate the possible effect of antihypertensive medication on serum levels of these two proteins. Materials and Methods: Fifty patients with essential arterial hypertension, without a history of previous neurological disease and 30 apparently healthy persons were included. Information on the antihypertensive drugs the patients were receiving was collected. Serum S100B and NSE were determined employing immunoassay kits from CanAg Diagnostics AB. Results and Discussion: S-100B and NSE levels were significantly higher in hypertensive patients than in controls, the highest levels being observed in those with retinopathy and with more severe white matter lesions as detected by MRI. To evaluate the effect of antihypertensive treatment on blood levels of S-100B and NSE, two analyses were carried out: 1) effect of one or two antihypertensive drugs vs joint administration of more than two drugs (polytherapy) and 2) effect of individual groups of antihypertensive drugs (ACE inhibitors, calcium channel blockers, β-blockers, diuretics). No significant differences were observed when patients treated with polytherapy were compared with those receiving one or two drugs. None of the individual groups of antihypertensive drugs increased the serum concentrations of S-100B and NSE; nevertheless, calcium channel blockers decreased serum NSE. These findings indicate that antihypertensive medication is not associated with elevated serum concentrations of these two proteins. Conclusions: Raised serum S-100B and NSE observed in hypertensive patients is not associated with the antihypertensive medication. This finding supports our suggestion that increased S-100B and NSE levels are possibly associated with subclinical neurological involvement in a group of hypertensive patients.</p>
<p>PFC 45</p>	<p>MOVEMENT DISORDERS DURING THE SLEEP IN SCA2 MUTATION: LISURIDE IMPROVE THE PERIODIC LEGS MOVEMENTS Luis Velázquez-Pérez, Roberto Rodríguez-Labrada¹, Nalia Canales Ochoa¹, Lourdes Galicia Polo², Reyes Haro Valencia², Lázaro Alvarez³, Gilberto Sánchez Cruz¹, Jacqueline Medrano Montero¹, José M. Laffita-Mesa¹, Yanetza González Zaldívar¹, Inca Tuin⁴, Arnoy Peña Acosta¹, Georg Auburger^{4*}.</p> <p>¹Centro para la Investigación y Rehabilitación de las Ataxias Hereditarias (CIRAH), Holguín, Cuba ²Universidad Nacional Autónoma de México (UNAM), México, DF ³Centro Internacional de Restauración Neurológica. ⁴Department of Neurology, University Hospital, Frankfurt am Main, Germany.</p> <p>Objective: To characterize the sleep pathology in SCA2 mutation by videopolysomnographic studies, also to check if the disorders appeared since preclinical stages of the disease and to identify therapeutic targets for treatment strategies. Background: The sleep disorders are common complaints of SCA2 patients, fundamentally towards the final stages of the disease. The study of SCA2 patients and presymptomatic</p>

	<p>relatives provides an opportunity to examine a molecularly homogeneous patient and presymptomatic relative with the SCA2 mutation group, in which disease stages can be defined based on disease duration, ataxia scores and polyglutamine expansion size. Methods: We analyzed thirty six genetically confirmed SCA2 patients with disease durations of 1 to 20 years, all with size SCA2 expansions (CAG 34 to 44), Thirty two presymptomatics with SCA2 polyglutamine expansions sizes (CAG 32 to 43) and thirty six sex- and age-matched healthy controls were studied by two all-night video polysomnographies and sleep interviews. The polyglutamine expansion size and the clinical score were obtained in all SCA2 mutation carriers and SCA2 patients respectively. Results: Almost all patients and presymptomatics reported good subjective sleep quality and negated incidents of REM behavior disorders (RBD). Nevertheless, REM sleep was abnormal. The most striking and consistent pathology of REM sleep was its significant reduction in 60% of SCA2 patients and presymptomatics, insufficient muscle atonia suggested subclinical RBD and decrease of REM density in the 32.3%. Abnormal motor control during sleep with periodic legs movements (PLMs) occurs in the 40% of patients. SCA2 patients and presymptomatics showed significant reduction of sleep efficiency and increase of arousal index and slow wave sleep. Central apnea appear in the 23% of these patients, but, not in the presymptomatic relatives. The most important findings in the prospective follow up study in the SCA2 patients were an increase in the PLMs sequences and index, a progressive reduction of the REM sleep and slow wave sleep and increased in the central apnea. Conclusions: The most prominent PSG alterations in SCA2 are: REM sleep pathology, which precedes the disease onset, and Periodic legs movements. PLMs get worse Progressively, indicating an increase of PLMs index about 17.3 PLMs/sleep hours pers year. These stages correspond to the progressive atrophy from the pons, nigrostriatal projection, and locus ceruleus to the thalamus. PLMs are comorbid with ataxin 2 expansions perhaps proposing gene products interaction or <i>trans</i>-acting factors undescribed linked with nigro-striatal structures.</p>
<p>PFC 46</p>	<p>THE POLYGLUTAMINE EXPANSION SIZE INFLUENCES NEGATIVELY IN THE INCREASE OF ZINC LEVELS IN SERUM AND THE CEREBRAL SPINAL FLUID. Luis Velázquez Pérez, Julio César García Rodríguez, Jorge E. Rodríguez Chanfrau, Gilberto Sánchez Cruz, MSc. Consuelo González Triana, Dr. Raúl Aguilera, Lic. Osvaldo Hernández Sosa, Lic. Iverlys Díaz Polanco, Juana Hernández Estrada, Yamila Rodríguez Cruz, Dennis Almaguer Gotay, Luis E. Almaguer Mederos, Ramona Núñez Gomero, Diurys Blanco Gamez, Belkis Pérez Lemus, Nalia Canales Ochoa, Julio C. Rodríguez Díaz, Héctor O. Soto, García, María Carmen Rodríguez Ávila.</p> <p>Centro para la Investigación y Rehabilitación de las Ataxias Hereditarias (CIRAH), Holguín, Cuba, CENPALAB, CIDEM.