Pan American Health Organization

Regional Office of the World Health Organization

PAN AMERICAN NETWORK FOR DRUG REGULATORY HARMONIZATION

MINUTES

IV PAN AMERICAN CONFERENCE FOR DRUG REGULATORY HARMONIZATION

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2-4 March 2005

IV PAN AMERICAN CONFERENCE ON DRUG REGULATORY HARMONIZATION[1]
Boca Chica, Dominican Republic
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Session 1

I. OPENING CEREMONY

The opening ceremony was conducted by,
Dr. Hector Otero, Assistant Secretary of the Ministry of Health and Social Welfare of the Dominican Republic, on behalf of the Minister, Dr. Sabino Baez,
Dr. Socorro Gross, PAHO/WHO Representative in the Dominican Republic,
Mr. Gustavo Rojas, Executive Advisor on International Politics, Ministry of Health and Social Welfare,
Dr. Elena Fernandez, Pharmaceutical Policy Advisor and Director of PROMESE, Ministry of Health and Social Welfare,
Dr. German Velasquez, Assistant Director of the WHO Department of Technical Cooperation for Essential Medicines,
Dr. Hans Hogerzeil, Director of the WHO Department of Medicines Policy and Standards,
Dr. José Luis Di Fabio, Manager of Technology and Health Services, PAHO/WHO
Dr. Jorge Bermudez, Chief of Unit of Essential Medicines and Technology, PAHO/WHO.

The opening ceremony began with a speech by **Jorge Bermudez**, who greeted the members of the committee, the health authorities, and the other participants at the Fourth Conference. He indicated that, although he began working at the PAHO recently, he has been involved in this struggle and the same battles for several years. As Unit Chief he is in charge of coordinating this work in the Region of the Americas. He is doing so with respect, determination, and his cumulative professional experience but, above all, with confidence, since he is joined by professionals who have acquired vast experience, firsthand knowledge, and expertise in the different countries in the Americas.

He stated that he has been working on the issue of access to medicines for several years within the context of the right to health. This context of access to medicines has been discussed in the health care reforms implemented by our countries; the concept of essential medicines has been discussed for 25 years, in conjunction with the rational use of medicines, national drug policies, subregional harmonization, and many other issues that encourage one to continue in the constant and at times endless or utopian battle to help build a world characterized by social justice, in which there are no more inequalities, disparities, contrasts, or imbalances that one sees in daily life in the developing world.

Dr. Bermudez greeted and acknowledged his predecessor at the Essential Medicines, Vaccines, and Health Technology Unit of PAHO/WHO, Rosario D'Alessio, who headed the Unit prior to his arrival and knew how to maintain interest so that the program was always considered to be one the priorities of the countries in the Region. Dr. D'Alessio has spent much of these past months working to ensure that the countries in the Region would play an active role in the Fourth Conference, which would include participation by the national

regulatory authorities, agencies, NGOs and the pharmaceutical industry in a meaningful discussion and search for consensus. On this occasion, he also publicly stated his appreciation for the support of the Manager of the Area of Technology and Health Services Delivery of PAHO, José Luis Di Fabio; as well as the ongoing and consistent support of the World Health Organization for the activities carried out in the Region of the Americas, through his friend German Velasquez, Assistant Director of Technical Cooperation for Essential Drugs and Traditional Medicine, and Hans Hogerzeil, Director of Medicines Policy and Standards.

He also expressed his appreciation to all those present for their interest, and to the PAHO/WHO Representative, Dr. Socorro Gross, for her enthusiasm and work in the organization of the Conference. He noted that the country has made a political decision to ensure that providing access to drugs is an effective activity of the present government, which he considers to be an example for the rest of the world.

Dr. Bermudez emphasized the need to support countries in which access to drugs is a priority on the health agenda. The PAHO must play a leading role in this Region and set an example for other regions of the world. This market, filled with the pressures and disputes that characterize the pharmaceutical sector, must be regulated and operated to respond to the social needs of our peoples. Social and economic development demand clear proposals with a commitment to the most vulnerable populations. Research and development of new products will have no impact if the products are not distributed rationally in health systems and made available to those who need them.

Therefore, this Fourth Conference, with a carefully prepared and balanced program, is considered to be timely. The PANDRH undoubtedly represents one of the most important initiatives in the Region and one with the greatest potential impact. He emphasized the strength that the presence of all the regulatory authorities from the countries of the Region represented as a driving force at the Conference, noting its broad scope, which included other agencies, the pharmaceutical industry, and NGOs.

Sensitive subjects of political importance such as the impact of the free trade agreements on the health sector, as well as other bilateral, regional, or global trade agreements, must be addressed. Even though the number of persons who have access to drugs has increased, an estimated 2 billion persons, or roughly one-third of the world’s population, still lack access to drugs.

The challenges faced by the Member States in increasing access to essential health supplies are primarily in the areas of selection of quality products, financing, procurement, supply systems, rational use, cost containment, and the regulation of intellectual property. The continued availability and sustainability of the programs should be an ongoing concern of the managers of our health systems, and we support them in this task.

We have been confronted with an extremely sensitive political period in past decades; the recent process of exclusive globalization marginalizes developing

countries, leads to an increased concentration of wealth among minorities, and challenges us to search for inclusive and equitable measures.

During these three days of work, we will be committed to fully satisfying the mandate of the Member States, following adoption of the resolution on access to medicines at the last session of the PAHO Steering Committee in September 2004. This reflects the desire of the most long-suffering and vulnerable populations, which live with difficulties, but never lose hope that there will be better days if we continue in our intentions with strength and firmness.

Let us be combative and supportive in consistently proceeding in the same direction and meaning, searching for the utopia which, as Eduardo Galeano said, one never reaches, but helps us take each step. I appreciate the sacrifice by all during these days far from your homes, your jobs, families and friends.

Welcome. Thank you again for being here. Keep your spirits up and let's get to work!

Next, Dr. **Socorro Gross**, PAHO/WHO Representative in the Dominican Republic, took the floor. She greeted the members of the committee, the national regulatory authorities, the industry, and other sectors. She gave Conference participants the most cordial welcome on behalf of Dr. Lee Jong-wook and Dr. Mirta Roses.

For the PAHO/WHO this meeting represents one more step of progress in health. In the Region of the Americas the life or death of persons is often determined by a drug. For a low income family, on most occasions access to drugs entails sacrificing other priority needs.

When we speak of health services we must also speak of medicines. To protect the population, in their respective areas, the health ministries discuss regulation and management; the pharmaceutical companies discuss their role in producing and marketing drugs; and, finally, the NGOs discuss ensuring effective access and availability of medicines. She pointed out that development is not possible without health and, finally, expressed her appreciation to the authorities for having provided their consent to hold this Fourth Conference.

Next, Dr. **Héctor Otero**, Assistant Secretary of the Ministry of Health and Social Welfare of the Dominican Republic, took the floor. He greeted the members of the committee and those attending the event.

On behalf of the Minister of Public Health and Social Welfare, Dr. Sabino Báez García, at the opening of this Fourth Conference on Drug Regulatory Harmonization, a meeting which, in accordance with its mission, will undertake an in-depth and highly responsible discussion on specific items as regards drugs of everyday use, in the name of the Minister, he extended his greetings to the conference, which will undoubtedly be successful.

Moreover, on this occasion, he would like to introduce in this magnificent setting some of the ideas that they are presently attempting to introduce in the Ministry of Public Health.

As established in the decennial health plan of the Dominican Republic, document based on the consensus of a series of requests closely linked to health, the Dominican Republic, with an area of 48,442 km^2, located in the eastern half of the island of Hispaniola, has a population of 8,562,541 inhabitants, 49.8% of which are men and 60% over 18 years-old. Sixty per cent of the population lives in the major cities, with a population density of 169 inhabitants per km^2. This density has had a direct impact on the social composition of the country and on increasing the contrasts due to the unequal distribution of income, migration, and marginalization.

As regards education, in the Dominican Republic, there is still an inequitable relationship between poverty and education. The illiteracy rate for the population of this charming nation is 12.7%. Moreover, there is a significant difference between the urban area, with 9.5% illiteracy, and the rural region, with 18.6%.

According to the 2002 report of the United Nations Development Programme (UNDP), the country was in 94th place of the 177 countries studied in the worldwide area and in 26th place of the countries in Latin America and the Caribbean.

In spite of the fact that some experts on the problem consider that the poverty level has begun to decrease, the distribution of income is still very unbalanced. The inequality in this country is below the extreme levels prevailing in Latin America. In spite of the progress under the previous management of the current president, Leonel Fernandez, in 1998, 20% of the population earned 4.6% of the income, whereas 10% of the wealthiest population earned 40.8% of the income, and 10% of the latter earned 70% of the income of the Dominican Republic.

Creation of stable and well-paid employment is one of the major challenges of the current model of development in the Dominican Republic. The employment generated in an economy that in recent years led economic growth in the Region has been lower than expected. One important noteworthy aspect that represents a serious challenge for the country is the high level of informal employment, situation that has worsened in recent years. Employment in the informal sector is characterized by high instability and very low pay. In 1998, 61.1% of the working population was located in the informal sector. In this context, in 2001 two new laws were enacted to reform the health sector, the General Health Act (4201) and the legislation which established the national insurance system in the Dominican Republic (8701).

These laws are oriented towards decentralization and establishment of a new political, institutional and financial framework to provide health services and guarantee national insurance for the population. Reform and modernization of the health sector are necessary conditions so that the Nation can guarantee

health. Therefore, changes that allow the institutions of the sector to satisfy this mandate must be promoted. For these transformations to occur, the public institutions responsible for designing and promoting national health policies must achieve high levels of cooperation and coordination so that their efforts are oriented in a single direction and the resources assigned to the sector reflect strategies of rationalization, lack of concentration, and decentralization of health expenditures.

It is quite clear that in-depth corrective measures must be introduced, which no longer insist on attempting to revive the old model of centralized health ministries responsible for all functions of the healthcare system, from management to providing services. This model has been extremely useful in the past four decades, but it has been demonstrated that it is insufficient and ineffective for facing modern health challenges.

In accordance with the health laws, work is being done to ensure effective decentralization of healthcare services, primary care, and social and community participation, as a form of social control that promotes the balance and transparency of processes; as well as creation of service networks that facilitate entry to a healthcare system that can offer the services included in the basic health plan of the national insurance system in the Dominican Republic.

Precisely a key point is access by the population to drugs that are essential for treatment and management of major diseases. As explained clearly by Federico Tobar, the options involved in the medicines policy could be represented by a triangle, with industrial policy, scientific and technological policy, and health policy as the vertices.

