PAN AMERICAN NETWORK FOR DRUG REGULATORY HARMONIZATION:

AN OVERVIEW

Index

I. Introduction and Background 4

II. The World Health Organization and harmonization of drug regulation 5

III Pan American Conferences for Drug Regulatory Harmonization (PACDRH) 5

First Pan American Conference for DRH: 6
Second Pan American Conference for DRH: 7
Third Pan American Conference for DRH: 7
Fourth Pan American Conference for DRH 8

IV. The Pan American network for Drug Regulatory Harmonization (PANDRH) 9

PANDRH' Operational Process 10
PANDRH Working Groups 11
1. *Working Group on Good Manufacturing Practices (WG/GMP)* 11
2. *Working Group on Bioequivalence and Bioavailability (WG/BE)* 12
3. *Working Group on Good Clinical Practices (WG/GCP)* 13
4. *Working Group on Drug Registration (WG/DR)* 13
5. *Working Group on Drug Classification (WG/DC)* 14
6. *Working Group on Combating Drug Counterfeit (WG/CDC)* 14
7. *Working Group on Pharmacopoeia (PWG)* 15
8. *Others WG and Projects* 15

Finance of PANDRH 17
Advantages of PANDRH 18

Final comment 19

Author:

Rosario D'Alessio, PAHO/WHO[1]

[1] *Rosario D'Alessio is the Regional Advisor in Medicines and Pharmaceutical Services of the Pan American Health Organization and has been the coordinator of PANDRH'Secretariat.*

I. Introduction and Background

Access to pharmaceutical products is based on the availability of national drug policies as part of the health policies, and is directly related with the quality of health care. Furthermore, since the purpose of the drugs is to diagnose, to prevent or to treat diseases or illnesses of the human beings, drugs are also an element of social order, justice, and equity. [2] Access to essential drugs is considered an issue of human rights.

Drug Regulatory harmonization processes contribute to access to quality public health services by developing consensus on common standards on the quality, safety and efficacy of medicines. It also allows avoiding duplication, rationalizing time and costs, and promotes faster introducing into the market of new priorities drugs. It can also facilitate developing transparent and fair regulatory processes and are part of open market policies at sub-regional, regional and global levels.[3] In the past twenty years, much progress has been in regulatory harmonization throughout regions. Some of the significant initiatives include the Association of South East Asian Nations (ASEAN), and the Collaboration Agreement of Drug Regulatory Authorities in European Union Associated Countries (CADREAC). The European Union is one of particular success with a centralized system in place for drug registration for products to be marketed at the regional market, whereas countries continue to operate their own registration systems for products whose circulation is limited to national markets.[4]

There are also inter-regional initiatives: the International Conference on Harmonization (ICH) among Europe, Japan, and the United States, and the International Conference of Drug Regulatory Authorities (ICDRA), a biannual Conference organized by the WHO and the national authorities of the country where the Conference takes place.

In the Region of the Americas, countries are increasingly involved in drug regulatory harmonization and all five sub-regional free trade integration groups in the Region, are addressing this issue with different degree of development and different strategies. Free trade initiatives between countries include the North American Free Trade Agreement "NAFTA"; the Central American Integration Agency "CAIS"; the Andean Community of Nations "CAN"; the Caribbean Community and Common Market—"CARICOM"; the Southern Cone Common Market "MERCOSUR" and other regional organizations such as the Latin American Integration Association , know as ALADI for its Spanish acronyms (Asociación Latinoamericana de Integración.[5]

---

[2] Executive Committee document, CE 126-15 on Drug Harmonization in the Americas, presented at the 42nd PAHO/WHO Directing Council

[3] 11th ICDRA Proceeding. Madrid 2004. MSCE, AEM, WHO.

[4] Doc IV-1 IV Pan American Conference on Drug Regulatory Harmonization. GMP Report and Proposal

[5] Executive Committee document, CE 126-15 on Drug Harmonization in the Americas, presented at the 42nd PAHO/WHO Directing Council.

II. The World Health Organization and harmonization of drug regulation

The Constitution of the World Health Organization (1946) specifically directs WHO "…to develop, establish, and promote international standards with respect to food, biologics and pharmaceuticals and similar products." Expert Technical Committees develops such standards and recommendations for internationally accepted standards, policies and reference materials. Those standards contribute to the global harmonization of essential pharmaceutical regulation. Some of them include the International Common Denominations proposed by the WHO; the International Pharmacopeias; standards of Good Manufacturing Practices (GMPs); the certification system for quality control of pharmaceutical products traded internationally; Good Clinical Practice (GCP) standards, and guidelines on requirements for the registration of interchangeable generic drugs. It also includes the automated system for drug registration, the guideline for the Evaluation of Medicinal Products used in the Self-medication, among others The International Conference of Drug Regulatory Authorities (ICDRA), already mentioned in this document, is also a WHO activity that promotes regulatory harmonization. It have been organized by WHO every two years since 1980 with the objectives of promoting harmonization, exchange of information and development of collaborative approaches to problems of common concern to all drug and biologic regulatory authorities in the world.[6]