</p> <p>Background: The prevalence of the SCA2 mutation in the Holguin province of Cuba is the highest reported worldwide, and reflects most likely a founder effect. The recent development of the roles of this Zinc as a crucial intra-and intercellular signalling ion of the CNS, and hence of the neurophysiological importance of zinc-dependent pathways and the injurious effects of zinc dyshomeostasis. The development of some innovative therapeutic strategies is aimed at controlling and preventing the damaging effects of this cation in neurodegenerative disorders. Objective: To test whether Zinc Sulfate is tolerated and safe and improve the nerve conduction, the lipid peroxidation was develop a clinical trials with Zinc Sulpate in SCA2 patients. Serum Zn and Cerebral Spinal Fluid (CSF) levels were significantly decreased in patients with Cuban SCA2 in relation to the controls groups. Methods: A randomized, double-blind, placebo-controlled study in 36 subjects with Cuban SCA2 disease was carry up. Eligible subjects were randomized to 50mg/day of Zinc Sulfate administered for three months. Results: The most important results were: the Zinc Sulfate was well tolerated and safe. Serum and cerebral Spinal fluid Zinc concentrations increased in the Zinc Sulfate -treated group. The treatment improve the postural stability, incoordination of the upper limb, saccade latency, peripheral nerve conduction studies of the median and sural nerves and the oxidative stress. May be that the different types of zinc transporter found in the cerebellum play a neuroprotective rather than a signalling role. However, the polyglutamine expansion size influences negatively in the increase of Zinc levels in serum and the cerebral Spinal fluid.</p>
<p>PFC 47</p>	<p>PENICILLIN SUSCEPTIBILITY OF <i>Neisseria meningitidis</i> ISOLATES FROM PATIENTS AND ASYMPTOMATIC CARRIERS IN CUBA Martínez I¹, Rodríguez PA¹, Sierra G¹, Izquierdo L¹</p>

	<p>¹Finlay Institute. Ave. 27 No. 19805. La Lisa, Havana, Cuba. email: isamartinez@finlay.edu.cu; isabelm.motas@infomed.sld.cu</p> <p>Introduction: <i>Neisseria meningitidis</i> represents a pathogen of great public health importance in both developed and developing countries and Penicillin has been the treatment of meningococcal infections for many years. However, strains of decreased susceptibility to Penicillin have been recognized in several countries. Knowledge of trends in the Penicillin susceptibility may be of great value in establishing a policy for empirical antimicrobial treatment of meningococcal disease. The aim of this study was to compare the levels of susceptibility to Penicillin from meningococcus strains obtained from patients and carriers in Cuba during a 26 year-period (1982-2008). Material and Methos: These strains were grouped into two stages: epidemic stage including isolates from 1982-1992 and post-epidemic stage including isolates from 1993-2008. A total of 283 strains were investigated, of these, 90 were from clinical isolates and 193 from carriers. All of them were identified as meningococcus by the API NH system (<i>bioMérieux</i>) and there classification in serogroup, serotype, subtype and immunotype was made by whole cell ELISA wit monoclonal antibodies. The Penicillin susceptibility was determined by agar dilution methods. The breakpoints used were those recommended by the NCCLS. The strains were identified as susceptible (MIC ≤ 0.06 $\mu\text{g/ml}$), moderate resistance (MIC = 0.12-1$\mu\text{g/ml}$) and resistant (MIC ≥ 2 $\mu\text{g/ml}$). Results and Discussion: During both periods the strains sensible to Penicillin (87.27%) predominated but 12.73% showed decreased susceptibility. The highest percentages of meningococcus strains with decreased susceptibility to Penicillin of epidemic period corresponded to B:15:P1.19,15:L3,7,9 (5.26%) and B:4:P1.19,15: L3,7,9 (2.63%). However, among the carrier's strains obtained in the post-epidemic period the phenotype NA:NT:P1.NST:L3,7,9 predominated and the 20.31% showed decreased susceptibility to Penicillin. Conclusions: These data show that continued surveillance of trends in antimicrobial susceptibility of <i>N. meningitidis</i> is important for detecting the emergence of meningococcal strains with penicillin resistance, which may pose serious therapeutic problems.</p>
PFC 48	<p>RESISTANCE TO HIV-1 REVERSE TRANSCRIPTASE INHIBITORS IN UNTREATED SEROPOSITIVE, FROM HAVANA CITY, CUBA Dubed M, Machado LY, Diaz HM, Blanco M, Ruiz N, Romay D</p> <p>AIDS Research Laboratory (LISIDA). Carretera de Tapaste y Autopista Nacional. San José de las Lajas, La Habana. email: cicdc@infomed.sld.cu</p> <p>Introduction: The therapy with reverse transcriptase inhibitors (RTI) has helped to improve the quality of life in human immunodeficiency virus type 1 (HIV-1) seropositive patients but these people may develop resistant strains to these drugs and transmit. The aim of this study is to determine the presence of mutations that confer resistance to the RTI in treatment naive persons. Material and Methods: The viral RNA was extracted from the plasma of 50 untreated HIV-positive during the second half of 2009, in Havana. The genomic region encoding the RT was amplified and sequenced with CEQ 8800 sequencer. The subtype was determined by phylogenetic analysis by MEGA v 3.1. The mutations associated with resistance to the RTI and the levels of resistance were defined with the database at Stanford University. Results and Discussion: The 81.4% of the tested samples belonged to men who have sex with men. The genetic classification showed a predominance of subtype B (42%), circulation of recombinant forms: 18 cpx (8%) and 19 cpx (28%), BF (2%), unique recombinant form: BG (18%) and non-typeable sample (2%). The capital with a higher incidence in the HIV/AIDS Cuban showed a similar pattern to that described for the country. The resistance mutations were detected in 40% of the cases, of which 17.5% had loss of sensitivity to RTI (usually low-level resistance), probably by the transmission of resistant virus. Conclusions: We confirmed the circulation of different genetic variants and RTI resistance in the population studied, hence the importance of surveillance of drug resistance in the capital and spread it to other provinces of Cuba.</p>
PFC 49	<p>STUDY OF THE HAEMOLYTIC ACTIVITY OF SYNTHETIC 1-O-ALKYLGlycerols ON ERYTHROCYTES OF PATIENTS WITH SICKLE CELL DISEASE Castan L¹, Del Toro García G², Ortíz Beatón E¹</p>

