SUMMARY OF CONCLUSIONS

1. OPENING
   1.1 Dr. Brandling-Bennett - DDPAHO

2. PRESENTATIONS
   2.1 Development of Common Policies and Strategies as a Path Toward the Free Trade Area of the Americas. Dr. Sherry Stephenson - OAS
   2.2 Update on the International Conference of Harmonization (ICH). Dr. Stuart Nightingale - FDA
   2.3 Impact of Economic Integration on Regulatory Harmonization in Latin America. Mr. Thomas Andrew O’Keefe, MERCOSUR Consulting Group
   2.4 Update on Current Normative Activities. Dr. J. Indanpaan Heikkila – WHO
   2.5 Harmonization of Drug Regulations in the Americas. Dr. Enrique Fefer - PAHO
   2.6 Toward Harmonization of the Requirements for Drug Registration. Dr. José Manuel Cossiño - FIFARMA
   2.7 Drug Regulatory Harmonisation in the European Union: Evolution and Results. Prof. Rolf Bass
3. PANELS

3.1 Panel A: The Perspective from the Health Sector - Potential Impact of Regulatory Harmonization on Drug Availability and Use

3.1.1 Dr. Marta Nóbrega Martinez - Brazil
3.1.2 Dr. María Guillermína Albarrazín - Colombia
3.1.3 Ms. Silvia Martínez de Sanchinelli - Guatemala
3.1.4 Dr. Jorge Reyes Salas - Ecuador
3.1.5 Dr. Francisco J. Higuera - Mexico

3.2 Panel B: Perspectives from the Economic Sector: The Expected Impact of Regulatory Harmonization on Regional Production, Trade, Markets, and Prices.

3.2.1 Mr. Huáscar Hirazoque: Latin American Integration Association (LAIA).
3.2.2 Mr. John Kissoon - (CARICOM)
3.2.3 Mr. Raúl Boccone - MERCOSUR
3.2.4 Ms. Juana Mejía de Rodríguez - Central America

4. WORKING GROUPS

4.1 Working group A: Technical Requirements for Drug Registration
4.2 Working group B: Institutions and Mechanisms for Implementation
4.3 Work by subregional groups:
   4.3.1 MERCOSUR
   4.3.2 NAFTA-CARICOM
   4.3.3 Andean Community

5. PANEL ON REACTIONS TO THE CONFERENCE

5.1 Dr. José Manuel Cousiño - Representing FIFARMA
5.2 Dr. José Vargas Mielo, Consumer Association for the Region of Latin America
5.3 Dr. Huasquar Hirazoque, LAIA
5.4 Mr. Dan Michols, Health Protection Branch, Canada.
5.5 Dr. Stuart Nightingale, Food and Drug Administration of the United States
5.7 Dr. Pablo Bazerque, National Administration of Drugs, Foods and Medical Technology, Argentina

6. CLOSURE

6.1 Dr. Brandling-Bennett DDPAHO

ANNEX 1. The Development of Common Policies and Strategies as a Path Towards the Free Trade Area of the Americas. Dr. Sherry Stephenson - OAS
SUMMARY OF CONCLUSIONS

1. The participants reiterated the need to give priority to health considerations in trade and economic integration processes, which implies that drugs should have a differentiated treatment in such processes. They expressed unanimous concern over such measures as the decentralization of drug registration and tacit approval where the administration fails to take action, which in some subregions and individual countries have been incorporated into the modernization processes, making it possible for products to appear on the market that are unacceptable from the health standpoint.

2. The following aspects were identified as priority components of harmonization processes:

   • The Standards for Good Manufacturing Practices and the advantages of using those recommended by WHO as a reference were recognized. The need to provide training for inspectors and to conduct joint inspections as way to facilitate future mutual recognition among them also became evident. It was also emphasized that the Certification Scheme recommended by WHO for the international trade in pharmaceuticals is not being employed properly despite its advantages over other systems such as that of the certificate of free sale.

   • It was recognized that uniform criteria were needed for: a) accreditation of laboratories for the analysis of drug samples, b) requirements for bioavailability and bioequivalence, c) product stability studies, d) conversion from the requirement for sale by medical prescription to sale without prescription (OTC), and e) the observance of Good Clinical Practices. For all of these the guidelines already developed by WHO and the ICH should be taken into account.

3. The need to define and disseminate the criteria used by some regulatory authorities to construct their lists of “reference countries” for the registration of drugs was recognized, mainly because of the manifest concern of some participants over a possible reduction in the autonomy or decision-making capacity of recipient countries in the issuance of marketing authorizations.

4. It was unanimously recognized that, to operate properly and efficiently, the regulatory agencies needed to be strengthened by: a) making them administratively and financially autonomous while keeping them attached to the ministry of health, b) establishing adequate schedules of registration fees and providing for the direct and exclusive use of the resources so obtained, c) endowing them with qualified human resources and up-to-date technology, and d) establishing procedures for updating and training in all areas of drug surveillance.

5. Adequate communication and coordination between ministries of health and the specialized commerce and trade agencies became evident as essential for: a) obtaining information about the ownership of the products to be registered, b) ensuring that the use of trademarks, registered or not, does not lead to misuse or confusion about their therapeutic use, and c) that the trade names do not make improper use of International Nonproprietary Names (INN).
6. It was recognized that, in compliance with current international legislation, it is important to respect the confidentiality of unpublished information used in registration procedures.

7. With regard to the harmonization processes under way, the participants acknowledged the necessity of: a) continuing them through the specific agencies and mechanisms currently operating in the Region, such as MERCOSUR, NAFTA, LAIA, and the Andean Community, while recognizing the serious limitations existing in other subregions, such as Central America, where there is no legal framework to authorize and operationalize the commitments made by technical groups at the subregional level, b) taking the particular needs of each subregional bloc and the different degrees of development of their constituent countries into account in order to implement the subregional agreements in the countries, which means that the agreements must be implemented gradually, and c) setting up a system for circulating detailed information on the standards, requirements, and procedures in place in every country and geographical bloc, to develop a common terminology.

8. As for global harmonization mechanisms, it was recommended that two representatives from the Region of the Americas as well as the six regions of WHO be included in the meetings of the ICH to ensure that countries with different degrees of development are represented.

9. It was unanimously recommended that a hemispheric Forum be established, with PAHO as its Secretariat, to articulate the different subregional blocs on the subject of drug regulation. There was emphasis on the importance of: a) having a Steering Committee in which the subregional groups active in the drug regulatory harmonization process are represented to coordinate the activities in preparation for the Forum and lend continuity to its recommendations; b) including in the Forum all actors involved in addressing the problems connected with drugs: the regulatory authorities, industry (domestic and multinational), representatives of the integration entities, consumers, and professional associations, c) guaranteeing financing for the forum as well as the work of the Steering Committee, for which the support of industry (domestic and multinational) and the governments was recommended.

10. Finally, PAHO was asked to support the countries and integration blocs in the following areas:

   • Information on pharmaceutical legislation.
   • Collection and dissemination of documents, experiences, and procedures on drug regulatory harmonization in each country and subregional bloc.
   • Research to document compliance with existing harmonization agreements.
   • Definition of the analytical methodology for addressing common problems and charting of lines of work.
   • Exchange of information among the harmonization efforts of the different integration processes.
   • Institutionalization of a hemispheric forum that articulates the countries and different subregional blocs.
1. OPENING

1.1 Dr. Brandling-Bennett - DDPAHO

Dr. Bennett welcomed the participants on behalf of the Director of PAHO and for himself. He recalled the tasks entrusted to PAHO by the Heads of State and Government of 34 countries at the Summit of the Americas (Miami, 1994), making the present Conference a party to the fulfillment of this mandate. In this regard he noted:

- That even the Constitution of PAHO (the pioneering intergovernmental organization of its kind in the world, now on the eve of its first centennial) expresses an awareness of the close links between health and trade, and
- The original nature of the Organization as both the Regional Office of WHO and the inter-American system’s agency specializing in health.

