BULLETIN OF MEDICINES AND HEALTH FOR THE AMERICAS

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## Over half the medicines sold online are substandard

The European Alliance for Access to Safe Medicines published a report on online pharmacies. This group ordered medicines from 100 online drug sellers. These had to fulfill some requirements, like having a telephone number, apparent access to a pharmacist and good English language, aspects that could create the illusion of a reliable on line pharmacy. The investigators bought 30 common drugs, as atorvastatin, olanzapine, clopidogrel, lanzoprazol, among others. After receiving the medicines, these were evaluated in two stages.

First, a panel of experts carried out a visual evaluation of the packaging and authenticity of the products. Fifty percent of the medicines were delivered without the patient information leaflet and only 47 percent seemed to present a proper, original packaging.

In the second stage, the products were subjected to laboratory analysis. Sixty-two percent of the medicines were counterfeit or substandard, even some that were considered original by the expert panel of the first stage.


Online buying of medicines is a growing practice, presenting serious risks to health due to lack of authenticity, guarantee of quality and access to prescription medicines without professional monitoring. In some countries of the region of the Americas this practice seems to be consolidating, without a regulatory response capable of stopping illegal sellers.

**Read the full report in:**
http://www.eaasm.eu/Media_centre/EAASM_reports
**Working group on Drug Counterfeiting (PAHO):**
http://www.paho.org/english/ad/ths/ev/GCFM-hp.htm

## More contributions to neglected diseases treatment from Brazil and DNDi

The partnership between the national laboratories of Brazil, in this occasion the Pharmaceutical Laboratory of the State of Pernambuco (Lafepe), and the "Drugs for Neglected Diseases Initiative" (DNDi) has made another contribution to the treatment of neglected diseases.

This laboratory will develop and produce a pediatric formulation of benzonidazol for the treatment of Chagas disease. This medicine, marketed in the 70´s, doesn´t present any pediatric formulation in the market. At present children are treated with pills formulated for adults, which must be fractioned to reach the pediatric dose. This practice makes the dose received by the patient uncertain, inducing medication errors and treatment failure.

The product will be sold at production cost in Latin America. DNDi recently reached a similar agreement with another Brazilian national laboratory for the production of a malaria fix dose combination medicine.

Source:
http://www.lafepe.pe.gov.br/LAFEPE/noticias/noticiario/17072008.html
www.dndi.org.br

## PHARMACY ACREDITATION PROPOSAL FOR LATIN AMERICA

The preliminary document on accreditation for all Latin America is already available. The same was developed by representatives from nine countries and with the contribution of PAHO/WHO. The document will be revised and discussed during the VI Pan American Conference on Pharmaceutical Education (for more information on this event read page 6).

If you wish to read the document please send a mail to medicamentos@ffyb.uba.ar

## AIDS Congress in Mexico

The XVII International AIDS Conference (AIDS 2008) was held in Mexico on August 3rd-8th. This is a biannual meeting, set in Latin America for the first time.
Nearly two million people are estimated to be infected with HIV in Latin America and the Caribbean. Recently UNAIDS finished their regional update on the epidemiology of AIDS, which includes the situation of each country and the Region as a whole.
**Latin America**: The average HIV prevalence rate in adults is 0.5%. The HIV epidemic in Latin America remains stable, but HIV transmission continues to occur among the population at higher risk of exposure and without proper access to education and health care.
**Caribbean**: This Region presents a prevalence of HIV of 1%, the second higher after sub-Saharan Africa. The prevalence has stabilized in several countries as in Haiti and Honduras, but HIV remains one of the leading causes of death among people aged 25 to 44 years in the region.