	<p>¹Biomedical Engineering department, Electrical Engineering Faculty, Universidad de Oriente. Patricio Lumumba s/n Santiago de Cuba, Cuba. email: castan@fie.uo.edu.cu</p> <p>²Biophysics Department, Medical Biophysics Center, Universidad de Oriente. Patricio Lumumba s/n Santiago de Cuba, Cuba. Santiago de Cuba, Cuba.</p> <p>Introduction: Sickle Cell Disease is high incidence pathology. Studies carried out with 1-O-alkylglycerols naturals or marine origin and with their similar synthetic decylglycerol (C10) and dodecylglycerol (C12), show that the same ones possess activity against this illness without increasing the haemolytic events. In this work is presented a spectrophotometric study of the haemolytic activity of 1-O-alkylglycerols synthetic of 11 (C11) and 14 (C14) carbon atoms in the main chain. Materials and Methods: They were carried out 5 tests in Vitro with blood coming Sickle patients and 5 tests with normal patients. The blood was centrifuged and, the erythrocytes were subjected to three laundries with PBS pH=7.4. The molars relationships evaluated were 1:1 and 1: 10 Haemoglobin: compound in AA and SS erythrocytes. A positive control with NaCO3 0, 1%, negative PBS pH = 7.4 and a negative (*) control with vehicle were prepared. The determination of the haemolytic effect was carried out for the spectrofotometric method. Results and discussion: The haemolysis caused by these compounds was inferior to 10 % accepted in the literature like permissible. It was determined that the molar relationship 1:10 haemoglobin: compound the haemolytic events are increased with regard to the relationship 1:1, suggesting an increase of the haemolysis with the concentration. The analysis of the effect of C11 and C14, to the same molars relationships, on erythrocytes AA and SS, didn't show statistically significant differences (p>0,05). This demonstrated in preliminary way that the haemolytic component of these compounds is independent of the chain longitude. Conclusions: The study revealed that the effects of 1-O-alkylglycerols analyzed are similar in normal erythrocytes and SS, although the haemolysis caused in the seconds can be higher. These results reveal the low toxicity of C11 y C14 and the possibility of using them as potential anti sickle cell disease agents.</p>
PFC 50	<p>EFFECT OF HEMODIALYSIS ON OXIDATIVE STRESS INDEXES IN HUMAN IMMUNODEFICIENCY VIRUS INFECTED PATIENTS WITH CHRONIC RENAL FAILURE Gil L¹, Castaño O¹, Ajete D¹, Caballero M¹, Abad Y¹, Calderón O¹, Luzardo C¹, Tápanes R¹. Institute of Tropical Medicine “Pedro Kouri” (IPK), Autopista Novia del Mediodía km 61/2, P.O. Box 601, Marianao 13, Ciudad de La Habana (Cuba). email: lgil@ipk.sld.cu</p> <p>Introduction: Patients with Human immunodeficiency virus (HIV) and Chronic Kidney Disease (CKD) often have cardiovascular diseases as the main cause of morbidity and mortality. Oxidative stress and a subclinical inflammation are crucial factors for its development. The aim of this study was to assess oxidative stress indexes in patients on hemodialysis treatment (HD) and to determine its effect on this stress. Material and method: We performed an observational case control study. Peroxidation potential (PP), glutathione (GSH), malondialdehyde (MDA), total hydroperoxides (HPO), superoxide dismutase (SOD), catalase (CAT), advanced oxidation protein products (AOPP), CD4+T lymphocytes subsets, and viral load were measured at baseline, 1 and 4 hours during dialysis in 12 patients compared with the values obtained in a control group (1:2 relation). Results and Discussion: All biomarkers showed important differences in comparison with the control subjects (p<0.05). Significant increased levels of oxidative damage (MDA, PAOP, OP) and low levels of antioxidant status (SOD, GSH, CAT, PP) were observed. During HD treatment the oxidation indexes (p<0.05) were increased and significant reduction of antioxidant level (p<0.05) were observed too. Significant differences respect control values persist. Plasmatic viral load reduces significantly during HD (p<0.05). Conclusions: There is an important oxidative stress in patients with CKD, probably established during the early stages of disease. The possible mechanisms involved in the oxidative status changes during HD are discussed in order to improve the quality of life of HIV patients with CKD. It may be also methodologically important for the follow-up of further clinical studies.</p> <p>References: Oberg BP, McMenamin E, Lucas FL, McMonagle E, Morrow J, Ikizler TA, Himmelfarb J. Increased prevalence of oxidant stress and inflammation in patients with moderate to severe chronic kidney disease. <i>Kidney Int</i> 2004; 65: 1009-16.</p>
PFC 51	<p>ALTERED REDOX STATUS IN PATIENTS WITH DIABETES MELLITUS TYPE 1 Gil L¹, Milian L², Toledo A³, Vilaró N², Tápanes R¹, Otero MA². ¹Hospital, Institute “Pedro Kouri”, Autopista Novia del Mediodía km 61/2, La Lisa, Havana, Cuba.</p>

	<p>²Laboratorios LIORAD, Ave 27 A # 26402 e/ 264 y 268 La Lisa. Havana, Cuba. Email: lazaracmd@liorad.quimefa.cu</p> <p>³Molecular Immunology Center, 216 St. & 15th Ave, 1600, Playa, Cuba</p> <p>Introduction: Diabetes mellitus is a complex metabolic disorder characterized by a disturbance in glucose metabolism. Recent evidences suggest that increased oxidative damage as well as deficits in antioxidants defence systems could be related to the complications in Diabetes patients' type I. Material and Methods: The aim of this study was to investigate an extensive array of redox status indices: glutathione (GSH), malondialdehyde (MDA), peroxidation potential, superoxide dismutase (SOD), catalase (CAT), total hydroperoxide (TH) and advanced oxidation protein products (AOPP) in relation to blood glucose and glucose indicators control such as glycosylated haemoglobin (HbA_{1c}) and fructosamine by spectrophotometric techniques. 40 Diabetes Mellitus patients' type I and 40 healthy subjects were recruited. Results and discussion: Both a reduction of GSH levels and an increase in MDA and TH levels were observed in the serum of patients. These patients also showed an increase of AOPP and PP levels as well as an increase of both CAT and SOD activity. Relatively to the control group, patients had significant differences in global indices of oxidant/antioxidant status and indicators of glycaemia control. Conclusions: These results contribute both to the evidences that substantial oxidative stress occurs during Diabetes Mellitus type 1 without early complications and to an integral overview of the oxidant / antioxidant balance in these patients. Reference: Yarek. MA. The Role of Oxidative Stress in Diabetic Vascular and Neural Disease. Free Rad Res 2003; 37 (5):471-80.</p>