Dr. Brandling-Bennett described the current programming guidelines of PAHO and its priorities, emphasizing the link between poverty and health, and the Organization’s central commitment to progress toward equity in a Region characterized by enormous inequities among and within countries. In the pharmaceutical area this means promoting access by all to good quality essential drugs at reasonable prices.

He concluded by noting the importance of the results of the Conference as health sector inputs at the next Summit of the Americas, to be held in Santiago, Chile, in 1998.

2. PRESENTATIONS

2.1 Development of Common Policies and Strategies as a Path Toward the Free Trade Area of the Americas. Dr. Sherry Stephenson - OAS

Dr. Stephenson referred to the Summit of the Americas (Miami, 1994) as a fundamental end-of-century event, and the decision to promote a Free Trade Area of the Americas (FTAA) as conducive to realization of the integrationist dream of Simón Bolivar.

She gave a detailed account of the progress being made in setting up the FTAA and emphasized the compatibility of the process with current subregional integration efforts and with the progress in consolidating the World Trade Organization (WTO) (Annex 1).
2.2 Update on the International Conference of Harmonization (ICH).
Dr. Stuart Nightingale - FDA

Dr. Nightingale was gratified by the relevance of the material on the ICH in the Conference reference document, which made his presentation easier. He pointed out the type of government-industry cooperation that characterizes the ICH as essential to its success, measured by the more than 40 scientific and technical guidelines approved. The ICH has worked so well, he said, that it tends to serve as model for other initiatives, such as those in the areas of veterinary medicine, medical equipment, etc.

The Conference is held every two years, but the work of the ICH is ongoing. Dr. Nightingale noted that the importance of industry’s participation was borne out by the fact that while previous FDA initiatives (with Japan in 1960, with PAHO in 1979, and with the European Union in 1980) that did not include it were interesting and led to an exchange of information, they yielded no progress in harmonization. Industry’s presence is essential to the current progress because industry knows where the problems are and has a special interest in avoiding the duplication of efforts.

The ICH is not supranational, but the need for formal mechanisms to make its recommendations official was recognized. Dr. Nightingale also noted that participation in the ICH and acceptance of its findings is voluntary. The FDA has modified its guidelines in keeping with the recommendations of the ICH.

The permanent Secretariat in Geneva has been a decisive factor, and its neutrality has been essential for success, even though it consists of representatives of industry. Without this neutrality, the regulatory authorities would reject its proposals.

The ICH has been branded and attacked as “heavily biased in favor of industry,” although it actually has not operated that way. It is well to recall that the decisions in its typical guideline approval process are the exclusive responsibility of the governments, and industry has no part in them.

WHO participates as an observer of the ICH, which is of primary importance because it opens up the prospect of the globalization of ICH agreements. (Annex 2)
2.3 Impact of Economic Integration on Regulatory Harmonization in Latin America.
Mr. Thomas Andrew O’Keefe, MERCOSUR Consulting Group

This presentation concentrated on an analysis of the legal nature, evolution, economic results, and impact on the health sector and drugs of four subregional integration processes: MERCOSUR, the Andean Community, SICA, and LAIA. (Annex 3)

2.4 Update on Current Normative Activities.
Dr. J. Indanpaan Heikkila – WHO

Dr. Heikkila described WHO and its membership (191 Member States), the mandate in its Constitution from which their efforts (from 1948 to the present) derive for international harmonization in the field of pharmaceuticals, and the main results obtained (Pharmacopeia, GMPs, Generics, etc).

He emphasized the importance of involving all interested actors (governments, industry, consumers) in the harmonization efforts (Annex 4).

2.5 Harmonization of Drug Regulations in the Americas. Dr. Enrique Fefer - PAHO

Dr. Fefer said that deregulation, patent protection, and the economic integration processes would define the framework in which the Region’s pharmaceutical market would develop. He referred to the various international forums involved in the harmonization of drug regulations: the ICH, ICDRA (the International Conference of Drug Regulation Agencies), and EMEA (the European Medicine Evaluation Agency).

In the Region of the Americas there are a large number of institutions of different origins involved in the integration processes, which affords an opportunity to promote articulation among them. Dr. Fefer particularly emphasized the processes under way in three subregions: MERCOSUR, Central America, and the Andean Community, and noted the points at which they converged and the differences in their structures and modes of operation.

In light of the liberalization of markets, he emphasized, it was important for the countries to have efficient and effective regulatory and control agencies to ensure the quality and proper use of the pharmaceutical products on the market. He mentioned the existing barriers that impair the performance of most of these entities and was of the view that only their radical restructuring would enable them to accomplish their primary purpose: protecting public health (Annex 5).
2.6 Toward Harmonization of the Requirements for Drug Registration.
Dr. José Manuel Cousiño - FIFARMA

Professor Cousiño presented the results of the FIFARMA study on the requirements for drug registration in the countries of the Region. He identified the aspects of the registration process that make for significant differences among the countries, some of them because of a lack of managerial capacity, others because of conceptual differences. Professor Cousiño presented details on these differences linked with the financing of registration, the stages of the process, samples for quality control, the acceptance of reference countries, the need for local clinical studies, the use of good manufacturing practices, and the treatment of similar products. The general diagnosis resulting from this analysis served as the basis for Dr. Cousiño to formulate proposals on technical and institutional aspects for optimizing the registration process while promoting harmonization of the requirements of this process (Annex 6).

2.7 Drug Regulatory Harmonisation in the European Union: Evolution and Results.
Prof. Rolf Bass

Professor Bass gave an account of recent European experience in drug regulatory harmonization and concentrated on the responsibilities and performance of the European Medicine Evaluation Agency (EMEA) as an instrument for developing a unified drug market in the European Union. The Agency, which is headquartered in London, commenced operations in 1995 with a staff of 70 and a budget of ECU $14.4 million and is expected to grow to 210 staff members and ECU$44 million in 1999. The function of the EMEA is the evaluation of drugs presented for centralized registry (that is, its approval is valid in all the countries of the European Union), this centralized process being mandatory for every biotechnology product and optional for other new molecules. In 1997 some 66 applications for evaluation by the centralized registry were received. The Agency is also available to arbitrate differences between countries generated by the decentralized evaluation and approval processes in the individual countries. Additional responsibilities include the coordination of drug control and of inspections to ensure adherence to good clinical, laboratory and manufacturing practices, and the provision of advisory services to the pharmaceutical industry.

The EMEA aims for completion of the process in 300 days, at the end of which the product must be authorized for marketing and the appraisal report publicly available. (Professor Bass emphasized that all the Agency’s documents are available in Spanish, one of the four principal languages of the institution). From February 1995 to October 1997 the process took 472 days for biotechnology products and 376 days for other new products.

The EMEA also participates in international cooperation activities, particularly with Nordic and Central and Eastern European countries, and attends the meetings of the ICH and the World Health Organization (Annex 7).
3. PANELS

3.1 Panel A: The Perspective from the Health Sector - Potential Impact of Regulatory Harmonization on Drug Availability and Use

Perspectives of the national regulatory authorities on the “Potential Impact of Harmonization Processes on the Availability, Quality, and Use of Drugs.” The presenters were:

3.1.1 Dr. Marta Nóbrega Martinez - Brazil

The Dr. Nóbrega emphasized that the harmonization processes should be intensified in every subregion. In Brazil, efforts are going forward in the framework of MERCOSUR, and their purpose is to protect the health of the population. She cited the different macro functions:

- Regulation. The harmonization process in MERCOSUR covers not only the registration of drugs but their monitoring and industrial manufacture, the finished products, post-marketing surveillance, and advertising and dissemination of information.

- Drug control.

- Research: on safety, effectiveness, and the riskbenefit ratio.

- Cultural aspects: all those that affect the rational use of the drugs.

Dr. Nóbrega also noted Brazil’s priorities in regard to drugs:

- Restructuring of the government unit in charge of health surveillance, and

- Harmonization of regulations and equivalences in the MERCOSUR framework.

