



Regional Office of the  
World Health Organization

PAN AMERICAN NETWORK FOR DRUG  
REGULATORY HARMONIZATION

**WORKING GROUP ON  
BIOEQUIVALENCE AND BIOAVAILABILITY  
V MEETING  
Panama, 8 – 11, August 2005**

**Participants:**

Members:

**EUA:** Justina Molzon, Coordinadora. Associate Director for International Affairs. FDA

**ARGENTINA:** Ricardo Bolaños. Departamento Estudios y Proyectos. ANMAT.  
Docente de Farmacología. Universidad de Buenos Aires.

**BRAZIL:** Silvia Storpirtis. Associate Profesor, Consultant Division of Generic  
(essential – similarity) ANVISA

**CANADA:** Conrad Pereira. Dirección de Productos Terapéuticos, Health Canada

**CHILE:** Regina Pezoa Reyes, Jefa Sección Biofarmacia, Instituto de Salud Pública de Chile

**COSTA RICA:** Lidiette Fonseca. Directora Instituto Investigaciones Farmacéuticas  
INIFAR. Escuela de Farmacia. Universidad de Costa Rica

**University of Texas:** Salomon Stavchansky. Alcon Centennial Professor of  
Pharmaceutics. The University of Texas at Austin. College of Pharmacy

**USP:** Vinod Shah, Consultant United States Pharmacopoeia

**VENEZUELA:** Irene Goncalves. Farmacéutico Jefe del Departamento de Evaluación  
Científico Legal. Instituto Nacional de Higiene Rafael Rangel

**ALIFAR:** Silvia Giarcovich. Directora Técnica y Gerente de Estudios Clínicos.  
Diffucap-eurand SA. Profesora Universidad de Buenos Aires Dpto Farmacología

**FIFARMA:** Janeth Mora, in liú of Loreta Marquez, Executive Director International  
Medical Organizational-Latin America- (Bristol-Myers Squibb)

Resource person:

Sanchez Aida. Division of Bioequivalence. Office of Generic Drugs. FDA

Observer:

Wilma Turner, MOH Panama

Secretariat:

Rosario D'Alessio, OPS/OMS

## AGENDA / MINUTES

- The group was welcomed by Guadalupe Verdejo, PWR-PAHO/WHO Panama and by Pablo Solis, Drug Regulatory Authority of Panama and Alternate member of the PANDRH Steering Committee.
- Rosario D'Alessio, PAHO/WHO provided an update on achievements and work under developing by other PANDRH Working Groups.
- Justina Molzon, Working Group Coordinator provided a review of the Conclusions and Recommendations for the working group from the IV Pan American Conference.
- The proposed agenda was modified to allow for the participation of Salomon Stavchansky who would be arriving later in the day.

### 1. Review of the WG/BE Mission:

This subject was introduced by the Secretariat based upon a comment received from Silvia Giarcovich (ALIFAR). The current Mission states: "*The working group should contribute to harmonized bioequivalence criteria for the interchangeability of pharmaceutical products in the Americas.*" It was developed in the third meeting of the group (February 2003) and approved by the IV Conference (March 2005). Members were asked if they wished to modify or comment.

#### Comments:

- Silvia Giarcovich, ALIFAR, suggested that the mission should end after - *the working group should contribute to harmonized BE*, as only four countries provide BE for interchangeability at this time in Americas: US, Canada, Brazil, and Mexico. She indicated that ALIFAR preferred a more conservative approach. The mission cannot address interchangeable at this time.
- During the discussion various members of the working group pointed out that the main purpose of implementing BE studies is to assure a link to the innovator's safety and efficacy, and to assure interchangeability between the innovator with another medicines (generic).
- Wilma Turner PAHO/Panama indicated that some countries are using BE as requirement for registration.
- Regina Pezoa Reyes, Chile proposed to add language to the mission statement to include the concept of the working group's efforts *facilitating* bioequivalence
- Justina Molzon, USA suggested that the Working Group should contribute to harmonized bioequivalence criteria to assure a link to the reference product's safety and efficacy studies as a foundation for interchangeability of pharmaceutical products in the Americas. It is important to link a generic (multisource) product to the innovator's safety and efficacy studies.

- Ricardo Bolanos, Argentina, indicated that there were three problems with interchangeability: It was created in countries where there were only innovator and generic; and Latin America has "similar" which add the idea of interchangeability product by product; there are restricted interchangeability—NTI; and he also mentioned the concept of "*transivity*" which implies interchangeability between generics.