PFC 52	<p>ANTIOXIDANT DOSIFICATION IN PATIENTS WITH DIABETES MELLITUS</p> <p>Mildrey Vales Almodovar, Danay Heredia Ruiz, Juan Rubén Tandrón Echeverría, Douglas Fernández Caraballo, Jesús Alfonso Rodríguez.</p> <p>Medical Sciences University "Dr. Serafin Ruiz of Zárata Ruiz". Santa Clara. Villa Clara. Cuba. email:mildreyva@ucm.vcl.sld.cu</p> <p>Introduction: the main manifestation of diabetes mellitus (DM) is hyperglycemia and this condition produces an oxidative stress status due to the selfoxidation of glucose that leads to the formation of alphacetoacids, hydrogen peroxide and superoxid radical, amongst other. Objective: To determine the values of the activity of Superoxide Dismutase (SOD), and Cathalase (CAT) enzymes and seric concentrations of Reduced Glutation (GSH) in diabetic patients. Materials and Methods: there were taken 120 patients with a recent diagnose of diabetes mellitus type I which were dispensarized in the Diabetic Clinic of Santa Clara city. All the determinations were made using 10 ml of venous blood and by means of spectrophotometric UV-visible techniques. SOD and CAT activities were measured using the Marklund method and the Aebi procedure, respectively and for GSH was used Beutler method. All the comparison were made with blood from 100 healthy individuals. Results: a marked diminution in values of CAT (2,87- 27,36 U/mL) and GSH (2,24 - 6,98 nmol/mL) in diabetic patients was observed, whilst in SOD (0, 00 -18, 87 U/mL) the difference was slight when compared to normal controls (3,56 - 17,56 U/mL). Those results showed that diabetic patients are subjected to stress and that could be due to that hypoinsulinemia increases the values of acil CoA fat oxidase which initiates the beta oxidation of fatty acids with a greater production of hydrogen peroxide. Conclusion: there were stabilised the pathological levels of SOD, CAT and GSH in the diabetic patients studied sample, and a significant diminution in the values of CAT and GSH with respect to normal patients was also observed.</p>
PFC 53	<p>DETERMINATION OF ANTIOXIDANT/PRO-OXIDANT MARKERS IN THE SEMEN OF HEALTHY SUBJECTS</p> <p>Hernández Y¹, Delgado L¹, López R²</p> <p>¹ Center of Studies for Research and Biological Evaluations, Pharmacy and Food Sciences Collage, University of Havana. email: yanet@cieb.sld.cu</p> <p>²Department of Pharmacy, Pharmacy and Food Science College, University of Havana.</p> <p>One of the significant developments, in the last two decades, in the study of human infertility has been the discovery that reactive oxygen species and oxidative stress play a critical role in the etiology of defective sperm function and male infertility. But also reactive oxygen species have been recently associated with the capacitation process, the acquisition of fertilizing ability, when they are generated at very low levels.</p>

	<p>The aim of the present study was to investigate the behaviour of biochemical parameters of oxidative stress in the sperm of 40 healthy subjects. The levels of biomolecules damage indices (malondialdehyde and advanced oxidation protein products), the activity of antioxidant enzymes (superoxide dismutase and catalase) and the antioxidant status (reduced glutathione, peroxidation potential and ferric reducing ability of plasma) were tested spectrophotometrically. These indicators could be extrapolated to routine clinical analysis and contribute to an integral overview of the antioxidant/pro-oxidant balance in infertile men and could also be used as indices of treatment efficacy.</p> <p>Key words: Reactive oxygen species, oxidative stress, sperm capacitation, male infertility.</p>
PFC 54	<p>MODIFICATION IN REDOX STATUS OF DIABETES MELLITUS TYPE 1 PATIENTS AFTER INSULIN TRANSITION Milian L¹, Gil L², Toledo A³, Avila J⁴, Vilaró N¹, Llera I⁴, Tápanes R², Otero MA¹, Martínez G⁵</p> <p>¹ Laboratories LIORAD, Ave 27 A # 26402 e/ 264 y 268 La Lisa, Ciudad de La Habana, Cuba. email: lazaracmd@liorad.quimefa.cu ² Institute of Tropical Medicine “Pedro Kouri” (IPK), Autopista Novia del Mediodía km 61/2, La Lisa, Ciudad de La Habana (Cuba). ³ Center for Molecular Immunology, 216 St. & 15th Ave, 1600, Playa, Ciudad de La Habana (Cuba). ⁴ Center for Pharmacoepidemiology Development, 5ta esq 44, Playa, Ciudad de La Habana, Cuba. ⁵ College of Pharmacy and Food Science, Ave 222, La Lisa, Havana University, Ciudad de la Habana, Cuba.</p> <p>Introduction: To determine and compare an extensive array of biochemical redox indices before and 2 months after insulin type change in DM patients’ type 1. Material and Methods: Glutathione, malondialdehyde, peroxidation potential, superoxide dismutase, catalase, total hydroperoxide and advanced oxidation protein products in relation to blood glucose and glucose indicators control such as glycosylated haemoglobin and fructosamine were measured in 40 patients before and after 2 months since pork insulin was changed to human insulin in type 1 diabetic patients. These data was compared to gender and age matched healthy control. Results and Discussion: After 2 months of changing, all indicator measured were favourable evolved and were significantly modified (p<0.05) except activity of erythrocyte enzymes superoxide dismutase and catalase. Adverse reactions (hypoglycaemic events) were observed in 7 patients with 0.7 % of incidence. It was related to concomitant use of captopril, clortalidone and nitropental for hypertension treatment. Simultaneous beneficial change in glucose, glucose control indices and redox markers were noted in 27 (68%) of total patients of study. Conclusion: These results contribute to both evidences that transition process from animal to human insulin could be beneficial to diabetes mellitus type 1 patients and an integral overview about metabolic events involved could be valid for evaluate treatment effects. The results contribute to evidences that transition to human insulin can improve the antioxidant status of diabetic patients. Reference: Perez-Matute P, Zulet MA, Martínez JA. Reactive species and diabetes: counteracting oxidative stress to improve health. <i>Curr Opin Pharmacol</i> 2009; 9: 771-9.</p>
PEF 01-12	<p>PHARMACOLOGY TEACHING / ENSEÑANZA DE LA FARMACOLOGÍA</p>