Technical and scientific commissions made up of representatives of government, industry, and consumers have been created to move forward in the regulation of products and of drug registration and control systems. The criteria for analyzing new products, sound manufacturing practices, and other subjects are also under discussion. Courses are being arranged for health inspectors of the four countries. Work is also being done on information exchange in order to advance toward harmonization of the evaluation of basic documentation and quality assurance. A project for a network of analytical laboratories will be executed in cooperation with the IDB. Clinical and preclinical experiments, patents, and research are also priority matters for Brazil. The aim is to coordinate governments, industries, and universities with a view to increasing innovation.

Finally Dr. Nóbrega noted that efforts were being made to harmonize systems for controlling the use and abuse of products. This is a matter for the individual society to determine;
there are products that are prohibited in some countries and permitted in others. Hence, harmonization is directed at systems and not at drugs themselves. She concluded by noting that the harmonization process is very dynamic in MERCOSUR and that Resolution 2395 is considered a very important step in this process.

3.1.2 **Dr. María Guillermina Albarrazín - Colombia**

Dr. Albarrazín pointed out that Colombia’s basic policy on drugs is to guarantee access to essential drugs by all the population. To this end the recommendations of WHO on essential drugs and on the use of generic drugs in prescriptions and marketing have been adopted. The current policy covers the subjects of rational use, science and technology development, quality assurance, drug control, post-marketing surveillance, essential requirements for service delivery, information, training of human resources (in coordination with universities), and the joint efforts of the health sector and the ministries of development and trade.

Dr. Albarrazín also said that harmonization work is under way in the Andean Community. She mentioned a group working in Colombia concerned with good manufacturing practices and cited a bilateral harmonization effort with Venezuela.

She expressed concern about Andean Community Resolution 418, in whose preparation the health sector had not participated. She stressed the need to recognize and accept that drug registration entails an assessment of the product and its quality, which takes a reasonable amount of time to perform.

3.1.3 **Ms. Silvia Martínez de Sanchinelli - Guatemala**

Ms. Martínez pointed out that globalization facilitates access to products, but for it to contribute to the health of populations it is necessary for the health sector to increase and improve its capacity for surveillance and control. Prerequisites for this are that the legal framework be improved and regulatory agencies strengthened.

Ms. Martínez analyzed the various dimensions of the drug policy and emphasized the need to intensify the subregional harmonization processes (Annex 8).

3.1.4 **Dr. Jorge Reyes Salas - Ecuador**

Dr. Reyes first made it clear that he was making his presentation as a member of the Andean Community. He then presented a document (Annex 9) prepared especially for this Conference by the official representatives of the Andean Community at its recent meeting in Bogotá. The document proposes the principal tasks that should be pursued in the Andean Community in regard to drugs.
3.1.5 Dr. Francisco J. Higuera - Mexico

Dr. Higuera said that Mexico has 189 drug manufacturing plants and 4 distribution enterprises operating 1,200 warehouses. There are 14,560 registered drugs, of which only 7,150 are marketed, and 133 are export products.

Dr. Higuera described the government structures responsible for drug regulation. He emphasized that they are immersed in the NAFTA process and engage in exchanges of information on drug registration, tissue culture, clinical tests, post-marketing, quality control of exported and imported products, and the issuance of marketing permits.

He noted the importance of the national public health laboratory and of the body of requirements to guarantee the quality of drugs. He reported the establishment of an electronic system that has expedited registration procedures and that noted many procedures have been decentralized to the states.

3.2 Panel B: Perspectives from the Economic Sector: The Expected Impact of Regulatory Harmonization on Regional Production, Trade, Markets, and Prices

This Panel was responsible for presenting the perspectives of the economic sector on the foreseeable impact of drug regulatory harmonization on drug production, marketing, and prices. Its members were:

3.2.1 Mr. Huáscar Hirazoque: Latin American Integration Association (LAIA)

Mr. Hirazoque said that LAIA has an agreement on Scientific and Technical Cooperation that provides for initiatives to harmonize standards relating to product registration, technical barriers to trade, and intellectual property. It is essential to relate these initiatives to the agreements that are developed in the World Trade Organization (WTO).

He emphasized that consumers are increasingly demanding assurances of good manufacturing standards. LAIA is concerned about the fact that legitimate GMP requirements can be too expensive for the smaller countries and hinder the exportation of their products and that small industrial enterprises do not always have testing and assay laboratories. He proposes technical cooperation among countries to correct such problems. Cooperation in the accreditation of institutions by government to enable it to certify the quality of products requires the development of mutual trust and the formation of networks. This is accomplished by bringing the countries closer together, and LAIA has collaborated in this direction. Mr. Hirazoque emphasized that drugs are a complicated subject. Beyond harmonization it is essential to promote technology transfer and technical cooperation.
3.2.2 Mr. John Kissoon - (CARICOM)

Mr. Kissoon said that it is necessary to go beyond limited views in which companies see regulation as something that raises costs and holds back and stifles trade, and governments, concerned about product safety, do not worry about the flexibility needed to make drugs available to the population. He reported that there are 11 drug manufacturers in the Caribbean, which supply only 10% of the demand. There are no taxes in the Region. There is a regional quality control laboratory for drugs, with a Technical Advisory Committee. A Regional Advisory Body on Drugs and Therapeutics has been set up to address other aspects of drug policy and is exploring forms of cooperation that will benefit the Region’s 14 constituent territories—forms that include the establishment of a regional registry agency. The second CARICOM Conference recommended the harmonization of legislation, institutions and procedures.

3.2.3 Mr. Raúl Boccone - MERCOSUR

Mr. Boccone reported that the harmonization of drug regulations was being addressed in Working Subgroup 3, where it has been under consideration since 1991. Tariff reduction makes the technical barriers to trade more visible, he said, and he proceeded to refine some concepts, distinguishing technical standards from technical regulations, and harmonization from evaluation of compliance and mutual recognition. He pointed out that MERCOSUR is adopting the ISO standards, that it is based on transparency, and that the results of harmonization (resolutions) must be implemented by the member countries themselves (i.e. MERCOSUR is not supranational).

Finally, he analyzed the establishment of the FTAA, emphasizing that the negotiation phase has not yet been reached, and he referred to the processes for admitting Bolivia and Chile into MERCOSUR, which has prompted the beginning of work to explore harmonization with Chile.

3.2.4 Ms. Juana Mejia de Rodríguez - Central America

Ms. Rodríguez referred to the situation in Central America with regard to trademarks, patents, production, free trade, standardization, and prices:

Concerning brands she explained that the Central American agreement requires a registered trademark to market a pharmaceutical product. This trademark must be registered in each country of the area. One of the system’s difficulties is the fragmented procedure for registration. To resolve these difficulties, meetings of the heads of the offices for the registry of industrial property have been held, with advisory services of the WIPO. A draft Central American agreement on trademarks has been drawn up and accepted by the highest political authorities (the ministers of the economy), who have sent it to their respective legislatures for ratification. Some interest groups have objected to it and have withdrawn from subregional congresses, and amendments have been made that address their objections. With these modifications it will again
be submitted to the national legislatures for ratification and will become Central American law when approved by three countries of the subregion. This new agreement will afford the advantage of allowing a product to be marketed with the same name all over Central America.

In regard to patents she noted that in Central America some technological items, including chemical products, were not patentable. With the treaty of Paris patent laws began to be revised, and different levels of protection were established for intellectual property. With the accession of the countries in the subregion to the WTO and to the TRIPS agreement, the need to harmonize Central American laws on patents, industrial designs, and trade secrets emerged. With the advice of WIPO as the forum for discussion, meetings of registrars of industrial property of Central America and Panama have been held, and a widely discussed bill has been drafted that is under review for signature by the ministers of the economy responsible for integration. The Central American countries have assumed the commitments of the WTO; therefore, even if this draft legislation fails to be ratified, they must adopt it as law within their respective borders. It will have no effect on the availability of drugs to the population in the short term; it will be tested only with the introduction of new patented molecules, for which prices will be charged that are set by the products with no market regulatory mechanism. This may make these produces difficult for some sectors of the population to afford. However, the possibility has opened for contracts between research-based laboratories and local manufacturers aimed at specific markets such as government, social security, and low-income sectors.

