V PAN AMERICAN CONFERENCE ON DRUG REGULATORY HARMONIZATION

Buenos Aires, 17 - 19 November 2008

Preliminary Report, Conclusions and Recommendations

V CONFERENCE OF THE PAN AMERICAN NETWORK FOR DRUG REGULATORY HARMONIZATION (PANDRH)

REPORT ON ACTIVITIES WITH CONCLUSIONS AND RECOMMENDATIONS

AGENDA

16 November
5:00 to 7:00 p.m. Registration of participants

17 November
8:00 to 9:00 a.m. Registration of participants

9:00 to 9:30 a.m. **Opening Session**
Remarks by the national authorities and PAHO/WHO.

9:30 to 10:00 a.m. **Regulation and Public Health. Video of Dr. Mirta Roses, Director of PAHO/WHO**

10:00a 10:30 a.m. **PANDRH Operational Guidelines.** Secretariat, PAHO/WHO

10:30a 10:45 a.m. *Break*

10:45 to 12:30 a.m. **Panel on Drug Regulatory Harmonization Initiatives**

Coordinator: Drug Regulatory Authority of Colombia

ICDRA: Dr. Lembit Rägo (WHO); ICH: Dr. Justina Molzon (FDA); PANDRH Network: Dr. José Luis Di Fabio (PAHO/WHO); ASEAN: Dr. Selvaraja Seerangam (Ministry of Health of Malaysia)

12:30 to 2:00 p.m. *Luncheon*

2:00 to 2:45 p.m. **System for Recognition by Regulatory Authorities**
Dr. Rafael Pérez Cristiá, CECMED-Cuba and Dr. José Peña, PAHO/WHO

2:45 to 4:15 p.m. **Presentation of Progress Made by Working Groups (WG).**
Coordinator: Drug Regulatory Authority of Costa Rica
Bioequivalence (BE): Dr. Justina Molzon (FDA, USA), Dr. Ricardo Bolaños (ANMAT, Argentina), Dr. Silvia Giarcovich (ALIFAR, Argentina). Pharmacovigilance (FV): Dr. Rubiela Méndez (INVIMA, Colombia), Dr. Claudia Vacca, (UNAL, Colombia). Vaccines (V): Dr. Olga Lidia Jacobo (CECMED, Cuba).

4:15 to 5:30 p.m. **Break and WG Discussion Tables**

5:30 to 6:30 p.m. **PANDRH session**

18 November

8:30 to 9:15 a.m. **Essential Functions of Drug Regulation and Challenges for Regulatory Authorities.** Dr. José Luis Di Fabio, PAHO/WHO

9:15 to 09::45 a.m. **Drug Counterfeiting as a Public Health Problem.**
Dr. Valerio Reggi, WHO

09:45 to 10:15 a.m. **WHO Prequalification System.** Dr. Lembit Rägo, WHO

10:15 to 10:45 a.m. *Break*

10:45 to 12:30 p.m. **Presentation of the Progress made by Working Groups Coordinator: Drug Regulatory Authority Argentina**
Registration of medication (MR): Dr. María Teresa Ibarz (INHRR, Venezuela). Good laboratory practice (GLP): Dr. María Gloria Olate (ISPCH, Chile). Counterfeit drugs (FM): Dr. Tiago Rauber (ANVISA, Brazil).

12:30 to 2:00 p.m. *Luncheon*

2:00 to 3:30 p.m.. **Presentation of Progress made by Working Groups. Coordinator: RNA Jamaica**
Good clinical practice (GCP): Dr. Analía Pérez (ANMAT, Argentina). Drug promotion (PM): Dr. María José Delgado (ANVISA, Brazil). Good Manufacturing Practices (GMP): Dr. Justina Molzon (FDA, U.S.), Dr. Rodolfo Mochetto (ANMAT, Argentina), Dr. Rosalba Alzate de Saldarriaga (Consultant, PAHO/WHO)

3:30 to 4:30 p.m.. **Break and Working Group Roundtables**

4:30 to 6:30 p.m.. **PANDRH Session**

19 November

8:30 to 9:00 a.m. **Rational Drug Use as a Component of Regulatory Decisions**
Dr. Perla de Buschiazzo, CUFAR, PAHO/WHO Collaborating Center, Argentina.

9:00 to 10:30 a.m. **Roundtable - Biotechnological Biologic Products Coordinator: Dr. María Ángeles Cortes Castillo, PAHO/WHO**
PAHO/WHO: Dr. Maria Luz Pombo, ALIFAR: Dr. Néstor Anníbali, FIFARMA: Dr. Lucas Marletta, Canadian Regulatory Agency (Health Canada): Dr. Elwin Griffiths

10:30 to 11:00 a.m. *Break*

11:00 to 12:30 a.m. **Panel on Progress Made in Integrating PANDRH's Recommendations into Regional Integration Processes. Coordinator: Drug Regulatory Authority of Brazil**

MERCOSUR, ANDEAN COMMUNITY, CUSTOMS UNION, CARICOM

12:30 to 2:00 p.m.. *Luncheon*

2:00 to 4:00 p.m.. **Conclusions and Recommendations**

4:00 to 4:45 p.m.. **Closing Session** ANMAT, PAHO, ALIFAR, FIFARMA, Directing Council of PANDRH

MINUTES OF THE MEETING

OPENING SESSION

The opening was chaired by Dr. Ricardo Martínez, Director of Argentina's National Administration of Drugs, Food, and Medical Technology (ANMAT) and Dr. José Antonio Pages, PAHO/WHO Representative in Argentina.

Remarks of the National Authorities and PAHO/WHO

The opening remarks were delivered by Dr. Ricardo Martínez who, on behalf of ANMAT, welcomed all participants to the V Conference of the Pan American Network for Drug Regulatory Harmonization, emphasizing PAHO/WHO's efforts to support the drug regulatory harmonization initiative. He invited participants to discuss and debate the subjects in a positive spirit. He recognized PANDRH's operations as a means to help ensure quality, safe, and effective drugs. At the end of his remarks, he wished everyone a happy stay in Buenos Aires and conveyed the greetings of Dr. Ocaña, Argentina's Minister of Health. She predicted this meeting would have its eyes on a much brighter future.

For his part, Dr. Pagés offered special thanks to the Government of Argentina for the opportunity to hold the meeting in Buenos Aires. He welcomed the participants to the Conference as PAHO/WHO Representative in Argentina, and on behalf of our Director, Dr. Mirta Roses. He especially welcomed Dr. Ricardo Martínez, Director of ANMAT, together with the officials from other institutions.

Dr. Pagés emphasized PAHO's role as Secretariat of the network and recognized the work of Dr. Rosario D'Alessio in her excellent performance overseeing its activities. He welcomed Dr. José Luis Di Fabio, and all the PAHO and WHO colleagues attending the Conference. He thanked the Government of Argentina for providing the opportunity to hold the meeting in Buenos Aires. In his presentation Dr. Pagés reported on the network's achievements and challenges, stating that access to drugs is a fundamental human right and noting the importance of constructive dialogue among all regulatory entities in our countries, the pharmaceutical industry (public and private), and other related sectors. He pointed out that one of the most important goals for Pan American countries is developing cooperation among countries, and in particular strengthening South-South cooperation. Promoting drug regulatory harmonization requirements among our countries is an excellent example of solidarity and cooperation. He concluded by saying that at this meeting, the challenges will be reviewed and addressed in a discussion of imaginative alternatives that go beyond strengthening partnerships and implementing joint plans to continue this successful work, which clearly strengthens health services for our peoples.

Regulation and Public Health. Video of Dr. Mirta Roses, Director of PAHO/WHO.

In this 10-minute video, Dr. Roses discussed the matter in the context of the Essential Public Health Functions, with special mention of Function No. 6 and public health regulation and control. She emphasized PAHO's role in strengthening the governance of the national regulatory authorities. She presented a brief overview of the development of PANDRH and the benefits of its activities, emphasizing that true to the principle of Pan-Americanism, the most developed drug regulatory authorities have helped to mentor the less developed ones. She concluded her presentation

wishing for a highly productive and constructive conference with the intensity and dedication that Dr. Rosario D'Alessio knew how to provide from the first convocation.

PANDRH Operating Guidelines

Next, Dr. Nelly Marín, on behalf of the PAHO/WHO Secretariat, presented the PANDRH operating guidelines and the methodology for the organization of the V Conference. During her talk, she presented a historical summary of PANDRH, its members, and objectives.

She pointed out that although participation in the previous conferences had focused on the authorities, industry representatives, academia, and consumer advocacy representatives, for the V conference, in a session of the Directing Council, approval was given to expand participation to include international agencies, harmonization mechanisms, sub regional integration systems, and NGOs accredited with PAHO, in order to achieve greater dissemination and ownership of the documents and work agreements.

She presented an overview of the Conference's agenda and explained that there would be two types of activities:

Conferences, roundtables, and presentations by the Working Groups (WGs) in which all members would participate.

Networking sessions, which would be held at the end of the afternoon on Monday and Tuesday, in which only these members would participate: national regulatory authorities, ALIFAR, FIFARMA, and the Secretariat.

At the end of the Conference, a spokesperson would present a report with the main conclusions and the general proposals approved.

Each WG coordinator would submit a report on the principal decisions adopted.

Discussion Panel: Initiatives in Drug Regulatory Harmonization

Four harmonization systems from different regions were presented – ICDRA, ICH, PAHO/WHO-PANDRH, and ASEAN – to understand their dynamic, scope, strengths and accomplishments, and identify opportunities for mutual feedback. A summary of the experiences cited is presented.

