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II Pan American Conference on Drug Regulatory Harmonization

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Program on Essential Drugs and Technology (HSE)
Division of Health Systems and Services Development (HSP)

Pan American Health Organization
World Health Organization

1. CONCLUSIONS AND RECOMMENDATIONS

1.1 General Conclusions

1) Drug regulatory harmonization is part of the global integration processes and is consequently influenced by factors outside the health sector. Hence, there is a need for the health authorities in the drug field to assume leadership in these processes.

2) The present Conference recognizes that progress has been made in regulation and harmonization in the Region since the I Conference, although it was also aware that a greater, more continuos effort should be made.

3) The evaluation of drug regulatory harmonization should be accompanied by an evaluation on access to pharmaceutical products. In this regard, the join effort of the public and private sector and specially, the pharmaceutical industry was considered basic to the implementation of policies to improve that access.

4) Harmonization should be understood as the search for common ground within the framework of recognized standards, taking into account and respecting the existence of different political, health, and legislative realities among the countries of the Region. It is necessary to continue strengthening the health authorities to overcome the weaknesses described in the process report on drug regulatory harmonization, adjusting implementation schedules when significant difficulties are observed.

5) PAHO/WHO has promoted criteria for quality in the production, distribution, and use of drugs, as can be observed in the existing and proposed guidelines of the Organization. PAHO/WHO support for the countries regardless of their developmental situation was noted; however, responsibility for the response to this support falls to the national authorities.

6) The regulatory authorities expressed concern about the extend of drug advertising, which leads to irrational use of drugs.

7) The retail drug trade is affected by the establishment, operation, and control of pharmacies in the Region area regulated, which has contributed to irrational use of drugs.

8) There is a clear need for conceptualizing quality as a continuous process, incorporating it into both the drug distribution chain—including drugstores and pharmacies—and the rational use of drugs.

1.1.1 BIOEQUIVALENCE

9) With regard to bioequivalence, a consensus has not yet been reached among national and international industrial sectors on the following:

- Definition of "generic drug"
- Interchangeability of pharmaceutical products
- Identification and prioritization of products requiring in vivo trials
- Preparation of lists of interchangeable, bioequivalent drugs.

Despite all of this, the health authorities expressed interest in promoting the marketing of generic drugs, based on the WHO guidelines.

10) The conclusion of the report experts in bioequivalence experts (Caracas 1999) regarding the need for all drugs, including generics, to meet standards of quality, safety, and efficacy, was reaffirmed. These requirements extend to labeling and adherence to Good Manufacturing Practices.

11) The need for strict, temporary provisions for enforcement of the technical and scientific requirements within a generic drug policy was confirmed. These standards should not be distorted alleging a lack of financial resources, despite the provisions in point 4 of the general conclusions.

12) The cost of bioequivalence studies poses an obstacle for some countries of the Region, since these studies require both infrastructure and expert human resources. Thus, cost-effective mechanisms should be considered, such as recognition of reference institutions in the Region and technical cooperation among countries. In this regard, it was pointed out the support offered by the U.S. FDA for the preparation of guidelines for *in-vitro* studies of products that can demonstrate their therapeutic equivalence.

13) The importance for the Region of programs for bioequivalence studies on high-risk drugs initiated by some countries was pointed out.

1.1.2 GOOD CLINICAL PRACTICE

14) The report of the expert group on good clinical practice (Buenos Aires 1999) is considered a major step forward to achieve harmonization in this field. This report welcomes the recommendations of the *International Conference on Harmonization* (ICH) in this area, with some modifications to suit the reality of the Region.

15) In the past, the few clinical trials that were conducted in Latin America were Phase IV trials and those of a promotional nature. Currently, an increase in Phase II and Phase III studies is being observed. The lack of trained personnel in the countries' regulatory

authorities, as well as in the institutions that conduct the research, limit development in this area. The contributions of private enterprise to the training of investigators were recognized.

16) To date, the majority of the countries do not have programs for monitoring clinical trials, their oversight being limited to the authorization of the protocol.