The Pan American Sanitary Conference of the Regional Office of WHO for the Americas also supports the development of essential drug policies. Technical cooperation in the area of drugs includes drug legislation and registration; drug manufacturing and marketing; drug use and drug financing; that promotes the establishment of pharmaceutical services and drug information for health workers and public education promoting the rational use of medicines. Access and intellectual property rights are also becoming part of the technical cooperation of the Organization. Drug regulatory harmonization has become part of PAHO technical cooperation and the main strategy to deliver support in the area of drug regulation.

III Pan American Conferences for Drug Regulatory Harmonization (PACDRH)

PAHO has convened three Pan American Conferences on Drug Regulatory Harmonization. Those Conferences are based on the Panamericanism spirit that is carried out in PAHO continental activities. The Conferences bring together all regulatory authorities of PAHO Member States, together with other members of regulatory agencies and representatives of regional associations of the pharmaceutical industry. The academia, consumer groups, professional associations and representatives form all five sub-regional trade integration groups in the Americas, are also invited to participate at the Conferences. The Conferences are open forum to discuss issues of common interest in drug regulations.

The Conferences are held every two-three years and is the highest level of authority within the Pan American Network for Drug Regulatory Harmonization (PANDRH), to approve or adopt harmonized proposals referred to standards, guidelines, and other recommendations to be

[6] *Doc IV-1 IV Pan American Conference on Drug Regulatory Harmonization. GMP Report and Proposal.*

implemented or considered by all countries in the Region. Thos proposals are developed by technical working groups, and are presented for adoption by the Conferences through the Steering Committee (SC). Conclusions and recommendations of the Conference are to be adopted by consensus and in case there is no consensus in plenary sessions. If consensus cannot be reached, the different points of view will be recorded. [7]

First Pan American Conference for DRH[8]:

The first PACDRH took place in 1997 and it is considered the first step toward the establishment of PANDRH. Among the main conclusions of the Conference are:

- Definition of the term "Harmonization", which should be understood as the search for common ground within the framework of recognized standards, taking into account the existence of different political, health, and legislative realities among the countries of the Region.

- Establishment of the Mission of the Conferences as: to promote regulatory harmonization for all aspects of quality, safety and efficacy of pharmaceutical products as a contribution to the quality of life and health care of the citizens of the countries of the Americas.

- A "Pan American Network for Drug Regulatory Harmonization" as a hemisphere initiative with biennial Pan American Conferences was recommended to be established to provide an open forum for interested parties. That initiative should have:

    - PAHO as Secretariat to coordinate technical cooperation, act as a clearinghouse of the Network, among other responsibilities , and
    - A Steering Committee to enable progress between Conferences by coordinating, promoting, facilitating and monitoring harmonization processes in the Americas.

- All parties concerned with pharmaceuticals from the public and private sectors should be involved and participate in the initiative.

- Financial support should be provided by industry, governments and international agencies and organizations.

- The priority areas to work in DRH are GMP, BE and GCP. However, effort should be made to address other important areas.

- Special attention should be given to:

7 Norms and Procedures of PANDRH. www.paho.org

8 Report of the First Pan American Conference for Drug Regulatory Harmonization. November 1997. Washington DC. www.paho.org

- Health consideration in trade and economic integration processes
- Support to ongoing harmonization process in the region
- Strengthen of regulatory agencies
- Confidentiality of unpublished information

Second Pan American Conference for DRH[9]:

The Second Conference took place in 1999. The main subjects addressed were:

- Advances in Drug Regulation in the Region through sub-regional trade groups were reviewed and reports from the ad-hoc working group on BE and GCP.
- GMP was confirmed once more as key subject to be enforced.
- The Pan American Network for Drug Regulatory Harmonization (PANDRH) which is described in this document.
- The first Steering Committee (SC) was elected with the responsibility of promoting progress between conferences through the coordination, promotion, facilitation, and monitoring of the harmonization processes in the Americas.
- Processes of harmonization should encompass not only the aspects of regulation in the registration of medication but also drug marketing and be analyzed from the standpoint of its impact on improving the access to the drugs.

Third Pan American Conference for DRH[10]:

As the previous two conferences the III Conference took place at PAHO premises, in 2003. Some of the subjects addressed in this Conference were:

- An update on ICDRA, and regulatory harmonization in the five trade groups in the Region were reviewed by their representatives; the impact of ICH in underdeveloped countries; the use of active control in clinical trials and the Helsinki declaration; a case study on Drug Counterfeiting in Colombia; and promotion & sale of drugs through Internet. Resolution CD42/R11CD from the 42nd PAHO Directive Council was also presented.