PEF 01	<p>CHANGING WSU CLINICAL ASSOCIATE STUDENTS’ PERCEPTIONS OF THEIR PHARMACOTHERAPEUTIC COMPETENCIES: A ‘BEFORE’ AND ‘AFTER’ SURVEY”. JH Aguirre, EN Kwizera</p> <p>Department of Pharmacology, Faculty of Health Sciences, Walter Sisulu University, Mthatha 05117, South Africa.</p> <p>Background: Walter Sisulu University (WSU) pioneered the South African undergraduate training of Clinical Associates in 2008, and the students were introduced to Pharmacology and Therapeutics at the beginning of their 3rd and final year in February 2010. Their acquired pharmacotherapeutic knowledge, skills, and attitudes were assessed summatively using written and oral examinations. The present study sought to supplement these assessments by looking at the students’ perceptions of their pharmacotherapeutic competencies before and after exposure to a 4-week intensive course of basic and clinical Pharmacology. Summary of work: Just before they were given their first Pharmacology lecture at the beginning of February 2010, 23 WSU Clinical Associate students in their 3rd and final year were asked to voluntarily complete a very short (6-item) questionnaire on their perceived pharmacotherapeutic competencies, on a Likert scale of: ‘strongly agree’, ‘agree’, ‘neutral’, ‘disagree’, and ‘strongly disagree’.</p>

	<p>After 4 weeks of learning Pharmacology mainly from daily interactive lectures the students completed the same questionnaire at the beginning of March 2010. Responses were analysed statistically for ‘before’ and ‘after’ differences. Summary of results: The response rate was 100%. Regarding ‘strongly agree’ or ‘agree’, there were significant ($p < 0.05$) differences in favour of ‘after’ and the converse was the case with regard to ‘disagree’ or ‘strongly disagree’. There were no significant differences related to the ‘neutral’ or ‘no opinion’ responses. Conclusions: From comparing their ‘before’ and ‘after’ responses, it is clear that in February 2010, WSU 3rd year Clinical Associate students felt that their pharmacotherapeutic competencies improved over an intensive 4-week pharmacology course; and results from such surveys could be used to evaluate the impact of a given course on student’s perceptions of their acquired knowledge, skills and attitudes and thus the success of the course.</p>
PEF 02	<p>A SET OF EDUCATIONAL SOFTWARES AIMED AT THE DEVELOPMENT OF THE TEACHING-LEARNING PROCESS IN THE PHARMACOLOGY FUNDAMENTALS SUBJECT FOR THE NURSING DEGREE STUDENTS Oliva A¹, Reina M¹, Pollán J A¹, Cordero J M¹, Torres M², Rodríguez N², Ortíz R², Pompa M², Boza M²</p> <p>¹ Department for Educational Softwares Development for the Medical Sciences, Filial de Ciencias Médicas “Haydée Santamaría Cuadrado”. Campechuela Road Km 1, Manzanillo City, Granma Province, Cuba. e-mail: galenomanzanillo@infomed.sld.cu aoliva@ftc.grm.sld.cu ² Filial de Ciencias Médicas “Haydée Santamaría Cuadrado”. Campechuela Road km 1, Manzanillo City, Granma Province, Cuba.</p> <p>Introduction: A set of educational hyperlinks that offer the user (students and professors) the contents taken in the pharmacology fundamentals subject is proposed. They were created since the curricular approach. It allows students the development of abilities since a more interactive form by achieving support to the teaching-learning process. The main objective sought with these ten educational hyperlinks posted to first year students of nursing degree is to present them some contents through texts, images, and animations among other media resources. Materials and Methods: A multidisciplinary group was in charge of the design and setting up processes of the proposed hyperlinks. The technology used for the graphical design was the Adobe Photoshop CS3 making possible the media treatment; Macromedia Flash MX 2004, for the animations creation; and the SadHea Web Tool made possible to set up the contents related to the pharmacology fundamentals subject. Conclusions: Based on the results achieved we may demonstrate the fulfillment of the Pharmacology Learning Educational Hyperlinks’ (LEH) functions: They contributed to reveal the importance and ways of using the scientific knowledge for the life. They link students to the daily life practice. They turn students into direct interactors inside the teaching-learning process. They develop on students cognitive qualities and capacities. They relate the theoretical teaching to the practice. They raise the teaching possibilities when controlling the students’ knowledge acquisition. They offer concrete models for the logical process development. The fulfillment of these functions becomes the Learning Educational Hyperlinks (LEH) into an invaluable assistant in the teaching duty practice, aspect by which their rapid development must be considered according to the incessant improvement of plans, programs and audiovisual means.</p>
PEF 03	<p>SOFTWARE EDUCATIVO PARA LA ENSEÑANZA-APRENDIZAJE DE VÍAS DE ADMINISTRACIÓN DE MEDICAMENTOS Y FORMAS FARMACÉUTICAS Bosch Núñez AI, Rodríguez Reyes O, Díaz Sánchez LS, Páez Delgado D</p> <p>Universidad de Ciencias Médicas. Facultad de Estomatología. Santiago de Cuba. Cuba. Avenida las Américas. e/ e y i. Reparto Sueño. Santiago de Cuba. Cuba. email: aibosch@sierra.scu.sld.cu</p> <p>The raising of the new Technologies of the Information and the Communications (ICTs) has brought about their overuse at large scale in the different human knowledge spheres, showing benefits with their application. The use of the educational software as a teaching aid facilitates the teaching-learning process in the different careers of the Medical Sciences. An educational software of multimedia type titled Ways of drugs administration and its pharmaceutical forms was designed in the period from September 2009 to February 2010 motivated by the difficult access to the up-to-date bibliographies about the topic faced in the University of Medical Sciences in Santiago de Cuba. The objective of this software is to better the teaching-learning process on this topic to both professors and students of the 2nd year of the Dentistry career. All the necessary information was gathered, organized and digitized; a virtual gallery of images was</p>

	also included to support it. For the assembly of the multimedia the software Mediator 8.0 was used as a computer tool.