International Conference of Drug Regulatory Authorities (ICDRA). Dr. Lembit Rägo

DR. Rägo pointed out that the International Conference of Drug Regulatory Authorities (ICDRA) is an annual WHO conference in which regulatory staff members of all WHO member states participate, as well as regional advisors of the technical programs in WHO Regional Offices: AFRO, AMOR, EMRO, EURO, SEARO, and WPRO.

The conferences have been held since 1980 to promote the exchange of information and collaboration among authorities on matters of mutual interest.

As ICDRA is an environment restricted to the authorities, the implications and importance of accomplishing the recommendations has shown that it is necessary to involve other stakeholders.

In order to delve deeper into priority issues, pre-conferences open to all stakeholders have been organized. The criterion used to select topics is based on whether they represent public health interest, the dynamic of the market. Recommendations from these conferences are presented to WHO. With the results and recommendations, interventions are promoted to address the relevant regulatory issues.

The 13th ICDRA Conference was held in Berne in September 2008 and the subject of the pre-conference was "Better Medicines for Children: The Way Forward." The recommendations presented to WHO as a result of this pre-conference were: Convene and collaborate with the global working group on pediatric drug regulation; work with civil society to mobilize and empower consumers, parents, patient groups, and health professionals to advocate improved drugs for children; focus on the high-priority needs with attainable results, including: zinc for diarrhea; treatment of pneumonia; neonatal sepsis; treatment of HIV, TB, malaria, analgesia; drugs for chronic diseases in children; steps to identify treatment priorities and guidelines for newborns; establish mechanisms to support the development of essential new drugs for children.

In the conference's plenary sessions, the progress made in each WHO region since the previous meeting was presented, and these topics were developed: Forging mutual trust as a key for access; Regulatory systems in a changing environment; Crisis management of crises: Safeguarding health and current issues

Workshops were also held on the following subjects: Regulatory aspects of pediatric drugs; Regulations for herbal medicines; Safety and preparation in the case of pandemics; Regulatory approaches to verify interchangeability; Strategies to combat drug counterfeiting; Emerging regulatory aspects on biosimilars and biologics; Emerging diseases: blood derivative regulation; Contribution of the regulatory authorities to access; Updating harmonization initiatives; Role of the regulatory authorities in approval of pivotal clinical studies; Creating regulatory capacity: Best practices for the future, and GMP inspections: impact of sharing information and risk management.

Dr. Rägo also pointed out that during the ICDRA work sessions, retrospective analyses are made, the concrete achievements and results (based on monitoring) of the agreements and recommendations of each previous conference are evaluated. He concluded by reiterating the need for regulatory authorities to have a suitable structure that makes it possible for them to better channel resources, and commented that both the conference report and the pre-conference report have been uploaded on the website and are in printed version and that the next conference will be held in Singapore in 2010.

Evolution of the International Conference on Harmonization (ICH). Dr. Justina Molzon (FDA)

Dr. Molzon presented an overview of the International Conference on Harmonization (ICH) – a harmonization initiative between Europe, the United States, and Japan. It was created in 1990 with a view to harmonize the different regional requirements existing on drug registration. Canada, European Free Trade Association (EFTA), and

WHO participate as observers in the ICH. It is a unique experience due to the joint effort of the regulatory authorities and the pharmaceutical industry associations.

Dr. Molzon pointed out that the ICH has produced harmonized directives in different subjects: 16 on effectiveness, 16 on safety, 24 on quality and two multidisciplinary communications – Medical Dictionary (MedDRA) and Electronic Standards (ESTRI, E2B).

She then gave an overview of the 1996 proposal from industry representatives to organize the information generated by these harmonized directives in exactly the same order in all countries; at first the proposal had little reception by regulatory authorities in each country, and they required that a feasibility study be conducted to justify such a request.

The industry conducted the study to determine the number of weeks that it would take to convert a request that had been presented to one regulatory authority, for example, the FDA, to be presented to another regulatory authority, for example, EMEA. The number and type of personnel required for the conversion were also evaluated. The study's results showed that it would take significant investments of time and energy to reorganize the roles for the presentation of a request in the format of one ICH region to another one, that this caused a delay in the request for that ICH region, which meant for patients in that region, there was a delay in access to new innovative drugs.

From there the initiative of the Common Technical Document (CTD) emerged. This initiative incorporated a change in work dynamic, which is regarded as progress. Initially the ICH process focused on the directives through discussions between regulators and industry, trying to standardize a common directive format. This dynamic has changed and now focuses on the definition of production of supplies for review.

Dr. Molzon reported that, from the FDA's perspective, adoption of the CTD has brought multiple benefits, revisions are more coherent, uniform, there is better analysis between requests in the same therapeutic category and a more fluid exchange between regulatory authorities and reviewers.

The FDA implemented an "Electronic Submission Gateway" so requests can be sent electronically, which has been critical for improving efficiency, the material to be reviewed arrives promptly to the reviewer, FDA processes have been automated through the use of electronic forms that can be filled out online, promoting the paperless review.

It helps promote adoption of good review practices and selectivity, including only data worth presenting and requesting only useful information.

It promotes transparency and facilitates electronic communication and thus system management.

It has helped the FDA implement good review practices (GRPs). A great deal of similarity between the ICH documents and the GRPs. Due to the complexity of the various disciplines involved in the review, there should be GRPs to review the different products, with harmonized formats. Having a common style and a common plan for review will help regulatory authority personnel, the industry, and the public

understand the data review process for interpretation, recommendations and decisions, and for subsequent regulatory actions.

In summary, the CTD influences the content of the review, giving consistent order to the information and data provided. It gives shape to the realization of the review and to the presentation of the review results. The consistency of the CTD will promote consistent review practices that lead to GRPs. As more countries use the ICH directives and the CTD, a common regulatory language will evolve that promotes greater interaction among drug regulatory authorities.

Pan American Network for Drug Regulatory Harmonization (PANDRH)
Dr. José Luis Di Fabio (PAHO)

Dr. Di Fabio thanked Argentina's Ministry of Health and the ANMAT group and PAHO Argentina. He acknowledged Dr. Enrique Fefer, who first envisioned the PANDRH Network.

The Pan American Network for Drug Regulatory Harmonization (PANDRH) is made up of the national drug regulatory authorities of 35 member states and representatives of FIFARMA and ALIFAR as well as the regional pharmaceutical industry associations in the Americas. Its mission is to promote the harmonization of all aspects of drug regulation – quality, safety, and efficacy – as a contribution to the quality of life and health care of the national populations in the Americas.

PAHO gets involved in this process under the WHO mandate that grants authority in management and coordination of international health work in development, establishment, and promotion of international standards on biologics, drugs and similar products. Also, the Pan American Sanitary Conference states that PAHO shall support the implementation of essential drug policies encompassing legislation and regulation, production, promotion, use, and financing of drugs. Through Resolution of the 42nd Directing Council of PAHO (September 2000), the Ministers of Health of the Region of the Americas support the Pan American Network for Drug Regulatory Harmonization (PANDRH).

He added that the network establishes a Pan American forum of national drug regulatory agencies in the Region to discuss and identify solutions to common problems, as the agencies themselves will lead and participate in the process. The network strengthens the setting of priorities in drug regulatory harmonization processes and aspires to the convergence of regional drug regulatory systems. It improves access to quality, safe and effective drugs to improve the quality of the pharmaceutical markets. It promotes technical cooperation where the more developed regulatory authorities support and share their experience with the less developed authorities.

Dr. Di Fabio stated that harmonization as a policy of cooperation among countries in the Region of the Americas is one of the oldest strategies in the search for solution to common problems. It was, in fact, a joint effort among countries that gave rise to the Pan American Sanitary Conference. For years the countries were organized in different economic blocs (Andean Area, Central America, Southern Common Market (MERCOSUR), CARICOM, and later, the North American Free Trade Agreement (NAFTA). These sub regional initiatives are changing with the incorporation of various countries in other initiatives. All these initiatives arise from the countries'

interest in improving and strengthening consumer markets, including the drug market; which means that they include subgroups or commissions to discussion technical subjects that were initially limited to tariff issues but that later addressed the issue of quality. Today these groups also discuss drug policy-making, its implementation and monitoring. The degree of development of these commissions or subgroups varies widely, as well as PAHO's participation in them. In light of these various economic integration initiatives, the need became evident for an entity in which the different countries of the Region, based on the Pan American principle that historically unites them, share experiences and countries could benefit from the work of initiatives that are different in each country.

In addition to these initiatives, there are other more regional ones as well, but none include all the countries of the Americas: bilateral or multilateral agreements: usually economic accords that integrate only countries that are part of them and that may or may not include pharmaceutical products.

The Pan American Conference on Drug Regulatory Harmonization has become the forum that, based on Pan-Americanism/cooperation in the Region, is coming to fill that gap in the sharing of experiences and strengthening of regulatory authorities, especially drug regulation policies. The Pan American conferences started in 1997 and since then four conferences have been held. The Network as such was established in the second conference in 1999.

He explained the structure of the Pan American Network, which includes four components:

- The conference, held every two of three years, is the highest authority of the Network since the decisions to adopt technical documents and subjects to be addressed are made with the participation of all the drug regulatory authorities of PAHO member countries. The conference is also a forum in which representatives from the two regional pharmaceutical industry associations (FIFARMA and ALIFAR) participate, as well as consumer advocates, academia, and members of professional associations. Up until now, attendance at these conferences has been by invitation only, but in the statutes there are provisions to open the conferences to interested public;

- The Steering Committee made up of five drug regulatory authorities (DRAs) and five alternates as well as a representative from each of the two previously mentioned regional pharmaceutical industry associations;

- The Secretariat, performed by PAHO; and

- The working groups, made up of national experts in specific subjects assigned by the conference. These experts are mostly from the regulatory offices in representation of the five economic integration blocs in the Region, and also from academia and one from each of the two industry associations.