From the perspective of industrial policy, the primary concern could be summarized as the search for domestic and worldwide competitiveness. The instruments used for this purpose are the changes in tariffs and taxes applicable to the sector, as well as changes brought about by monetary policy, including price fixing. In scientific and technological policy, concern focuses on research and development, different tools of promoting research and innovation, patent protection, joint programs of development by universities and enterprises, etc. There is a complex area of work that involves regulation and surveillance of drugs.

All of the aforementioned is accepted with great concern by the current president, who outlined lines of regulation and surveillance from the manufacture of drugs to their distribution. Presently this policy has been accepted and relaunched by the Minister of Public Health as an expression of the need to join efforts for a National Pharmaceutical Policy.

Finally, I hope that the meeting of experts is an encounter where the rules of the game are discussed and harmonized, so that the patients are the primary beneficiaries.

Session 2

II. CURRENT HARMONIZATION INITIATIVES:

Moderator Victoria Urioste, Regulatory Authority/Bolivia

1) International Conference of Drug Regulatory Authorities, Hans Hogerzeil PSM / WHO, Sabine Kopp, QSM / WHO.

Hans Hogerzeil, recently designated to the post of Director of Medicines Policy and Standards of the WHO, stated that he had two important reasons for participating in this event. First reason, in order to share with the DRA what is being done in Geneva, and secondly to take advantage of the opportunity to meet the representatives from each country. He emphasized that the work being done in Geneva seeks to serve the countries. Therefore, it is worthwhile to know what is being done in each country in order to improve the material produced by the WHO for better use.

Three challenges or problems are evident, the problem of international trade, the challenges that this involves, and the work by regulatory bodies. In the field of drugs there are many pressures involved as regards importation, trade, AIDS programs, and there is much work to be done in terms of regulation and quality. In the WHO program for prequalification of drugs (e.g., drugs that combat AIDS, malaria and tuberculosis), it has been necessary to eliminate some products from the list. In some cases there are no alternatives and there has been pressure, but quality must be ensured. Since they do not have access to drugs at good prices, the patients take the risk of buying them outside of the system of pharmaceutical control. This risk must be evaluated.

Establishment of a regulatory system is essential and is associated with important demands. Harmonization (e.g., harmonization on the regional level, such as the Americas) is an important task which is supported by the WHO. The WHO establishes global standards. In order to do so, they must know what is happening in the countries in the different regions. The task involves joining the best initiatives, making them available, and then submitting them for consultations and, finally, worldwide acceptance by consensus. What is being done on this subject in Geneva? There are expert committees on pharmaceutical specifications which usually meet every two years to discuss standards, with the exception of the AIDS committee, that meets every year.

A series of guides have been prepared on subjects such as quality control, drug combinations, guidelines for regulatory bodies, monographs of the international pharmacopoeia, and for drugs designed specifically to combat AIDS. In addition to the model list provided by the WHO, there are also monographs for each of the drugs on the list, as well as radiopharmaceuticals and traditional medicines, and a guide on interchangeability of drugs. Achieving harmonization of stability test requirements has been difficult, as we have had to join the work performed by the different groups in a very tactful system of negotiation. There are new guidelines for GMP and distribution, as well as guidelines for herbal products. The international pharmacopoeia has been

printed on CD-ROM and GMP training modules have been updated. An international framework convention on counterfeit drugs has been held, etc.

Once again, WHO participation in the ICH is being discussed, in order to ensure that all Member States are taken into account through the WHO. For the new drugs against AIDS, malaria, tuberculosis, and other forgotten diseases, work is being done in Africa and in some developing countries in Asia, where the pharmacosurveillance systems are weak. These systems are in one country, and the drugs are in another country. The advisory committee for quality assurance of medicinal products would not only be a monitoring system but also an international center for analysis.

Finally, the WHO welcomes participation in the processes of preparation of global standards through regional harmonization. There is a need to hear what will be more useful and more necessary.

Next, **Sabine Koop** took the floor. She described similar regulatory activities being conducted in different regions such as the work being done in Asia, the European Union, or South Africa, which has a similar forum, etc. She mentioned that the goal of the WHO is for all persons to have access to safe, effective, and quality essential medicines; ensuring rational prescription and use of these medicines; and the four primary objectives with regard to policy, access, quality and safety, and rational use.

She informed that quality and safety, information exchange activities, and the activity of the International Conference of Drug Regulatory Authorities (ICDRA) would be discussed. She described the ICDRA as a specialized worldwide forum of regulatory authorities from countries that are WHO members that seeks to strengthen collaboration. It is important to know what is happening and what is going to be done in the future, so that priorities for action will be established in national and international regulations. The objectives of the forum are to promote collaboration between regulatory authorities, consensus on subjects of interest, suitable and timely exchange of information, and discuss subjects of international interest.

There are challenges for the DRA, such as increased globalization and the free trade area, sophisticated products, new technologies, increased communication by Internet, counterfeiting, etc.

She encouraged those present to become familiar with the history of ICDRA meetings through the WHO Web site on drugs. These meetings have been held in different continents. At the ninth meeting there were 280 participants from 90 member states. This has increased over time to the 110 Member States which participated at the most recent meeting in Madrid. A preliminary meeting on counterfeiting of drugs with the participation of other stakeholders such as customs offices, INTERPOL, etc. was held in Madrid This forum gave many Member States the opportunity to participate. The report will be available on the Web site. It reflects the progress and shows that the recommendations made at previous meetings have been taken seriously.

For example, as regards access to drugs, the following was recommended to the WHO:

1. Promote good practices in Member States for distribution of raw materials to ensure the quality of these materials; the action taken by the WHO on this point was to prepare two new guides, Good Distribution and Trade Practices and the Outline for Certification of Pharmaceutical Ingredients, with inspection and certification by the manufacturer. Both guides were approved by the Executive Committee of the WHO and are already available for official use.

2. Promote regulation of blood and plasma collection centers; in response, a GMP program for these centers was created, which was begun in Argentina.

3. Promote regulation of biotechnology products; in response, the WHO will monitor progress and promote guidelines that guarantee quality, efficacy and safety. The WHO has established 29 new biotechnological reference products in the past 2 years.

4. As regards counterfeiting, strengthen the current network of responsible officials through a Web site; tools have been prepared for filling out reports, which can be downloaded from the WHO site, in order to promote regional communication.

At the eleventh meeting of the ICDRA in Madrid, important issues were considered, such as the pharmacopoeias in a changing regulatory environment, advice on regulation of combined products, regulatory aspects of GCP and ethics, public health needs with regard to markets, ensuring quality and safety of blood and blood products, etc. All of these regulations are included in “WHO Drug Information Vol. 18, No. 1, 2004”. Moreover, as mentioned previously, the complete report with all of the presentations is available on the Web site.

In some sessions, such as that on pharmacopoeias in a changing regulatory environment, it was recommended that the Member States provide incentives for collaboration between regulatory authorities and the committees and/or secretariats of pharmacopoeias; that the WHO promote an international conference to discuss problems in collaboration with the parties involved; and provide specifications for international validation of drugs for emerging diseases, or high risk drugs for public health. In response, the WHO included seven new antiretroviral drugs in 2004, with the collaboration of the generic drug and patent industries.

For combined products, it was recommended that the WHO prepare guides on regulation of these drugs. In order to do so, a speedy process was required, that was accepted by the expert committee last year. It was requested that the regulators participating implement measures for those who fail to comply.

The next ICDRA meeting will be held in Seoul in the spring of 2006. The subjects to be discussed at this meeting will be planned in April of this year in Geneva (Presentation in annex 1).

2) International Conference on Harmonization (ICH)
Mike Ward, Ministry of Health of Canada

Mike Ward began by mentioning that the most important part of the presentation by Hans Hogerzeil was the desire to integrate the different harmonization groups. He continued by acknowledging the work by Rosario D'Alessio, which has served as the conscience and driving force for this Conference.

He continued by explaining the single focus of the ICH and its objectives, which include identifying and eliminating the need to perform duplicate studies to satisfy the demands of different regulatory requirements, so that resources will be used more efficiently. Finally, they seek to make new drugs that are safe and effective more readily available to patients.

He mentioned the working groups in the ICH, which are the safety, efficacy, quality and multidisciplinary groups. All of them are under a Steering Committee that approves the subjects and supervises the processes. The structure is perhaps more controlled than the PANDRH, and less transparent. He offered a retrospective look at the history of the ICH, and pointed out that six conferences have already been held. Increased interest in ICH guidelines and their use has been observed on a worldwide level. It is time to evaluate the future of the ICH, and thus ensure a suitable balance between maintenance or new activities, more efficient use and management of resources, sufficient flexibility to deal with new developments in science and technology and, above all, greater transparency.

A significant amount has been produced by the ICH since the last Pan American Conference. There are five technical guidelines, three on quality and two on efficacy, with specifications established for electronic presentations; four documents with points to consider; responses to user needs, questions and answers documents, safety reports, etc.

The Global Cooperation Group (GCG) was established as a subcommittee of the Steering Committee in order to respond to the growing interest in ICH guidelines and establish bonds with regions that do not belong to the ICH. The GCG consists of:

i. Six members of the ICH
ii. Two observers (WHO and Ministry of Health of Canada)
iii. Secretariat of the ICH

The mandate is to interchange information, and the commitment to respond to interest in the ICH and its guidelines.

This is the best time for technology transfer. There are many problems in our countries. It is important that the professors, the members of the academic community in our countries, participate in the public consultation process, as a first step so that subsequently the specialists in Latin America are included in the ICH. For example, the ICH approved the resolution to change the stability parameters in tropical countries. A professor from Indonesia used the same methodology to prove that the result was not applicable in his country. This late reaction in changing the stability parameters could have been avoided by previous participation in the ICH. Therefore, the specialists in our countries must be identified so that they have an active voice in these English speaking resolutions.

In summary, the ICH continues to balance the development of important new subjects with maintenance and implementation activities. The new lists of procedures and business cases seek to improve the effectiveness and value of the ICH process. The transparency, communication and commitment of the GCG are considered increasingly important (Presentation in annex 2 in English and annex 3 in Spanish).

3) General Report of the PANDRH Secretariat**.**
Rosario D'Alessio, PAHO/WHO, Washington D.C.

Rosario D'Alessio expressed her appreciation to Jorge Bermudez, Mike Ward, and each and every one of the members of the working groups, personally as well as the institutions they represent, for all of the time and effort they have dedicated. Moreover, she indicated that she appreciates the spirit of collaboration shown by the national regulatory authorities, the pharmaceutical industry, and other groups that have participated in the Network for the common good.

During the period from the Third Conference to the present a series of reports and proposals have been produced that will be presented during these days. A Report of the Secretariat has been written that presents the achievements of the PANDRH, and reflects the experiences and knowledge acquired in the Network during the past five years, has also been prepared.