[9] *Report of the Second Pan American Conference for Drug Regulatory Harmonization. November 1997. Washington DC.* www.paho.org
[10] *Report of the Third Pan American Conference for Drug Regulatory Harmonization. November 1997. Washington DC.* www.paho.org

- Jointly with the Essential Medicine Department of WHO a pre-conference workshop was held on Evaluation of multisource pharmaceutical products with special focus on antiretroviral drugs quality pre-qualification project[11]

- For the first time, technical working groups presented preliminary reports of their work and the Conference made recommendations to each of them. Some of the specific recommendations are:
    - GMP continued to represent a challenge in the Americas and compliance with GMP is a prior condition to the implementation of Bioequivalence, thus the importance of reducing the time frame for total GMP implementation. It was also widely recognized the importance of implementing a WHO-type Certificate of Quality of Pharmaceutical Products Subject to International Commerce;
    - The BE Working Group was aimed to develop specific criteria to prioritize the necessary BD/BE studies and explore the possibility of carrying out such studies prospectively and not retrospectively. BE studies at country level are tied to taking into account the drugs of most use and the available resources; and the Conference recognized that the use of the same reference product for BE studies would facilitate the harmonization process;
    - Harmonization of procedures to evaluate clinical trials protocols was also identified as priority for health authorities and it was recommended to develop an Inspection Guidelines for audits on Good Clinical Practices;
    - The definition of Counterfeit Drugs be expanded to include the concept of fraudulent drugs;
    - The importance of a WHO representative participating in all International Conference on Harmonization (ICH) meetings was recognized as a means of informing the countries of the Americas (that are not ICH members) on the activities and the impact of implementing ICH recommendations.
    - The Conference recognized the effort made by the WG/GMP in training activities and encouraged its members to continue giving priority to these training activities aimed at the implementation of GMP.

Fourth Pan American Conference for DRH

This Conference will take place in March 2005. It will be the first time working groups will present final harmonized proposals requested by previous Conferences to be adopted by regulatory authorities that will participate. There is no doubt that continuity and impact of the Pan American Network fir Drug Regulatory Harmonization as initiative to support harmonization processes in the Americas, will depend on what will happen after the IV Conference. Moreover, it will depend on the degree of acceptance and implementation of PANDRH' recommendations by national regulatory authorities.

[11] *PAHO/WHO. Workshop on Evaluation of multisource pharmaceutical products with special focus on antiretroviral drugs quality pre-qualification project. 24-25 April, 2003. Report*

IV. The Pan American network for Drug Regulatory Harmonization (PANDRH)

PANDRH was established by the II Pan American Conference for DRH in 1999 to support processes on drug regulatory harmonization in the Region. National authorities of countries in the Americas and different interest groups in the area of pharmaceuticals including the pharmaceutical industry and academia participate in the PANDRH initiative, and the Pan American Health Organization is the Secretariat of the Network.

Participation of the public and private sectors are essential in processes of drug regulatory harmonization. It is also expected that Minister of Health, as responsible for national public health, should lead the process generally through national regulatory authorities at national level with and an active participation in sub-regional and international initiatives that deal with drug regulations. Along with the ministries of health, other national institutions are involved in harmonization processes such as those of trade, finances, and the private sector. Within the private sector, the pharmaceutical industry is a key player. It is the industry who has to adopt and implement most requirements to improve the quality of drugs (Q,S,E) and of the pharmaceutical market. Another essential player with a clear responsibility in drug regulatory harmonization process is the academia. The educational sector has the unequivocal responsibility of disseminate knowledge and combining the updated knowledge with the real capability of implementing them in different settings. Their work is directed to improving the present (professional practice) and seeding for the future (teaching at schools). Agencies of consumer protection and other groups of interest in the field of the drugs can also make contributions to regulatory processes. Among all the above, the political will is THE essential element for a successful harmonization process.

The support of the political will is needed not only for all decision that should be made within the process, but also because regulatory harmonization may imply the renewal of legislations and regulations to adopt the agreed standards and guidelines; strengthening the organization, administrative, and financing alternatives of existing structures. In addition, renewal and updating of its physical structures and personnel are part of the commitments that the governments and the private sector make in favor of the harmonization processes.

PANDRH is composed by four components: The Pan American Conference, the Steering Committee, the working groups and the Secretariat. Operational norms and regulation for all four were approved during the Second Conference and updated during the Third Conference[12].

The Steering Committee is formed by 12 members: 10 regulatory authorities (five main members and 5 alternates) representing the five sub-regional geographical groups in the Region and two industry representatives, with substitute members.