Find the Regional and country profiles in: www.unaids.org

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## Pioneers in the elimination of vertical transmission of HIV and syphilis

Public health authorities and experts in the field agreed to eliminate the vertical transmission of HIV and syphilis in the Caribbean by 2015. The technical meeting was organized by PAHO/WHO and UNICEF during the XVII International AIDS Conference. The efforts to eliminate the vertical transmission of syphilis started several years ago, but it is the first time that a developing Region also proposes to eliminate the vertical transmission of HIV. Maternal transmission in 2007 was estimated to represent the 8% to 10% of all HIV transmissions in the Caribbean.
The region has achieved important steps towards the objective. In Trinidad and Tobago the syphilis sero-reactivity rate for infants declined from 31% in 2002 to 9% in 2005. Antiretroviral treatment is available to 100% of HIV infected pregnant women in several countries such as Cuba, Dominica, St. Kits and Nevis, and St. Vincent and the Grenadines. On the other hand, some areas have to be strengthened, such as the screening and treatment of syphilis and the access to antiretroviral therapy in some countries.
The technical meeting established an incidence rate of less than 2 HIV cases per 100 infected mothers and an incidence rate of 0.5 or lower of syphilis cases per 1,000 live births as the criteria to declare the elimination of vertical transmission for each infection.

Source:
http://www.paho.org/english/dd/pin/pr080807b.htm

## Hospital admissions due to adverse effects

The journal "The Annals of Pharmacotherapy" published a review of observation studies designed to determinate the prevalence of hospital admissions caused by adverse effects. The review included 25 studies including over 100,000 patients.
The study found an enormous dispersion in the prevalence rates of adverse effects, an overall median of 5.3% (interquartile range [IQR] 2.7–9.0%) with a range of 0.16% to 15.7%. This difference was explained by the authors as due to the different methods of detection of adverse effects; studies with multiple methods of detection (such as patient interview plus the conventional records review) had the highest prevalence rates.
The study estimated the prevalence rate of different age groups: children, 4.1% (IQR 0.16–5.3%); adults, 6.3% (IQR 3.9–9.0%) and elderly, 10.7% (IQR 9.6–13.3%).

Source:
The Annals of Pharmacotherapy: 2008; Vol. 42; No. 7; pp. 1017-1025

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## Assessment of the impact of clinical pharmacy in drug related problems

A multi center study was conducted in six French hospitals to document the value of clinical pharmacist interventions (PI) in the detection and correction of drug related problems, and to assess the impact and acceptance of the pharmacist´s recommendation. The sample consisted in 300 PI per hospital, a total of 1,800 PIs. Drug related problems were detected during medication order validation by a clinical pharmacist.
Over 38,000 medications orders were analyzed, leading to a PI rate of 4.66 PIs per 100 medication orders. The most common drug related problems were nonconformity to guidelines or contraindication (21.3%), improper administration (20.6%) and supratherapeutic dose (19.2%). The rate of physicians' acceptance of the pharmacist´s recommendation was 73.4%, in 15.3% of the cases the physician refused to accept the pharmacist' recommendation and 11.3% of the responses could not be evaluated.
This study exemplifies that value of a pharmacist based validation of medication orders, especially when it is done with good communication and in coordination with the rest of the health team.

Source:
The Annals of Pharmacotherapy: 2008; Vol. 42; No. 7; pp. 1095-1103

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## Increase in strength for warnings of fluoroquinolones

FDA added a black box warning for tendinitis and tendon rupture associated with the use of fluoroquinolones. Furthermore, a Patient Medication Guide will have to be dispensed with these medicines.
The agency is strengthening this warning, present in the labeling information since 1995, due to the lack of a decrease in the reports of this adverse effect, which could be prevented with an appropriate patient risk-benefit assessment and avoiding unnecessary treatments. This adverse effect presents most frequently in patients over 60 years of age, receiving concomitant corticoid therapy and/or transplant recipients.
Public Citizen petitioned to the FDA this measure in 2006. After two years of inaction from the FDA, Public Citizen started legal actions against the agency, which finally decided to accede to the petition.

Source:
http://www.fda.gov/cder/drug/InfoSheets/HCP/fluoroquinolonesHCP.htm
http://www.citizen.org/publications/release.cfm?ID=7453

## EMEA withdrew an indication of norfloxacin

The European Medicines Agency finished a review of oral formulations containing norfloxacin for the treatment of chronic or acute complicated pyelonephritis. The agency concluded that there is not enough evidence to support the use of oral norfloxacin for this indication, and recommends to switch patients to other oral or parenteral fluoroquinolones.