The network operates from the base (the working groups) toward the top (the conference). It is presumed that the conclusions and recommendations, as well as the technical documents adopted, are in turn internalized both at the national level and in the different sub regional initiatives in which the DRAs participate. The conference is not a supranational entity; its decisions represent recommendations to be assimilated into the sub regional integration initiatives.

This new phase of the network calls for various changes in the statutes, at the levels of the conference, the steering committee, the working groups and changes in the functions of the Secretariat, its active role in monitoring the working groups, the steering committee, and implementation of targeted actions. Due to the industry's active participation in this conference, it became necessary to create opportunities for a "closed" meeting of the PANDRH network for decision-making.

Many documents have been approved and it is hoped to that others will be in the present Conference. It is necessary to identify mechanisms for their implementation.

Association of Southeast Asian Nations (ASEAN) Dr. Selvaraja Seerangam. National Pharmaceutical Control Bureau. Ministry of Health, Malaysia

Dr. Seerangam presented an overview of the Association of Southeast Asian Nations (ASEAN), which was originally established in 1967 in Bangkok as a geopolitical and economic bloc with five member states: Indonesia, Malaysia, the Philippines, Singapore, and Thailand. Between 1984 and 1999, more countries joined: Brunei Darussalam, Viet Nam, Lao PDR, Myanmar, and Cambodia. ASEAN's goal is to be a single market by the year 2015 with a single production base. The ASEAN Free Trade Area (AFTA) is a joint effort of this association to reduce or eliminate tariffs on the exchange of products. AFTA's objective is above all to coalesce its position as a competitive production base for both for regional and global markets.

In 1992 the ASEAN Consultative Committee on Standards & Quality (ACCSQ) was formed to facilitate and complement the ASEAN free trade area. The concept of drug harmonization was presented by Malaysia and approved by the Senior Economic Officials Meeting (SEOM) in 1999. The Pharmaceutical Product Working Group (PPWG) was created that same year.

The objective of the ASEAN Consultative Committee for Standards and Quality (ACCSQ) is to facilitate cooperation among the working groups of the ASEAN economic community, among the working groups for specific products, and dialogue with other related organizations.

The goal of the Pharmaceutical Product Working Group (PPWG) is to develop drug regulation harmonization plans for member countries, to complement and facilitate AFTA's objectives, in particular, elimination of technical barriers to trade presented by the regulations, without compromising product quality, efficacy and safety.

The group works to improve the exchange of available information on regulation requirements, review the requirements and regulations and conduct comparative studies, analyze other harmonized procedures and regulation systems, and establish common technical documents to accomplish MRA objectives.

He presented a historical account of the milestones in harmonization and recent developments in economic integration.

He pointed out that ASEAN's main challenges include political uncertainty, economic changes, free trade negotiations, differences in legal regulatory frameworks, public health issues, and global competition.

Global trade calls for strategic partnerships. Harmonization of standards is important to facilitate foreign trade and investment. Regional harmonization can be reached only by bridging the gaps among member countries in establishment of regulatory systems and implementation of common requirements. Global cooperation provides opportunities for development and improvements, identifying concrete mechanisms for international recognition.

The System for Recognition by Regulatory Authorities: A Strategy to Improve Public Health Dr. José Peña (PAHO/WHO)

Dr. José Peña presented the background and dynamic that this official assessment team has had. He spoke of the first Meeting of Regulatory Agencies of Latin America held in February 2006 in Oaxaca, Mexico, with the objective of strengthening the implementation of PANDRH's guidelines and recommendations and generating collaborative mechanisms among the countries of the Region. Subsequently, from September 2007 to July 2008, three meetings were held to involve the drug regulatory authorities (DRAs) in PAHO's prequalification system, define the instrument for DRA evaluation, and establish a procedure for the qualification of national reference authorities.

Dr. Peña said an instrument for prequalification of vaccines was already available in 2004, and then in 2007 the data collection tool was used to prepare a draft on drugs, which was open for public consultation, and presented at the Oaxaca meeting; this DRA evaluation tool consists of 16 modules. At the working meeting held in São Paulo in December 2007, the modules and indicators were defined that would be included in PAHO's national regulatory authorities reference drug evaluation tool. In February 2008, contributions were received from the countries to categorize the indicators as critical, necessary, and informative; comments were received until late June 2008, after that, the reclassification of indicators began. At the Mexico meeting in July 2008, with seven DRAs present, full consensus was reached on the categorization of indicators.

The indicators for the different evaluation tool modules were presented and the definitions of the indicators were explained.

In terms of the Standard Operating Procedure (SOP) for DRA evaluation, Dr. Peña commented that the SOP is applied to all DRA evaluations conducted by PAHO as a part of PAHO's DRA reference medicine qualification system.

He added that the purpose of this regulatory authority recognition system is to establish a uniform and transparent methodology for evaluating DRA performance in Latin America, in its relevant basic functions.

The DRAs that successfully pass the qualification process will collaborate as PAHO reference authorities in the discussion of strategic drug regulation issues in the Region, and when relevant, coordinate with the drug regulatory harmonization processes in the Americas, participating as reference authorities for PAHO in the prequalification of drugs, collaborate as reference authorities for PAHO in the implementation and monitoring of PANDRH-approved recommendations, establish joint strategic programs with PAHO to strengthen other authorities in the region to reach the grade of DRA reference.

In the last part of his presentation, Dr. Peña reviewed the results: the definition o a DRA evaluation tool (10 modules), the definition and categorization of indicators; the Standard Operating Procedures for evaluation of reference DRAs and selection of experts, the definition of a work program for 2009 and the commitment of the group's seven DRA members (Argentina, Brazil, Chile, Colombia, Cuba, Mexico and Venezuela). He concluded by saying that the greatest challenge of 2009 is to accomplish the evaluation of the seven DRAs.

The System for Recognition by Regulatory Authorities. PAHO/WHO Qualification: Impact on the Performance of Cuba's National Drug Regulatory Authority Dr. Rafael Pérez Cristiá

Dr. Rafael Pérez Cristiá presented the organizational chart of the Cuban regulatory system, and explained that the Regulatory Bureau for Health Protection, a dependent of the Ministry of Public Health, oversees the State Drug Control Center (CECMED), which was created in 1989 as the national regulatory authority on medications and diagnostic equipment. He presented an overview of the different institutes in the Cuban biotechnology industry and related products, and he presented the DRA's operations on vaccines, referring to a publication of WHO's Department of Vaccines and Biologics (WHO/V&B/99.10).

Dr. Pérez Cristiá then presented CECMED's regulatory functions and some general information on the experience of that entity in the PAHO/WHO evaluations and the impact of these evaluations. He described how the evaluations conducted and how corrections were incorporated to reach the qualification that they today have.

In order to apply the evaluation guidelines proposed by PAHO/WHO, CECMED organized a multi-stage plan, mainly: the creation of a central working group and subgroups for each basic function, organization of the technical and legal documentation for each basic function, the development of self-evaluation using the PAHO/WHO indicators to reach a diagnosis for each basic function; the self-identification of weaknesses and strengths and the application of immediate solutions to the findings, also defining an action plan to correct inconsistencies. A file was opened for each function with all the self-evaluation information according to the selected tools.

Dr. Pérez Cristiá then presented a summary of the objectives and results of the PAHO/WHO evaluations to CECMED and the benefits obtained from such evaluations, including the following:

Knowledge gained from the sharing of experiences by CECMED specialists and PAHO/WHO experts.
Better utilization of the basic functions.
Complete review of all processes.
List of strengths and weaknesses.
Strategies to resolve shortcomings.
Identification of training needs.
More objective institutional development plan.
Strengthened vaccine and drug regulation system.

He then described the impact of PAHO/WHO evaluations on CECMED's institutional development, pointing out the changes in organizational structure, the consolidation of CECMED as a DRA and greater governmental support for CECMED's activities,

participation of CECMED specialists in the Global Training Network and PAHO's courses for the region, and increased cooperation with PAHO/WHO and other DRAs.

He finished the presentation reporting the approval of certification of CECMED's quality management system and summarizing the participation of CECMED personnel in training courses on basic regulatory functions for vaccines and in the evaluation of other DRAs. He commended the lessons learned and ended with a series of recommendations for PAHO and the DRAs.

Presentation of the Progress of the Working Groups, coordinated by Dr. María de los Angeles Morales, Costa Rica

Bioequivalence (BE): Justina Molzon (FDA, USA), Ricardo Bolaños (ANMAT, Argentina), Silvia Giarcovich (ALIFAR, Argentina).
Pharmacogivilance (PV): Rubiela Mendez (INVIMA, Colombia), Claudia Vacca (UNAL, Colombia).
Vaccines (V): Olga Lidia Jacobo (CECMED, Cuba).

Bioequivalence (BE)

Dr. Justina Molzon presented the members of the BE working group and details on the different meetings and activities conducted by this group. The document presented by the group analyzed the active ingredients subject to requirements of bioequivalence studies in nine countries in the Region compiled from a survey to determine the reality of the situation.

The document incorporated the WHO technical recommendations that refer to the comparative product. The possible scenarios for this product were presented and it was left open to the countries to select the reference products.

The conference adopted the document: "Framework for Implementation of Equivalence Requirements for Pharmaceutical Products."

The conference recommended training to promote implementation by regulatory authorities both in the document and in bioequivalence statistics and the development of indicators to evaluate implementation of the document in the Americas.

Later Dr. Silvia Giarcovich referred to the scientific criteria for implementation of drug equivalence and the pertinent WHO documents.

Dr. Ricardo Bolaños (below) presented the strategic framework for implementation.

Pharmacovigilance (PV)

Dr. Claudia Vacca of the National University of Colombia and Dr. Rubiela Méndez of INVIMA participated in the presentation. The presentation gave an overview of the origin of the working group and the meetings held. Results and recommendations were presented on the diagnosis of the regional pharmacovigilance system of the Americas, carried out by Esperanza Briceño.