Steering Committee (Period 1999- 2001)

Regulatory Authorities

Members	Alternate
• Mexico	*USA
• Guatemala	*Costa Rica
• Jamaica	*Trinidad &Tobago
• Brazil	*Argentina
• Colombia	*Bolivia
▫ One rep from FIFARMA	----------
▫ One rep from ALIFAR	----------

[12] *Information on Norms and Procedures of PANDRH at See PAHO web page* http://www.paho.org/english/ad/ths/ev/Norms-pandrh.pdf

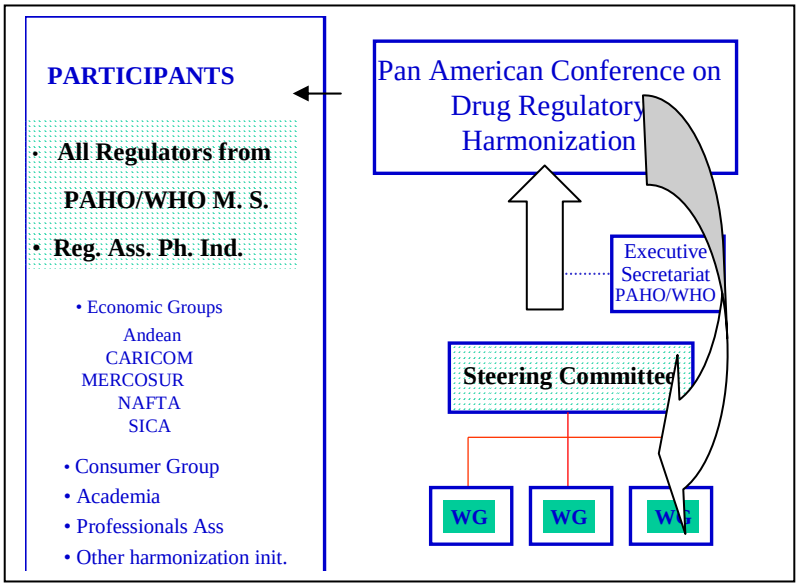
PAHO as Secretariat facilitates technical and administrative support and is the clearinghouse of information to the Conference, the SC and working groups of the Network.

The 42nd Directive Council of the Pan American Health Organization (September 2000) approved Resolution CD42/R11. The Resolution was a strong support from Minister of Health of Members States in the Region to PANDRH and the process of drug regulatory harmonization. The Resolution urges to the Governments to reexamine the pharmaceutical policies with a view to adopting new policies that will guarantee the access to the drugs that are safe, effective and of the acceptable quality; strengthen the infrastructures for the drug regulation; and that recommendations that arise from the PANDRH are carried out. Also, the Resolution requests to the Director of PAHO/WHO to support the establishment of the PANDRH by strengthening the function of PAHO as its Secretariat; promote the progress toward the technical agreements on the drug regulation among the Member States, including the multilateral agreements, bilateral and sub-regional; and promote the search for the sources of financing for the Network. [13]

Since November 2003, PANDRH has become a member of the Global Cooperation Group (GCG) of the International Conference of Harmonization (ICH), an initiative that focuses the requirements to evaluate quality, safety and efficacy of new drugs. The GCG is an opportunity for non-ICH countries to learn and share difficulties and concerns about ICH guidelines and standards. PANDRH representative in the GCG does not represent his/her country but the entire Region. The SC decided that a member of PANDRH Steering Committee represents PANDRH in the ICH/GCG.

PANDRH' Operational Process

The processes of work within the Network are simple and open (See Figure). The highest level of authority is the Pan American Conference which defines the priority areas to work in harmonization processes. The main objective of the Steering Committee is to follow up the Conference' recommendations and monitor the work being developed by working groups. WGs analyze the subject and, if necessary, develop consensual harmonized proposals or adapt international standard and guidelines. Those proposals are developed based on available international documents, primarily those developed by the WHO, other international documents and national regulations.



The documents, guidelines and proposals developed by WGs are reviewed

[13] http://www.paho.org/English/GOV/CD/cd42_r11-e.pdf

by the SC and presented for adoption and implementation in the Region. The Conference may decide to send the proposal back to the WH for further modifications. Since regulatory authorities of all countries in the Region re participating at the Conference it is expected that proposals, documents and guidelines will be adopted by individual countries and are incorporated in the discussion at sub-regional economic groups.

Countries interested in adopting PANDRH proposals, are expected to receive technical support from the Working Group in their national processes.

PANDRH Working Groups

Nine working groups have been established within PANDRH since the start; however, only eight are operating regularly. Minutes of their meeting are available in PAHO web page on PANDRH[14], as well as draft of their documents to facilitate dissemination and participation of regulators and interested groups that are not members of the group. All comments are consolidated by the Secretariat and analyzed by the WG in developing their final proposal. Working groups are coordinated by representatives form regulatory offices but one, WG on Pharmacopoeia) which is coordinated by the USP. This exception was approved by the Conference.