Decision:

1. The group modified the mission statement to include the words *TO PROMOTE*, as follows: "*The working group should contribute to harmonized bioequivalence criteria TO PROMOTE the interchangeability of pharmaceutical products in the Americas.* However, since according to PANDRH rules only the Pan American Conference can approve the Group Mission and the current Mission was approved by the IV Conference, it was decided that this change will be reviewed again a few months before proposing the change to the next Conference.

**2. Nacional Strategies for BE Implementation.**

The IV Conference recommended the WG/BE discuss other strategies for BE implementation. *Silvia Storpirtis*, member representing ANVISA was asked to present the Brazil experience. (PP attached).

Silvia pointed out that ANVISA created numerous guidance to help implement BE regulations; they also created a commission to determine the appropriate reference listed; and that ANVISA does not permit pharmaceutical alternatives (i.e. no salts or esters) however interchangeability of tablets /capsules is being discussed.

Comments:

- The point was made that BE can be seen as an obstacle to access to medicines and there is a need to convince government and consumers that generics are needed if drug access is to be improved through interchangeability. Supportive arguments toward the need for BE implementation as well as commercial and political concerns on generics and BE implementation should be dealt with at conferences and at Minister of Health level. A basic concept underlying BE is that poor people don't deserve poor drugs, and politicians need to justify why not requiring BE when it is scientifically recommended.
- Silvia Giarcovich pointed out that there is a big difference between retrospective implementation and prospective implementation. Similar are already on the market and would be expensive to retest. So there is great difficulty in trying to clean up the market place do all products are safe, effective and reliable.
- In Panama- politicians reduce costs through competition. Law of 2001: if want to increase competition must introduce quality and therapeutic equivalence. Only public health institutions other products can still be on market. In March this year came up with a regulation on how to prove BE. In Panama there are no

similar but there is a general impression by consumers that generics are of poor quality.

- Justina distributed copies of a PR campaign by the FDA's Office of Generic Drugs attesting to the quality, safety and efficacy of generic drugs. The ads were provided in both English and Spanish.

In order to have a better context as to the state of BE in Latin America, the WG went around the table so each WG member could describe major problems in their country

### **Chile:**

Regulation is under the responsibility of the ISP (Instituto Salud Publica). Currently they are working on regulation for BE studies. Their emphasis is on in-vitro testing and are making a list taking into consideration drugs from different diseases that government covered cost of treatment (high cost conditions). The new law is named Plan Auge. Documents being drafted will be ready hopefully by October, which explain new rules on medications in Chile

Educating physicians and pharmacists is of high priority. It was also decided that by 2006 all industry must have GMP regulations implemented

### **Costa Rica:**

In 2000 the new regulations for registering medicines was published requiring BE for multisource products. That requirement (BE) would be effective as the regulation for BE will be published. That regulations on BE was published last week in the national Gazette and it will start in 6 months.

In 2000 an Advisory Commission in Quality of Drugs was established to assess (industry, laboratories, health), to develop proposal for regulation and to assess need for training. There were sub-commissions in different topics (GMP, BE, Stability, Validation etc.).

The Commission on BE, reviewed USA and EU regulations on the topic, have also received help on documents from Brazil, USA and Canada. They developed a List of drugs to require in-vivo BE studies based on SUPAC. Other criteria were pK and NTI, and frequency of use on national system—largest number of people taking them to help cut costs. They published in 2001 the first list of 7 active pharmaceutical ingredients that require BE: Valporic acid, fenitoin, carbamazepine, cyclosporine, digoxin, levotiroxine, and verapamil based on largest number of people taking these drugs (measure of exposure).

They are focusing on GMP and have approved modifications on GMP regulations. Cost is of high concern pressure and need additional resources to implement new modifications.

They need training for reviewers and still need to establish BE unit within the NRA. Situation in Central America is more or less the same.

They are also working on list of reference products.

Need to recognize that PANDRH BE WG group membership has broadened exposure to national experts.

## **Venezuela:**

Crawling in terms of implementation; the country has a law on BE from 1998. Deadlines were set on BE but since the country has no infrastructure to start BE delayed the implementation for 3 years to help the industry to adapt infrastructure to BE studies requirements.

RLD is still a problem (which one?). Firms will not start in vivo testing until this issue is resolved.

Pilot center for BE studies available.

Staff training is ongoing. The academia will develop training in Pharmacy seminars.