Sources:
http://emea.europa.eu/pdfs/human/press/pr/38026008en.pd
http://emea.europa.eu/pdfs/human/press/pr/Q&A_Norfloxacin_37886708en.pdf

## Suspected serious adverse effects of montelukast

FDA is evaluating a possible link between the use of montelukast and behavioral changes, suicidality and suicide. The agency is analyzing available studies and post marketing information and estimates that the report will be published in about nine months.
Montelukast is a leukotriene receptor antagonist used to treat asthma, symptoms of allergic rhinitis and to prevent exercise-induced asthma.

Source:
http://www.fda.gov/cder/drug/early_comm/montelukast.htm
WHO Drug Information, Volume 22, Number 2, 2008

## Worst Pills requests the FDA to withdraw propoxyphene medicines

The medicines section of Public Citizen, an important nonprofit consumer advocacy organization of the EEUU, requested the FDA to withdraw the marketing authorization of all medicines containing the propoxyphene in 2006. Due to the complete silence of the agency on this subject, Worst Pills is suing the medicines agency in order to force a resolution.
The organization argues that propoxyphene is no more effective than safer alternatives and has been associated with more than 2,000 accidental deaths in America since 1981. Propoxyphene was withdrawn from the UK in January 2005 after an evaluation of the Committee on the Safety of Medicines. This work group stated that the efficacy of this drug was not well established, couldn´t find a sub group of patients with a positive risk-benefit profile, and the risk of toxicity due to overdose was unacceptable.

Sources:
http://www.citizen.org/publications/release.cfm?ID=7420
http://www.citizen.org/documents/FDAComplaint1.pdf

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## European agencies warn about two cases of progressive multifocal leukoencephalopathy with natalizumab

EMEA and several other agencies have launched a warning on natalizumab. The warning is motivated by the report of two confirmed cases of progressive multifocal leukoencephalopathy (PML) in patients with relapsing-remitting multiple sclerosis treated for over one year with natalizumab only. This medicine, commercialized in 2006, had two pre-marketing reports of PML when used in combination with beta-interferon, which led to contraindicating the simultaneous use of these two medicines.
EMEA is reviewing all available information and requesting health professionals to report all suspected cases of PML in patients treated with natalizumab. If PML is suspected, natalizumab must be discontinued and all proper testing must be performed.
PML is a sub acute evolving CNS disease caused by the reactivation of JC virus, predominantly in immunocompromised patients. PML usually leads to severe disability or death.

Sources:
http://www.agemed.es/actividad/alertas/usoHumano/seguridad/natalizumab-agosto08.htm
http://www.emea.europa.eu/humandocs/PDFs/EPAR/tysabri/42455408en.pdf