Since PANDRH working groups initiated their work an estimated of 140 professional, mostly from drug regulatory offices of the Americas have participated in technical meetings. Of those, 73 are permanent members of the PANDRH'WGs. Seventy-eight per-cent (78%) of the total members is form regulatory offices, 15% from the industry and 7% from other institutions, mostly from universities. Members are either selected by the SC or are volunteer form NRA interested in the particular subject of the WG. In any case, members should have large experience in the subject and be internationally or nationally recognized expert in the field of the WG. Observers, advisors and resource persons may be required when the group needs eventual technical support is specific aspect the WG is addressing. It should be recognized that Working Groups are based on voluntary work. No member received any payment for their work within PANDRH.

1. Working Group on Good Manufacturing Practices (WG/GMP)

The WG/GMP has 12 members and is coordinated by the FDA/USA. Eighth members are from national regulatory agencies, two from the pharmaceutical industry and two resource persons from FDA. Its Mission is "*To promote the knowledge and implementation of GMPs as a strategy for improving the quality of medications in the countries of the Americas.*" and four major areas are covered by the WG: Education/Training; Development of a Harmonized Guideline for GMP Inspection; Monitoring GMP implementation; and Support to Regulatory Authorities.[15]

[14] *www.paho.org/english/ad/ths/ev/redparf-home.htm*
[15] *II Pan AmericanConference on Drug Regulatory Harmonization. Report www paho.org*

After analyzing the results of a study on GMP Implementation in the Region, presented by FIFARMA in the First Pan American Conference on Drug Regulatory Harmonization, GMP was identified as the main priority subject to address by PANDRH and by countries in harmonization processes. The study presented at that time, pointed out the dissimilar requirements among countries in the application of GMP standards. The Conference recommended that there was a need for implementing GMP standards as those recommended by the WHO. At the Second Conference, emphasis was placed on the responsibility of regulatory authorities for the monitoring and implementation of GMPs.[16]

During these past five years, the WG focus their work in the development of a Regional Guideline for GMP inspection which will be presented for adoption at the IV Pan American Conference in March 2005. The Guideline is based on WHO-92 Technical Report for GMP standards and addendums until date. The approval of a common guideline will help to improve the quality of drugs by requiring better standards and also in building trust among regulatory agencies in the region.

2. Working Group on Bioequivalence and Bioavailability (WG/BE)

The WG/BE is composed by 12 members and coordinated by the FDA/USA. Seven members are from regulatory agencies, two from the industry, one from the academia, one resource person and one from the USP. The proposed Mission for the WG is *"to contribute to harmonize bioequivalence criteria for the interchangeability of pharmaceutical products in the Americas"*, and some of its objective are: develop science based criteria for products requiring BE studies; develop a strategy for harmonizing requirement of BE studies; prioritized lists of products that where BE studies are necessary; and develop a list of comparator drug products for use in the Americas region. [17]

Implementation of BE studies in the Region is variable. In a comparative study developed by the WG/BE 96 active ingredients from the WHO list were compared in 10 countries and the study find out that: a) only 4 active ingredients commonly require BE studies in all 10 countries: valproic acid, carbamazepine, cyclosporine and phenytoin. All of them are considered high health risks; b) the country with higher number of AFI requiring BE studies is the USA (88) followed by Canada (60); in Latin America the countries with more AFI requiring BE studies are Cuba (40), Mexico (39) and Brazil (32); and countries with less number of active ingredient with BE study requirements are Colombia (5) followed by Costa Rica (7). The wide divergence observed among countries in their requirement for BE studies, indicates the need to continue working toward harmonization[18].

In the Americas, many countries are engaged in developing Generic drug policies as a strategy to increase drug access and BE has become a key issue in addressing interchangeability of drugs. The group is currently developing a harmonized proposal on Criteria for implementing BE

[16] *Document IV- 1 WG/GMP Pan American Conference for Drug Regulatory Harmonization: Report and Proposal 2005.*
[17] *Document IV-2 WG/BE Pan American Conference for Drug Regulatory Harmonization: Report and Proposal 2005*
[18] *Science Based Criteria for bioequivalence testing (in vitro and in vivo), Bio-Waivers and Strategy for Implementation*

studies and a list of products that require BE studies. A draft of the document will be presented at the next Conference. [19]

3. Working Group on Good Clinical Practices (WG/GCP)

The WG/GCP is coordinated by the *Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (*ANMAT/Argentina) and is composed by 10 members: 8 from regulatory agencies and two from the industry. The Group mission is "*to promote harmonization of GCP in the Americas"*; and its objectives is to support adoption of GCP by national legislations and implementation, and development and promotion of educational programs on GCP mainly directed to regulatory personnel.[20]