On the subject of production she said that under the Central American treaty of the 1960s, the pharmaceutical industry was one of the first to be established in the subregion, in response to the prospect of supplying a market of fourteen million inhabitants. In 1965 international laboratories began to set up shop in Central America, most of them in Guatemala (16), one in El Salvador, and three in Costa Rica. There never was tariff protection for drugs because they were a sensitive class of products; instead they enjoyed tax exemptions on imports and raw materials, capital goods, and income. In the 1980s with the loss of these benefits and in the absence of tariff protection, the laboratories began to withdraw. Globalization and economies of scale also contributed to the withdrawal of international industry in order to serve blocs of countries. Moreover, the international firms trained local personnel, which has helped the development of national industries, which in recent years have increased their market share, and in some cases have formed small regional transnational laboratories. The national industries make generic or similar drugs, and since they do not engage in research, are able to offer drugs at more affordable prices.

In each country of Central America there has been Standardization, with sovereign autonomous entities choosing the type of regulation that has seemed best to them; in all but one country the regulatory entity is a government office. Adoption of the standard blank form for exports constitutes harmonization with international sanitary standards. Central America undergoing is absorbed in a process of harmonization that involves standardization. Some aspects of drug registration have been successfully harmonized. However, it is imperative that a political decision for free trade be taken and that the authorities be given time to comply with the decisions handed down in the harmonization meetings. In the new agreements NAFTA with Mexico, as well as in the FTAA and the treaties in which the countries of Central America have an interest, such as those with Panama and the Dominican Republic, there has been insistence on the harmonization of health standards.
4. WORKING GROUPS

Two working groups were formed to seek possible consensus in regard to:

• Basic technical requirements for the harmonization of drug registration.
• Development of institutional frameworks at the hemisphere and subregional levels to support and coordinate the harmonization process.
• Mechanisms for national implementation level of decisions made at the subregional or hemisphere level.
• Responsibilities of the actors involved.

4.1 Working group A: Technical Requirements for Drug Registration

Entrusted primarily to the registration authorities. They had a discussion Guide (Annex 10), which they followed as structured. The discussion topics were the elements of an evaluation and registration process and the legal, institutional, and administrative aspects of drug registration.

As an introduction to the topic, several participants emphasized the need for the technical requirements for approving drugs for marketing and for the control during marketing to conform to the social cultural, political, and economic needs of each country so that they could be more effectively applied. However, the standards must serve as a guide to future development, keeping up with technology advances and health needs, and preventing persistence of the status quo in the countries.

Similarly, in discussing the subjects it was taken into account that they are only part of drug policy; other aspects, such as rational use, accessibility, prices, etc., are very important but lie outside the main purpose of this meeting.

The working group also emphasized that inspection should focus on determining the extent to which reality conforms to the standards.

The following recommendations were made on the specific topics in the discussion guide:

**Common pharmaceutical requirements for drug registration:** The group discussed the common pharmaceutical requirements mentioned in the Guide. Many observations were made on the need for gradual application of the GMPs in keeping with the level of development of each country, using those recommended by WHO as a reference. It was emphasized that these standards should be implemented in stages, and that they are now being implemented in many countries, including European countries.

There was emphasis on the need to train inspectors using on-site training and inspection guides.
The group noted that joint inspections were being conducted in MERCOSUR, which helps bolster trust among the countries and will facilitate mutual recognition of inspections in future.

Given the volume of work of the government laboratories, which are used for the analysis of preregistration samples, regarded by several participants as inappropriate, consideration was given to the possibility of accrediting institutions to support registration and control work, which will require precise and harmonized criteria for accreditation and clear rules governing disqualification and incompatibility.

The urgent need for criteria for stability studies was noted. Another point raised was concern over the participation of third parties in manufacturing, chiefly in the case of imported products.

**Common pharmacological requirements for drug registration:** With regard to requirements for product interchangeability, there was acceptance of the general need to establish bioequivalence, which should best be done gradually, taking the health risk of products as the preferred criterion, including in the demonstration of bioequivalence products already on the market. It was recalled that at the last meeting of the IDCRA it had been suggested that the guidelines recommended by WHO be used for interchangeable products; it was also recognized that there were products that, while similar, were nevertheless not interchangeable.

**Common clinical requirements for drug registration:** The conditions that must be met by clinical trials in third countries for the data to be considered acceptable for the registration of products were examined, and it was felt that, whatever the standards in force in some Latin American countries, it is advisable to use criteria such as the WHO good practices for clinical trials and the criteria approved by the ICH.

**Classification of conditions for sale:** Several countries emphasized that establishment of conditions for sale must suit the local characteristics and supply of health services, as well as the cultural situation and other aspects, and should be part of a rational drug policy. There was general concern about the failure by vendors to request prescriptions from customers for the sale of drugs that require them. Criteria for considering changing the conditions of sale by prescription to over-the-counter sale were considered; among those mentioned were safety and efficacy, economic criteria, how a product is sold in reference countries, and the low concentration of products.

**Registration processes differentiated in time and requirements:** In general, registration systems differ for new or similar products, and some countries offer incentives for the registration of similar drugs.

**Legal aspects of drug registration:** The group examined several aspects of this point, indicating that given the short- or medium-term lifespan of the legislation on intellectual property, even though the ministries of health are not specialized in or in charge of the awarding of patents and similar rights, it is very important that there be adequate communication and coordination between them and the responsible agencies for the purpose of:

- Obtaining information on the ownership of products to be registered, though this is not a prerequisite for registration.
• Ensuring the use of trademarks, whether registered or not, that do not cause or lead to inappropriate uses or therapeutic confusion.

• Preventing registered commercial trademarks from infringing on or making improper use of official names, especially those included in the list of International Nonproprietary Names recommended by WHO, and

• Ensuring respect by the regulatory authorities for the confidentiality of private information furnished in the registration process, in compliance with the international and domestic legislation in force.

**Use of reference countries:** Concerning the use in reference countries of products imported and marketed in these countries, divergent opinions were expressed, in part because some participants declared that this administrative arrangement deprives their countries of autonomy or decision-making capacity on the issuance of marketing permits. Some participants requested that, because of this, ways be found to disclose in more detail the procedures that have facilitated or simplified registration formalities in order to determine whether they could be applied in others countries. At the same time, concern was expressed over the vagueness of the criteria for the selection of countries or for their inclusion on lists of reference countries, and over the discrepancies observed among the lists of countries that have adopted this system. Because of this, the group emphasized the need to define and disseminate selection criteria.

**Free sale certificates and the WHO Certificate:** It was clear that not enough is known either about the usefulness of the WHO-recommended scheme for certification of the quality of pharmaceutical products traded internationally, which causes it to be little used, or about the continued use of inappropriate systems such as certificates of free sale, which can even be issued by non-health authorities. It was noted with pleasure that both the U. S. FDA and regulatory agencies of Europe, especially that of the United Kingdom, are taking the necessary steps to issue certificates that conform to the recommendations of WHO.

**Institutional and administrative aspects:** When attention turned to the need to strengthen the regulatory agencies so that they could function properly and efficiently, there was broad consensus on the need to enhance the standing of these organizations, preferably by making them administratively and financially autonomous, setting rate schedules, and assigning the resources so obtained to their direct and exclusive use. These rate schedules must cover a significant part of the operating costs and contribute to the upgrading of the human resources involved. In addition, they must be in line with the costs in each country and not appreciably hinder the entry of pharmaceutical products of prime necessity to the market.

The regulatory agency, an autonomous unit attached to the ministry of health, must be an integrated unit that performs the functions of registration, inspection, and analytical control using transparent and predictable procedures without needless red tape.

The participants highlighted the importance of having qualified human resources and using up-to-date technologies. Special emphasis was placed on the establishment of procedures for instruction and for basic and refresher training in all areas of drug regulation including product assessment and pharmacological surveillance. They stressed the role that universities must play in this process, mainly because of the multiplier effect of educational processes.
Specific mention was made of regulating the activities of regulatory agencies and their personnel in order to prevent conflicts of interest in regard to the employment of third parties, relations with other entities, and the activities of their own staff, especially with regard to regulated industry.