1.1.3 GOOD MANUFACTURING PRACTICE

17) There is consensus that Good Manufacturing Practices are the basis for quality assurance of pharmaceutical products. Consequently, ongoing training of professionals in both government and industry is required in this field.

18) Some countries still are in the process of implementing Good Current Manufacturing Practices recommended by WHO. An important point to consider is the recognition of current weaknesses so that they can be overcome within a strict time frame.

19) The FDA issued a joint proposal with the University of Puerto Rico and the Pan American Health Organization to provide training in Good Manufacturing Practice for Latin American and Caribbean countries, geared specifically to the health authorities and industry. This proposal was welcomed, with the suggestion that it include courses in distance learning to take advantage of the installed capacity in the Region.

20) It was emphasized that the responsibility of the regulatory authorities includes not only surveillance of conformity with Good Manufacturing Practices, but also surveillance of the chain of distribution and the rational use of drugs.

1.1.4 COUNTERFEIT PRODUCTS

21) Counterfeit products, which exists to one extent or another in the majority of the countries of the Region, is a problem that the authorities are aware of. Some countries have taken forceful steps that have already helped to reduce it.

22) The guidelines for developing of measures for combating counterfeit drugs, recently published by WHO, are a good tool that can be used by the countries for developing their own strategies.

23) The majority of the countries lack up-to-date legislation for combating this crime and imposing exemplary sanctions. Addressing the problem requires the health authorities to coordinate their activities not only with the police and judicial authorities, but with manufacturers and distributors as well.

24) The uncontrolled proliferation of distribution channels and pharmacies in some countries can contribute to this crime.

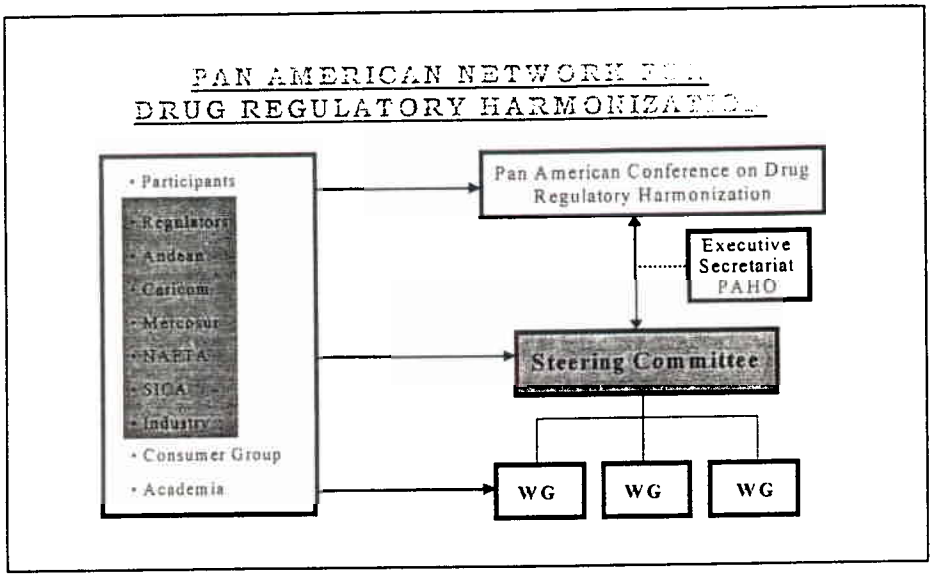
1.1.5 CLASSIFICATION OF DRUGS

25) The classification of drugs will not be regarded as a matter for regulatory harmonization but rather as an area for cooperation.

1.1.6 PAN AMERICAN NETWORK FOR DRUG REGULATORY HARMONIZATION

26) The establishment of the Pan American Network for Drug Regulatory Harmonization was approved, together with the holding of biannual Pan American Conferences as open forums for stakeholders and the formation of a Steering Committee to follow up on Conference recommendations. The operating scheme in the Network is reflected in Figure N°1.

Figure 1



27) The Steering Committee is made up of:

- Five (5) regulatory authorities (or their representatives) from five countries, one for each subregional group (Andean Area, CARICOM, Central America, MERCOSUR and NAFTA)
- One representative from FIFARMA
- One representative from ALIFAR

It could also participate in the Steering Committee:

- Five (5) alternates or regulatory authorities (or their representatives) from five countries, one for each subregional group

- Representatives of NGOs recognized by PAHO/WHO, as well as representatives from other interested sectors invited by the Steering Committee, could participate as observers.