# The Role of the Pharmacist

Medicines, as an indispensable component of health care, are part of the essential right to health.
Nevertheless, medicines are linked to economic factors, pressures and interests, even though medicines are considered social goods. For example, consider that the pharmaceutical industry billed over 602,000 million dollars in 2005 (1), and in some Latin American countries pharmaceutical expenditures are above 20% of the total health expenditure (2).
This is the reason why PAHO/WHO, in its medicines strategy, places access inside the frame of right to health but strongly connected to rational use. Access without rationality is not a strategy that benefits the health of the population in a frame of equity. As a global example, approximately the 15% of the global population consumes over the 80% of medicines and the 85% of population (Asia, Africa, Latin America, and Eastern Europe) consumes the rest, which is below 20% (2). An abundant availability of medicines is far from being a recommendable policy. Such situation leads to an over-utilization by a sector of the population accompanied by an infra-utilization by the poorer sectors. In addition, it is impossible to guarantee that in this scenario that medicines will be used using the criteria of efficacy, safety, convenience and cost-effectiveness. States must assure access to essential medicines, with a guaranteed quality and under a rational use policy.
The selection of medicines, far from being a restrictive activity, is a resource to rescue from the "flood" of molecules those that have a superior and adequate profile of efficacy, safety, convenience and better comparative cost. Selective financing of medicines is the necessary complement of a rational pharmaceutical use policy.
There is a process that begins with the selection of a medicine and finishes with the use of the medicine by the patient. This process includes committee of pharmacotherapeutics, the prescribing physician or dentist, the dispensing pharmacist and the final consumer. The pharmacotherapy of hypertension, described by Vicente Ortún Rubio, gives us an example of what happens along the different steps of this process. Antihypertensive medicines lose over 70% of their effectiveness when used by the population compared with the efficacy evidenced in the clinical trials. This occurs due to errors that propagate through this chain, such as inaccurate diagnosis, prescription errors, incorrect interpretation of the treatment, presence of adverse effects and adherence. In regard with the previous example, despite the efficacy evidenced in clinical trials, a high percentage of hypertensive patients do not have their arterial pressure controlled, despite receiving their treatment.
In the frame of medicines as social goods and the medicines utilization process, the community- and hospital pharmacist performs an important role in supporting the adequate use of medicines and the achievement of therapeutic goals. The use of medicines implies not only the expected beneficial effect, but also potential adverse effects or, even more frequent, problems related to the administration of the medicine to the patient. The pharmacist, an expert in medicines and the most accessible health agent by the patient, has a fundamental role in the implementation of measures for the resolution of medication problems. The pharmacist is who, by means of his knowledge and professional field, masters the administration of medicines, the aspects of management and storing, quality, dispensation with information, pharmacotherapeutic counseling and pharmaceutical care. Specific university training is required for these activities; otherwise valuable opportunities to intervene in the therapeutic benefit of the patient are lost.
In particular, "Pharmaceutical Care" is not related to the services that the pharmacist offers every day, but the conjunction of professional practices and standards that collaborate to achieve the pharmacologic and non pharmacologic therapeutic goals.
The role the pharmacist has been evolving around the world and several documents of WHO have discussed those changes. In 1988, the WHO consultative group gathered in Nueva Delhi elaborated the document: "The Role of the Pharmacist in the Health Care System" (3), some years later it was revised by the WHO second meeting in Tokyo, 1993. This last group elaborated the document "The Role of the Pharmacist: Quality pharmaceutical services – benefits for the governments and the public" (4), where the group defined the term "pharmaceutical care" as the professional practice committed with the achievement of defined therapeutic goals related to the patient´s health and quality of life. The document recommends governments, authorities and national or international organizations, including WHO, to support the concept of pharmaceutical care and adopt policies to promote it. The document highlights, among the recommendations for the achievement of this objective, the importance of a satisfactory pharmaceutical service, carried out or supervised by pharmacists, in the community and in hospitals.
The WHO member states would reach a definitive consensus in 1994, through the resolution WHA 47.12: "Role of the pharmacist in support of the WHO revised drug strategy" (5). This resolution recognizes "…that the pharmacist can play a key role in public health and particularly in the field of Medicines…", and states "…Concerned about the continued poor state of development of pharmaceutical services in many countries…". The resolution also calls upon pharmacists and their associations "…to promote, in collaboration with other health professionals, the concept of pharmaceutical care as a means of furthering the rational use of drugs and of actively participating-

in illness prevention and health promotion…" and urges member states, among other things, "…to make full use of the expertise of the pharmacist at all levels of the health care system…"

The relevant participation of the pharmacist is confirmed in these recommendations, along with his responsibility over the management of supplies, the provision of good quality medicines, adequate storage, preparation and dispensation. The role of the pharmacist in patient counseling, information to health professionals, participation in pharmacovigilance programs and as a collaborator inside the health team participating to resolve problems related to the use of medicines is also reassured.

These recommendations have been reaffirmed and expanded in successive documents of the WHO consultative groups: "The Role of the Pharmacist in the Health Care System" (6) Vancouver, 1997; and "The Role of the Pharmacist in Self-Care and Self-Medication" (7) The Netherlands, 1998.