PEF 04	<p>PHARMACOLOGY IN THE POSTGRADUATE TEACHING. AN EXPERIENCE IN OPHTHALMOLOGY <u>Ariana Fernández García</u>¹, Aleida Lavandero Espina², Elizet Jackson Horruitiner³, Rosendo Villar Valdés⁴.</p> <p>¹ MINSAP. Línea e I, C. Havana City. email: ariana.fdez@infomed.sld.cu ² Medical University. Carlos III e Infanta. Havana City ³ Medical University. Santiago of Cuba. ⁴ Medical University. Havana City</p> <p>Introduction: Pharmacology is a basic subject of the clinic that takes into account the scientific essentials for the rational use of medications. The main objective of this paper is to describe the teaching strategy used to teach pharmacology to the residents in ophthalmology in the “Ophthalmologic Cuban School”.</p> <p>Material and methods: This work constitutes the first experience in Cuba in which pharmacology is taught as a part of the program used in the formation of ophthalmologists. After some multidisciplinary methodological meetings the program of pharmacology was divided into two main topics: the general pharmacological bases of the therapeutic of ocular diseases and the pharmacological bases of the treatment of painful, inflammatory and infectious ocular processes. The ways of organization of teaching selected were the conference, the workshop and the independent study with the methodological orientations and the corresponding teaching aids.</p> <p>Results and discussion: The integral methodological preparation of the professors led us to the teaching of pharmacology related to the morpho-functional aspects that comprise the basic sciences in medicine. The guide of the good prescription was used as the active teaching method. The solution of problems of the clinical practice in ophthalmology was taken into consideration. The integral evaluation of the contents in the tests was carried out. The subject was taught in the country and abroad. The incorporation of the new tendencies of the high education to the Cuban medical education is an element of a great priority.</p> <p>Conclusions: The teaching of pharmacology applied to ophthalmology, contributed to the development of the rational thinking during the prescription. It is possible to apply these transformations to other medical specialties.</p> <p>References: Fernández A, Jackson E. The Guide to Good Prescribing: a teaching method applied to Ophthalmology. Rev Misión Milagro, 2 (3), 2009. Disponible en: http://www.misionmilagro.sld.cu/vol2no3/orig3.php.</p>
PEF 05	<p>IDENTIFICATION OF LEARNING NEEDS IN THE TREATMENT OF PAIN AND PALLIATIVE MEDICINE IN THE MEDICAL SCHOOL <u>Peña Fleites C</u>¹, Yodú Ferral N¹</p> <p>¹ “10 de Octubre” Medical School, Medical University of Havana. Calzada 10 de Octubre No 130 Cerro, Havana City, Cuba. email: caridad.pena@infomed.sld.cu</p> <p>Introduction: The scientific and technological advancement of medicine has influenced on the increase in life expectancy and population aging, which also explains that the number of patients with incurable chronic illnesses requiring palliative care to relieve their symptoms and improve quality of life has increased. Since 1993 Cuba enjoys the benefits of the Program for Attention to Pain and Palliative Care. However the curriculum of the medical career does not include the Palliative Medicine and devote little time to pain treatment. In order to evaluate the knowledge of 5th year Medicine students on pain treatment and palliative medicine, a descriptive study was conducted in March 2010 in “10 de Octubre” Medical School. Materials and Methods: 58 students were interviewed and the contents of two topics were evaluated: pharmacology of analgesics (non-opioid and opioid) and pain treatment and palliative medicine. The primary endpoint was to assess knowledge on pain pharmacotherapy. Results and Discussions: 84.5% of the students considered the association between non-opioid analgesics a correct practice. Less than half (41.3%) knew in what consist the analgesic ladder the World Health Organization for pain treatment. 77.6% reported cancer treatment as the sole use of morphine and 60.3% considered that the route of choice for their administration is the subcutaneous. 84.5% manifested that analgesics should be administered according to patient demands. 82.7% considered palliative care are exclusively for cancer</p>

	<p>patients and only 48.3% pointed its purpose is to improve life quality. Conclusions: We conclude that the knowledge acquired in the medical career about pain management and palliative care are insufficient, so it would be appropriate to include Palliative Medicine in the undergraduate curriculum.</p>
PEF 06	<p>DIFFICULTIES IN THE LEARNING OF PHARMACOLOGY IN MEDICINE STUDENTS IN THE UNIVERSITARY POLICLINIC RAÚL GÓMEZ GARCÍA. <u>Álvarez A IM</u>¹, Taboada CM ²</p> <p>Communitary Policlinic "Raúl Gómez García" 53 Coco street between Rabí and General Lee streets, Santos Suarez, 10 de October, Havana City, Cuba. Email: ¹ Ileana.alvarez @ infomed.sld.cu e- mail ² marta.taboada @ infomed.sld.cu</p> <p>Introduction: The medicine teaching in the community faces changes, challenges and new docent experiences. The Raúl Gómez Policlinic began in 2006 with the University Policlinic Project (known as PPU) and has two Pharmacologic experiences courses. Historically, students have faced many difficulties in the learning of that discipline. With this study we tried to define the most difficult topic to focus strategies for perfecting the teaching methodologies. Materials and Methods: A retrospective study of the third year student` evaluations results was made in the forenamed policlinic. This was developed in classes, seminars and term controls during two consecutive courses with the same teaching staff and teaching program. Through this research we could identify the most difficult topics in both materias and we pointed out probable causes.</p> <p>Results and Discussion: Pharmacology as discipline is the base for the rational use of medications. It uses teaching methods such as video lectures, seminars, workshops, practical classes, independent works and partial controls. When we analysed different evaluations, we defined the most difficult topic were: Pharmacology I: Theory of the receptors and autonomous nervous system. Pharmacology II: Antimicrobians (Beta-lactamic and inhibitors of the protein synthesis), medications for the treatment of cardiovascular diseases and Diabetes Mellitus.</p> <p>Conclusions: The more deficient topics were the more complex with faults owed to failures in precedent materias. Better methodologic strategies must be applied to avoid these difficulties and improve this discipline learning.</p>
PEF 07	<p>PHARMACOLOGY LAB PRACTICES. IMPORTANCE FOR PHARMACEUTICAL PROFESSIONAL FORMATION <u>Ivón González</u>, María Teresa Díaz Soto, Marian Hernández, Olga sonia León</p> <p>Pharmacology and Toxicology Dept., Food and Pharmacy Institute. University of Havana email: ivongb@ifal.uh.cu, olga@infomed.sld.cu, marianhc@uh.cu</p> <p>In Pharmaceutical Sciences career, one of the teaching forms is by laboratory practices. From the concept of D plan for this career, the number of frontal hours is highly reduced, and the time for practical activities rises. We propose to improve design and organizing of lab practices as responsible for this process. Because of the importance of practical skills in pharmaceutical professional, which are indispensable tools in preclinical evaluation, and in consolidation of knowledge for clinical applications, the aim of this work is to show the changes in practical course, directed to re-elaborate objectives, insert new practices as expression of the impact of research in direct teaching, and the analysis of possible substitutions by alternative methods. We also analyzed the influence of some contents of the practical course (Pharmacological Screening) in values formation in students.</p>