28) The first Steering Committee was approved. Representative from Canada, Guatemala, Jamaica, Brazil, and Venezuela form it. The alternates for this period will be representative from Mexico, Costa Rica, Trinidad and Tobago, Argentina, and Colombia.

29) The mission, objectives, goals, and functions of the Conference and the Steering Committee were established, together with the functions of the Secretariat and the financing of the Network, as indicated below:

MISSION OF THE CONFERENCE

The Conference should promote drug regulatory harmonization in all aspects related to the quality, safety, and efficacy of pharmaceutical products as a contribution to the quality of life and health care of the citizens of the Member Countries of the Americas.

MISSION OF THE STEERING COMMITTEE

The Steering Committee should enable progress between Conferences by coordinating, promoting, facilitating, and monitoring harmonization processes in the Americas.

OBJECTIVES OF THE CONFERENCE

- Promote and maintain a constructive dialogue between the regulatory entities, the pharmaceutical industry, and other sectors through periodic Conferences.
- Encourage convergence of drug regulatory systems in the Region of the Americas.
- Adopt recommendations for their implementation at the national and regional level.
- Promote and facilitate technical cooperation among countries.
- Promote the harmonization of drug regulatory requirements and guidelines for special regulatory issues.

OBJECTIVES OF THE STEERING COMMITTEE

- Ensure the effectiveness of the Conference and the relevance of the topics it deals with.
- Facilitate and monitor implementation of the Conference recommendations.

- Safeguard the continuity of pharmaceutical harmonization activities in the period between Conferences.
- Facilitate consensus building and resolutions of issues between and during the Conferences.

GOALS OF THE CONFERENCE

- Examine global regulatory systems.
- Formulate and adopt proposals for technical and regulatory harmonization.
- Review the existing drug regulatory requirements and the guidelines for special issues.
- Identify and discuss drug regulation implementation issues.

GOALS OF THE STEERING COMMITTEE

- Identify experts and promote broader scientific consultation to facilitate consensus at the Conferences.
- Develop and maintain an information system to disseminate information on progress in the harmonization process at the national and subregional level.
- Identify mechanisms to promote capacity-building and scientific and technical cooperation.
- Provide up-to-date, accurate information on regulatory systems in a timely manner.

FUNCTIONS OF THE CONFERENCE

- Promote involvement in the Conference by all stakeholders in the Americas and those invited by the Steering Committee.

  National and regional drug regulatory authorities, subregional integration organizations, pharmaceutical industries, pharmacy associations, academic institutions, and consumer associations should be encourage to attend the Conferences.

- Convene the Conference every two years on the date and at the place determined by the Steering Committee.
- Adopt all recommendations and conclusions by consensus at the plenary sessions. If no consensus is reached, the different viewpoints will be indicated in the reports.

FUNCTIONS OF THE STEERING COMMITTEE

- Organize meetings, workshops, and other related activities to put the recommendations of the Conferences into practice.
- Establish study groups on regulatory topics identified by the Conference as more relevant.
- Determine the preparatory activities needed for subsequent Conferences.
- Determine the best problem-solving methodologies to achieve consensus.
- Convene meetings at which a quorum of two-thirds of the members is present.

FINANCING

The financing for the Conferences, meetings of the Steering Committee, and preparatory activities will be sough from the following sources:

- Associations of the pharmaceutical industries
- Professional associations
- Governments
- Conference registration fees
- PAHO contributions
- NGOs
- Other

SECRETARIAT

The Pan American Health Organization/World Health Organization will serve as the Secretariat of the Network, the Conference, and the Steering Committee. The Secretariat should:

- Provide administrative and technical support for the Network
- Coordinate the activities deriving from the recommendations issued by the Conference
- Act as a clearing house for information

- Arrange for experts advise and consultants to assist regulatory authorities to promote drug regulatory harmonization, and

- Provide liaison, when appropriate, with similar programs such as ICDRA (organized by WHO), ICH, other national or regional trade organizations, and others, as necessary.