Other topics of importance addressed with regard to administrative procedures and the modernization of procedures such as decentralization and tacit approval. On this last subject reference was made to the concern aroused by the excessively limited time allowed to the health authority to decide on the registration of a pharmaceutical product, because it can result in the entry of unacceptable drugs to the market. Hence it would be desirable that tacit approval become operative only after a reasonable time has passed that ensures that the drugs on the market are effective, safe, and of satisfactory quality.

In this regard it was noted even greater cause for concern is that tacit approval in one country can permit the entry of unassessed products to regional markets and third countries.

4.2 Working group B: Institutions and Mechanisms for Implementation

This group also had a discussion guide (Annex 11); most of its members were representatives of integration agencies and the economic sector. Some of its conclusions and recommendations are as follows:

*Institutions in charge of the integration process and mechanisms for implementation:* The group reiterated the priority of health considerations in trade and economic integration processes, which implies that drugs should receive differentiated treatment.

It was agreed that one way to energize this process is to harmonize drug regulations, although this harmonization must not be limited to registration requirements but must cover matters such as consumer protection and access to and rational use of drugs.

The group decided by consensus to ask PAHO to act as the agency for articulating the existing subregional integration blocs (MERCOSUR, Andean Community, NAFTA, CARICOM, SICA, LAIA) in the processes for drug regulatory harmonization. To this end it was considered advisable to continue the subregional forums and to follow up on the efforts of the present regional forum to promote its continuation.

The actors who must be involved in this forum are: regulatory authorities, representatives of integration structures, representatives of domestic and multinational industrial enterprises, consumers, and professional associations.

It has become necessary to draw up an agreement on the topics that must be included in a minimum common agenda on harmonization processes.

Harmonization requires an effort to circulate detailed information on the standards, requirements, and procedures in each country and in the different geographical blocs, to ensure the use of a common terminology.
Coordination at the national level is essential among the ministries of trade and health and other parties concerned, such as consumers and professional associations.

The Group agreed to ask to PAHO to support the countries and integration blocs in the following matters:

1. Information on pharmaceutical legislation.
3. Collection and dissemination of documents, experiences, and procedures on drug regulatory harmonization in each country and subregional bloc.
5. Research to document compliance with existing harmonization agreements.
7. Definition of the analytical methodology for addressing common problems and the charting of lines of work.
9. Exchanges of information among the harmonization efforts of the different integration processes.
11. Institutionalization of a hemispheric forum that articulates the countries and different subregional blocs.

The Group considers it important to make use of the technical and scientific guidelines and other documents generated by the ICH as useful inputs to the harmonization processes under way in the Region. It also recommends facilitating the inclusion of two representatives of the Region of the Americas in the meetings of the ICH in keeping with a WHO proposal suggesting that the same be done in regard to the six Regions of WHO.

4.3 Work by subregional groups:

The purpose of these groups was to review and adapt the harmonization proposals (requirements, institutions, mechanisms) that emerge from the discussions of Working Groups A and B to the subregions.

4.3.1 MERCOSUR

The group reviewed the recommendations of Groups A and B in previous meetings and considered at the last plenary session. The participants expressed their interest and agreement regarding promotion of the distribution, dissemination, and use of the information on pharmaceutical legislation in the development of the subregional economic blocs and in regulatory harmonization.

While reiterating the priority of health considerations in trade and the economic integration processes, the group took due note that harmonization is driven by the political decisions that have led to the trade integration processes under free-trade and common market agreements and other modalities.

The group attached importance to and supported the establishment of a hemispheric forum to articulate the different subregional blocs with regard to the development of drug legislation.
and regulation. It regarded PAHO as the proper organization (at the regional and subregional level) to organize and serve as secretariat to that forum, provided that “the problems of financing this activity are solved.” It recommended that support be provided by domestic and multinational industry and the use of the procedure that has made the MERCOSUR meetings viable—that is, that each government delegation finance its own participation in the events.

The PAHO office in Brasília offered the support of its consultant on drugs as the focal point in MERCOSUR.

On the topic of intellectual property in the report of Group A, concern was expressed that it not be taken as a prerequisite for the registration of drugs, and it was agreed that this point would be discussed in the plenary session.

Note: This point was discussed in plenary and the adjustments of the wording were made in the conclusions of Group A, as shown in the present report.

4.3.2 NAFTA-CARICOM

General discussion:

• The five subregional groups in the Americas could contribute to the formation of a permanent forum to discuss issues of regulatory harmonization in the Americas. The present meeting would constitute the first meeting of the forum.

• Science and technical issues for discussion might include the following topics: efficacy, safety, quality, GMPs, the GLPs, and GCPs, pharmacopoeial issues, quality control in the marketplace, drug surveillance, and advertising and promotion.

• More general topics and areas of focus might include: information exchange, legal and administrative approaches, access and transparency issues, and financial topics.

• Participants in the forum must have good representation from interested parties (regulators, industry, trade groups, governments, legislators, consumer representatives, financial representatives, etc.)

• The group also addressed the steps in harmonization and how it should take place in the Americas. A consensus was reached that harmonization should first occur at the subregional level in the five trading blocs. The main reason for this approach was that the trading blocs have special needs and are at different stages of development.

• The participants acknowledged that some subregional approaches and mechanisms exist and are working to harmonize regulatory approaches. In this area, communication among the subregional groups must be strengthened. An area of particular importance is harmonization of the format of the information submitted to the regulatory agency.

• The ICH is beginning to consider the common technical document (CTD), which might facilitate regional and subregional harmonization in the format of an application. The ICH approach will focus on summaries and reports, in the recognition that access to primary data is not a consideration for most regulatory agencies.
Harmonization is a complex procedure that should focus on understanding and agreement in the following areas: administrative and legal approaches, and scientific and technical issues. With good information exchange further progress could be made.

The participants agreed that harmonization should be a step-by-step process, with easily accomplished tasks considered first. NAFTA may wish to expand the opportunities for harmonization, recognizing that much progress has already been made under the Memorandum of Cooperation. This progress has been particularly valuable in the areas of information exchange, health insurance fraud, analysis of procedures and legal regulatory approaches.

Information exchange is considered of special importance. The present models must be studied to understand the successes and failures. Mutual recognition is a complex issue and should be considered at a later date. Administrative harmonization is tied more to regional and subregional elements. All views should be respected. The goals of harmonization should be clear, practical, and pragmatic.

WHO and PAHO can facilitate general approaches and serve as secretariat for selected regional and subregional activities. The ICH achievements could be disseminated better at the regional and subregional level.

The participants considered various ways to obtain financing, including funding from governments, industry, conferences, and other sources. The possibility of obtaining matching funds should be explored.

The forum could meet every two years, in the understanding that a steering committee could meet more often, given sufficient resources. Terms of reference could include the structure and procedures of the forum, areas of focus and methods to allow interaction with subregional harmonization activities in the five trading blocs. General administrative and financial subjects should be considered. Scientific and technical topics (noted above) could be developed, in the understanding that subregional efforts in these areas might occur first. To avoid duplication of efforts, all participants must recognize that a great deal of progress has already been made in harmonization in scientific and technical areas in WHO and the ICH.

Participation of all interested parties should be considered at both the subregional and regional levels.

Based on the general discussion above, the participants agreed to propose the following general model for regional and subregional regulatory harmonization in the Americas:

**Regional harmonization approaches:**

A forum composed of representatives from the regulatory offices of each of the five subregional trading blocs should be created. It should also include other interested parties, such as representatives of industry, consumer groups, professional societies, and governments, and could meet every two years, perhaps in collaboration with ICDRA.

Because of the rapid pace of change in the area of drug development and harmonization, a steering committee could be formed to oversee regional and subregional regulatory
harmonization activities. Membership in this steering committee could be drawn from regulatory representatives from each of the five blocs and others, as appropriate. The steering committee would meet yearly or more often, as resources permit.

PAHOWHO will act as a facilitator for both the forum and the steering committee, perhaps serving as executive secretariat.