PEF 08	<p>MASTER IN PHARMACOLOGY: A NECESSARY SPECIALIZATION <u>Marian Hernández</u>, Eduardo Fernández Sánchez</p> <p>Pharmacology and Toxicology Dept., Food and Pharmacy Institute. University of Havana. email: marianhc@uh.cu</p> <p>Food and Pharmacy Institute. University of Havana, has a long and remarkable tradition in national and international academic post grade, with 2 PhD programs, 8 master programs and 2 specialties, and several diplomats and courses. Among these trajectory takes place Pharmacology master program, with 6 editions, and many graduates of different centers and specialties. This program has born to accomplish specialized formation that makes the new professional capable for research in basic and clinical pharmacodynamic and pharmacokinetic aspects, to contribute to pharmaco-toxicological file of a new drug. We count with an</p>

	<p>excellent panel of professors, in improving process in order to supply pharmacological research needs of interested professionals. The aim of this work is to proudly present the master program in Pharmacology of University of Havana, to favor professional's incorporation and contribute to their integral formation, and to our country development in this brand.</p>
PEF 09	<p>RESEARCH SKILLS TRAINING IN MEDICAL STUDENTS THROUGH THE PHARMACOLOGY DISCIPLINE <u>González O</u>, Pérez M.</p> <p>University of Medical Sciences in Villa Clara. email: orestesgc@ucm.vcl.sld.cu</p> <p>The insertion of research as a strategy in the university curriculum is of vital importance if one starts from the premise that the University is a center of knowledge generated and mentor of new generations, to produce knowledge and ideally perform its role in the development economic, political and social life. All subjects can deploy scientific thinking in students and help achieve the research skills that society demands to the University today. That is why an investigation was conducted a qualitative development in order to propose measures for their training in the third year students of medicine through discipline Pharmacology. To succeed in this order is necessary to: take responsibility and actions are not common in a traditional learning environment, to modify the class methodologically based on the interrelationship, interdisciplinarity and transdisciplinarity of content; get students to devote more time to work independently depending on the solution of tasks teachers, train teachers in Scientific Research Methodology and strengthen the methodological work of the groups in terms of achieving this purpose. The integration of academic and clinical components to the researcher, both through the content taught, as teaching methods used and the tasks assigned, will contribute to the development of cognitive independence and with the active thinking and creator of the students which prepares graduates to meet again with his social role.</p>
PEF 10	<p>INTRODUCTION OF BIOINFORMATICS IN PHARMACOLOGY AND OTHER UNDERGRADUATE MEDICAL SUBJECTS TEACHING. <u>O Serrano Barrera</u>, N Orive Rodríguez Provincial Center of Medical Genetics, PO Box 27, Las Tunas 75100, Las Tunas, Cuba. email: orlando@cucalambe.ltu.sld.cu</p> <p>Introduction: Bioinformatics has recently emerged as a high level multidisciplinary area with many potential applications in the biomedical fields, including drug developing processes and pharmacogenomics. Nevertheless, no elements of bioinformatics are included in undergraduate or graduate medical curricula in Cuba. Design: In the present work current programs of basic and preclinical subjects in undergraduate medical teaching were reviewed with the objective to propose some contents and skills related to bioinformatics to be incorporated into ongoing programs. A number of activities were considered, including all forms of teaching: lectures, seminars and online practical activities as well as both electronic and print review documents. A website covering news and resources on bioinformatics was also designed. Results: In the case of Pharmacology, a lecture was planned to update on pharmacogenetics and pharmacogenomics: molecular basis, diagnostic technologies, clinical applications and regulatory implications. Besides, a practical activity was added to deal with online resources on single nucleotide polymorphisms, variations at nucleotide and protein levels and three-dimensional structures of drugs and biologicals. For a number of other medical subjects, related bioinformatics contents were also included, such as Morphophysiology (sequence retrieval, secondary and tertiary structures, protein-protein interactions, metabolic pathways), Microbiology (pathogen genomes, immune response prediction) and Genetics (human genome, chromosomes sequences, gene variation, OMIM). Core contents, objectives, skills and evaluations were considered. A new website is currently available at http://blogs.sld.cu/oserranob/, covering all aspects of bioinformatics and with links to the most important databases and resources in the field. Conclusions: A first attempt was made to incorporate bioinformatics into Pharmacology teaching. Updating on bioinformatic skills are essential for present and future scenarios in the biomedical field, and it is mandatory to accelerate the inclusion of its contents and resources into medical subjects.</p>
PEF 11	<p>NECESSITY OF CONTINUOUS FORMATION OF PHARMACOLOGY PROFESSORS <u>Ortíz Y</u>¹, Suárez H¹, Ramos K¹</p>

	<p>¹ University of Medical Sciences of Granma. Branch Bayamo. email: yurisnel.grm@infomed.sld.cu</p> <p>Introduction: Traditionally the professor formation has received two meanings: initial and permanent or continuous, in function of the professional moment the teacher is although most of the studies that approach this topic points toward the formation of the professor as a continuous one that should be present along the professor's professional trajectory, being stood out the coordination necessity between both formation types, integrating both in an unique sense. Materials and methods: With the employment of qualitative methods of scientific investigation, it was carried out a non experimental design of descriptive transeccional type with the objective of characterizing the continuous formation of the professors of pharmacology of Medical Science Collage Branch Bayamo in the period from July to December 2009. Results and discussion: 25 professors that teach the subject of pharmacology in the central and municipal areas were interviewed, the prevalence of models, focuses or traditionalist conceptions was verified in which importance is granted to the possession of the knowledge teaching that the professors should possess and transmitte in the classroom; the professor hopes the training prioritizes the transmission of the theoretical contents; inadequate plan of postgraduate course; inadequacies in the coherent integration among the qualification, the methodological preparation and the investigation or innovation. Conclusions: The pharmacology professors need of the implementation and evaluation of a model of continuous formation, with pedagogic foundations that allows them to introduce educational innovations with the purpose of perfecting the educational process and obtain as product a graduate one with in the preparation that society demands.</p>