There is a need for specific training on analytical and biopharm;

The industry is very open to perform in vitro and BCS. The problem is the lack of a technical document classifying drugs in BCS. The industry is also waiting for guides to certify CRO BE studies;

In the DRA there is no unit for BE evaluation and no BE studies is done inside country. There are 29 critical drugs and studies are done 100% outside of the country.

The question raised on: If countries can accept studies from outside country why have infrastructure inside country to do studies.

The WG discussed the possibility of Inter country collaboration. Mutual recognition in Central could lead to marketing in all LA countries. The group could cooperate in developing a list of comparator products; however the problem is that RLD is different in the different countries of LA.

The difficulties of reaching mutual recognition was exemplified by the decision of the FIRST CONFERENCE- on the proposal introduced to create a single agency in the Americas. However, considering the existence of several sub-regional groups and the difficulties of recognizing registration among participating countries, the SC decided to work on harmonization of regulations as a preparation for a possible single agency for drug regulation in the future.

## **Argentina—ANMAT:**

In Argentina there is no law for generic drugs. Similar are registered and can be BE or pharmaceutical alternatives. That includes different salts and esters, different dosage forms but same route.

BE studies programs are prospectively and retrospectively based on health risk.

There are 76 products with BE analyzed, which include revision of data from original products.

Protocols are submitted to ANMAT who review and approve protocols if they comply with current legislation.

ANMAT inspects clinical centers and those where the bioanalytical assay are conducted.

RLD innovator marketed in the country. ANMAT follows the 2002 WHO decision tree.

Foreign studies are accepted only when the RLD used formulation is the same as the test formulation. Issue if the formulation changes over time.

ANMAT requires consistency in GMP 3 batches and ANMAT analyses batch records.

Conclusion:

1. To implement BE successfully need: regulations, guidelines, reference listed drug, and resources in terms of staff and funding. In other word there is a string need for increasing the capacity and strengthening of NRA.

**3. Update on WHO meeting on BE held on July 18.**

Silvia Storpirtis participated at the WHO meeting on BE held in July in Geneva representing PANDRH and provided her comments (see slide presentation).

The aim of the document is to be guidance for countries that intend to adopt BE. They tried to keep the text simple to avoid misunderstanding. Maintenance of any statement was always based on science and wide experience. Proposal to waive in vivo BE requirements for WHO model list of essential medicines IR solid oral dosage forms

Comments:

- Salomon states that we can't have two different quality product standards—can also foresee problems. Don't want products with different profiles. Market issues come into play. The goal of the WHO guideline is the minimum requirements
- The BE WG doesn't want to duplicate or contradict WHO document. Rather, there is a need to provide information relevant to the region to help with implementation of BE in the region

**4. Note from ALIFAR on WHO definition of Multisource Drugs**

Silvia G. presented ALIFAR's considerations regarding the WHO definition of Multisource drugs. The letter was sent directly to WHO and a copy to PANDRH Secretariat. The concern was that the new definition of multisource developed by WHO leaves out the definition of sanitary risk, and that the definition cannot be applied to the concept of "similar products".

Comments:

- Silvia's main concerns was that by requiring BE studies, DRAs may interpret that those similar products should be withdrawn from the market if not found BE. On this issue, Lizzy explain what were the experience of the FDA. There is no need to withdraw some of the similar products if they are shown to be in the therapeutic window for that drug, and are shown not to be in either at sub-therapeutic or toxic levels. The FDA experience was not to withdraw approved products but characterize their therapeutic equivalence. If the products where not BE, they would be rated to denote nonequivalence. So maybe a rating system like the FDA would be an alternative.

- The discussion went on Vinod Shah mentioned that the goal of the WHO document is to promote interchangeability, depending on a country's health risk analysis and its priorities. The goal is that all multisource products will have BE studies done. Very important that each country can do what they feel is necessary for their country.
- One important point is the consideration that prospective and retrospective implementation is different. Similar products were not designed with RLD in mind. RLD frequently not BE to original innovator.
- Members that participated at the WHO meeting (Vinod Shaw and Silvia Storpirtis) confirmed that the global group reviewed all comments received including the letter from ALIFAR and the decision made was not to modify the definition.