The diagnosis was presented at the meeting in Salvador de Bahia and served as a framework for the work plan of the region. It described the results of the evaluation and the mission and objectives that the working group had agreed upon.

José Luis Castro of PAHO was commended as technical secretariat.

The presentation described the dynamic developed to produce the technical proposal and also the objective and contents and structure of the document proposed for discussion.

The structure of the document was presented: a description of pharmacovigilance in the context of drug use; good pharmocovigilance practices to set up a center, from materials to operation; good practices to analyze and manage the risks identified in the system and their communication.

Tasks and responsibilities of pharmacovigilance agents.

Vaccines (V)

Dr. Olga Lidia Jacobo submitted the background documentation on the Vaccines Working Group's meetings and activities, summarized below:

(June-November 2005) Survey on requirements for vaccine registration. Surveys were sent to 19 countries, and responses were received from 16 DRAs.

(December 2005) Second working-group meeting in Caracas to present and analyze survey results.

(April 2006) A first draft of the requirements and an industry guide with details of the information to present, taking into account the elements defined by the Working Group and the WHO and ICH recommendations.

(June 2006) Third working group meeting in Ottawa, the draft of the document and the guide were discussed.

(Beginning in July 2006) Review of the documents and comments compiled. Tailoring of document and guide. Translated into English and French.

(April-June 2008) Submitted to public opinion review through mass media. Posted on websites of PAHO, WHO, and Health Canada. Sent to industry representatives.

(October 2008) A meeting was held at PAHO/WDC with DRAs and the industry participants in public opinion to review all the observations in the discussion process. Glaxo, Pasteur, and ICFA participated.

The document was updated and sent to meeting and conference participants.

The proposals submitted to the V Conference are:

Proposal of harmonized requirements for vaccine registration in the Region of the Americas.

Guidelines for preparation of request for Health Registration

Current work

Presentation of documents for their approval at the V Conference
Official publication
Implementation stage
Training workshop for implementation
Evaluation of adoption of the document by the DRAs

Work objectives for 2009
Promote the sharing, convergence, and recognition of the vaccine regulation systems among DRAs of the region.
Product of public consultation. Develop a mechanism for recognition among the regulatory agencies of the Americas to inspect vaccine production in compliance with Good Manufacturing Practices.
Development of inspection guidelines for vaccine producers to adhere to Good Manufacturing Practices.

Essential Functions of Drug Regulation and Challenges for the Regulatory Authorities Dr. José Luis Di Fabio, Technology, Health Care and Research, PAHO/WHO

During the presentation, the DRA's broad competencies were described, the need for effective regulation not to be fragmented, as fragmentation does not permit effective regulation. Regulatory processes should be transparent, and there should be punitive measures for violation of the functions.

Dr. Di Fabio discussed the need for creating a regulatory culture, with independently thinking personnel with technical, ethical, and legal training (see transparency).

He emphasized that drug regulation is an essential function since the public is not in a position to evaluate drug quality, efficacy, and safety.

He spoke about the key elements of regulation--legal, administrative, and technical--that ensure that drugs are effective, safe and of acceptable quality, that they are used rationally and are accessible to people. He also listed the basic functions of regulation: issuance of manufacturing licenses, importation and marketing of products, authorization of clinical studies, monitoring promotion, and prescription and dispensing practices.

He argued that regulation needs to include accountability and transparency for the government and the public through public reports, publication of decisions, processes, and policies, mechanisms for appealing DRA decisions, code of conduct for DRA personnel, thus accomplishing the DRA mission to protect the public and prevent corruption. He added that regulatory authorities are subject to pressures from major economic interests and lobbying.

He discussed the mutual recognition and established procedures, adding that the procedures are based on the confidence in the countries' regulatory authorities; such confidence in turn is based on the certainty of implementation of PANDRH guidelines and recommendations. He added that 65% of the countries in the Region have a regulatory authority but most do not have the capacity to evaluate and regulate products, they lack harmonization in drug regulation in the different countries, that human resources do not have the capacity to accomplish their roles and that many

official laboratories do not have the skilled personnel nor other resources needed to implement the GLPs.

He explained that a reference regulatory authority is one that has been submitted to an evaluation process through a transparent methodology that qualifies it to successfully meet the critical indicators. He justified that the DRA qualification process means that DRAs can collaborate as reference authorities for PAHO in the discussion of strategic issues in drug regulation in the Region, and when apt, coordinate with the drug regulatory harmonization processes in the Americas.

He urged renovation of processes such as the one used by the EMEA (exchange of product evaluation reports with the consent of the head of registration. Availability and circulation of a list of approved products and their evaluation reports), which has benefits such as the promotion of good evaluation practices based on risk analysis with limited resources, reduced evaluation time, the sharing of evaluation reports on new drugs in the research phase, new drugs, among others.

He proposed new challenges for DRAs: the approval of new drugs only when they are an improvement over existing ones; to counteract the current inconsistency in the approval of a drug for a specific indication and dosage and then that drug is prescribed, dispensed, and used in another way; inclusion of rational use in regulatory functions; regulatory authority participation in patent system control; a balance between the preapproval phases and minimum controls in the post-approval phase; application of risk management concepts applied to drug quality systems.

He concluded by pointing out that regulation models are not importable and they should be in harmony with the resources available for their implementation, and that the DRA has the challenge of differentiating the criteria and standards that ensure public health from the ones that only constitute barriers to access.

Drug Counterfeiting as a Public Health Problem Dr. Valerio Reggi (WHO)

Dr Reggi spoke about the reported deaths of people from consuming counterfeit drugs, about people who know how to copy the original very well and people who do not, the informal information systems and participation of organized crime rings in national and international drug trade.

He explained that WHO began receiving reports on counterfeit products in 1980 and that there is a chronology in WHO's participation in the issue:

In 1988, Resolution WHA 41.16 was adopted, which requests that governments and pharmaceutical manufacturers cooperate in "the prevention and detection of the export, import and smuggling of falsely labeled, spurious, counterfeit or substandard pharmaceutical preparations."

In 1992, the first international conference on counterfeit drugs was held with the participation of WHO, CIOMs, and IFPMA, which led to the definition of counterfeit drug and the commitment to work with the Ministries of Health in the struggle against drug counterfeiting.

In 1994, Resolution WHA 47.13 was issued, requesting that WHO assist member countries in their efforts to combat the use of counterfeit drugs. In 1996 a specific WHO project on drug counterfeiting was already underway. In 1999, a guide for

action against drug counterfeitin was issued. In 2000, a working group was formed to combat drug counterfeiting. From 1994-2004, the issue of counterfeiting was being addressed. Starting in 2006, the international task force on counterfeiting was established, which brought together experts in working groups. The IMPACT document on principle elements and conceptual framework was prepared; IMPACT is a coalition of interested parties whose purpose is to coordinate international activities to combat the counterfeiting of health products, involving all the different stakeholders.

He emphasized that WHO's leadership role helps ensure that the activities hold at their core the implications of counterfeiting for public health and not issues of intellectual property.

He explained IMPACT's conceptual framework and its operations. Member countries in America include Argentina, Brazil, Colombia, Mexico, and the United States: There is a Secretariat in WHO and five working groups: legislative and regulatory infrastructure; implementation of regulation (document under discussion on good practices in standards for distribution); research and repression (inter-country coordination of operations, monitoring and purchasing on the Internet, training materials, guidelines); technology (supply system safety, mobile assessment technologies) and communication (messages, website, participation in events, model materials for health professionals, distribution system, patients, police, customs, justice. Short films).
He reported that INTERPOL and WHO are in close collaboration, and a network of focal contact points is in the process of being launched.

He stressed that drug counterfeiting is not a problem of intellectual property rights.

He spoke about the myth of the 'perfect copy'. If a counterfeit is a perfect copy of an original product, there is no public health problem, and of the myth of the 'country source,' all the counterfeits come from some other country, never one's own. Importing and exporting countries need to share the responsibility.

He discussed the definitions of counterfeit drugs from 1992 and the IMPACT-2007 definition.

He described the next phases of IMPACT activities: Meeting in Bonn Germany, 24-26 November 2008, update to include medical equipment; the Third General Meeting of IMPACT in Hammamet, Tunisia, 3-5 December, 2008; and 19-24 January 2009, in Geneva, WHO's Executive Board has an agenda item on counterfeit medical products and is preparing a resolution on the issue for the 2009 World Health Assembly.

Finally, he concluded by pointing out that the action of WHO depends on its member countries and thus to report cases, contribute to the working groups to accomplish concrete results and develop a network of contacts and a national network of contacts among the different institutions that need to act.

The WHO Prequalification System Dr. Lembit Rägo, WHO.

Dr. Rägo began his presentation commenting that drug quality and safety continues to be a problem, and pointed out what WHO is doing to assist countries, including regulatory functions; INNs, ATC, DDD, international guidelines, standards and norms (mostly in quality assurance), international pharmacopeia, WHO's good

manufacturing practices, interchangeability, combinations of fixed doses, variations, guidelines for stability, etc. He gave the website, a DVD on planning and a compilation of all the regulatory standards that also contain material on international pharmacopeia.

He also spoke about training tools, commenting on the existence of the GMP training modules to train inspectors.

He explained the prequalification system for essential drugs, which is a U.N. action to expand the drugs for HIV/AIDS, TB, malaria, reproductive health and avian flu. This system ensures the quality, safety, and efficacy of drugs acquired by U.N. agencies; its existence has changed the environment of drug procurement so that quality drugs reach all people.

He discussed why prequalification is necessary, indicating that poor-quality drugs or counterfeits constitute a risk for the patients and also generate mistrust in the public.