Terms of reference for the forum and the steering committee could be defined by mutual agreement and could cover the following areas:

1) structure and operations;
3) legal, administrative and policy aspects of regulation;
5) exchanges of information and communications, focusing on Internet access and translations;
7) training to build expertise; and
9) other general topics of mutual interest.

Certain subregional topics may at times be presented for consideration by the steering committee and possible regional harmonization in the recognition that additional resources may be required for this purpose.

Financing to support the steering committee and the forum could come from government, industry, the registration fees from a major conference (modeled on the ICH) and other sources. PAHO and WHO might be able to provide resources, but given the general resource constraints, these funds should always be considered complementary. Special arrangements for smaller economies should be considered. Support might be provided by industries given clearly defined and agreed objectives and timelines. Industry can be asked for matching funds to supplement government support and resources.

Support for the general approach could be developed at the Presidential Summit in Chile in March 1998, which will include presentation of statements about the importance of pharmaceuticals in health care delivery systems.

Subregional harmonization:

For CARICOM and NAFTA, primary harmonization will take place at the subregional level based on the structures and processes currently established or to be developed.

CARICOM has a Secretariat in Guyana which convenes a meeting twice a year.

The NAFTA regulators meet trilaterally once a year.

Regulatory aspects of NAFTA are covered by a Memorandum of Cooperation that been in existence for several years. Good progress has been made under this agreement focusing on general exchanges of information, health insurance fraud, and selected scientific and technical topics. Further efforts may be required to strengthen and otherwise advance trilateral regulatory harmonization between Mexico, Canada, and the United States, with the expansion of current
structures and processes, where appropriate.

There was a preliminary agreement that ways to improve communications and interaction between regulators in NAFTA and CARICOM should be explored.

### 4.3.3 Andean Community

The Andean group emphasized the technical advances made in the harmonization of requirements for registration, good manufacturing practices, pharmacological standards and procedures for oversight committees, which have resulted in agreements on cosmetics, foods, and drugs.

It noted that its procedures differ from those of other integration blocs because of the supranational character of the Andean Community, which requires full technical agreement before decisions are made, usually without deadlines or domestic implementation processes.

It also highlighted the importance of subregional processes for the harmonized regulation of expanded markets, which increases the capacity for negotiation with other integration blocs.

Some countries expressed concern over the instrument of authorization by tacit approval as a mechanism for harmonization or mutual recognition because they feel that it lacks the necessary balance between the health and economic aspects of these processes.

The Group emphasized the progress made under the Hipólito Unanue Agreement and its three technical groups: good manufacturing practices, drug registration, and quality, and recommended that the continuity of their work be ensured by preserving their role under the Agreement or setting up a new technical negotiating entity. PAHO, moreover, was asked to continue its technical and logistical support to these technical working groups.

There are also bilateral harmonization processes that show different speeds of rapprochement among countries and are proceeding in a manner similar to that of the Andean Group.

Regarding the utility of forums such as the present one, it was reiterated that it is appropriate that PAHO, with its moral authority, serve as the organ for articulating the harmonization processes of the different trading blocs through mechanisms for monitoring, the collection and dissemination of information, and operations research.

The forum must respond to the need to set the topics of a common agenda for progressive development toward hemisphere-wide harmonization.

Its financing must be provided by PAHO from regional and country funds, and by governments and industry, with mechanisms such as registration fees. A forum of this nature has a political impact, but its fruits are basically technical agreements whose articulation with policy-making bodies are beyond its power and authority. It is for the participants to see to it that the information reaches those bodies.
Central America (Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica, Panama) and the Dominican Republic.

The group recognized the political pronouncements issued at the meetings of presidents of the Subregion, Panama, and the Dominican Republic on the efforts to be made to achieve economic integration in the short term.

Within these processes it recognized the existence of subregional entities that have been working on aspects of the harmonization of pharmaceutical regulation (meetings of drug regulatory authorities) and free trade (SIECA).

The group stated that some of the commitments undertaken at subregional meetings could not be fulfilled owing to a lack of financing and a legal framework for their implementation, and to lack of training of the human resources in charge of registration and control. Hence, it is necessary to revise the legal framework and search for an administrative structure that will allow the regulatory authority to use the resources it earns from the services it performs to strengthen its institutions and provide basic and refresher training for its human resources.

It is proposed that the higher development of some countries of the subregion be turned to account to support ongoing education and training for personnel from less developed countries.

It was recognized that implementing commitments in technical aspects requires gradual processes and lead times, and it was therefore recommended that a yearly plan of action with a work timetable be drawn up and semimonthly reports prepared on its progress and fulfillment.

It was urged that national working groups involving the sectors that operate in the field of drugs be formed to execute the plan of action.

These groups must establish ties with the integration entities so that a permanent body of information can be maintained and feedback provided on results in the field of harmonization and in that of the economic integration process.

PAHO was asked to provide support by monitoring this process and serving as secretariat for the collection of information and its transfer every two months to the national groups so that measures may be taken to carry out the plan of action according to its timetable.

5. PANEL ON REACTIONS TO THE CONFERENCE

5.1 Dr. José Manuel Cousiño - Representing FIFARMA

Dr. Cousiño opened his remarks by recognizing the moral authority of the Pan American Health Organization to bring about this Conference and remarked on the intensity of participation in its proceedings during the three-day period. The Conference provided a view of other parts of the world, particularly of what is being done by the United States and Europe in
matters of regulatory harmonization, an area in which he noted the excellent response capability of our Latin America. Dr. Cousiño observed firm resolve among the regulatory authorities and domestic and international pharmaceutical industrialists to move forward with the assessment of drugs. He also noted great concern over the levels in our countries compared with the progress being made elsewhere on the planet, and the determined reaction and resolve to continue to advance and improve. Regarding that reaction as an important achievement with which all the participants should be satisfied, Dr. Cousiño stressed that there was no longer any discussion of the need for industry and the private sector to participate in all these events. Latin America has strong and technically very well prepared domestic industries as well as an international industry; the domestic industries of yesterday are transnational today, and the transnational companies of yesterday already appear to be transcontinental. They all have something to say in the drug sphere, and so all must participate. He noted that FIFARMA, the Federation of the Latin American Pharmaceutical Industry, which he represented, is a member of the International Federation Pharmaceutical Associations (IFPMA), the secretariat of the great ICH project. Hence, the great interest in continuing to collaborate with the Pan American Health Organization and with all those who request our support for the realization of these projects in Latin America. Dr. Cousiño closed his remarks by stating that the declaration of principles of the Second Summit of the Americas, soon to be held in Santiago, Chile, asserts that harmonization of regulations will improve the availability and quality of drugs and prevent the marketing of ineffective or hazardous products. This statement, which is a declaration of principle, is on the agenda of all the countries today, and he invited the participants to continue working in this direction.

5.2 Dr. José Vargas Mielo, Consumer Association for the Region of Latin America

Dr. Mielo described briefly the Organization he represented, Consumers International, as an independent nonprofit foundation representing more than 250 national consumer organizations in over 100 countries. Its purpose is to promote the rights of consumers all over the world by proposing policies for the protection and defense of consumers and helping to raise the level of equity in social relations today. He referred to the importance of this meeting and consumer participation in it and said that his organization had recently entered into official relations with the Pan American Health Organization, which he thanked for the opportunity to participate in this meeting on a topic of particular interest to Latin American and Caribbean consumers. The Conference brought out our differences and shortcomings in the harmonization of drug regulation, he said. But what was most important about the meeting was the opportunity it afforded to move forward in a demonstration of political and professional will to address needs that affect the entire population, something that Dr. Vargas believed had been signally accomplished in the meeting. The consumers of our Region, he noted, are faced with a drug market that is imperfect in many ways with respect to quality, safety, efficacy and prices. This is accompanied by a profound lack of information and serious labeling problems, with no educational program to give consumers a more rational attitude in their use of drugs. This meeting provided an opportunity to rethink the situation, recognize weaknesses, put the rules into play, and improve and move forward, following those who have gone ahead of us while having due regard, of course, for the realities and the resources of individual countries. Dr. Vargas was of the view that in any harmonization process, in addition to consideration of the technical
aspects that had been discussed, efforts should also be made to give effect at the national level to harmonization at the regional level. He expressed the hope that efforts would lead to a policy of fair and affordable prices, to the regulation of advertising and labeling, to the establishment of regional cooperation in all information matters, to the establishment of mechanisms for the settlement of disputes, and to the pursuit of harmonization as part of an integrated process for commercial, economic, and technological development. Guidelines must also be established for the rational use of drugs and provision made for the participation of all sectors involved, in the understanding that, from this meeting forward, there will also be a place for consumers both at the national level in the subregions and at the regional level. Finally, he offered the support and professional skills of International Consumers in these discussions, and to support, in particular, the efforts that the Pan American Health Organization has been making. He regarded the conclusions and the discussion as a clear step forward that gives us a much better outlook than before.