The Network experience has been one of cooperation between countries, including countries with more developed regulatory systems as well as those with less developed systems. All of us have learned. All parties have been strengthened; the countries as well as the PAHO, which often provided advice or on some occasions acted as a mediator. We are sowing the seeds of the future. "The future is made of different moments in the present", as Silvia Linares said. The working groups in the Network as well as other groups have performed significant work, and developed different proposals. On this occasion, she asked that the authorities, the industry, the universities and the Network itself, pay close attention to what is requested of them.

She assessed the situation as regards the professionals from the Region who have participated in the different working groups: 78% are staffs from

regulatory offices in the Americas, 15% are specialists in pharmaceutical industries, and 7% are from other groups in the countries mostly as universities.

As regards the proposed sources of financing, initially not all of them have been active. Financing for the working groups has been provided by the governments and the PAHO. The Conferences have been financed by pharmaceutical industry associations, governments, and PAHO contributions. Finally, for educational activities, financing has come from the registration fees of those who participated in the courses and a PAHO subsidy.

As regards the impact of the Network, at present its impact has been in terms of process. Nine harmonized proposals have been created. Now, the regulatory authorities must decide what to do with these proposals, whether they will be used. Moreover, two resolutions have been made by Member States of the PAHO, one exclusively of support for the Network, and a second resolution that acknowledges the work carried out in the Network. Finally, it must be pointed out that the Network is one of the members of the ICH-GCG.

The challenges to be faced will be decided by the regulatory authorities of the Member States. The future is in their hands, as well the responsibility for approval or at least discussion of the proposals in their regional harmonization groups, after they have been reviewed and analyzed.

Next, Dr. D'Alessio gave an example of a plan for approval, and provided details on the different points to be followed (Presentation in annex 4).

4) Conference: Agenda and Procedures.
Rosario D'Alessio, PAHO/WHO
Dalia Castillo, PAHO/WHO, Dominican Republic.

Dalia Castillo and **Rosario D'Alessio** presented the agenda and procedures to be followed at the conference.

At each session, a regulatory authority will act as moderator. It is emphasized that time is important and it will be controlled by the moderators.

They informed that the authorities and members of the Network Steering Committee have microphones available and active participation is expected. The DRA can pose questions orally, whereas the other participants can do so in writing on the special forms available. If there is not enough time to respond to questions during the presentation, they will be answered in the consultation sessions.

At the end of each day, there will be an additional hour for consultation sessions on the subjects presented by each working group that day. All members of the WG who participate in the Conference will be present at the consultation sessions. The purpose of these sessions is to respond to questions which it has not been possible to resolve immediately after the presentations due to lack of time and facilitate participation in the discussions by all, direct

interchanges with WG members, information requests, and concerns to be submitted for analysis and consideration by the respective WGs.

At the end of each session an evaluation form will be provided for the group presentations in order to evaluate the speakers as well as the material.

It was clarified that the members of the working group will provide guidance in the process for countries that wish to adapt or adopt the proposals for implementation. Finally, it was informed that this afternoon the new members of the Network Steering Committee will also be selected, so that the DRA can already begin to discuss the possibilities with other DRA from each subregion.

Session 3

III. ***GOOD MANUFACTURING PRACTICES***:
Moderator Pamela Milla, Regulatory Authority/Chile.

1) Doc IV -1 Good Manufacturing Practices (GMP), Report and Proposal, GMP Inspection Guide, Group Coordinator Justina Molzon (FDA), Rodolfo Mochetto (ANMAT), Elsa Castejón MS-Venezuela, Millie Barber (FDA)

Justina Molzon made a general presentation on the work conducted by the group (Presentation in annex 5), highlighting that GMP are the number one priority for the Region. She informed on the different meetings held by the WG prior to preparation of the report and the proposal. She pointed out that the mission of the group consists of promoting knowledge and implementation of GMP as a strategy for improvement of the quality of drugs in the countries in the Americas.

The WG met after the Third Pan American Conference to define its priorities taking into account the recommendations made at the conference. They decided, first of all, to prepare the GMP Inspection Guide and, secondly, to study strategies for implementation of the guide and, finally, training /qualification.

The ANMAT prepared a draft of the guide based on WHO recommendations on GMP published in 1992. Next, the WG reviewed the draft and included the necessary recommendations. Subsequently the first draft of the guide was distributed and a pilot test was conducted in 2003. However, the WG considers that this test does not reflect the average in Latin America. Therefore, it was suggested that some members test the guide as part of a pilot test for validation in a pharmaceutical industry that would like to cooperate with the process.

Later some members of the WG requested that the guide be implemented in their countries and that subsequently the results and recommendations be sent to the Secretariat. As a result, a series of comments on the guide were received, which were very helpful. A third and fourth meeting were held, in which revision and editing of the document continued.

Next, three members of the Working Group, **Elsa Castejón, Millie Barber and Rodolfo Mochetto** made a brief presentation on the different chapters of the guideline for Good Manufacturing Practices Inspection, highlighting the most important aspects. (Presentation in annex 6,7 and 8)

Discussion:

Victoria de Urioste, DRA of Bolivia expressed her appreciation to the group and proposed that the regulatory authorities provide a space where they can interchange experiences on guide implementation.

José M. Cousiño (FIFARMA), congratulated the group for their excellent presentation. He highlighted the fact that throughout many years of work the group has consistently followed a single line, and that the guide is based on the WHO guide. It would be a pleasure for them to support the document and they congratulated the authors once again. They suggested some minor points that will be submitted to the Secretariat of the Conference. They also considered it to be a good instrument for training, and that the deadline dates on which it would take effect in the countries should be defined at this time.

He also recommended that they make a decision tree on how to progress in implementation of the guide and share mechanisms of mutual knowledge.

As a final point, it was also recommended that standards be developed for (pharmachemical) active ingredients to comply with GMP.

Rubén Abete (ALIFAR), congratulated the group and stated that they have some observations that will be sent to the Secretariat committee, especially as regards the wording, which should not be so imperative. Another recommendation was with regard to public consultation. It is a legal regulation that sets forth conditions for compliance. Therefore, the subject should be reviewed so that it does not create confusion and lead to objections. He stated his concern about its success if it is not implemented taking into account the reality of each of the countries.

He also stated that it should be established as national policy in which industrial policy and health policy are defined. This would provide a legal security that could be extended over time and would not depend on the authority at a given time. He proposed industrial rationalization to obtain safe and effective products. He reminded that the inspection guide is not an objective, but rather a tool.

Manuel Limeres, DRA of Argentina (ANMAT) congratulated this group for the work performed, and informed them that they have the full support and commitment of the regulatory authority for implementation of the guide in Argentina. He invited the conference to reflect on the importance of GMP because it is the only activity conducted by the regulatory authority in which they can control the process. GMP is essential in daily work. Finally he

requested that the conference approve this document prepared by the working group.

Moreover, different participants made contributions reflected by the following summary: Can the Guide be implemented by phases or stages? How many phases would be needed to implement the guide? Is 100% implementation necessary?

In response, the PAHO recommended that it be adopted with the support of the members of the working group. The adoption of the guideline as well as the effectiveness of its adoption, it will depend on each DRA. The working group is willing to provide guidance on the process at the request of the authorities.

Esperanza Briceño, DRA of Venezuela informed that in Venezuela three phases were established: compliance with a quality system, in which the industry is already sending its plans; at the same time, a retrospective validation of products already being sold on the market; and, finally, evaluation of the water system and essential products.

Justina Molzon (FDA) clarified that all aspects included in the guide are important to safeguard patient health and obtain quality products. It is up to the authorities to decide whether a plan should be defined for a group of products, phases, etc. Once again, she repeated the support that the group can provide as regards certain technical aspects or questions. Finally, she emphasized that this is not a qualified or approved guide.

Conclusion of session 3:

The proposal by the WG/GMP was accepted, and the comments stated will be included.

Session 4

IV. PHARMACOPOEIA AND QUALITY CONTROL:

Moderator Esperanza Briceño, Regulatory Authority/Venezuela

1) Doc. IV-8 Pharmacopoeia, Report and Proposal
Group Coordinator Horacio Pappa (USP)

Horacio Pappa provided a brief background of the pharmacopoeia working group. He had previous experience before the Network, at the meeting to harmonize procedures of American pharmacopoeias. Subsequently this group was included in the Network. The composition of the group includes the four pharmacopoeias from the Region, Argentina, Brazil, Mexico and the United States.

The working group conducts several activities, the most important of which are interchange of information and training, in addition to creation of an Electronic Information Network.

The mission of the WG is to create a forum for discussion and information interchange that facilitates adoption of the harmonization procedures. A possible objective of the WG would be to create a harmonized pharmacopoeia in the Americas.

The group has met eight times in the different member countries. The next meeting will be held in Washington during the USP convention. Four public meetings have also been held, in Brazil, Argentina, Mexico, as well as the United States.

At present work is being conducted on two initiatives, one in the Pharmacopoeia Discussion Group, which includes the European Pharmacopoeia and the Japanese Pharmacopoeia, and another in the PANDRH Working Group on Pharmacopoeia.

In his report he explained the difference between what is considered harmonized and what is harmonized based on attributes. This does not imply that all pharmacopoeias have the same text. The differences should not lead to different results. This allows mutual recognition of the procedures stated in each pharmacopoeia.

He clarified that a monograph does not necessarily have to include all of the specifications. If it only indicates which are harmonized and which are not; this is already progress.

Moreover, he described the steps in the harmonization process, presented for approval by the Conference, specifying the periods for harmonization of each pharmacopoeia. In summary, it begins by recognizing which pharmacopoeia will lead the process. Then, three rough drafts of the process are prepared. Next, there are consultations with the expert committee of each of the pharmacopoeias and a second level of consultation of users (public consultation). The USP “Pharmacopoeia Forum” is an example of the latter. After harmonization has been achieved, the pharmacopoeia that will make a change agrees to do so with the knowledge of the other pharmacopoeias in order to continue the harmonization process.

He continued informing on the work being done at present, including development of general chapters related to bacterial endotoxins, waste from ignition and particles in injectables. Moreover, the monographs on amiodarone (there are not yet agreements) and cat's claw, an herbal product in which all are interested, are also being prepared.

As regards future tasks, he indicated that they would like to reach a consensus on: dissolution (FA as leader of the pharmacopoeia); uniformity of unit doses (FEUM as leader); and disintegration (USP as leader). They would also like to make an effort to update a series of monographs that are already outdated: Aspirin, Morphine, Acetaminophen, Cod Liver Oil, Hydrocortisone, Iron Sulphate and Hydrochlorothiazide.

Finally he presented the dates for publication of each of the participating pharmacopoeias (See document) (Presentation in annex 9).

2) Doc IV-7, Report and Proposal of External Quality Control Program (EQCP)**,** José María Parisi, PAHO/WHO.