Dr. Rägo then outlined the basic principles of prequalification, emphasizing its legitimacy, since a committee of experts brings it before the meeting of member states and the executive committee. He indicated that the process is voluntary, widely discussed, and transparent, that all the information is available online, that it is opened to both innovative producers and multisource products (generics), that it helps strengthen capacities and does not cost anything to become prequalified. Through this system, the preparation facilities and laboratories are prequalified, the public lists of products and manufacturers are prepared, capacities are strengthened and harmonization achieved, as well as a permanent monitoring of quality, and greater access to treatment. He commented that quality products rely on good manufacturing and distribution practices.

He pointed out that WHO's role is to manage and organize the project on behalf of the United Nations, providing technical and scientific support to ensure compliance with international norms and application of standards.

Then Dr. Rägo explained that in the case of evaluation of innovative products, the regulatory entity is responsible. For multisource products, regulation is not harmonized, information is required including all the data, information on raw material and finished products, including specification details, data on stability, formulation, manufacturing method, packaging and labeling, efficacy, and bioequivalence. The manufacturing laboratories, active ingredients, and research laboratories all undergo inspection.

Prequalification is based on the standards approved by the WHO expert committee and also the applicable standards of ICH and Report 41.

He referred to a series of documents and reports available on the Internet that help in training and dissemination of information, for example, WHO public inspection reports.

Next Dr. Rägo commented that only a limited number of products meet the required standards, that it takes time to fulfill the request, due to the amount of data to generate, tests to perform, etc., in order to implement the GMP. He indicated that several products and suppliers have met the standards, most for antiretroviral drugs

(ARVs); many suppliers appreciate the feedback and would be willing to meet the standards. As a result of the prequalification procedure, an unprecedented level of technical knowledge on products has been compiled, especially for generic antiretroviral and anti-malaria drugs. Another positive component is capacity strengthening. The possibility of implementing joint efforts helps in recognition of others' work and reduces doubling of efforts.

He finished by saying that the list of prequalified products is not mandatory for any country; however, many mechanisms such as the Global Fund are obligated to purchase prequalified products, thus minimizing risks by eliminating products that do not meet all the standards. The world is free to follow any path, to promote whatever may be best for the population.

He commented on the fact that PAHO is in the process of prequalifying regulatory authorities, and in the future these authorities could ensure this prequalification step. A regional perspective is different from a global perspective. Some things are easier to make happen at a regional level; a consensus may be reached in the region but not be applicable at the global level.

Progress Report of the Working Groups, coordinated by Dr. Carlos Chiale, Argentina

Drug Registration (DR): María Teresa Ibarz (INHRR, Venezuela)
Good laboratory practices (GLP): María Gloria Olate (ISPCH, Chile)
Combat Drug Counterfeiting: Tiago Rauber (ANVISA, Brazil)

Drug Registration (DR)

Dr. María Teresa Ibarz presented an overview of the working group's background and activities: a survey in the different countries on requirements for drug registration and renewal in the Region. A document presenting the survey results was prepared. Dr. Ibarz believed this document should be disseminated and open to receiving feedback and suggestions.

She presented the current work plan:

In November 2008: Completed document on harmonized registration requirements

In 2009: Preparation of the guidelines for application of the document on requirements in registration, preparation of a document on the requirements for health registration renovation and subsequent changes in registration, and preparation of an updated list of DRA websites in the network (links to relevant legislation)

Proposals for the V Conference

Document submitted for approval: "Harmonized Requirements for Drug Registration in the Americas"

Good Laboratory Practices (GLP)

Dr. María Gloria Olate commented that since the 1980s different actions have been accomplished to strengthen and establish official drug quality-control laboratories. In 2000, during the II Conference that created PANDRH, an external quality control program was created. The program was launched that same year under PAHO's leadership and with technical support from USP. Performance control tests. The laboratories were classified in three groups, laboratories with excellent results in all performance tests; those with average performance, and those with low performance.

A series of training courses in high-performance liquid chromatography (HPLC) techniques has been offered, which has helped raise the performance level in laboratories. In the IV Conference, a Working Group on Good Laboratory Practices (GLPs) was formed. The group's mission was defined, as well as general and specific objectives, and a two-year work plan. The group has held six meetings with defined agenda, whose results have been accomplished.

GLP courses: general concepts of a quality-control system, WHO Report 36 Annex 3, comparison with ISO standards on laboratories, workshops on practical application.

Implementation of the self-evaluation guidelines, consisting of a checklist based on Report 36. Thirteen courses have been offered in 13 countries to 168 lab technicians in quality-control laboratories and 28 training institutions.

Replication of the GLP courses in Chile with the University of Chile, in Brazil in national health laboratories.

Monitoring GLP implementation.

Preparation of documents.

Two new stages of the external control evaluation program, modification of the USP criteria for classification of laboratories by performance results.

Initial proposal for the control of other analytical techniques in line with equipment, infrastructure and development of official control laboratories.

Other WG activities:

Principal agreements. Obtain prequalification to become United Nations reference laboratories. Exchange visits with other countries with GLP- and ISO17025-compliant labs.

Send information material for preparing application for prequalification to interested countries (Brazil, Bolivia, Uruguay, Argentina, Costa Rica and Panama)

Continue offering GLP courses in remaining countries and in those that request it again

Prepare a work agenda for monitoring GLP implementation

Establish procedures to foster the WHO prequalification

Improve dissemination of WG activities and exchange among countries in the region

Establish solid strong relationships among the official control laboratories for mutual recognition of results

Participate in ongoing exchange of information and experiences among the official laboratories

Coordinate a network of quality control laboratories

Preventing and Combating Drug Counterfeiting

Dr. Tiago Rauber presented the group's background and meetings, summarized below:

In 2001, the first WG meeting was held, in which a survey was presented to help diagnose the drug-counterfeiting situation in the countries.

In April 2002, the survey was presented at the III Pan American Conference on Drug Regulatory Harmonization, and the WG's work plan was also approved.

In August 2003, the second WG meeting was held in Mexico City in which the group's mission and objectives were developed.

In August 2004, at the third WG meeting in São Paulo, the group reviewed the commitments and discussed, among other topics, the proposal for a regional training course for health authorities.

In March 2005, in the IV Pan American Conference on Drug Regulatory Harmonization held in the Dominican Republic, in addition to establishing some recommendations, several documents prepared by the group were approved, including the road-map proposal, the implementation unit, indicators, educational program.

Proposals for the V Conference

The WG on Drug Counterfeiting proposes several priorities to put into action in the next period, based on review of the work plan prepared at the last meeting (November 2006 in Buenos Aires) and in consideration of the evolution of international discussions – mainly with the activities developed by WHO, which often are the same proposed by the WG – the educational program presented at the IV Conference should be updated.

Brazil and Argentina implemented a joint project, based on the experience of the two countries and also that of MERCOSUR, and held a seminar in Montevideo in September 2007. International WHO references also helped construct the content of the event.

A pilot seminar on discussion of tools and generation of proposals for the prevention and combat of counterfeit drugs was held in Panama, 5-8 August 2008.

Priority actions

Establish an effective network of national and regional focal points. Time period: by 2009

Conduct workshops on discussion of tools, generation of proposals for prevention and combat of drug counterfeiting
Time period: ongoing activity, as formally requested by countries

Preparation of guidelines for identification of divergent drugs in the market
Time period: by 2009

Review and update the documents: road-map and implementation unit
Time period: by 2010

Introduce the subjects of traceability and e-trade (Internet) of products under discussion.
Time period: ongoing activity

Develop a distance-learning program based on ANMAT course
Time period: by 2010

He presented the objectives of the workshop on discussion of tools and generation of proposals for prevention and combat of counterfeit drugs, and the pilot seminar project held in Panama City, 3- 8 August 2008.

He presented a model for the network of focal points to combat counterfeit drugs; addressing objectives, structure of the national network, emphasizing national focal points. Objectives of the national network, the profile and operation of the focal points to combat drug counterfeiting within the network, responsibilities, tasks, and objectives of the focal points. The important tool is communication among the different stakeholders. The proposed structure for the subregional network is that each stakeholder entity participate as a focal point. Responsibilities, tasks, and objectives of the subregional focal point. Network installation and maintenance.

Presentation of Working Group Progress, coordinated by Dr. Princess Thomas Osbourne, Jamaica

Good Clinical Practices (GCP): Analía Pérez (ANMAT, Argentina)
Drug promotion (DP): María José Delgado (ANVISA, Brazil)
Good Manufacturing Practices (GMP): Justina Molzon (FDA, USA), Rodolfo Mochetto (ANMAT, Argentina), Rosalba Alzate de Saldarriaga (Consultant, PAHO/WHO)

Good Clinical Practices (GCP)

Dr. Analía Pérez presented the group's objectives and mission and accomplishments. The Document of the Americas, underscoring the importance of its Annexes: Operational Guidelines for Ethics Committees, A Self-Evaluation Questionnaire for Independent Ethics Committees (IECs). Document for widespread use.

She reported that the WG had already prepared the pediatrics document; the document is important for the region, based on the ICH document, and available

online for contributions from the countries. The document coincides with others emerging from other regional meetings, for example, ICDRA.

She presented the work plan under discussion and the WG's tasks, including: validate participating members and countries, revisit the work agenda to capitalize on experiences in the countries, review the research environment in the countries, strengthen the educational component with participation of other stakeholders.

Drug Promotion (DP)

Dr. María José Delgado presented an overview of the group's background and activities, including:

First meeting of the Working Group in August 2006. The mission was defined: promote and harmonize the criteria for drug promotion as contribution to rational use, in the framework of the health policies in the countries of the Americas. The vision to expand and strengthen awareness. A work plan was prepared, objectives defined.