5.3 Dr. Huasquar Hirazoque, LAIA

Dr. Hirazoque began by thanking the Pan American Health Organization for taking another step towards the harmonization of drug regulations and above all for emphasizing that the ultimate object of all efforts made in international forums is the human being. There is great interest in advancing down the road not only toward a common market, but also toward a shared ethics of public health. He noted that the Pan American Health Organization is the ideal forum for this subject, notably because it stresses the priority of the sanitary aspects over the economic, which they would not have if they were being addressed in the FTAA or LAIA. He viewed with satisfaction the participation of all and expressed concern at the magnitude of the task ahead because of the vast differences among the countries and among the regions, which compels a strengthening of efforts to establish technical cooperation programs and to prevent countries from lagging behind or being left out. Dr. Hirazoque was of the view that working toward harmonization must lead the way not only to sharing the market, but also to collaboration among all to improve the well-being of our populations. By mandate of its countries, the Latin American Integration Association has been collaborating with great interest in all these tasks not only in the pharmaceutical area. He stressed that the integration is not only commercial, but also has cultural and social aspects, which are the most important ones. He noted that one of the conclusions is to go on working and to ask the governments for the support, political will, and financial resources that are so necessary to complete these undertakings. He commended the organizers and participants, and hoped that this effort might culminate in a more just market that would make it easier for small laboratories working so hard in many of our countries to operate—not just the large laboratories—and that our efforts might make it easier for all to take part on equal terms. There is no greater injustice than to apply a law equally to unequal situations, and he reiterated the need to complete technical cooperation and technology transfer programs in the short term so that harmonization may truly be the path for all, not just for some.
Mr. Dan Michols. Health Protection Branch, Canada.

Mr. Michols began by thanking PAHO for the invitation to participate in the Conference, which he considered very useful. He explained that his statements on the conclusions and recommendations of the Conference expressed his personal views, which came from a specific context surrounding his regulatory agency. He next gave a brief description of that agency and said that it had just completed a four-year period of renewal and renovation of both drug and medical device regulation. All aspects of the process had been examined and many changes made. The organization’s mission is to ensure that the drugs and medical equipment available to Canadians are safe, effective and of high quality. No economic parameters were taken into consideration in the review, but there was recognition of the tremendous benefits in both timely access and marketing accruing to the national economy from a strong regulatory agency.

The agency is responsible for the regulation of pharmaceuticals, biologicals, herbal and other traditional remedies, blood and blood products, tissues and organs, and medical devices. Cost recovery or fees for its operations was introduced three years ago, and today 70% of its operations are funded from these fees and only 30% of them are financed by revenues from the government. One of the key elements of the country’s drug regulation strategy, he said, is international harmonization. The agency actively participates in activities of the ICH and WHO. It recently signed an agreement with the European Community on good manufacturing practices; when this agreement is fully implemented there will be mutual recognition of the certificates and licenses produced by inspections. Switzerland, Australia, and New Zealand have expressed interest in similar agreements, and Canada is negotiating with the USFDA and the Ministry of Health and Welfare of Japan for a similar arrangement based on the exchange of inspection reports. It has also signed agreements with Russia and China on matters of harmonizing drug regulatory activities.

For Canada harmonization is much more than a slogan. It is a way of doing business, and Canada takes very seriously its commitment to drug regulation. Consequently, Mr. Michols applauded the Conference as the start of what can be a serious exercise in the harmonization of regulatory activities in the Americas. He supported the proposition in the Conference’s working document that we must harmonize regulation in this area and work together to strengthen the regulatory agencies (emphasizing that we must also work to streamline their operations so that they may be as efficient as they can be), and agreed with the third recommendation, that a forum of this nature must be institutionalized. He also commended the FIFARMA study as an effort to present a synopsis of the situation in each country and identify some of the problems facing all of them. He noted that the material on Canada is out of date and undertook to send updated information.

Regarding the discussion on NAFTA and CARICOM, he was of the view that harmonization work is needed at the subregional level. There is a memorandum of understanding in NAFTA, but it must be strengthened in two ways: the memorandum is an agreement between governments and ought to be broadened to include representatives from
industry, the health professions, and consumers. It also needs to be further developed in the regulation of medical devices. Secondly, he felt there was need for coordination and motivation to harmonize regulation at the hemispheric level, and applauded PAHO’s initiative in this exercise. There are very few who can go it alone, and it would be foolish to reinvent the wheel in regulatory activities. Much can be learned from experience at the country and regional levels. Canada is prepared to share its experience and support this continuing forum. He regarded PAHO as an excellent choice as coordinator and facilitator of this activity and considered that a committee of representatives from the subregional organizations would be of help to the Organization in developing the agendas and exchanging information between meetings and conferences. Thirdly, he noted that Canada is prepared to provide technical assistance to other countries as its resources allow.

5.5 Dr. Stuart Nightingale, Food and Drug Administration of the United States

Dr. Nightingale said that he spoke on behalf of the Food and Drug Administration, but for himself as well. He noted that the conclusions reached in the Conference are very concrete proposals that would be highly useful and indicate that there is much to be done. He regarded this as an excellent meeting because of its organization and the opportunity it afforded for intercourse among subregional groups on specific aspects of harmonization and the mechanisms to be used. He regretted that he had not had a chance to describe the work being done by the FDA at home and abroad. He said that the FDA was pleased and proud of the enormous work it had done through the ICH in furtherance of international harmonization. He noted that the FDA could be visited on its Web page, where information could be found on its international activities. The present Conference was an excellent opportunity to bring together industrialists and government in joint work which, though different, recalled some of the characteristics of the ICH. He recognized that the Conference made it possible to lay the foundations for what are regarded as basic activities in harmonization processes.

Dr. Nightingale also noted that for work at the hemispheric level it is essential to have scientific and technical guidelines. Much has been done by the ICH, WHO, and the subregional groups, whose documents must be revised long before the subject of possible mutual recognition agreements is addressed. The Conference also made it possible to recognize the importance of exchanging information and of reaching agreement on the type of information to exchange. He agreed that PAHO must serve as secretariat for the hemispheric forum and suggested that it be held every two years to exchange information and review the progress made. He also suggested that these forums be open to participation by industry and government. This follows the pattern of the ICH meetings, which are held every two years, and helps to put a little pressure on the harmonization process. He agreed that there must be an Advisory Committee, which might meet twice a year; placing representatives of the different subregional groups on it will be a valid way to support progress and keep exchanges of information going. He ratified the usefulness of having PAHO as facilitator and emphasized that this is not a supranational role in regulation matters. Finally, he remarked on the significance of this Conference for the future: there is much to be done and, though there are differences and complexities, it is possible to move forward; what is done bilaterally, trilaterally or with another regulatory agency will benefit from the information and the kind of perspective gained from this Conference. He considered excellent Dr. Heikkila’s proposal to request representation for two additional governments from the
Region of the Americas in the discussions of the ICH; this would make it easier for this regional
group and the ICH to work together. He was grateful for the idea of sharing the documents
produced by the ICH and analyzing their importance in the Region.