Decision:

1. To accept all WHO definitions including the Multisource drugs; and
  2. To recognize the existence of similar products in the Americas in the PANDRH BE document specifically in the implementation strategy.
- 5. Document "SCIENCE BASED CRITERIA FOR BIOEQUIVALENCE TESTING (*IN VITRO* AND *IN VIVO*), BIO-WAIVERS, AND THE STRATEGIC FRAMEWORK FOR ITS IMPLEMENTATION.**

WG is developing a document to help countries and guide understanding of BE studies. It will guide to determine when they are necessary and when not necessary. One important point is that DRA do not ask for studies when they are not necessary. At the same time WHO is developing a document to be used globally. PANDRH WG has access to development of WHO document and we can increase our participation to provide a better understanding of the situation in Latin America

We want our document to complement the WHO document and we can contribute with our comments to the WHO doc. AMRO/PAHO can serve as a model and work with countries on how to implement. These activities would be in line with Dr. Lee's mandate to work with countries. Each WHO region should do the same. This could be a paradigm shift.

The group then went around the table to give their individual opinions on the WG three draft documents: version before Salomon major edit (as presented at the IV Conference), version with Salomon's major edit (known as VERSION # 9 (12-15-04)), and the WHO document (as per July 18). The goal is to keep in mind is that the WG wants to be helpful to countries of the Americas in implementing the WHO document in their own reality.

Salomon Stavchansky: It is not coincidental that WHO is developing a document on BE of multisource products. Reality is that this is an important document which WHO will be using globally. We can't isolate ourselves from that activity. Our document from Antigua didn't include some of WHO recommendations. He

suggested avoiding a lot of duplication with WHO document. If the WHO document is not sensitive to the needs of the Region we can mention those specifics in our document. For the Americas this is what we need to do. Scientific BE principles are the same. We can make our document more precise and make it helpful. Salomon feels that the WHO section on comparator could still be improved. In terms of definitions, we could discuss but we should respect those definitions. We can contribute to the document but shouldn't try to change the document as will go into circle. He tried to include WHO concepts in his edits but that may have been a mistake.

Regina Pezoa (Chile): The WHO document is very important and in a meeting with MOH has gone beyond academia. Since Chile is part of WHO must follow guidelines. This is very important as representatives of national industry are maintaining that this is a capricious idea. So the WHO document and implementation of BE in Chile is important to act in a short time. There is a huge interest in biowaivers. Uruguay, Paraguay, Peru and Bolivia are in the same situation. She suggested starting with in vitro dissolution and small list of drugs needing in vivo studies. The last draft document version # 9 is highly repetitive from WHO document. Agrees with Salomon in supporting WHO document and focus in document on Latin American concerns.

She considers that WG should have a role in the implementation phase of WHO document. The Group should act as a catalyst to provide resources, and to foster implementation. Governments agree philosophically, but don't have resources to support the philosophy. Most countries only have minimal staff to work on this topic. Currently it is very difficult and the same situation is in Bolivia, Peru, Uruguay and Paraguay.

She also said that there is a strong link between academia and two strong groups in academia conducting BE studies. No CRO's at this time in Chile conducting studies. There is a lot of interest from other groups to conduct studies in Chile. There is a pool of pharmacists so, no lack of professionals available to help implements. Regina is also head of FEFA and can create a movement to encourage BE.

Lidiette Fonseca/Costa Rica- WHO document is fundamental to Costa Rica and countries of Central America. WHO documents serve as a basis for laws and recommendations for industry. There is a high interest in biowaivers and how to conduct in vivo testing.

Justina –proposed a possible strategy might be to get biowaivers products out of the way and then work on problem products. Will help calm industry and then can focus on real issues of public health. Remove duplication of WHO info in version 9. Explanation of BCS should be an addendum. Training is something the WG should be focusing on. WG should support effort so government can be more willing to establish CROs. Look for strategy to motivate government so will support educational institutions and country level CRO's . PAHO can act as an intermediary.

Salomon pointed out that the government is the key issue. If government pushes enterprise companies will see the opportunity. If show commitment private investors will show up and help the economy. For example phase 2 and 3 studies being done

in LA all the time. This coincides with government desire to have studies done in their own country. Brazil exerted pressure and negotiated for commercial development.

Justina mentioned that centers of excellence within a region can share resources. It may be possible to have MR between countries to encourage companies to submit BE studies in return for marketing in region.

Lidiette /UCR is thinking of implementing post graduate studies and just found out that Panama started one in 2003.

Ricardo Bolanos (ANMAT) He agrees with WHO document and suggested that that our document should be a guideline based on different scenarios in various countries; a guideline on how to implement WHO based on country experience; and an operational one to explain what country should do to implement interchangeable drug system. He proposed scenarios--BE in vivo, BE waivers and health risk. Every country should focus on health risk of product. This is a political decision by each country. Biowaivers are a strategic tool to convince politicians to support the requirement of the need to demonstrate BE. This would be a better way to concentrate our efforts.