José María Parisi explained to us that the EQCP is a technical cooperation program of the PAHO that is carried out in conjunction with the USP, with the participation of the official drug quality control laboratories of the Member States. This program seeks to optimize their testing capacity and the form in which results are presented; evaluate the quality of drugs used in priority programs such as AIDS, tuberculosis and malaria; identify areas that require greater technical cooperation; and finally develop the concept of quality control reference laboratories in the Region.

The USP provides technical support and financial aid for the program. Next, he presented the objectives of the program. He informed that the countries that do not have laboratories are encouraged to implemente them, whereas the countries that already have laboratories are strengthened.

He commented that there are three phases in the EQCP. In phase I a diagnosis and a laboratory study are performed; in phase II performance is evaluated; and in phase III the human resources in the laboratories that require strengthening are trained /qualified. He also presented the findings and results of laboratories studied for each of the phases. Finally, he reported that at present 23 laboratories are participating (See document) (Presentation in annex 10).

Discussion:

As regards the Pharmacopoeia, the WG is congratulated. It is recommended that the group be open to the possible participation of representatives from all countries, thus contributing to progress towards a common pharmacopoeia.

The WG responded that this would be the ideal situation. If there is a regional pharmacopoeia, there should be continental legal support to ensure uniform standards for all countries. The political decision requires a supranational structure that comprises all countries. When work on this aspect begins, other countries could be invited; meanwhile, it is extremely difficult to do so.

There were unanimous congratulations for inclusion of herbal products, since sometimes there are native products that do not exist in other continents.

Conclusion of session 4:

- The proposal of the WG/Pharmacopoeias was accepted with the comments made.

- The EQCP report was recognized and the proposal to establish a WG in Good Laboratory Practices was approved.

Session 5

V. ELECTION OF MEMBERS OF THE PAN AMERICAN NETWORK STEERING COMMITTEE:

Moderator Rosario D'Alessio, PAHO/WHO

Rosario D'Alessio referred to that established in the standard as regards the members of the Steering Committee in terms of time, origin, geographic groups, etc. She informed on the composition of this Committee, which includes five members (DRA), one for each subregion; five alternate members (DRA), one for each subregion; and two members and their respective substitute members, one for FIFARMA and another for ALIFAR.

The present composition of the Committee is as follows:

- ✓ *North America*
  Member: Mexico
  Alternate Member: USA

- ✓ *Central America, Dominican Republic and Cuba*
  Member: Guatemala
  Alternate Member: Costa Rica

- ✓ *CARICOM*
  Member: Jamaica
  Alternate Member: Trinidad and Tobago

- ✓ *MERCOSUR*
  Member: Brazil
  Alternate Member: Argentina

- ✓ *AA*
  Member: Colombia
  Alternate Member: Bolivia

In accordance with the standards of the Network, three of the oldest members of the Steering Committee should be changed, which on this occasion refers to the subregion of Central America, Caribbean and MERCOSUR (Presentation in annex 11).

After the presentation, the DRA of each subgroup met and agreed to replace the members with alternate members, and to include a new alternate member.

Conclusion of session 5:

Election of the new SC was conducted by consensus of the DRA, and the new SC was established as follows:

- ✓ *Central America, Dominican Republic and Cuba (New)*
  Member: Costa Rica
  Alternate Member: Panama

- ✓ *CARICOM (New)*
  Member: Trinidad and Tobago
  Alternate Member: Barbados

- ✓ *MERCOSUR (New)*
  Member: Argentina
  Alternate Member: Chile

There was no change in the members and alternate members of the North America and Andean Region subregions.

Session 6

VI. DRUG REGISTRATION AND CLASSIFICATION:

Moderator Zoila Navarrete, Regulatory Authority/Ecuador

1) Regional Study: Requirements for Drug Registration in the Americas. Doc. IV-4: Working Group on Drug Registration, Report and Proposal, Group Coordinator, Esperanza Briceño, MS- Venezuela, Pamela Milla, ISP-Chile.

Esperanza Briceño presented the report and the group proposal. She mentioned that this is a subject that has been worked on for many years in the Americas and it is a very important subject for the regulatory authorities. It is the frame of reference for all matters related to drug regulation, subsequent surveillance, and drug control. It is where marketing authorization is defined. Therefore, it is an important subject for health and trade.

The efficacy, quality, and safety profile can be approved based on the documentation and tests. The stakeholders involved have different positions. The regulatory authorities are primarily concerned with ensuring the necessary requirements to guarantee safe, effective and quality drugs and access to drugs, benefiting public health.

For the economic integration blocks, the subject of drug registration involves non-tariff technical barriers. In the Andean Community the subject has been on the agendas of health and trade. There has been significant progress. However, since it was not binding it could not be implemented in all countries. Work has been conducted for four years, since 2002, but presently the subject is at a standstill and harmonization has not been achieved. In the MERCOSUR there has been progress in resolutions on specific standards, but harmonization of requirements has not yet been introduced. In Central America the standards have already been harmonized, and there has been progress in registration

requirements. In CARICOM there are no initiatives on drugs registration. In NAFTA, each country establishes its requirements individually; they have not been harmonized. Nevertheless, the regulatory authorities as well as the industry are interested in harmonization that facilitates the processes.

Recalling the background of the PANDRH WG on Drug Registration, she pointed out that this group was created recently and that it was identified as a need by the drug regulatory authorities. The group defined its mission, which is to promote and facilitate harmonization of suitable regionally recognized technical criteria for drug registration in order to contribute to quality, efficacy, safety and availability of drugs in the Americas.

After defining its mission, the WG decided on its objectives, and prepared a work plan for two years. Most of the tasks have already been completed. The selection of indicators is pending for 2005.

Subsequently she presented a diagnosis of the situation as regards drug registration requirements in the Americas; indicated which variables were taken into account and explained the methodology followed by the WG. The DRA of nineteen countries participated in the study. Three other countries provided information through another valid source. Information on products included active ingredients as well as final products. Next, she presented the results of the diagnosis. The survey only measured which country requested the requirement, but it did not consider the definitions established.

Finally, she presented the conclusions reached by the WG:

- ✓ There are similarities in some registration requirements;
- ✓ There are some differences in requirements that the WG considered critical;
- ✓ It is necessary to conduct a technical assessment of the present regulatory situation and present a Proposal of Requirements for Drug Registration.

Therefore, the WG made an initial proposal on requirements and a proposal on requirements for biological products. She stated that this is only one step forward. Moreover, she requested that other observations be made during this session, at the round tables for discussion at the end of the day, or by electronic submission to the PANDRH Web site, to ensure future consensus and approval at the next Conference.

Finally, she presented the proposal addressed to the Network and Working Group, the regulatory authorities, the pharmaceutical industry, and the Universities (See document) (Presentation in annex 12).

Discussion:

Julio C. Aldana, DRA of Colombia recognized the work of the group and recommended that other subjects associated with other groups, such as

bioequivalence, should be coordinated with the appropriate group, so that they can be included as registration requirements, because they are non-exclusive subjects. Pamela Milla, DRA of Chile and the members of the WG/Registration responded to this suggestion, emphasizing that the subject of registration is transversal to the rest of the subjects. Therefore, at the suitable time it was established that the appropriate group be responsible for providing a response, reviewing and approving work.

Marta de Álvarez, DRA of Guatemala congratulated the group for their extensive work. She shared their experience in Central America and the requirements they have faced, and stated that the objectives set forth in the legislation regarding registration with health authorities must be coherent. For some it is a reference standard, whereas for others it is a mechanism to monitor quality, safety and efficacy. A requirement can generate a standard or regulation that must be considered, improved, and they must arrive at an agreement on the requirement. If there is a related standard or regulation, the requirement is feasible. If not, prior work is needed before defining the requirement.

Rafael Pérez, DRA of Cuba acknowledged the work by the group. He made available to the Network the experience on registration harmonization acquired by Cuba and Venezuela. In this subject, competence to evaluate the information must be taken into account; at times the requirements become a series of administrative tasks. Some criteria for recognition of registration should be harmonized by different countries. This would provide support for the less developed countries that require a level of competence to conduct revision of requirements. The risk criteria should be stated in the requirements, according to the type of products. Safe, effective and quality products, as well as access to these products, should be guaranteed.

Esperanza Briceño responded by pointing out the need to strengthen the Human Resources responsible for registration review so that they can perform their duties properly.

Maria de los Ángeles Morales, DRA of Costa Rica congratulated the group for this highly valuable instrument that could lead to a recognition process by different countries. This instrument must not remain as such; dates should be defined to conduct internal analyses in the countries and define when the products will be decided on. She believes that it is important to establish a more comprehensive glossary of the variables included. Also, with regard to the database on legislation of the Region, she would like to know if this objective was achieved or is pending.

The WG responded that preparation of the glossary has been postponed. The database is pending. Some authorities have not sent their information. In fact, very few have sent it. They are waiting for the remaining 50% of the countries to send the information.

Rosario D'Alessio invited the countries that have not yet sent information regarding drug legislation and regulations to do so in order to make this

information available on the Web site. She also clarified that as soon as the different working groups have their own glossary, these would be integrated to form a single glossary for the Network.

R. Abete (ALIFAR) congratulated the working group. He pointed out that in the guide 115 items have been evaluated for 10 possible registration schemes, and identified critical items related to the working groups on Bioequivalence, Good Manufacturing Practices and Pharmacopoeia. He emphasized that it is essential to provide support, so that all of the groups are coordinated. He also considers that the proposal should be developed further. It is important to put both documents on the Web site so that they are widely discussed. The proposal should be developed further so that the recommendations will be applicable.

José M. Cousiño (FIFARMA) acknowledged the work done by the WG in such a short time, and considers the results interesting. Some points should be revised to guarantee quality, efficacy and safety. He invited the WG to include presentation of evidence demonstrating that the active ingredients comply with the requirements. Moreover, the characterization of raw material should be revised, because this is not requested for generic products and other similar products. This also applies to the guides for synthesis, production and stability.

In some countries, abbreviated requirements are accepted for biological products; therefore, changes should be included. It would be worthwhile to create a group of experts to prepare requirements for these products based on the WHO recommendations. He repeated once again that it would be interesting to have a glossary.

As regards renewal, it is a very complex administrative procedure; it is why this point should be reevaluated and Registration of OTC with health authorities should also be reviewed. He concluded his contribution by informing that all of the aforementioned recommendations are included in a written proposal that will be sent to the Secretariat.

Esperanza Briceño expressed appreciation for the comments and clarified that technical requirements should be evaluated on an ongoing basis and not only during the renewal process. As regards active ingredients, the requirements should include the items needed to safeguard public health. The Secretariat and the group agreed on the need to establish a specific group for biologicals.