Proposal of the WG's initial work plan to combine Objectives 1 and 2; the condensed work plan was proposed and validated in 2007-2008

Later the new proposals were presented: Facilitate the WG's work in order to accomplish the proposed objectives in the shortest time period possible.

Establish the ethical criteria for the promotion of drug advertising

Prepare a comparative study based on review of legislation, promotion and advertising

Good Manufacturing Practices (GMP)

Dr. Justina Molzon presented an overview of the WG's meetings and work plan, and reported that at the last conference the document "Guidelines for the Verification of Good Manufacturing Practice for the Pharmaceutical Industry" was adopted.

Proposals for the Conference

Decision tree for the implementation of the guidelines for GMP inspections.
Adoption of ICH Q7 guidelines for good manufacturing practices for active ingredients.
Code of ethics
Mutual recognition of GMP inspections
The network can promote harmonized procedures and exchange of information among the countries of the Americas.

Rodolfo Mochetto explained the decision tree for the implementation of the guidelines for GMP inspection.

He presented the background that led to preparation of the document. Adoption of WHO 1992 GMPs as standard base, inviting member countries to adopt it. The guidelines for GMP inspections were prepared, validated in fieldwork, and approved

in 2005 in the Dominican Republic. Development of national plans for the implementation of the guidelines with participation of all those involved.

Rosalba Alzate submitted a detailed report on the WG's educational activities.

Rational Drug Use as a Component in Regulatory Decisions Dr. Perla de Buschiazzo

In her presentation, Dr. Buschiazzo reflected on rational drug use and regulatory decisions, identifying regulatory weaknesses and strengths that influence decision-making, as well as the importance of regulatory measures in improving access and equity based on this concept.

She emphasized educational strategies, management and regulation for the promotion of rational drug use and the use of this concept as a strategy to improve access to drugs, the principal functions of regulation and rational drug use (registration, information, monitoring the marketing). She added that clinical studies to measure efficacy are based on tests that measure subrogated and non-variable clinically relevant variables.

She described the difference between efficacy and effectiveness, presented an analysis of the efficacy balance and safety of some new drugs, the withdrawal of drugs from the market for safety reasons, in many cases due to weaknesses and limitations in their process of regulation.

Dr. Buscchiazzo concluded by saying that regulatory decisions should have as goals the health and safety of the population, that the new drugs should be studied to demonstrate their efficacy in relevant clinical results and that shortening the drugs' pre-registration evaluation period has an economic component and in general does not serve health needs. She also emphasized that it is necessary to promote initiatives designed to introduce the culture of protecting the safety of the population through institutionalizing educational programs aimed at all stakeholders.

ROUNDTABLE Biotechnological Biologic Products
Coordinator: Dr. María Ángeles Cortes Castillo, PAHO/WHO
PAHO/WHO: María Luz Pombo, ALIFAR: Néstor Anníbali, FIFARMA: Lucas Marletta, Health Canada: Elwin Griffiths

Regulation of Biotechnological Biologic Production in Latin America and the Caribbean Dr. María Luz Pombo (PAHO)

In her introduction, Dr. Pombo presented WHO's definition of biologics. She emphasized the need for clear uniform definitions for biotechnological products, biotherapeutics and biosimilars, and referred to existing reference documents for biosimilar products.

She analyzed PAHO's role in providing technical support in biotechnological biologic regulatory matters to the national regulatory authorities in member countries, and summarized the initiatives in this area.

She presented the results of the study on current regulations in biotechnological biologic production in Latin America and the Caribbean. In that study, a survey was

designed and sent to 27 member countries in Latin America and the Caribbean. Seventeen countries responded to the survey.

In the last part she reviewed drug regulatory authorities' needs for biotechnological biologic regulation, from an item in the meeting held in June 2008 in the Dominican Republic.

Conclusions
Biotechnological biologic regulation faces unique challenges compared with regulation of traditional pharmaceutical products.

Biologics do not fall within the criteria established for generic drugs.

Currently the source or not, in the use of the definition "biosimilars," as well as the mechanism followed for their regulation, depend on the legislation in effect in each country.

The global trend is toward harmonization; however, to date a harmonized document to help regulate biotechnological biologics does not exist.

Regulatory Aspects of Biotechnological Biologic Products. Dr. Lucas Marletta, Roche, Argentina

He emphasized the characteristics and features of biotechnological/biologic products and the risk that could arise from the approval of biosimilars; he developed some key concepts for the regulatory framework to help minimize the cited risks.

Biopharmaceutical Products. Dr. Nestor Annibali, ALIFAR

In his presentation, Dr. Annibali outlined a series of technical concepts and criteria that characterize biopharmaceutical products. He also reviewed the regulatory framework that several countries and integration groups (the United States, EMEA, etc.) have implemented for this type of product, which include evaluation of efficacy and safety.

He defined the criteria that must be met to be considered a biosimilar drug, the characteristics of the production method, manufacturing (expression, separation and "downstream"), the search for relevant standards. He also pointed out that introduction of GMP and new technologies helps ensure replicability even between different producers, pointing out the very high value of bioassays in this regard.

Dr. Annibali concluded by pointing out that the quality of the biologics is closely related to their manufacturing process and that even though two products have different production processes, criteria of similarity and comparability can be established to compare them. He also concluded that from the regulatory standpoint, they are not generic drugs, and that they could demonstrate their similarity with the innovative biologic through a complete physical, chemical, biological, and preclinical characterization.

Global View of Biotechnological and Biologic Products (Health Canada) Dr. Elwin Griffits

Dr. Griffits based his presentation on concepts and criteria for the production and regulation of biotechnological and biologic products and the basic aspects and criteria of the so-called biosimilar products.

He pointed out the differences of biotechnological biologic products from products of chemical origin, the tests needed for their characterization, the regulatory aspects that must be met, the critical points in their production process, the characterization of the products, and the controls in process, pointing out the need for surveillance of their immunogenicity, mainly for new products or when changes have been made in the manufacturing process.

Dr. Griffits pointed out recent developments in the so-called biosimilar products, their potential contribution to access, their growth in the market, management of their commercial authorization, WHO initiatives for regulation in this type of product, its denomination. He emphasized that these products cannot be classified as generic drugs, that due to their nature, biotechnological products are never identical and are highly complex in nature and production; he agrees with the possibility of authorizing licensing for this type of product based on demonstration of similarity with an already-licensed product, with the need for extensive product characterization and then an analysis of the possible regulatory paths, the type of product to which they may apply, as well as aspects on standards and criteria to apply. He especially emphasized the state of the proposed standards that WHO is preparing for this type of product.

Panel on Progress in Integrating PANDRH Recommendations into the Integration Processes in the Region
Coordinator: NRA of Brazil

MERCOSUR, Dr. Carlos Chiale

Dr. Carlos Chiale, representing MERCOSUR, reported that in line with MERCOSUR policies, related activities are being developed.

He emphasized that the progress in the field of Good Manufacturing Practices (GMP) includes ongoing training and joint inspections of pharmaceutical manufacturing facilities (both intraregional and in other latitudes). He also reported that to date there is no mutual recognition. Dr. Chiale pointed out that a quality assurance program for inspections is in process.

The group has developed a strategic program on vaccine regulation and control that includes a variety of regulatory functions.

The registration of synthetic pharmaceutical active ingredients follows the MERCOSUR drug policy and each member state's policies, in accordance with each country's particular administrative procedures.

He pointed out that in combating counterfeit drugs and medical equipment, there are declarations and resolutions defining the problematic nature, a training program, and an action plan for suspected cases.

He concluded by pointing out that the issue of biotechnological biologic products is addressed in the guidelines for 2009-2010.

Central American Integration System (SICA) Dr. Julio Valdés

Dr. Julio Valdés, on behalf of SICA, pointed out the legal bases that form this integration system, citing the scenarios of discussion on the topic of drugs, their composition, resolutions, the decision-making bodies (COMISCA, RESSCAD) and the Subregional Technical Drug Commission, its lines of action.

He commended the importance of the accomplishments in 2007-2008 in the framework of this commission as well as the expectations for progress in 2009, specifically, joint negotiation on drugs, the basis for quality assurance of drugs, a pharmacovigilance system, a regional program for rational drug use and a profile for regional academic preparation.

Looming challenges include the coordination of decisions, maintaining joint efforts among concerned parties and donors, providing regional guidance to empower national decisions and actions, recognizing the priority of the health perspective over the economic perspective, and strengthening human resources in the countries.

Andean Community Dr. Víctor Dongo

Dr. Víctor Dongo, on behalf of the Andean Integration System (Andean Community), reviewed the group's member countries, regulatory framework, their decisions on drugs and other products for human consumption, the responsibilities of the health registration system that changed to mandatory notification of compliance. He also emphasized the participation of technical personnel of the Andean regulatory authorities in the PANDRH working groups.

Dr. Dongo emphasized the Andean Social Agenda, especially in the projects led by the Hipolito Unanue Agreement, the Andean health agency.
He referred to the circulation of goods, services and people in the Andean Community.

He concluded by pointing out the group's commitment to PANDRH, including work in the different harmonization groups, defining a focal point in every country for each technical group, and presenting the resulting PANDRH products to Andean Community entities.

CARICOM Dr. Beverly Reynolds

Dr. Beverly Reynolds, on behalf of the Caribbean community (CARICOM), reviewed the structure of governance, the regulatory framework, the mechanisms of mandate and support, the challenges in the region in drug harmonization, the activities underway and projects for the future in the field of drug regulation.

Dr. Reynolds pointed out that regional integration facilitates the exchange of goods, services, people, and the free exercise to negotiate in any member country.

She emphasized that the group has challenges in drug harmonization issues in terms of size of country and cost of structuring a regulatory system, limited human and financial resources in relation to institutional capacity, lack of legislative frameworks and policies, the need for establishing a drug procurement system to ensure the efficacy and safety of drugs marketed in the Caribbean region.