Implementation of GCP in the Region varies from one country to another. In 2000, in a study conducted by the WG/GCP on GCP implementation in Latin America in terms of GCPs regulation, found that 10 of the 12 countries that participated in the study, have regulation in place on clinical trials, with different contents, requirements, and application of aspects regarding ethics committees, informed consent, research on vulnerable populations, and certification of researchers and research centers. Inspections of institutions where clinical trials were conducted, were only carried out in three countries. This situation indicated the need in the Region for harmonizing aspects regarding the authorization and follow-up of clinical research.[21]

In many LA countries, clinical researches were limited to IV phase; however, during the last decade, there has been an increase of phase II and III of clinical trials. PANDRH' WG/GCP advocated their work to the development of the document on *Good Clinical Practices: document of the Americas,* which include guideline for Ethics Committees, Informed Consent, GCP inspection, essential documents, responsibilities of researchers and sponsors, among others. This guideline will be presented for adoption to the IV Pan American Conference.[22]

4. Working Group on Drug Registration (WG/DR)

This WG has 10 members and is coordinated by the Regulatory Authority of Venezuela. Eight members are from regulatory offices and two from the industry. The mission of the Group is "*to promote and facilitate the harmonization of regionally recognized and appropriate technical criteria for drug registration to contribute to their QSE and availability in the Americas".*[23]

Laws and regulations for drug registration, marketing and control throughout the Region are frequently inconsistent and incomplete, thus hampering the attainment of health policy objectives.

---

[19] *Ibid*
[20] *Doc IV-3 WG/GCP. IV Pan American Conference for Drug Regulatory Harmonization: Report and Proposal 2005*
[21] *PAHO, Report on the assessment of the situation of Good Clinical Practices in 12 Latin American countries, 2000.*
[22] *GCP: Document of the Americas. PANDRH- GCP/WG. 2005*
[23] *Doc IV-4. WG/DR IV Pan American Conference for Drug Regulatory Harmonization: Report and Proposal 2005*

Moreover, thousands of different pharmaceutical drugs are available from a large number of manufacturers, importers, and distributors. [24]

The first step the WG/DR to work toward harmonization of registration and marketing approval was the developed of a comparative study on drug registration requirements in the Americas to identify differences and similarities in drug registration requirements of pharmaceutical products and to analyze possible effects of differences in the Q,S & E.[25]

At the same time, the WG identified the requirements that should be present in all countries, and from the results of the study, the group selected those that are essential to assure quality, safety and efficacy. The requirements are referred to new entities, generic drug (and similars), new formulation, new strength, new associations, renewal, and biologic (vaccines, recombinant and blood products).[26]

5. Working Group on Drug Classification (WG/DC)

The group has six members and is coordinated by the Regulatory Authority of Guatemala. Five members are form regulatory offices and one from the industry.

Proper drug classification can contribute effectively to public health, and several countries of the region have included in their pharmaceutical policies modification of their legislation to make drugs that can be sold without a prescription more accessible to the population. Harmonization of criteria and marketing strategies of OTC drugs of participating countries is essential for countries in an open pharmaceutical market. Drug Classification has been addressed in the first two Conferences (1997 and 1990).[27],[28]

Through PAHO, the Working Group on Drug Classification conducted a comparative analysis of current legislation. The study was the basis for an integrated proposal for criteria for drug classification to be presented at the IV Pan American Conference (March 2005).[29]

6. Working Group on Combating Drug Counterfeit (WG/CDC)

The WG is coordinated by ANVISA-Brazil, and is composed by nine members, seven from regulatory offices and two from the industry. Their mission is to *" promote, facilitate, and motivate*

---

[24] *WHO, The World Medicines Situation, 2004.*
[25] *PANDRH' Working Group on Drug Registration. A regional Assessment on registration requirements in the Americas. 2005.*
[26] *Doc IV-4. WG/DR IV Pan American Conference for Drug Regulatory Harmonization: Report and Proposal 2005*
[27] *Report of the First Pan American Conference on Drug Regulatory Harmonization, Washington, D.C. November, 1997.*
[28] *Report of the Second Pan American Conference on Drug Regulatory Harmonization, Washington, D.C. November, 1999.*
[29] *Doc IV-6 WG/Drug Classification: Report and Porposal. IV Pan American Conference fro Drug Regulatory Harmonization. March 2005*

implementation of proactive strategies for preventing and fighting drug counterfeiting and thus contribute to the improvement of health care in our countries in the Americas.[30]

In 2002, the WG conducted a regional study to determine the situation of drug counterfeiting in the countries of the region, which was answered by fifteen countries (60%). Drug counterfeiting is a problem that exists in varying degrees in most of the countries of the region. Some of them have taken strong measures to reduce the problem; but, most countries lack up-to-date legislation that would make it possible to address this crime and enforce compliance.[31]