1.2 GENERAL RECOMMENDATIONS

1) PAHO/WHO should continue and even increase its support for the countries, especially those with less development in the area of harmonization, strengthening the capacity of the regulatory agencies involved in the harmonization processes. Among this support are the promotion and adoption of The Certification Scheme for Pharmaceuticals Moving in International Commerce, proposed by WHO.

2) The health authorities should make a commitment to move forward with the application of scientific standards, at three levels:

   - Normative: Move closer in line with international recommendations.
   - Timetable for the work: establish strict timetables for meeting regional harmonization goals.
   - Operational: promote the involvement of academia and the private sector to ensure the availability of human resources and the necessary infrastructure. There is a pressing need for reference institutions and reference laboratories.

3) Conduct a study on the feasibility and viability of having a regional entity or other mechanisms for evaluating drug registration applications that will be recognized by country authorities. The findings will be submitted to the subregional harmonization groups for their approval and will be presented at the next Pan American Conference on Drug Regulatory Harmonization.

4) Involve the four existing pharmacopeias in the Region in the harmonization processes and set up a communications network among them.

5) Develop a strategy for shared financing between the governments, the pharmaceutical companies, and cooperation entities to support the drug regulatory harmonization process.

6) Support cooperation initiatives for drug regulatory harmonization in the subregional blocs, within the framework of the economic integration processes.

7) Recommend that the countries promote activities for implementing the Good Pharmacy Practices recommended by the International Pharmaceutical Federation and WHO, and professionalize the dispensing of drugs in order to have specific standards for control and improvement of the retail drug trade in the countries of the Region.

1.2.1 BIOEQUIVALENCE

8) Disseminate the report of the expert group on Bioequivalence (Caracas 1999) through working groups, to achieve a national and regional consensus on the concept and its

applicability, developing specific proposals aimed at achieving that applicability in the short term.

9) Identify cost-effective mechanisms for conducting bioequivalence tests; for example, the recognition of reference institutions in the Region and technical cooperation among countries.

10) Continue to promote generic drugs in the countries as a strategy for improving access to drugs, using the WHO guidelines as the frame of reference.

1.2.2 GOOD CLINICAL PRACTICE

11) The report of the expert group on Good Clinical Practices (Buenos Aires, 1999) should be utilized by the countries as a guide for developing regulations for the application of Good Clinical Practice in drug studies.

12) Continue to support the working group on Good Clinical Practices.

13) Standard procedures should be established in the Region to facilitate the development and oversight of clinical research, including procedures for the importation of experimental drugs and the shipment of samples for analysis.

14) Training should be developed for the application of Good Clinical Practices, geared to investigators, the evaluators of clinical protocols, ethics committees, and the inspectors of clinical trials.

1.2.3 GOOD MANUFACTURING PRACTICE

15) The countries (government and industry) should move ahead with the application of up-to-date international standards on good manufacturing practice, establishing a strict timetable, without prejudice to the provisions in point 4.

16) Institutionalize the training program on GMP that the FDA plans to develop with the University of Puerto Rico and PAHO/WHO. This program, which should incorporate the contributions of the interested countries (authorities and industry), should include distance learning modalities and take advantage of the installed capacity of the Region.

1.2.4 COUNTERFEITING

17) Countries should review and modernize their legislation, reviewing the existing provisions in order to identify possible mechanisms that would permit the imposition of sanctions under the current law.

18) Disseminate and share information among the countries on counterfeit products, with the Executive Committee proposing strategies in this area.

19) Promotion of the development of integrated control systems in the regulatory area and the other sectors involved (courts, police, entities responsible for protecting intellectual property, etc.).

1.2.5 CLASSIFICATION OF DRUGS

20) Create discussion groups in the Americas on the classification of non-prescription drugs. PAHO/WHO is requested to issue recommendations or criteria to assist these groups.

21) Create a working group for the adoption of classification systems for pharmaceutical products. This group will examine the various drug classification systems and criteria in the Americas in order to determine similarities and differences. It will also identify those that can be validated and adopted by the countries.