2) Regional Study: Drug Classification Requirements in the Americas. Doc. IV-6: Working Group on Drug Classification, Report and Proposal. Group Coordinator, Beatriz B. Jimenez, MS-Guatemala, H. Bolaños (FIFARMA).

Beatriz B. de Jimenez began by describing the previous events that led to establishment of the working group. Next, she presented the objectives of the working group, which is to have knowledge of and compare legislation and

practices in the countries in the Region as regards drug classification; identify similarities and differences; and seek points of agreement for preparation of a harmonized proposal on over-the-counter (OTC) drugs.

The methodology used by the WG was to prepare a survey that was distributed by the Secretariat of the Network to all countries in the Region that are members of the PAHO/WHO (32 countries). A total of 21 countries responded to the survey (65%): 18 Spanish speaking countries and 3 English speaking countries. After the responses were received they were consolidated and the WG analyzed the results.

Subsequently the results obtained in the study and the conclusions were presented.

She informed on the proposed definition of OTC drugs; the criteria for classification of over-the-counter drugs (OTC); additional criteria that enables a product sold under medical prescription to change to unrestricted sales; information included in labeling, insert or directions for use; and requirements for advertising over-the-counter drugs (OTC). Some actions and recommendations for these products were also proposed. (See document) (Presentation in annex 13)

Discussion:

E. Briceño, DRA of Venezuela congratulated the group and made two observations. One of the concerns of the authorities is to identify the different forms of the drug; there is a need to deal with classification, and she requested that the working group strengthen this aspect. There has been a great deal of progress, but there is a need to continue working hard as regards classification of certain products that are difficult to classify and are "in limbo" (e.g., herbal medicines). Sometimes it is not clear whether it is a drug or a cosmetic. As regards prescription drugs and OTCs, it would be worthwhile for the group to work on counterfeiting of OTC drugs, since in some cases this has been documented.

J. Cousiño (FIFARMA) congratulated the group for their excellent work. The group has presented a solid proposal, and they recommended to the Conference that the group continue. There should be a proposal agreed on by consensus for active ingredients. FIFARMA and ILAR will make a proposal. He proposed preparation of a Code of Ethics for advertising. The lack of consensus on drug sales outside of pharmaceutical establishments should be reviewed. ILAR will use its experience to analyze this subject again based on developed countries with positive experience in promotion.

R. Abete (ALIFAR) agreed with the statement made by FIFARMA as regards sales in non-pharmaceutical establishments. He stated that they are concerned about sales of energy drinks which include products that alter central nervous system function and interfere with alcoholic beverages. He requested that the regulatory authorities take action on this subject.

3) Special Presentations:

a) Drug Promotion. Franklin Rubenstein (ANVISA)

This subject was requested by the Network Steering Committee in order to justify the possible creation of a specific Working group for Drug Promotion and Advertising. It was assigned to the ANVISA as regulatory authority for Brazil. **Franklin Rubenstein** presented the activities conducted on this subject in different countries. He pointed out that, according to the WHO, drug promotion requires increased communication between health authorities, creation of an active policy on rational use of drugs, and information for consumers (WHO 1999). The WHO identified the following basic problems in drug advertising: inadequate information on risks, exaggeration of benefits, and unapproved indications (Bulletin on Essential Medicines No. 31/2002). Monitoring advertising is a form of post-marketing control (guidance on therapeutic indications disseminated, including new, unregistered and erroneous and/or outdated indications).

Next, he informed on the objectives of the proposal. First of all, they seek to have knowledge of how this subject is dealt with in each country participating in the Conference and promote discussions on this subject. He considers that harmonization of health regulations on monitoring and oversight of drug advertising can be achieved. Secondly, they aim to create a large database on drug promotion based on information received from the health authorities.

He concluded by informing that an international seminar on Drug Advertising will be held in Brazil from 4 - 7 April, with the participation of the MERCOSUR countries, Australia, and Portugal. Brief information was provided on the subjects to be dealt with at the seminar (Presentation in annex 14).

b) Vaccine Control and Support for Drug DRA. José Peña, (PAHO/WHO)

José Peña began the presentation by defining the producers, drug regulatory authorities, and consumers as the principal stakeholders which guarantee that a national system ensures the quality of drugs and vaccines. The challenges are from the government, patients, healthcare professionals, and regulatory authorities. Safe, effective and quality products are needed, that ensure compliance with the regulations and standards for use. In order to achieve this, regulatory authorities should be strengthened. Therefore, the strengths and weaknesses of the authorities were identified, and an action plan to provide support was prepared.

He mentioned the components of the regulatory system, and evaluated the functions with regard to related indicators. This process enables authorities to review their actions and validate them or introduce the appropriate changes so that their work has an impact. He mentioned this assessment process.

Vaccines must undergo prequalification. There is no such requirement for drugs. The WHO recommends that countries fulfill some of the basic functions such as regulatory system, lot release, supervision, and clinical trial authorization. Manufactures must comply with the three functions. By 2004 only two countries in the Region complied with this function, and over 60% complied with implementation of the functions poorly. Nevertheless, significant changes are foreseen in 2006.

Providing support for the DRA is primarily achieved by training. In 2005 important subjects such as ethics committees, clinical trial authorization, lot release, pharmacosurveillance, biostatistics and good manufacturing practices are expected to be addressed.

They also have the collaboration of Centers such as the National Institute of Public Health in Quebec, Canada; CECMED of Cuba; and the laboratory of the Rafael Rangel Institute of Health in Venezuela.

There is a regional network that consists of the regional network of quality control laboratories, the regional vaccine surveillance network, and the virtual network which provides information such as news and a calendar of activities.

As regards harmonization of registration requirements, activities have been conducted in order to do so; as an alternative measure, identifying countries of reference and establishing mutual recognition of registration is proposed (Presentation in annex 15).

c) Training Proposal. Rosario D'Alessio, (PAHO/WHO)

Rosario D'Alessio informed on the proposal prepared by the Secretariat. She acknowledged that the training activities have been an important element in the regional network.

She presented the events that have occurred in five years, highlighting the 24 national seminars with the GMP modules established by the WHO. She mentioned that most of the working groups propose training activities. Therefore, There is a need for improvement in the management of the demand for training activities.

She presented the proposal, financing mechanisms, and requested responses on this subject (Presentation in annex 16).

Discussion:

Hans Hogerzeil requested that for future participation he would appreciate receiving comments on the training instruments developed by the WHO.

Rafael Pérez, DRA of Cuba stated that evaluation of vaccine registration by regulatory authorities has contributed to improving work. The same evaluation is being performed for drugs. He encouraged review of the instruments being used; the fact of implementation or self-implementation of these instruments provides a diagnosis of the areas in which work is needed.

M. Limeres, DRA of Argentina suggested that it would be advisable to have a working group on drug promotion and advertising.

M. Hinds, DRA of Barbados requested that Caribbean English be included in these training courses.

Cousiño (FIFARMA) recommended that the subject of promotion should be submitted for approval by the Steering Committee. He considers that, given the number of working groups, it is not a priority subject. As regards the vaccine group, it could be included in the subgroup for biologicals. Nevertheless, the subject of training should be a global working group.

José Peña responded by saying that he only intended to show what is being done in vaccines. He was not proposing anything specific, but he does think that vaccines should be included. The invitation for the Steering Committee to discuss this subject is still open, with availability for the requests made by countries.

F. Rubenstein emphasized that legislation is not the most important aspect of promotion; what is important is surveillance and the extent of compliance with legislation.

F. Meixueiro, DRA of Mexico congratulated the committee that made the presentation. With regard to the advertising group, he stated that the medical paradigm is changing. There is a need for a guide so that those who take part in the health system can participate in this paradigm and this subject is not left exclusively to the media.

P. Milla, DRA of Chile stated that advertising is a new subject. Although there are regulations, he considers the program proposed by Brazil to be interesting. We should learn to consider the subject from a different perspective, and have bases for evaluation of advertising.

Conclusion of session 6:

- The respective studies conducted by the WG/Drug Registration and the WG/Drug Classification were recognized;
- The proposal of the WG/Drug Registration was accepted as a draft;
- The proposal of the WG/Drug Classification was accepted with the observations stated;
- The Training Proposal was accepted with the observations stated.
- The WG/Biologicals was created;
- The WG/Promotion was created.

Session 7

VII. GOOD CLINICAL PRACTICES

Moderator: María de los Ángeles Morales, Regulatory Authority/Costa Rica

1). Doc. IV-3: Working Group on Good Clinical Practices (GCP/WG), Report and Proposal, Group Coordinator, Patricia Saidón (ANMAT), Stan Woollen (FDA).

Patricia Saidón began her presentation by updating the members of the working group. She also provided background information on good clinical practices (GCPs). Following, she presented the report *Good Clinical Practices: Document of the Americas*, and the group's proposal, including the mission, the objectives, the adoption of the document, and specific requests to drug regulatory authorities, to national universities, to pharmaceutical industry, to PANDRH and working group.

She indicated that the working group completed the pediatric research document (See document). (Presentation in annex 17)

Discussion:

M. Álvarez, DRA of Guatemala enquired about who is responsible for supervising research sponsors. In response, it was indicated that the proposal of Good Clinical Practices provides a guideline for establishing a program to perform supervision, and that the regulatory authority can also perform this role with a view to authorizing a document. Currently, however, there is only an inspection guide to monitor researchers. Each country must develop a program for monitoring good clinical practices.

J. M. Cousiño (FIFARMA) offered congratulations on the quality of the document, qualifying it as "excellent"—an observation with which the rest of those present agreed. He also praised the authors of the document, stating it can help facilitate early access to new drugs, and that it represents a technology transfer to the countries of the Region of the Americas. Although acknowledging that the document meets the criteria established by the International Conference on Harmonization (ICH), Cousiño conceded that some aspects merit additional consideration, i.e., the need to include a biostatistician on the Ethics Committee. He agreed to put his opinion on the matter in writing and distribute it to the working group.

Conclusion of session 7:

The proposal of the Good Clinical Practices Working Group (GCP/WG) was accepted with the additional comments.

Session 8

VIII. DRUG COUNTERFEITING

Moderator: Princess Osbourne
Regulatory Authority/Jamaica

1). Doc. IV-5: Working Group to Combat Drug Counterfeiting (CDC/WG), Report and Proposal, Group Coordinator Maria da Graca Santana Hofmeister (ANVISA), Francis Burnett (CARICOM), and Miguel Maito (ALIFAR)

Maria da Graca Santana Hofmeister introduced the members of the working group and provided background information on drug counterfeiting, touching on the recommendations issued at each of the previous conferences.

She informed that the group prepared its proposal based on four components:

- ✓ National programs and plan of action ("Road map");
- ✓ Executing unit to develop the program;
- ✓ Interaction with other stakeholders; and
- ✓ Training.