5.7 Dr. Pablo Bazerque, National Administration of Drugs, Foods and Medical Technology, Argentina

Dr. Bazerque was expressing his own opinions rather than speaking as a member of MERCOSUR because he had not had time to canvass the views of the representatives of the other countries in his subregion. Firstly, he noted the importance of the meeting not only because of the breadth of the spectrum of entities represented, but because of the quality and importance of the representatives, and also the seriousness of the contributions to the proceedings. He felt that marked a beginning for harmonization in Latin America, in which the problems were being presented and a start was being made in learning how to solve them. This requires reflection both inside and outside of MERCOSUR. In the first case we are amazed at how far we have been able to advance, at everything that has been done. In retrospect we see that much progress in harmonization has been made, not only in regard to the requirements or conditions for registration, but also the needed far-reaching harmonization of procedures, such as changing the existing situation with a view to improving the health of the population through the quality of the products available to it. It has been possible to advance in procedures by validating things, and the process has advanced far enough to attain positions and harmonizations at the subregional level instead in individual countries. In MERCOSUR the stances are not those of individual members of the subregion but one view, that of MERCOSUR, on harmonization vis-à-vis other countries of Latin America and the rest of the world. This has been accomplished by dint of many hours of work, many hours of discussing, seeking consensus and making concessions, in addition to conducting training and implementing procedures that make it possible to modify that situation. He said he agreed with what was said by the delegate of Canada about the importance of exchanges of inspections and joint inspections. This sets the pace toward harmonization, and a dialogue is under way between harmonization and specific control on how that harmonization is to be accomplished. He was of the view that we must harmonize what can be harmonized, and that this is possible if we are dealing with actual situations in joint inspections.

Regarding reflection outside MERCOSUR, he said that many gains have been made in some regions, such as the European Union, which has been working on harmonization for many years, has accomplished many things, and has blazed trails so that the wheel does not have to be invented. He noted that it is important to know how to adapt the good things available that have worked in similar situations. In this regard, too, it is noteworthy that the European Union, with all its technological advances and all the effort it has made over so many years, has not yet been able to arrive at mutual recognition, which once again shows that mutual recognition is an outcome of a series of processes that must already be present and cannot be established by laws or decrees. He also noted that another of MERCOSUR’s achievements is the positive and significant collaboration of industry, which is the product of far-reaching communication, transparency in procedures, and an explanation of the problems and interests of every sector.
6. CLOSURE

6.1 Dr. Brandling-Bennett – DDPAHO

Dr. Brandling-Bennett reminded the participants that PAHO is called upon to work for equity and quality in health services, an important component of which is access to safe, effective and quality drugs. Regulatory harmonization is an important mechanism that contributes to this end, and the work of the participants of this Conference during these three days, guides us on how to proceed. It was clear from the conclusions of the Working Groups the existing subregional initiatives must serve as a foundation and that views differ widely. It also became clear it will be necessary to strengthen the national regulatory entities and their participation in the subregional processes. Progress will not come easily, but it is important to act. To this end, PAHO offers an forum open to all interested parties, in which it will facilitate exchanges of information and support the measures agreed upon, but will at no time impose standards or regulations.

Dr. Brandling-Bennett added that many matters related to resources and the financing needed to ensure the continuity of this line of regional work remain pending. Again, in this area, it is essential that all interested parties play their part. In addition, political support will have to be secured, and it is hoped that the declaration to be issued by the Presidential Summit in Santiago, Chile, in April 1998 will make reference to the topic of drugs.

Dr. Brandling-Bennett concluded by saying that the Conference has given direction to the hemispheric process, though the steps to be followed remain to be charted in detail. It is important to keep clearly in mind the ultimate objective, which is to improve the health of the Hemisphere’s peoples. If we advance successfully in regulatory harmonization, we will have helped to reach this goal. Certainly, success will depend on the commitment and efforts of all those present, for PAHO cannot do it alone.
1. The establishment of the FTAA may be viewed as one of the more important events of the end of this century. It realizes the aspiration expressed by Simón Bolivar two centuries ago. The FTAA initiative was launched at the Summit of the Americas, held in Miami in 1994, by the decision of 37 Heads of State who launched the Partnership for Development and Prosperity: Democracy, Free Trade, and Sustainable Development in the Americas by progressively eliminating barriers to trade and investment.

3. The Ministers of Trade in charge of defining guidelines for setting up the FTAA said that it must be balanced, not raise barriers to countries outside the Region, be consistent with the obligations assumed by the countries under the World Trade Organization (WTO) agreement, respect the existing multilateral and bilateral arrangements in the Region, and be implemented through a single agreement that spells out mutual rights and duties.

5. It is necessary to emphasize the importance of the FTAA process, which includes countries representing one-third of the world’s gross product (US$8 trillion in 1992, out of the world total of US$25 trillion). These countries account for 30% of world trade. Hence, their great importance in the world economy.

7. The purpose is to lift barriers to trade (customs and noncustoms, investments, and services).

9. The Region is highly diverse. Some of the countries are twice as developed economically (Brazil, Canada, the United States, and Mexico) as others (Honduras, Jamaica, Nicaragua, Trinidad and Tobago). As a result, there are wide disparities in per capita income.

11. The establishment of the FTAA began with the Miami Summit and is being moved forward in meetings. The next one will be take place in Chile in 1998. The one in Miami was followed by ministerial meetings in Denver, Colorado (United States), Cartagena (Colombia), and Belo Horizonte (Brazil). The next one will be held in Costa Rica (March 1998) immediately prior to the Presidential Summit in Chile.

13. Trade has soared in the past 10 years. It doubled to more than US$500 million in 1995 owing to the unilateral negotiations carried out by the countries of the Region.

15. The process of establishing FTAA is structured in three levels:

• Summit of Heads of State

• Meetings of Ministers of Trade (which define the objectives and the overall program of work).

• Meetings of Vice-Ministers (which schedule meetings to analyze the results of the working groups, and chart measures for the future).
• Working groups. There are 12, created in succession. The following ones were established in Denver: Customs, Rules of Origin, Small Economies, Sanitary and Phytosanitary Aspects, Investment, Technical Standards and Barriers, Subsidies, “Anti-dumping” Measures and Countervailing Duties. In Cartagena the following were added: Policies on Competition, Intellectual Property, Services, and Ministerial Procurement, and in Belo Horizonte: Settlement of Disputes. The working groups are chaired by different countries.

• Working meetings have been held in 13 countries.

9. There is a Tripartite Committee consisting of the OAS, the IDB and ECLAC, which provides technical support to the FTAA process.

11. At the Belo Horizonte meeting, the Ministers of Trade recommended to the Heads of State that they move forward with the procedures for creation of the area at the Summit in Chile. Several other decisions were also taken:

• Decisions will be made by consensus.
• The FTAA may coexist with the regional and subregional agreements in the Region.
• Countries may participate in the process as groups or individually.
• Provisions must be made in regard to the smaller economies.
• A Technical Secretariat must be established to coordinate these efforts.

11. The Ministers asked the working groups to present reports to the Vice Ministers to enable them to determine how to arrive at negotiations and technical considerations and so that alternative courses may be devised for their development. These reports were presented at the recent meeting of Vice Ministers in Costa Rica.

13. The Working Group on Technical Standards and Barriers to Trade, the one having to do with this meeting, has already met six times under the presidency of Canada. Its work is based on six mandates:

• To improve transparency in the production of standards. To this end it has already completed a census of barriers to trade.
• To collect and compile information on organs and procedures accordingly, especially in regard to accreditation at the hemispheric level. The Inter-American Accreditation Corporation was established in 1996 to promote mechanisms for establishing relations among accreditation entities.
• To promote better understanding of technical standards and barriers to trade. This work is done by disseminating information and promoting seminars. The latest of these was held in Trinidad and Tobago, and the next one will be held in Guatemala.
• To make recommendations on certification and promote mutual recognition. The results of this conference would be very useful in this regard, particularly in respect of recognition of
technical agreements at the different levels (governments, testing laboratories, etc.).

15. The harmonization of standards is essential for facilitating realization of the FTAA. It is also considered important to strengthen democracy and support the attainment of equity.