To better address the problem of drug counterfeiting, the WG has developed a road map to evaluate the cycle of implementation by the focal points of each country; a proposed executing unit to implement the actions of preventing and fighting drug counterfeiting as a part of the national health authority. The WG also developed a set of indicators for management and criteria for classification of counterfeit drugs and an educational program that has been tested in Brazil and will be applied in various countries. [32]

7. Working Group on Pharmacopoeia (PWG)

This WG is coordinated by the USP as approved by the II Conference. The PWG is composed of representatives from the four active pharmacopeias in the Americas: Pharmacopoeia of Argentina, Brazil, Mexico and the United States (USP/Secretariat). The mission of this working group is *to create a forum for discussion and exchange of information which will facilitate the adoption of harmonized procedures*; and, a possible objective of the PWG is to have a Harmonized PHARMACOPEIA of the Americas.[33]

8. Others WG and Projects

8.1 *WG/ Medicinal Plants*. Ten members are part of this WG coordinated by Health Canada with no representatives from the industry. The subject of medicinal plants has been addressed by technical cooperation of PAHO in collaboration with the WHO Program of Traditional Medicines, who have worked on the definition and regulations requirements for herbal product[34] and in quality, safety and use of herbal products. [35] The WG is being re-organized to address regulatory aspects.

---

[30] *Doc IV-5 WG/Combat Drug Counterfeiting: Report and Proposals. IV Pan American Conference for Drug Regulatory Harmonization. March 2005.*

[31] *Report on the II Pan American Conference on Drug Regulatory Harmonization. Washington, D.C., November 1999.*

[32] *Doc IV-5 WG/combat Drug counterfeiting: Report and Proposals. IV Pan American Conference for Drug Regulatory Harmonization. March 2005*

[33] *Doc IV-8 PWG Report and Proposals. IV Pan American Conference for Drug Regulatory. March 2005*

[34] *PAHO/WHO Report Regional Meeting on Regulatory Aspects of Herbal Products. Nov 2000, Jamaica.*

[35] *PAHO/WHO Report Regional Meeting on Traditional Medicines and Herbal Medicines. February 2003, Guatemala*

8.2 *WG/Pharmacovigilance*: PANDRH has also a working group on post-marketing surveillance, which has not yet been operational.

8.3 *The External Quality Control Program*. This is a special program implemented by PAHO in collaboration of USP. Its main objective is to strengthen official drug quality control laboratories. Twenty two laboratories are participating in this Program. The EQCP began with a new diagnostic study of official drug quality control laboratories of the Region, and up to date four phases of the External Quality Control Program for Official Drug Quality Control Laboratories (EQCP) have been performed. Parameters for evaluating laboratories performances include: weighing, equipment, precision, reproducibility, relative standard errors, reporting of data and interpretation, limitations of the monograph, and familiarity with USP methods. According to the results, labs are classified in four groups: Group 1: laboratories whose performance of the tests was excellent; Group 2: laboratories whose performance was good; and Group 3: laboratories whose performance was very poor. [36]

8.4 *Training*: Training activities are an important component of PANDRH. During the last five years specific educational seminars included:

8.4.1 Regional workshops on GMP organized by the FDA and the Pharmacy School of the University of Puerto Rico (UPR). Those activities are offered on an annual basis in the premises of the UPR during summer and professors and FDA personnel participate as trainers. Since June 2000 four regional seminars have been offered and participants included government officials and private industry.

8.4.1 Educational seminars on GMP were organized by PAHO in collaboration of professors from pharmacy school of Latin American universities. Those courses are based on WHO educational modules and are implemented at national level to facilitate participation of more professionals in each country. Trainers in those activities are professors of national universities and members of working groups that volunteer. Participation of both: faculty and inspectors are essential, the former for teaching methodology and inspector for their practical experience.

8.4.2 Workshops in HPLC use for quality control labs, organized by PAHO and the USP.

8.4.3 Sub-regional seminars on BE, organized by PAHO and the FDA.

8.4.4 Courses organized jointly with PAHO and national agencies for sub-regional level such as the one organized on GMP with ANMAT and INAME from Argentina, for MERCOSUR countries.

[36] *Doc IV-7 External Quality Control Program: Report and Proposal. IV Pan American Conference for Drug Regulatory Harmonization. March 2005.*

8.4.5 National seminars on GCP implemented as pre-meeting of the WG to help to disseminate GCP guidelines and practices.

During the period between 2000 and 2005 (February) there have been 30 workshops with 883 participants (two in BE, 4 in HPLC and 24 in GMP). Some basic characteristics of these educational activities are: Integration of Universities in the process; in general are open to all sectors: regulatory, academia and industry; and are organized jointly with the national regulatory authority.[37]

Finance of PANDRH

The activities in support of the processes of harmonization imply the availability of budgetary resources for the financing of the operation of the Network, which include the Steering Committee, the technical Working Groups and the Pan American Conferences.