WHO´s most recent document, the manual "Developing pharmacy practice: A focus on patient care" (8) was developed in collaboration with FIP in 2006 and with the support of the Department of Pharmaceutical normative and Technical Cooperation in Essential Medicines and Traditional Medicines of WHO. The manual describes and develops the twist in pharmaceutical professional practice, focusing in the responsibility over the patient: The introduction highlights that pharmacists, by taking direct responsibility over the needs related with the use of medicines, can make a particular contribution to the patient´s pharmacotherapy and quality of life.

A rigorous normative on the presence of the pharmacist in the establishments exists in countries as the United States of America. Even more, pharmacists working in some pharmacy chains participate in monitoring programs of patients with chronic diseases such as diabetes.

The recognition of the role of the pharmacist in relation with public health is even more advanced in other countries such as Great Britain. The Report N° 246, July 2005, of The Parliamentary Office of Science and Technology, "Changing role of pharmacies" (9), developed categories of medicines under pharmaceutical supervision. The report highlights the benefits of this practice, especially in chronic diseases, in which pharmacists can refill the initial prescription or interact with the patient in regard with modifications of the pharmacotherapy (the documents cites a shared monitoring intervention; in this experience the collaboration of pharmacist and physician reduced the number of hospital readmissions of patients with type 2 diabetes, compared to physician-care only).

Beyond these proposed "advanced" competencies, the importance of protecting the professional management of medicines until these (and even later) reach the hands of the patient is clear. As we have mentioned before, the adulteration and counterfeit of medicines, dispensation errors, - inadequate storage, counseling without proper knowledge, impossibility to answer basic problems in the interaction between the patient and the pharmaceuticals, and other undesirable situations occur more often in the absence of professional staff.

This document summary tries to show how incorporating pharmacists as a true component of the health team, trough the acquisition of responsibility over the patient represents a positive change in achieving better control and rational use of medicines. This approach, which is supported by WHO, tries to stimulate countries to take advantage of pharmacists, adding value to the supply chain, from the prescription to the use of medicines. This progress in the management of medicines requires the commitment of all the actors involved, sanitary authorities, universities, professional associations, consumer associations, etc. The cooperation of the actors is vital to achieve the dynamics necessary for the education of human resources, the integration of the pharmacists in working groups and in the health systems, and the coordination among all of them.

## References

(1) **Global Pharmaceutical Sales, 1998 – 2005,** IMS Health Total Market Estimates and Global Pharma Forecasts 2005.

(2) **WHO Medicines strategy: Countries at the Core 2004-2007**; World Health Organization 2004

(3) **The Role of the Pharmacist in the Health Care System**; Report of a WHO consultative group; Nueva Delhi, India. 13-16 December 1988.

(4) **The Role of the Pharmacist: Quality pharmaceutical services – benefits for the governments and the public**; WHO second meeting, Tokyo, Japan. 31 August-3 September 1993.

(5) **WHA47.12 Role of the pharmacist in support of the who revised drug strategy**, The forty-seventh World Health Assembly, Twelfth plenary meeting, 10 May 1994 - Committee A, second report.

(6) **The Role of the Pharmacist in the Health Care System; Preparing the Future Pharmacist: Curricular Development**. Report of the third WHO consultative group on the role of the pharmacist; Vancouver, Canada, 27-29 august 1997.

(7) **The Role of the Pharmacist in Self-Care and Self-Medication;** Report of the 4th WHO Consultative Group on the Role of the Pharmacist; The Hague, The Netherlands, 26-28 August 1998.

(8) **Developing pharmacy practice: A focus on patient care**. World Health Organization and International Pharmaceutical Federation, 2006.

(9) **Changing role of pharmacies;** Postnote**,** July 2005 Number 246, The Parliamentary Office of Science and Technology, UK.