She reported that a drug quality control laboratory is currently in operation. There is also a regional advisory body and a technical advisory group for patents and related matters.

Dr. Reynolds mentioned that since 1986 a procurement agency financed by the member countries has worked on harmonization of drug formulas, technical assistance, common pharmaceutical policy, donation of drugs, drug surveillance, combating counterfeit drugs and studies of drug use. This agency is an excellent example of economic and financial cooperation that increases access to effective, safe and quality drugs.

Current activities include development of a pharmaceutical policy model, standardization for qualification of pharmacies, evaluation of medicinal products, an authority in the Caribbean for management of drug procurement and supply, a drug surveillance network, meetings for training and sensitization on the TRIPS Agreement, and regional evaluation of patent legislation and related matters. A regional evaluation of registration and regulatory drug systems is also being carried out.

The new steps include monitoring the regional drug harmonization forums to evaluate their implementation, explore the broad application of the procurement system, and the strengthening of institutional capacity to oversee regulatory matters.

CONCLUSIONS AND RECOMMENDATIONS OF THE V CONFERENCE

Considering: that the regulations and standards of the Pan American Network for Drug Regulatory Harmonization (PANDRH) attribute to the Pan American Conferences on Drug Regulatory Harmonization the responsibility to:

Promote drug regulatory harmonization that covers all aspects of quality, safety, and efficacy of pharmaceutical products as a contribution to the quality of life and health care of the citizens of member countries of the Americas;

Adopt recommendations for implementation at both the national and regional levels;

Promote the harmonization of drug regulation requirements, and documents for guidance with special problems in regulation.

Formulate and adopt proposals for technical and regulatory harmonization;

CONSIDERING: That during the V Conference, the proposed technical documents presented by the different Working Groups were recognized and at the same time a series of recommendations were made.

That the different Working Groups took as a basis the recommendations from the IV Conference to prepare the work plan developed and the documents presented for consideration at the V Conference.

The V Pan American Conference issues the following conclusions, recommendations, and decisions on each proposal submitted by the PANDRH Working Groups and other subjects presented for consideration:

I. BIOEQUIVALENCE AND BIOAVAILABILITY (BE)

The Conference recommends to the Network:

Adopt the document "Framework for Implementation of Equivalence Requirements for Pharmaceutical Products" with the suggested changes.

Promote the development of training programs for the DRAs in document management for effective application, particularly in subjects such as bioequivalence statistics and BCS.

Develop a list of indicators to evaluate BE implementation in the Americas.

Make a regional effort to improve the sharing of experiences between countries.

Organize a strategic plan to form a Latin American network for development of BE studies, with solid bases, with profile defined not only for the center, human resources, and trainings, but also as a determinant factor in reaching the development capacity of BE studies in the Region.

Promote discussions on implementation of requirements to link the local innovative product with the product that has proven safety and efficacy in order to establish the local reference product.

Promote educational and information campaigns for the public, health professionals, DRAs, and the industry on the scope of the BE tests as requirement for some active drug ingredients and dosages.

To the Working Group

Incorporate the modifications proposed by the participants and send to the Secretariat to be uploaded on the PANDRH website.

To the DRA:

That in order to declare a local innovative product as a reference product, it should be linked (in accordance with the recommendations of the document) to the product with established safety and efficacy.

To the Secretariat:

Promote training programs including case studies to guide the countries in use of the technical document, with emphasis on BCS, prioritization and applied methodology to identify valid and reliable reference products.

Establish, during document implementation, a conduit to receive questions or observations, to be addressed by the working group members and sent to PAHO to be uploaded on the PANDRH website

To the Industry:

Develop training programs in application and use of the document.

Provide the information required to establish the link between the local reference product and the innovative product that has proven safety and efficacy.
Promote the establishment of centers for conducting local and regional BE studies.

To Academia:

Promote the carrying out of BE studies.

II. GOOD PHARMACOVIGILANCE PRACTICES (PV)

The Conference recommends:

To PANDRH:

Adopt the document GOOD PHARMACOVIGILANCE PRACTICES with the suggested changes.
Implement the document for validation and monitoring in two groups of countries, one with low PV development levels and the other with programs underway.

To the national drug regulatory authorities (DRAs):

Incorporate and position PV programs in the framework of agency regulatory activities and comprehensive monitoring of drug use, based on evaluation of clinical registration information, monitoring of clinical studies, and post-marketing surveillance.

Although problems in quality may be detected in the framework of the PV systems, it is best that these matters be prevented or denounced through the very mechanisms of the health surveillance systems.

Also, to recognize FAILED TREATMENT as a notifiable event incorporated in the dictionary of terms: WHOArt and ICH. However, it is recommended that the analysis not be exclusively associated with faulty quality and recognize that many other factors involved. It is recommended that strategies be developed to evaluate reports of treatment failure that first rule out all problems associated with the use, patient's clinical condition, problems in diagnosis, among other variables, and analyze quality only in the case of reasonable doubt, to avoid wasting resources.

To the WG on Pharmacoviglance and the Secretariat:

Consider linking Suriname to the resource personnel.

Update the diagnostics, adjust the schedule for accomplishing pending objectives, and evaluate the need for another meeting.

III. VACCINES (V)

Recommendations:

To PANDRH:

Adopt the proposal for harmonized requirements for the registration of vaccines in the Region of the Americas and the guidelines for preparation of a request for registration.

To the national drug regulatory authorities (DRAs):

Review and analysis of the documents by the personnel in charge of implementation.
Identify the steps to follow for implementation.
Staff training.
Adoption and implementation.
Update the WG's principal members and alternates.

To the Industry:

Review and analysis of the documents by the personnel in charge of implementation.

Apply after adoption by the DRA.

To Academia:

Assess the possibility of including aspects of vaccine regulation and production in university specialties.

Support DRA work through participating as outside experts in the evaluation process, in those DRAs requiring it.

To the PAHO Secretariat:

Official publication of the document and its dissemination.
Financial support to conduct training.
Coordinate the future meeting of the Vaccines WG in 2009.
Monitor the process of implementation of approved documents by the countries in the Region.

To the Directing Council:

Approval is requested for the inclusion of other countries as members of the Vaccines WG, especially those that have actively participated in the process of document implementation and DRA representatives from non-vaccine-producing countries.
Update the members and alternates from each DRA.

IV. DRUG REGISTRATION:

Recommends:

To the Regulatory Authorities:

Analyze the document “Harmonized Requirements for Drug Registration” and send comments and suggestions to the WG in the established time period in order to prepare the final document.
Raise the discussion of the proposed document with the subregional integration groups (MERCOSUR, CARICOM, NAFTA, Andean Community, Central America)
Participate actively in preparing the guidelines for application and the glossary of terms.
Send to the Registration WG and the Secretariat, to the email addresses of the DRAs, and when possible, link to legislation on drugs.

To the Industry:

Review proposed document and send comments and suggestions within the established time frame.
Participate in preparing the guidelines for application and glossary of terms.

To the PANDRH Secretariat:
Provide particular support for the Registration WG, to ensure achievement of the established goals and in particular upload on the network’s website the document under review and links to a mailbox for suggestions and feedback from the group and publication of a list of DRA websites, and links to legislation.

Promote joint efforts to integrate related WGs, especially with the Bioequivalence WG, to harmonize these aspects in the proposed document.

To the Technical Group/Registration:

Review the comments and suggestions for the proposed document, and prepare the final document.
Promote the preparation of guidelines for application and glossary of terms.
Monitor the respective activities, to upload on the network’s website the proposed documents and those in preparation, as well as the list of DRA websites.
Update the list of participants by country in the Registration WG, in order to ensure active participation of all members.

CONCLUSIONS:

A decision was reached at the Conference to submit the document "Harmonized Requirements for Drug Registration" to network members for their evaluation, until June 2009, in order to receive comments and suggestions, and it is hoped that the final document will be ready by October 2009, and also the guidelines for application and glossary of terms.

V. GOOD LABORATORY PRACTICES (GLP):

Recommendations to PANDRH:

Continue providing the GLP courses based on WHO Report 36, Annex 3, considering the national regulatory authorities’ recommendations on course design.

Continue the ongoing training and workshops on specific analytical techniques in accordance with the countries' needs and recommendations of the national regulatory authorities

Monitor implementation of the GLP-WHO in the official drug control laboratories that want to prequalify

Establish procedures to support prequalification of the official drug control laboratories that request it

Continue with the External Quality Control Program for improving the performance of official drug control laboratories that request it

Monitor document implementation (wait for requested proposal)

To the National Drug Regulatory Authorities:

Support GLP implementation activities, WHO Report 36, Annex 3 for the purpose of requesting WHO prequalification to be a U.N. reference laboratory.

Work actively in GLP implementation, WHO Report 36, Annex 3.

Participate in performance evaluation programs for continuous improvement.

VI. COMBATING DRUG COUNTERFEITING:

The Working Group on Combating Drug Counterfeiting approves the proposed documents and activities and adoption of the following concept of counterfeiting medical products:

"A medical product (medicine, vaccine, pharmaceutical starting material, diagnostic or medical device) is counterfeit when it is fraudulently and deliberately mislabeled in relation to its identity or source."

To the Working Group on Combating Drug Counterfeiting:

Expand the target of work action to include medical products, i.e. drugs, vaccines, pharmaceutical raw materials, and medical equipment;

Develop action strategies that take into consideration the situation of countries that have not yet implemented a regulatory structure for medical products and countries with small and vulnerable economies;

Prepare a proposal for a model of a network of focal points to combat drug counterfeiting;

Conduct seminars for discussion of tools and generation of proposals to prevent and combat drug counterfeiting

VII. GOOD CLINICAL PRACTICES (GCP)

The Conference approves the document:

"Guide for conducting clinical studies in pediatric population" with the modifications indicated below.