Moreover, she presented the work plan and proposal, including specific requests for drug regulatory authorities, the Conference, the pharmaceutical industry, and universities (See document). (Presentation in annex 18)

Discussion:

The DRA of Bahamas found the document very complete, but added that some countries lack the institutional support and human resources, especially CARICOM countries where there are no regulatory authorities. The representative also called for consideration of the Internet, qualifying it as the easiest vehicle for counterfeit drugs.

J. C. Aldana, DRA of Colombia shared his country's experience, relating that Colombia's national industry association includes both industries, together with the federation of businesses, in coordination with National Institute of Drug and Food Surveillance (INVIMA), law enforcement, and the offices of the government attorney, signed an agreement designed to disrupt the flow of commerce between the laboratories and distributors of counterfeit drugs. He explained that the criminal justice system is not very proactive in many countries of the Region, stating that in some cases these crimes do not carry prison sentences, and that many drug counterfeiters use a legally-established private drug distribution system. Aldana recommended that the industry be fully committed to a policy of refusing to sell products to any establishment found to possess counterfeit drug inventories. He stressed that this is a cooperative effort requiring coordination on the part of government institutions, the

pharmaceutical industry, and civil society, given that annual counterfeit drug operations worldwide generate as much as US$400 million.

R. Abete (ALIFAR) commented that a basic premise of the document is that all companies participating in the marketing network must be licensed to market drugs, and that marketing by any unlicensed company would be unlawful, thus emphasizing the very collaborative nature of this initiative.

The coordinator of the working group, Maria Graca Santana Hofmeister, noted that Brazil's anti-drug counterfeiting network has been further expanded to include the sale of any medical or surgical products.

M. Hinds, DRA of Barbados recommended that WHO organize a conference to take a fresh look at drug counterfeiting, and specifically marketing sanctions, as was agreed at the most recent International Conference of Drug Regulatory Authorities (ICDRA).

ALIFAR emphasized three areas that facilitate drug counterfeiting: legal systems that fail to punish these crimes with jail sentences; commerce conducted outside of normal channels; and public purchases derived from the bidding process. It suggests that pharmaceutical associations maintain controls on the marketing of drugs.

J. Villacorta, DRA of Peru congratulated the working group on its progress. He noted that Peru has an implementing agency charged with drug regulatory functions, inasmuch as drug counterfeiting is addressed by the offices of the government attorney, the customs authority, etc. He acknowledged that Peru has had a lot of problems with contraband products entering the country which are subsequently used in the production of pharmaceuticals. Villacorta suggests that the Region consider implementing systematic initiatives to facilitate coordination among the many different sectors participating in such processes.

The representative DRA of Dominican Republic shared the experiences of his country, noting that the Dominican Republic has a multisectoral agency in place to monitor drug counterfeiting and contraband activities, and that the agency coordinates with national and international industry. However, no measures are in place to severely punish criminals despite the fact that the appointment of a special government prosecutor charged to investigate drug counterfeiting. One strategy has been to publish the drug counterfeiters in the media, which has proved helpful. He proposed launching an international publication and network to share this information.

Sabine Kopp (WHO) noted that she was very pleased to hear that the document prepared by Geneva was being used as an instrument. She state that in keeping with the agreements reached at ICDRA, a meeting would be held this year, most likely in the last half of 2005, at which the countries of the Region of the Americas would be invited to participate.

J. M. Cousiño expressed his satisfaction with the proposal. He congratulated the Group and thanked the representative of Colombia for sharing that country's experiences. He noted that the problem of drug counterfeiting is worldwide phenomenon and that the participation of all pharmaceutical companies is needed in this regard. He also spoke to the need for countries to commit to a plan, ensuring confidentiality in plans of action, and incentives to report counterfeit drugs, versus than mandatory denunciation, so as not to compromise the brand. He suggested revisiting the term of sentences and called for longer sentences as a means to prevent recidivism.

P. Osbourne, DRA of Jamaica asked those countries that have a legal framework in place on drug counterfeiting to assist the smaller countries that do not have the relevant legislation.

Conclusion of session 8:

The CDC/WG proposal was accepted with the observations raised.

Session 9

IX. BIOEQUIVALENCE

Moderator: Pablo Solís, Regulatory Authority/Panama

1). Doc. IV-2: Bioequivalence Working Group (BE/WG), Report and Proposal: Criteria for Bioequivalency Trials, Bioavailability and Strategic Framework for its Implementation. Group Coordinator, Justina Molzon (FDA), Silvia Giarcovich (ALIFAR), Salomón Stavchansky (University of Texas), and Ricardo Bolaños (ANMAT).

Silvia Giarcovich presented background information on work carried out to date, the objective of the study, and detailed information gathered by the drug regulatory authorities of each participating country, as well as information obtained from a questionnaire administered in both English and Spanish regarding:

- ✓ The legislation of GCPs and BE;
- ✓ The demand for BE studies and prioritization criterias;
- ✓ The centers for *in vivo* studies;
- ✓ The potential for DRA to perform evaluation, monitoring, and inspection activities;
- ✓ The amount of reliable in vivo studies performed; and
- ✓ The training.

She reported on the methodology used to analyze responses and the general conclusions (Presentation in annex 19).

Justina Molzon presented background on the working group and on the work plan proposed in response to the prioritization of the work of this working

group at the last conference. She also provided a summary of the group members, the various meetings held, and the training programs carried out.

Following, the group defined its mission and prioritized the following four objectives:

- ✓ To develop scientific criteria for products requiring *in vitro* or *in vivo* BE studies and for those that do not;
- ✓ To develop a lists of pharmaceutical products requiring *in vivo* BE;
- ✓ To develop a lists of pharmaceutical products that do not require *in vivo* BE; and
- ✓ To develop a list of comparator drug products for use in the American Region.

Molzon reported on activities of the working group, and presented the working group study carried out by Silvia Giarcovich, including the proposal and specific requests for the regulatory authorities, the PANDRH Network, and for the Working Group (Presentation in annex 20).

Salomón Stavchansky presented the draft document, and provided background information on the Network and the mission of the working group.

He stated that all parties agree on the relationship between drug safety, efficacy, and its manufacture. He discussed aspects of the Group's proposal concerning the scientific bases of bioequivalency studies and comparator drug products, as well as the special consideration presented by antiretroviral drugs. His comments also addressed, to the classification of solubility and related concerns, methods of permeability, and considerations regarding critical drugs (Presentation in annex 21).

Ricardo Bolaños presented on the strategic framework for implementing BE studies, pointing out that because of the specific realities present in Latin America, simply copying models of the developed countries may not be possible. He stated that risk and graduality guided the development of the proposed model. He summarized precedents in Latin America regarding health risk (high, medium, and low) and quantitative selection model, with its two-stage, the score assignment, and the statistical model (Presentation in annex 22).

He mentioned that the pharmaceutical sciences journal will publish monographs that can be applied to biopharmaceutical models.

He asked the authorities to read the documents and submit their comments to the PAHO Secretariat in April (See document).

Discussion:

P. Milla, DRA of Chile proposed that the entire Region of the Americas use a single comparator with a view to minimizing studies between the different

countries. She suggested that once an agreement is reached regarding the document on bioequivalence, a list of key products could be compiled requiring supervision where bioequivalence studies exist.

D. Rumer, DRA of Brazil asked if the working group was open to other strategies to harmonize requirements of BE studies. Rumer asked that the group consider other strategies, such as the one being implemented in Brazil.

In response, R. Bolaños asked that the proposals be channeled through Brazil's member on the BE/WG. S. Stavchansky invited Brazil to submit its proposal to the working group for its consideration and to later issue its conclusions.

M Limeres, DRA of Argentina reflected on what bioequivalence means in terms of the drug registration process—that it is a controversial topic. He asked the members to remember the decision of the Committee in Venezuela; it recommended a strategy of gradual implementation, in accordance to the health risks associated with each drug. He stated that this is precisely the strategy Argentina has followed to date—for drugs with high, medium, and low health risks. He stated that currently, Argentina has been using GMPs as a compliance tool. Accordingly, this makes it possible to evaluate processes, not just isolated situations. Argentina requires BE studies for more than 100 products. "Different countries develop innovative products, but there is no bioequivalence among them. Thus, the analysis envisioned should focus more on product quality and not as a requirement to prevent a drug from being registered."

I. Galano, DRA of Honduras mentioned that this topic has been debated with the Customs Union, but that not much progress had been made since the meeting with the countries of Central America, it is why the documents developed inside the PANDRH Network, i.e., to Guatemala and Costa Rica, would constitute valuable input.

J. Aldana, DRA of Colombia suggested that the debate on bioequivalence continue not as a measure of drug interchangeability, but of drug quality. He pointed out that one must remember the political implications, recalling that Colombia, Ecuador and Peru are party to a free trade agreement, and requested that this document be limited to bioequivalence technical recommendations and not address intellectual property concerns.

He spoke to the need to develop a glossary to unify criteria. He pointed out that bioequivalence studies are required for antiretroviral drugs, and proposed that the problem be studied on a case-by-case basis, taking into account the country's conditions.

Hans Hogerzeil (WHO) congratulated the Group for its very technical and scientific approach to such a sensitive issue, and praised its work in the area of bioexemptions, entailing the need to reduce the number of *in vivo* studies and, consequently, their associated regulatory costs. He was also pleased that all of this is linked to public health risks.

Hogerzeil acknowledged that from the point of view of WHO, they are inclined to develop the global definitions, and to collaborate through personal exchanges and working through official and unofficial channels. He emphasized that these excellent regional initiatives must be pursued, as they can lead to international consensus, and thus, the objective is one of fine tuning international guidelines or guides. As part of the committee responsible for essential medicines, I am concerned about the great overlap in the list of essential medicines throughout the world. Ideally, it is possible to combine all drugs into a single list, together with all the pertinent information."

Conclusion of session 9:

The draft document on BE prepared by the BE/WG was acknowledged and the comments expressed in the proposal were incorporated.

Session 10

X. IMPLEMENTATION

Moderator Rosario D'Alessio (PAHO/WHO)

1). Implementation Strategies, Justina Molzon (FDA) and Mike Ward, Drug Regulatory Authority/Canada

Mike Ward stated that his presentation was extremely important to the implementation of working group products. He presented a diagram used by the ICH in hopes that it would be of use to conference participants.

He stated that implementation of harmonized technical guides by the countries can be such a major challenge as creating the guides. What this means? the results of such efforts will depend on the willingness and commitment of the authorities. The implementation does not have to be overly difficult if an analysis is done beforehand in terms of what is needed for implementation and how to go about it. So even when some guides are still in draft form feedback can still be routed."

He stated that regulatory authorities and the pharmaceutical industry have to work together, and to considerate different regional and national capacities and those areas that are most important. Moreover, he cautioned not to forget to identify high-risk products.