PEF 12	<p>SYSTEM OF METHODOLOGICAL ACTIVITIES WITH A DIDACTIC COMPETENCY APPROACH FOR PHARMACOLOGY PROFESSORS OF THE NEW PROJECT FOR THE FORMATION OF MEDICAL DOCTORS Romero MB¹</p> <p>¹Medical University of Matanzas “Dr. Juan Guiteras Gener”, Km 102 Carretera Central, Matanzas.</p> <p>Taking into account the changes that are taking place in the Medical High Education, it becomes a necessity; the dynamic, solid and scientific preparation of professors in the field of Didactics and Pedagogy. An educative research on Pharmacology I was carried out on the third year medical students of Matanzas Medical University in the conditions that characterizes the scenario of the University Teaching Polyclinic. The approach assumed, is the one concerning didactic competencies while the research is basically qualitative by means of empirical methods which allowed to collect useful data. To establish the diagnosis, and the final results, the theoretical methods made the study and their relation with the didactic competencies possible, they are considered fundamental for those professors who teach at the University Polyclinics (U.P.P.) Regarding the statistic procedures, the description statistics was taken into consideration showing frequency and percentage. The results were presented in tables and graphics which made easier the discussion of them. The main result is a system of methodological activities that provided the professors' staff with the pedagogical and didactic training. Some recommendations are also made in order to generalize the experience if it is possible.</p>
PDF 01-03	<p>BIOINFORMATIC AND MOLECULAR DRUGS DESIGN / BIOINFORMATICA Y DISEÑO MOLECULAR DE FARMACOS</p>
PDF 01	<p>MODELING OF MOLECULAR PROPERTIES OF BETALACTAMIC ANTIBIOTICS AND INHIBITORS OF THE BETALACTAMASES Cruz Elso M, Sánchez Esley</p> <p>Medical Sciences University, Las Tunas, Cuba. email Address: elso@cucalambe.ltu.sld.cu</p> <p>Introduction: The antibacterial properties of the betalactam antibiotics are the result of its molecular structure. The molecular modeling contributes to deepen on this relationship. Method: A theoretical study using methods of the quantum mechanics to model structural properties, density of the atomic charges and the frontier orbitals of betalactamic antibiotics and inhibitors of the betalactamases was carried out. The molecular structures were optimized with PM3 semiempiric calculus. The structure of the betalactamic ring in the different compounds was compared. The molecular properties were calculated according to the Density Functional Theory at a B3LYP/6-31G(d) level. The density of the atomic charges and the frontier</p>

	<p>orbitals were analyzed. The effect of the substituents on the properties of the betalactamic ring was evaluated. All the calculations were executed in personal computers. Results and Discussion: There are variations in the calculated properties that make possible to define two groups of compounds: one for the monobactams and the inhibitors of the betalactamases, with less planarity in the ring and more gap in the frontier orbitals and another one with the penicillins, cephalosporins and carbapenems, planer, more structurally stable and with less gap in the frontier orbitals. The structural parameters of the betalactamic ring do not change as a consequence of the modifications in the lateral chains of the modelled penicillins and cephalosporins. There are no important variations in the charge densities, mainly in the positive charge of the carbonylic carbon. The ceftobiprole is different from the others due to the spatial dispositions of the lateral chain that facilitates the access up to the carbonylic carbon. Conclusions: The modelled molecular properties of the betalactamic antibiotics and inhibitors of the betalactamases show agreement with its pharmacological behavior. The structures and electronic properties of the betalactamic ring do not have significant modifications among modelled betalactam antibiotics.</p> <p>Keywords: betalactam antibiotics; betalactamase inhibitors; molecular modeling.</p>
PDF 02	<p>IN SILICO IDENTIFICATION OF MANGIFERIN BINDING SITES ON HUMAN AND RAT SEROTRANSFERRINS Gutiérrez MA</p> <p>National Bioinformatics Center, Ave. Salvador Allende esq. a Luaces, CP 10600, Cuba. email: miguelagp@instec.cu</p> <p>Introduction: Serotransferrin (Tf) is the protein responsible for the transport of Fe³⁺ by the blood, avoiding the formation of free radicals. Mangiferin, a C-glucosylxanthone, is the main active compound from an extract with proved antioxidant activity. The aims of this in silico study are therefore: (a) to predict the complex between rat Tf and mangiferin; (b) to analyze a possible complex between mangiferin and human Tf; (c) to analyze the structure/function relationship in the corresponding complexes; and (d) understand, at the molecular level, why mangiferin has an antioxidant activity. Materials and methods: The binding site and the conformation of mangiferin into Tf_{rat} were predicted using a blind-docking experiment (i.e. with no prior definition of the possible binding site). The docking analysis was done with a software package called "Blind-docking tester", which extends the capabilities of AutoGrid/AutoDock for this kind of experiment. Results and discussion: The results of this docking analysis show a common binding site for mangiferin into Tf_{rat} that is independent of the form (apo or holo) and the lobe (N- or C-). The same docking experiment was done with Tf_{human} and the results were equivalent to those with Tf_{rat}. Conclusions: When mangiferin binds to this common binding site, it blocks the exit of Fe³⁺ and CO₃²⁻ from the holo forms of Tf_{rat} or blocks the load of these ions by the apo form.</p>
PDF 03	<p>SEARCH OF POTENTIAL VACCINE CANDIDATE OPEN READING FRAMES IN THE NEISSERIA MENINGITIDIS GENOME: AN IN SILICO SCREENING. García D¹, Cobas K¹, Sardiñas G¹, Delgado M¹, Climent Y^{1,2}, Niebla O¹, Yero D^{1,2}, Perera Y, Caballero E¹ and Pajón R³.</p> <p>¹Meningococcal Research Department, Division of Vaccines. Center for Genetic Engineering and Biotechnology. Ave 31, Cubanacan, Havana 10600, Cuba. ² Department of Molecular Biology, Division of Biotechnology. Finlay Institute. Ave 27, La Lisa, Habana 11600, Cuba. ³Faculty of Medicine, University of Calgary, Heritage Medical Research Building, Hospital Drive N.W., Calgary, Canada. email: darien.garcia@cigb.edu.cu</p> <p>Introduction: Reverse vaccinology has strongly enhanced the identification of vaccine candidates by replacing several experimental tasks, using <i>in silico</i> prediction steps. The development of new predictor softwares and the availability of an increasing number of genome sequences provide the opportunity to identify new and conserved proteins that could show protective and immunogenic properties. The use of an <i>in silico</i> approach to <i>Neisseria meningitidis</i> published genomes makes possible the pre-selection of a panel of novel conserved meningococcal antigens. By cloning, expressing and evaluating the immunological potential of these proteins we could propose novel vaccine candidates to control meningococcal disease. Materials and Methods: Sequence similarity searches, as well as motif, cellular location predictions, and</p>

domain analyses were structure in a pipeline based on free internet servers and databases, obtaining eight final candidates, that has not been characterized before. The genes were cloned and expressed in *E. coli*, purified, and used in an immunization schedule in mice. **Results and Discussion:** Although all resulted immunogenic, bactericidal response, considered the gold standard of functional responses against the meningococcus, was detected only in antisera elicited by six of them against the homologous strains. **Conclusions:** Our study demonstrated that utilization of genome sequences by application of bioinformatics is still possible to expedite the vaccine discovery process in *N. meningitidis* by rapidly providing a set of uncharacterized candidates for further testing.