Recommendations:

To PANDRH:
Approve the document: Guide for conducting clinical studies in pediatric populations, with the agreed-upon modifications.
Validate the members of the Good Clinical Practices Working Group.
Support the GCP Working Group's meeting in a time frame of less than four months.
Support the program of implementation in the countries of the Region and promote it in each country with cooperation from PAHO/WHO, health authorities, industry and academia.

To the Working Group:

Apply the following modifications to the approved document: Guide for conducting clinical studies in pediatric populations:

Consider including in the adolescent age group not only chronological age but also onset of puberty. That each country consider the ages of that group according to their own criteria and legislation.
Paragraphs 2.6 and 2.7 are eliminated and an Annex prepared, which is not part of the current approved document, on clinical studies of drugs from other countries as well as studies on the populations of the most vulnerable children.
Prepare guidelines for the design of studies on non-inferiority, among other things, in vulnerable populations.
Discuss the Annex at the next meeting
Validate the members of the WG
Hold the next WG meeting within four months.
Discuss the following points at the meeting:

Completed documents pending discussion in their final version. (Inspections, researcher manual, and use of placebo)
New topics to develop:
Aforementioned annexes
Public registration of clinical studies for transparency (WHO/Helsinki Declaration) (Experiences in Cuba, Argentina and Brazil)
Certification program for clinical sites in compliance with GCP

Update and prepare the group's work plan
Program for implementing Document of the Americas in the countries of the Region and modalities of cooperation that support and promote it (TCC, others)

To the Regulatory Authorities:

Initiate the implementation process in the countries where it has not started with the support of WG members through technical cooperation projects between two countries (or more) and seek alternatives for the support of human resources and materials.

VIII. DRUG ADVERTISING

The Conference recommends restructuring the WG and adopting the document on ethical criteria for the promotion of drug advertising, as the draft pending completion with other elements that address the needs of countries.

The Conference recommends:

To the National Drug Regulatory Authority (DRA):

Propose members for the WG to restructure the group and monitor its actions.
Respond to the questionnaire on the situation of promotion and send it to the group's coordinator before 10 December to prepare the comparative study and complete the database. The information should be sent to:
gprop@anvisa.gov.br
monitora.propaganda@anvisa.gov.br

Send contributions for the document

To the WG:
Training for health professionals and consumers – including a review of the existing modules on critical evaluation of promotional materials, in addition to other initiatives that address the theme for consumers. From that evaluation, the WG will work on a proposal for a Training Program.
Update the work plan – to encompass the proposal for evaluation and validation of WG members.

IX. GOOD MANUFACTURING PRACTICES (GMP)

The Conference adopts the documents presented by the WG:

"Decision tree for the implementation of the Guidelines for good manufacturing practices inspection"

"Good Manufacturing Practices for Pharmaceutical Ingredients (Guide ICH-Q7)"

"Code of Ethics for Inspectors of Good Manufacturing Practices."

Recommends

To the Network:

Promote harmonized procedures and exchange of information among countries of the Americas to promote mutual recognition of GMP inspections.
Promote the use of a common guide and participation in joint inspections to foster confidence building between authorities and efficient use of resources.
Explore mechanisms to promote mutual recognition

To the National Authorities:

Adopt the decision tree for the implementation of the Guidelines for good manufacturing practices inspection.
Set up the Guide for Good Manufacturing Practices for Pharmaceutical Ingredients (Guide ICH-Q7).
Adopt the Code of Ethics for Inspectors of Good Manufacturing Practices.
Share information on inspections as first phase in mutual recognition.

To the GMP Working Group:

Respond to the questions in the question-and-answer box.

To the Secretariat:

Establish a question-and-answer box when implementing the Guidelines for Good Manufacturing Practices Inspection for the pharmaceutical industry and the decision tree for the implementation of the guidelines.
Conduct a monitor process of the progress in implementing the guidelines and decision tree.
Send the most recent version of the Code of Ethics for Inspectors of Good Manufacturing Practices to member countries for their implementation.
Investigate training programs for high-level inspectors.
Invite the DRA from each country to continue making progress in GMPs and consider adopting the GMP regulations recommended by WHO in 2003.
Monitor the implementation of the technical document.

GENERAL RECOMMENDATIONS TO THE SECRETARIAT ON APPROVED DOCUMENTS:

Support the publication of all documents approved in the Conference
Support the holding of WG meetings
Support implementation of agreements and documents approved during the V Conference

X. REVIEW OF PANDRH STATUTES

Since it was not possible during the Conference to review the proposal on statutes, it was agreed that countries shall review the proposal and discuss it at the subregional level in a maximum period of five months. Such information will be presented by the subregional representative at the next Directing Council to be held in July 2009.

The decisions of the Directing Council will be submitted to the subregional groups for endorsement.

XI. RECONSTITUTION OF THE EXECUTIVE COMMITTEE (EC)

In compliance with PANDRH regulations, up to three of the five members of the EC shall be replaced during each conference. EC members each hold a four-year term. During the V Conference, three of the five principal members were replaced by their corresponding alternates, in the following subregional areas:

a) Central America, the Dominican Republic, and Cuba;
b) Andean Region; and
c) NAFTA

The new members were elected by consensus in their respective subregional groups and current EC members include the following:

Legal representatives of the Regulatory Authority

1- Central America: (from the V - VII Conference)
Member: PANAMA (Ministry of Health)
Alternate: El Salvador (Ministry of Health).

2- Andean Region: (from the V - VII Conference)
Member: PERU (DIGEMID)
Alternate: VENEZUELA (National Institute of Hygiene)

3- NAFTA: (from the V - VII Conference)
Member: USA (FDA)
Alternate: CANADA (Health Canada)

4- CARICOM: (NO CHANGE)
Member: Trinidad & Tobago
Alternate: Barbados

5- MERCOSUR (NO CHANGE)
Member: Argentina
Alternate: Chile

6- ALIFAR representative or alternate member
7- FIFARMA representative or alternate member

CLOSING SESSION

In conclusion, representatives of ANMAT, PAHO, ALIFAR, FIFARMA, and the PANDRH Directing Council presented their views on results of the V Conference and future PANDRH work.

The Director of ANMAT emphasized the importance of these meetings, in addition to strengthening interrelations, it is clear that similarities among participants far

outnumber their differences. He also commended the progress made by Regulatory Authorities in the Region and the need for more in-depth debate on the content of PANDRH's statutes and the network's strategic contribution to the progress of this forum.

The FIFARMA representative thanked the participants and recognized the progress made and the importance of working groups, which are the soul of the network. He appreciated the groups' work but declared that he believes there is a lack of progress in some working groups and that these should be better focused or dissolved, in the case of those that have not functioned well or that have not had continuity.

He stressed FIFARMA's ongoing commitment and support for PANDRH both for the working groups and the periodic Pan American Conferences, which have turned out to be an important forum for achieving harmonized regulations in the region. He stressed the importance of Pan-Americanism and the presence of the countries to the North with a longer history of drug regulatory development, which are vitally important for the progress and achievement of the objectives.

Dr. Rubén Abete of ALIFAR thanked ANMAT for hosting this event, all the Regulatory Authorities for their participation, Dr. Enrique Fefer who launched the initiative, Rosario D'Alessio for his dedication to the network's growth. He saluted the integration agencies, NGOs, academia, and the industry. He proceeded to present a summary of PANDRH, its mission, goals and objectives, the four previous conferences, and the achievements obtained, and proposed some reflections on issues such as drug counterfeiting, industry participation, the sense of Pan-Americanism among the countries, the need for relaunching PANDRH and decision-making based on consensus.

Dr. Victor Dongo, on behalf of the Directing Council of PANDRH and the Regulatory Authorities, thanked Argentina, its Ministry of Health, ANMAT, the immense and focused support provided by PAHO all along to the technical groups and now at this meeting, which succeeded in reaching consensus on the documents. He added that it is the responsibility of all countries to assume the roles that correspond to them in order to reach a time when drugs are reliable and high quality. Dr. Dongo considered that the Executive Committee is responsible for assuming a greater role in the network's operations, not only in the conferences but also in helping the technical groups accomplish their activities and evaluations on time. He suggested that for the next conference, the committee disseminate advance information. If each country can commit to a common action, there is greater opportunity for the documents emanating from the WGs to be accepted.

Dr. Martín Cañas, on behalf of Health Action International (HAI), presented HAI's view on what the objectives of drug regulation should be, his concern for biases in the agenda due to the influence of commercial interests and models and regulatory standards with no concrete advantages for public health in the network's member countries, that these become technical barriers to accessing drugs, since a country may adopt regulatory standards that do not correspond to its reality and disregard experiences and capacities. HAI salutes the proposal to include transparency of decision-making processes in the forum's agenda and in DRAs' agendas, as well as creation of the WG on Drug Promotion. The recommendation is that PANDRH make all its processes transparent.

The DRAs were advised that regulatory standards are often the result of commercial negotiations and so their participation is imperative; they salute the initiative to put the subject of cost of drugs on the agenda, one of the obstacles to access. He added that while the BE document presented at the conference included some of the technical advances in the theme, it is of concern that an erroneous interpretation could be used to pressure the countries for general adoption of the BE studies, and that it is necessary to distinguish between a reduced list of products that require in-vivo studies and the possibility of making an extensive list for their gradual requirement.

Dr. José Luís Di Fabio, on behalf of PAHO, thanked ANMAT, the Regulatory Authorities, and PAHO for their participation and collaboration. He pointed out that he considers that the Conference met the expectations, and hopes that the Regulatory Authorities continue to participate actively and support the WG's activities.

Dr. Di Fabio declared that the date for the next conference is still pending from headquarters.