Finally, regarding the challenges, Ward stated, we must decide between two things: why do we do this or that? The answer is that we must always do what we do in support of public health. The other question is: whether can we stop making progress toward the future?. And the answer is a resounding no."

Justina Molzon thanked all the different working groups for their excellent work. She offered a summary of the efforts being carried out in the ICH. She also mentioned the efforts of the working groups tasked to create the guides, and stated that these guides must be implemented in the countries. "This is the reason PhRMA and the FDA were asked to prepare a proposal for

implementing these guides. It is a joint process designed to ensure implementation. The value of this tool is that it can be used in the implementation of these guides and for monitoring once implementation is under way. It has a systems-level focus that helps us to identify the areas of greatest difficulty which require corrective measures."

Molzon stressed the importance of communicating. "We must keep the discussion at a scientific level. The way to communicate what we are doing can be done through publications, the Internet, or meetings so that we can provide notification that the guide will enter into force."

She went on to say that in order to ensure notification of the guidelines, they must be distributed through the legal channels and to the relevant stakeholders, i.e., the drug industry should receive guidelines directly.

Molzon also emphasized the importance of training, qualifying as essential that the relevant stakeholders be familiar with and receive training on the guides. When developing the plan for implementing the guide, she acknowledged that one must consider access to the guide: The guide must always be available and every step must be taken to ensure a smooth implementation of the document. If problems arise when implementing the guide, we need to provide people with an opportunity to ask questions."

She made a point of emphasizing that the pertinent information be made available through forums and workshops, and that the relevant stakeholders be provided with ample notification in order to plan activities. It is important to keep the profile of the participants in mind, and cross-training between the regulatory authorities and the pharmaceutical industry is also critically important, because by participating in the same training activities they are facilitating the implementation.

Molzon pointed out that implementation is the act of putting the guide into practice and that consequently, both drug industry and regulatory authority need to develop the implementation plan jointly, making sure to allocate the necessary resources to this end (i.e. time, budget, and personnel, etc). "Implementation is the most important stage, more so than the development of the guide. We must not forget to have a mechanism in place to identify elements requiring modification, even when scientific advances are present in this specific area."

Molzon affirmed that management includes monitoring to ensure that the guides are used correctly; communication and feedback. "An annual report from all the concerned parties makes it possible to identify any discrepancies between the ideal implementation and what occurs in reality. We need to have a mechanism in place to correct problems as they arise in a timely manner—to take the time needed to make corrections. Training should be ongoing throughout the entire process.

She presented a flowchart for implementation detailing the different stages, each including its own processes and activities. She pointed out that

this can be done in smaller steps and that one can return to the previous stage if necessary (Presentation in annex 23).

R. D'Alessio mentioned that the flowchart presented identifies three stages: the first is pre-implementation, followed by the actual implementation, and finally implementation management. "In recent years, the PANDRH Network has worked hard to select topics and develop proposals to introduce at the Conference. Some topics have yet to be developed; however, we need to focus on the 11 topics presented at this Conference. Everyone here can identify gaps in the three stages of implementation: some can be planned for in the pre-implementation stage, while others can be identified during the training stage, and still others can be determined during implementation."

Discussion:

M. Álvarez, DRA of Guatemala spoke about the potential anxiety experienced by regulatory authorities regarding implementation. Accordingly, the most important concern was the timing of implementation. A process is needed through which the documents that have been prepared can take effect. The priority assigned to each topic also needs to be considered. We have to use the documents we have available. These are a necessary element, although not necessarily one that has been followed with regard to training. We cannot enjoy the privilege of training if we are not convinced of implementing and using what we have developed.

R. D'Alessio pointed out that to that training activities to date have been based on educational materials prepared by WHO or the Working Groups on Good Manufacturing Practices (GMPs) and Bioequivalence (BE), but not the proposals developed by the Network. This Conference is the vehicle that facilitates the work of the Network in this area because we have already proposals that have been adopted by the Conference. We must also consider what the regulatory authorities' will accept in terms of a given topic—whether or not they consider the topic selected to be important, i.e., the guide on GMPs, in which case training activities on that topic would be carried out in those countries that want them."

I. Galano, DRA of Honduras pointed out that there must be a willingness to adopt the products of the different working groups, and that the stage proposed by some of the Groups is different. We need to begin a review in order to make the necessary adjustments little by little, but in some cases we can proceed with implementation. For this work, we need the support of the Regional team and PAHO.

M. A. Morales, DRA of Costa Rica pointed out that the work seen here is not suitable to be carried out individually and should be done jointly as a bloc in order to achieve levels as yet unattained. For example, we in Central America should analyze this as a bloc so that subsequently we might achieve levels reached by other countries, such as the MERCOSUR member countries. We

need to begin the process in the short term in order to achieve what we have proposed for ourselves in the medium term.

The workflow proposed should be adopted by all the countries and to convey it within our country, if we have as partner the part and counterpart can be initiated the implementation and show results faster.

R. Abete (ALIFAR) expressed the opinion that the focus was drifting from the technical aspects and that success means implementing the guidelines. We need to understand that the interests of science should not take precedence over human interests. If we conduct a strategic analysis, we should not focus solely on the strengths we have been hearing about—we must also take a look at the weaknesses we discover as we implement the process. We need only look to globalization for some big examples that did not foresee unemployment or exclusion. For this reason, I recommend that we take the time to carefully consider both sides before we move on to implementation.

D. Rume, DRA of Brazil indicated that by taking a close look at the history of health surveillance it is apparent that changes have been implemented where the political will exists. Implementation will be much easier once each country achieves a more autonomous structure, and provides its technical corps with greater legal strength and stability.

J. Cousiño (FIFARMA) stated that the selection of topics is key. Regulatory authorities can become overwhelmed if they are made to implement everything at the same time. We believe that the document on GMPs is a comprehensive instrument that facilitates implementation, as is the case with good clinical practices and drug counterfeiting. Bioequivalence is a topic that is not so 'selectable.'"

He indicated that implementation should be done at the subregion level and with the commitment of the Network to provided advisory services. These processes strengthen the implementation of drug policy; they carry more weight than a policy formulated in a given country.

In response, J. Molzon pointed out that the ICH had devoted no less than nine years of work to the strategy. This is a starting point; the ICH should join with other regional processes under way. Its development was called for because the drug regulatory authorities and the drug industry wanted an individual focus. This process was developed over a very long time—in the implementation of the guides that were prepared, based on recent experience. Of course, this implementation strategy is only one of many possibilities.

M. Ward recommended that the focus stay limited to the most important: "We cannot adopt all the guidelines or modify them if necessary. We need time to implement them. We need to look at this as a network of countries—to advance together as a bloc. The ICH has introduced a stage to analyze whether it is important to conduct feasibility studies for certain topics. We have to take a look at the usefulness of this tool, and all of the pertinent stakeholders must be on board."

2). Panel Discussion – National Regulatory Authorities (by subregion)
MERCOSUR: Pamela Milla, Regulatory Authority/Chile
Andean Community: Juan Villacorta, Regulatory Authority/Peru
Central America: Pablo Solís, Regulatory Authority/Panama
CARICOM: Ivette Silvester, Regulatory Authority/Trinidad & Tobago
NAFTA: Federico Meixueiro, Regulatory Authority/México.

Pamela Milla (MERCOSUR): There are still differences among countries. We have to work together on implementation and it is important to keep in mind the opportunities to hold training activities—not only traditional training but also Internet-based virtual training. We must face the challenges we have made for ourselves.

Juan Villacorta (Andean Community): The Andean Community evaluates and issues opinions on all of its activities, including the level of organization, high-quality technical solvency, and a great commitment. Very important in this regard is the meeting where specific products are provided that can be implemented and adopted by the countries. The Andean Community helps us to solve the problems that we face.

The Community sees the Network as a means of sharing information and that it is important to continue the process. With respect to the document on GMPs, the Community believes that the countries should review and implement it on a gradual basis. With regard to GCPs, the Community considers the document to be well-prepared from the technical standpoint. The document on drug counterfeiting needs to be consolidated, inasmuch as it constitutes a serious problem in our countries. The documents on the Registry and Bioequivalence are in transition and require more extensive work to get them in optimal order.

With respect to the implementation strategy, the proposed flow is acceptable. The Andean Community has passed a resolution requiring all of these points to be considered jointly in order to take stock of the progress made in each country.

I should like to take this opportunity to thank the organizers and ask the Conference to be forthcoming in its support for the work ahead and the sharing of information so that we can successfully implement the goal we have set for ourselves."

Pablo Solís (CA): It is an honor to represent the Region at this Conference of the Network. Central America (CA), Dominican Republic (RD), and Cuba have met on each of the topics, and, although small countries lacking resources in certain areas, especially in regard to academic capacities, our decision is that each of these products constitutes a resource that cannot be set

aside, and hence, our countries commit to implementing these documents in accordance with our capacities.

This Conference has not only stated what needs to be done, but it has also provided the tools to do it. Accordingly, we believe we can move forward and achieve harmonization.

We consider the problem at hand to be the structure of fundamental laws that hinder implementation of the changes planned as fast as we would like.

With regard to the documents, the document on GMPs is a technical instrument which has been discussed among the drug regulatory authorities of CA, DR and Cuba, with a view to studying and developing a plan of work for its implementation. We must not forget the challenge facing CA in terms of its Free Trade Agreement (FTA) with the United States, and likewise, Panama will enter into another bilateral FTA, so sooner or later we will have to address these issues.

With regard to the document on drug counterfeiting, we recommend a review of legislation and coordination with other agencies involved in this struggle.

With regard to GCPs, disparities exist among the regulatory frameworks in each country, thus a study is needed to determine how to go about implementing the document. Moreover, a self evaluation of national drug regulatory authorities is in order since we need to know where we are now in order to know where we want to go.

With regard to the Drugs Registration, our countries believe this is currently less problematic. We embrace the document, endorse its content, and propose that steps be taken to facilitate its distribution.

With regard to the document on Bioequivalence, our countries recommend that the experience of Cuba in this area be considered with a view to regional implementation; Costa Rica and Panama have a new document and hope to implement it.

Our countries wish to thank the Conference and the Working Groups for sharing their vision of the work ahead."

Ivette Silvester (CARICOM): She thanked PAHO/WHO for its efforts to ensure that the countries of the Region have access to safe, effective, and good-quality drugs. She affirmed that the discussions were productive and that more debate is needed in some areas. She considered the Working Groups were beneficial despite the existing language barriers.

The guidelines are ready to be implemented. They are safe and will be assisted with support from the Network for this purpose. Some legal aspects require that laws be modified. Our hope is that these guidelines will benefit the Caribbean and all the countries of the Americas.