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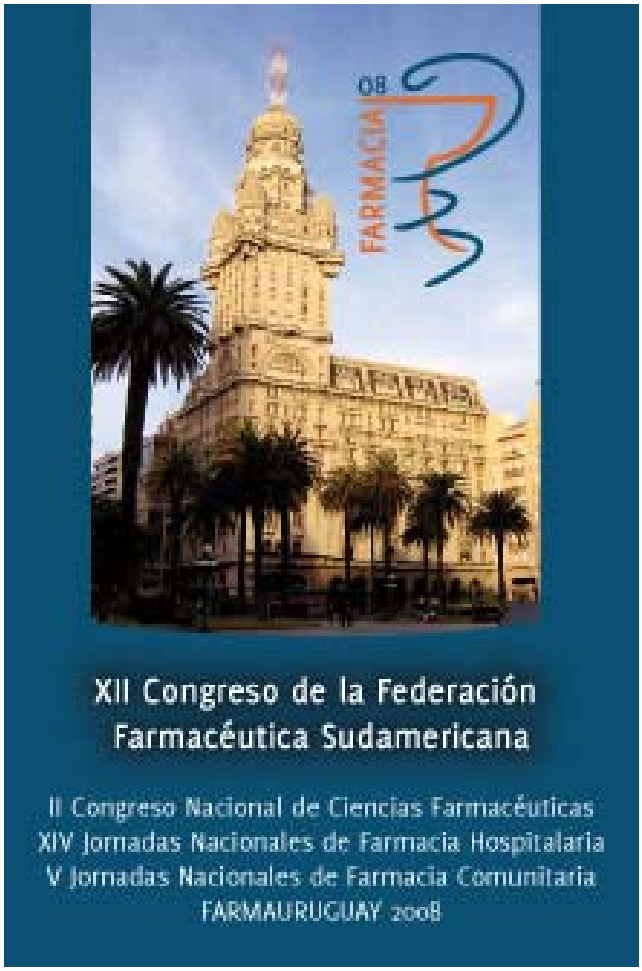
## Rimonabant was withdrawn in Europe

The Committee for Medicinal Products for Human Use (CHMP) decided to withdraw the marketing authorization of rimonabant, after the assessment of its psychiatric adverse effect (the incidence in the community is estimated to double the incidence shown in clinical trials) and its effectiveness (lower in actual clinical practice than in clinical trials).
EMEA communicated in July changes in the patient information leaflet of rimonabant, which highlighted the psychiatric adverse effects, which include low mood, depression and suicidal thoughts.
Rimonabant included information on psychiatric events since its authorization in 2006. In July 2007 EMEA set a contraindication for patients with major depressive disorders and patients receiving antidepressants. Rimonabant was approved in Europe as "an adjunct to diet and exercise for the treatment of obese patients (BMI≥30kg/m2) or overweight patients (BMI>27kg/m2) with associated risk factors as diabetes type 2 or dyslipidemia", but was rejected by the FDA.
After the announcement, several Latin American countries, as Argentina, Mexico and Colombia, followed the decision of the European agency.

Sources:
http://www.mhra.gov.uk/Safetyinformation/index.htm
http://www.agemed.es/actividad/alertas/usoHumano/seguridad/acomplia-julio08.htm




# Congresses and Meetings

### VI CONFERENCIA PANAMERICANA DE EDUCACIÓN FARMACÉUTICA

19 al 21 de noviembre de 2008
Sala Conference - Radisson Victoria Plaza Hotel

**Pharmaceutical education in America is responsible for the training of pharmacy students, including the acquisition of skills and knowledge, for their initial professional practice and their insertion in the health team as vital members. The Pan American Conference on Pharmaceutical Education have been taking place since 1990 every three years, to promote the cooperation among the Associations, Universities and Pharmacy departments of America.**

**Main topics of the Conference:**
**Accreditation, Education on Good Pharmacy Practice, Pharmaceutical Care and Rational Drug Use**

**The Proposal for the Latin American Accreditation will be discussed during the conference.**

**More information: http://www.fefas.org/paginas/vi_conferencia.html**
**Languages: Spanish and English, with simultaneous translation**

## Contact Information

Fernando Scarcella
Junín 956, Post Code 1113, Department of Pharmacology, 5th floor School of Pharmacy and Biochemistry, University of Buenos Aires, Argentina

Email: medicamentos@ffyb.uba.ar



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