PANDRH operations have been financed mainly with PAHO funds; and by regulatory agencies such as the FDA, who also contributed to financing working groups operation. The two Latin American associations of the pharmaceutical industry, FIFARMA and ALIFAR, have contributed to the Pan American Conferences. Registration fees at the Conferences and contributions from individual pharmaceutical industry are also acceptable sources as approved by PAHO Directing Council in Resolution CD-42, but until now none of these two sources have been used.

However, as it is stated in the background document of Resolution CD-42 on PANDRH the real cost of harmonization also demand specific cost from: [38]

Governments:

- Hours/man of regular staff of the institutions involved in working groups and at national institutions in developing documents, analyzing data etc;
- Cost of implementing at national level regional agreements that imply improvements in terms of physical plants, new or updating operational functions and organization; acquisition of new equipments; hiring new personnel and training existing human resources.

Industry

- The participation of its representatives at the technical meetings;
- The costs of implementing regional agreements terms of physical plants, new or updating operational functions and organization; acquisition of new equipments; hiring new personnel and training existing human resources.

[37] *Doc IV-9. PANDRH Educational Seminars. IV Pan American Conference on Drug Regulatory Harmonization. Report. March 2005*

[38] *Executive Committee document, CE 126-15 on Drug Harmonization in the Americas, presented at the 42nd PAHO/WHO Directing Council.*

PAHO/WHO

- Hours/staff member to meet the Secretariat responsibilities of the Network, of the Executive Committee, and of the Conference;
- The coordinating and/or delivery of technical assistance in the identified areas of priority for the harmonization processes at regional, sub-regional, and national levels;
- Production and dissemination of standards, guides, reports, and agreements.

Advantages of PANDRH

1. The Pan American Network has become a forum for most countries in the Region to discuss common issues on drug regulation. Not all countries are involved in actually developing the proposals, but all of them are participating in the decision of adopting them. Drug regulatory authorities, by participating in the process are strengthening their national process.

2. PANDRH has promoted to build a constructive dialog among all sectors that are participating in the process, through technical working groups. The involvement of the industry, through their technical experts have been a contribution to this constructive dialog and to the technical level of the guidelines and other proposals developed;

3. The work of PANDRH, have been beneficial to national universities that are participating in training activities in terms of updating program of studding for undergraduate as well as for postgraduate and continuing education programs. PANDRH facilitates access to most recent advances in the areas of drug regulations. National Drug Regulatory agencies also benefited from participation of the academia since through educational activities their human resources have had opportunities for updating and training;

4. National Regulatory Authorities lead the process of discussions and preparation of harmonized proposals, standards and guideline. Professional experts from regulatory offices are the majority of members of each technical group. And all but one WG are coordinated by national regulatory staff. Drug regulatory agencies of the Region drive and lead PANDRH work;

5. PANDRH promotes technical cooperation among countries. Those with more developed regulatory agencies share knowledge and experiences with less advanced agencies;

6. Being training an important component of PANDH, the network is a permanent opportunity for professional development. It improves knowledge of existing international guidelines, it is an opportunity to know what is happening in other part of the world on regulatory issues; and more important, PANDRH gives an opportunity to national experts to know their peers in other countries and jointly discuss common problems and look for most efficient solutions. PANDRH has also facilitate working groups members to participate at

national or international events by organizing their meeting as pre or post international or national meetings, promoting WG members participate as speaker at those events.

7. PANDRH also helps to prioritize health issues in economic integration processes in the region and in drug regulatory harmonization processes. It also facilitate continuity of technical agreements; and encourage convergence of drug regulatory systems in the Region;

8. By adopting PANDRH' proposals on standards, guidelines and strategies, countries in the Region will improve access to Q, S & E drugs because those proposals reduce unnecessary and duplicated requirements for drug registration while improving the quality of the regional pharmaceutical market;

9. PANDRH has also been an effective strategy for WHO and PAHO technical support in the area of regulation by helping to be more cost-efficient, productive in terms of supporting member states and to address impact of its work.

Final comment

In spite of the above advantages, PANDRH real benefit and impact is still to be seen. Since its conception, PANDRH has been producing harmonized proposals to be implemented by countries. Most of them will be presented for adoption at the IV Pan American Conference. It is from that event, that PANDRH will face the challenge of its real usefulness. This challenge is in most part in the hand of regulatory authorities and governments by adopting PANDRH recommendations and implementing them at national level and discussing them within the different trade groups that are operating in the Region.

As PANDRH being an initiative leaded by NRA with PAHO support; so it is expected that NRA will use the tools developed by them in the framework of the Network. The time for doing that will start right after the IV Pan American Conference assuming that harmonized proposals in GMP, BE, GCP, Registration, Classification, Counterfeit, Quality Control and Training will be adopted by the Conference.