Federico Meixueiro (NAFTA): He thanked the Conference for the opportunity to participate at this forum: As we know well, the icon of this era is change; change within change. Each new scientific discovery is being give sixty four times more rapidly than the previous. Not only are we witnessing a shift in the medical-scientific paradigm, but our entire lives are changed as well. In fact, some Mayan prophecies predict the world will come to an end in 2012.

We need not look to the future with fear and apprehension. This meeting brings together a proactive group for the purpose of regulating drugs. Today, illiteracy does not mean not knowing how to read, but not knowing how to think.

Mexico, as part of tripartite group, is a country that has dealt with several of these problems such as drug counterfeiting. We have been active participants, although we are not as far along as the United States and Canada, but in the context of globalization, we are feeling the pressure.

Mexico is making general progress in all of these areas. Drug inventories are renewed every five years, and of the 50,000 products registered only 7,000 are marketed. The discussions at this Conference will help us to get better organized in this area.

With regard to the documents, the one on GMPs is on the right track. The guide on GMPs is seen as a good contribution. As for the document on GCPs, t research protocols are under study and revision. We are working with authorized third parties on the BE document.

Finally congratulations are in order for the coordinator of the Working Groups and I would also like to congratulate them on the implementation proposals, which is the culmination of the entire process.

3) Conclusions and Recommendations
María Dolores Pérez-Rosales, (PAHO/WHO)

María D. Pérez-Rosales presented the conclusions and recommendations of the documents and proposals submitted to the Conference by the Working Groups. The conclusions and recommendations were compiled from the discussions held at the end of each session, from round table events held at the close of each day, and the written recommendations.

She pointed out that the Secretariat is in charge of preparing the final version of the Conclusions and Recommendations, but that preliminary drafts would be shared with the Working Group coordinators for their input. Finally, she indicated that all the material will be featured on PAHO's webpage dedicated to the PANDRH Network.

Session 11

XI. CLOSING CEREMONY

The closing ceremony was led by Dr. **Sabino Báez**, Minister of Health and Social Welfare; **Dr. María Villa**, Deputy Minister of Public Health and Social Welfare; **Dr. Socorro Gross**, PAHO/WHO Representative in the Dominican Republic; **Dr. Germán Velásquez**, Deputy Director of the Technical Cooperation and Essential Medicines Department of WHO; and **Dr. Jorge Bermúdez**, Unit Chief, Essential Medicines and Technology, PAHO/WHO.

Everyone congratulated the participants on their hard work during the Conference, and also emphasized the importance of the Network in terms of making progress in the harmonization of drug regulation in the Region, qualifying it as an example for other regions to follow.

The participants were urged to implement in their countries all the tools approved by the drug regulatory authorities, and were encouraged to continue working and sharing experiences at the subregional and country level.

The organizers of the Conference were congratulated, singling out the local organizers on their excellent logistical execution and hospitality. Finally, the Fourth Pan American Conference on Drug Regulatory Harmonization was declared closed.

IV PAN AMERI0CAN CONFERENCE ON DRUG EEGULATORY HARMONIZATION

2-4 MARCH, 2005

PARTICIPANTS

COUNTRY/NAME	INSTITUTION
ARGENTINA	
1. Manuel Limeres	ANMAT, NRA, S. Comittee PANDRH
2. Ricardo Bolaños	ANMAT, WG/BE
3. Patricia Saidon	ANMAT, WG/GCP
4. Rodolfo Mocchetto	ANMAT, WG/GMP
5. Perla Buzchiazzo	CC/RUD, UNIV. LA PLATA
6. Ruben Abete	ALIFAR, Steering Comité PANDRH
7. Miguel Maito	ALIFAR, WG/Regist; WG/Counterf.
8. Silvia Giarcovich	ALIFAR, WG/BE
9. Ana M. B. de Dehó	FIFARMA
10. Bautista Marinaro	FIFARMA
11. Gustavo Dodera	Pharmaceutical Forum
BAHAMAS	
12. Marvin Smith	NRA/MOH
BARBADOS	
13. Maryam Hinds	NRA/MOH; CC/Drug Suply
BELIZE	
14. Sharon Sanchez	NRA/MOH
BOLIVIA	
15. Victoria de Urioste	NRA; PANDRH Sttering Committee
BRAZIL	
16. Davi Rimel	AMVISA, NRA; S. Comité PANDRH
17. Dirceo Raposo	ANVISA
18. Franklin Rubienstein	ANVISA
19. Maria Graca Hofmeister	ANVISA, GT/Counterfeiting
20. Maria A. Oliveira	CC Drug Policy (Rio)
21. Marcela Saad	ALIFAR
22. Dante Alario	ALIFAR
23. Nelly Marin	PAHO/Brazil
CANADA	
24. Mike Ward	Health Canada/NRA
25. Conrad Pereira	Health Canada/ WG/BE

CHILE	
26. Pamela Milla	ISP/NRA
27. Magdalena Reyes	ISP/WG/GMP
28. Jose M. Cousiño	FIFARMA/S. Committee PANDRH
29. María A. Sánchez	ALIFAR
COLOMBIA	
30. Julio C. Aldana	INVIMA, NRA, S. Committee PANDRH
31. Claudia Mora	Univ. Nacional Colombia
32. Gina Buendía	INVIMA
33. Claudia Vacca	AIS/INVIMA
34. Maria Claudia García	FIFARMA
35. Claudia Osuna	FIFARMA
36. Alberto Bravo	ALIFAR
37. Rafael Cadena	ALIFAR
38. Maria A. Sanchez A	LIFAR
39. Juan Manuel Gutierrez	ANDI
40. Cristina La Torre	PAHO/Colombia
41. Amparo de Pacheco	ANDI
42. Cruz de Moncaleano	ANDI
43. Gloria Boenheim	ANDI
COSTA RICA	
44. María de Angeles Morales	NRA; PANDRH Steering Committee
45. Ana María Fallas	ALIFAR
CUBA	
46. Rafael Pérez Cristiá	MOH, NRA
ECUADOR	
47. Zoila Navarrete	MOH, NRA
48. Juan Arriola Colmenares	ALIFAR
49. Eduardo Mayorga	ALIFAR
50. Salomón Jiménez	FIFARMA
EL SALVADOR	
51. Patricia de Hernandez	MOH, NRA
52. Carlos Silva La Torre	ALIFAR
53. Carmen Estela Perez	ALIFAR
GUATEMALA	
54. Marta de Álvarez	NRA; PANDRH Steering Committee
55. Beatriz Batres Jiménez	MOH; WG/Classification
56. Luis Velásquez	ALIFAR

57. Enrique Pineda	ALIFAR
58. Rodolfo Lambur	FIFARMA
59. Virginia González	FIFARMA
60. Juanita Rodríguez	PAHO/Guatemala
GUYANA	
61. Lall Bahader Singh	MOH/NRA
62. Robert Brohim	CARICOM
HAITI	
63. Christophe Herat	PAHO/Haiti
HONDURAS	
64. Iris Galeano Barralaga	MOH/NRA
65. Isabel Reaman	PAHO/Honduras
JAMAICA	
66. Princess T. Osbourne	NRA, PANDRH Steering Committee
MEXICO	
67. Federico Meixueiro	NRA/Steering Committee PANDRH
68. Marisela Poot Grajales	FIFARMA, WG/GMP
69. Matilde Damian	FIFARMA
70. Rafael Gual Cosio	FIFARMA
71. Héctor Bolanos	FIFARMA, WG/Classification
NICARAGUA	
72. Nubia Lacano	MOH/NRA
73. María E. Berrios	PAHO/Nicaragua
74. Benito Merchant	AIS/Nicaragua
PANAMA	
75. Pablo Solís	MOH/NRA
76. Jeronimo Aversa	Official Lab Quality Control
PARAGUAY	
77. Gustavo A. Adorno	MOH/NRA
PUERTO RICO	
78. Ilia Oquendo	Univ. Puerto Rico
PERU	
79. Juan Villacorta	MOH/NRA
80. Rosario Vega Huanta	Official Lab Quality Control
81. Manuel Yzaga Salazar	ALIFAR
82. Corina N. Valdivia	FIFARMA
83. Martiza R. Valdivieso	FIFARMA
84. German Rojas	AIS-PERU

85. Mauricio Bustamante	ORAS
86. Alejandro Midzuaray	PAHO/Peru
87. Pedro Alvarez Falconi	INS
REP. DOM	
88. Sabino Baez Garcia	MOH
89. Socorro Gross	PWR/PAHO-WHO D. Rep.
90. Olanda Fermin	SS/ARN
91. Leila Mejia Roldan	ALIFAR
92. Dalia Castillo	OPS/Rep. Dom.
93. Elena Fernandez	PROMESE/CAL
94. Gustavo Rojas Lara	Executive
95. Bautista Rojas Gomez	CERSS
96. Mussetta Cedeño	Univ. Autonoma
97. Miguel Ureña	PROMESE/CAL
98. Dignora Mejia	Univ. Central del Este
99. Rhayza Almanzar de Mena	Univ. Pedro Herniquez Ureña
100. Maria E. Tapia	CERSS
101. Adolfo Sagredo	PROSISA
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102. Lilian E. Komproe	MS/NRA
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103. Francis Burnett	OECS, WG/Counterfeiting
T & T	
104. Yvette Sylvester	MS/NRA
URUGUAY	
105. Lourdes Galvan	MS/NRA
USA	
106. Justina Molzon	FDA, WG/GMP, WG/BE
107. Millie Barber	FDA, WG/GMP
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109. Stan Woollen	FDA, WG/GCP
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112. Jonathan Simon	CC, Policy (Boston)
113. Roger Williams	USP, WG/BE
114. Loreta Marquez	FIFARMA, WG/BE
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116. Anthony Ventura	FIFARMA, WG/GCP

117. Cynthia Wang	FIFARMA
118. Silvia Samaniego	FIFARMA
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121. Enrique Fefer	R/PAHO
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122. Esperanza Briceño	MOH/NRA; WG/Registration
123. Araminta Marin	MOH/INH
124. Elsa Castejón	MS; WG/GMP
125. Leopoldo Landaeta	MOH
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127. Rosangela de Sario	FIFARMA; WG/Registration
128. Estela Hidalgo	FIFARMA
129. Raul Cardona	ALIFAR
130. Miguel Angel Lopez	PAHO/Venezuela
PAHO/HQ	
131. Jose Luis Di Fabio	
132. Jorge Bermudez	
133. Rosario D'Alessio	
134. Olga Yuri	
135. Maria Dolores Perez	
136. James Fitzgerald	
137. Jose Luis Castro	
138. Jose Maria Parisi	
139. Jose Daniel Pena	
WHO	
140. Hans Hogerzeil	
141. German Velásquez	
142. Sabine Koop	
143. Daniela Bagozzi	