Irene Goncalves (VENEZUELA): She doesn't agree with scenarios because we as a group should focus on all situations in region. Venezuela needs in vitro studies and BCS at this time. It is important that WHO document consider situation in countries but countries also have high expectations for PANDRH BE WG document. The last document we have is not a friendly document may need to move some information to annex to make it more users friendly. She agrees with Lidiette and the need to focus on supporting government in implementing BE (at least countries represented in the WG).

Justina asked Rosario about resolution by PAHO's Directing Counsel and all MOH signed off. What does that mean? Do we need to remind them that they signed and should provide support to PANDRH products, documents, etc. Rosario indicated that when the MOH signed in support of PANDRH they promised to provide resources to PANDRH activities. Even though we can't really measure implementation and commitment per group, we need to include efforts in reviewing and developing regulations, restructuring of the regulatory unit etc. that are implemented in many countries that can be considered parts of the commitment of countries related to the Resolution. The PAHO Resolution is from 2000 and we are now in 2005; so it may be good time to report on it.

Silvia Storpirtis (ANVISA-Brazil): ANVISA always develops its own documents based on US, Canada, EU, etc. They had to adopt documents into new law. WHO documents are very important. ANVISA is interested in harmonizing with WHO and PANDRH as will give ANVISA credibility as a DRA. Only have doubts on BCS Not the scientific principles but have concern about source of API. They are working on regulation for certification of APIs, and have simultaneous development of regulations, guidance and laws. Soon after were able to purchase HPLC equipment as an example. Version 3 of WHO document felt to be more helpful as provided more background to DRA. She proposes that our document could have more details

to help implementation take place and explain requirements to industry. National experience with implementation should also be shared. For example ANVISA had a problem with the first cyclosporine generic. Now that they have experience and can share their experience.

Salomon: A "How to" course in doing calculations and making decision would be helpful. He mentioned Pharsight Corporation. Course 20-30 people on BE. SAS is not very friendly, while with Pharsight there is no need for any programming experience. Biowaiver monograph references are being published in J Pharm Sci. They need to be translated into Spanish.

Regina informed that FEFAS (Federacion Farmacéutica de Sur América) (Regina is current President) have already translated into Spanish but need permission from J Pharm Sci so can publish in FEFAS journal. Each paper is about 10 pages and reviews literature and formulations in public domain. Recommends biowaiver and complete document can be useful in making risk assessment. Point out it is a useful tool and resource. Reporting procedure was suggested to help countries understand how biowaivers decisions are being made such as in Brazil.

Silvia Giarcovich (ALIFAR): When we wrote our document we didn't know about WHO document. We agree with eliminating first part of document scientific. She suggested changing the title HIGH risk based to stress importance that strategy is risk based. Imposing BE on similars would generates great asymmetry between multisource and similars which goes against harmonization. Need to first address issue of comparator product. Actual definition of multisource in 1996 represented reality. Automatically knocks out of market similars not BE.

Justina-Suggested including the definition of similar in WHO document and devote some part of our document to explain current situation to help construct an implementation plan. DRA can decide what they want to do.

#### Decisions:

1. The WG/BE decided to adopt the scientific principles of WHO document. PANDRH document should have a more operational focus and explain how to implement that document in the Region. Every country can adapt the document from WHO according to its own reality and the role of the WG/BE is to help making the document implemental in the Region of the Americas.
2. PANDRH document will explain current situation on similares in the Region to help construct an implementation plan. DRA can decide what they want to do.
3. Wherever needed PANDRH document should expand any subject considered helpful to NRA in BE implementation.
4. To focus on specific aspects that we would find helpful in facilitating BE studies in Latin America. For example electronic submissions would be helpful in analyzing documents and would prevent the need to reenter data; harmonized submission format such as CTD; develop reviewer template for review.

5. PANDRH document shouldn't be more stringent than WHO document.
6. The document must be operational for DRA. It will include a decision tree on whole issue of BE based on sanitary risk of product.
7. To suggest to the PANDRH SC that it would be advisable to develop a follow up report on Resolution on PANDRH. Countries and PAHO would like to know how PANDRH is helping countries in harmonization processes.
8. Since the WHO document is not final and it is undergoing a process for comments. It is important to get comments to WHO in time (by the end of August the latest) to be incorporated into the document in time to be distributed to technical committee for October's meeting.
9. Exchange of information and experiences among countries should be promoted.

## **6. Regional Comparator for the Region**

The issue of RC was discussed in several meetings of the WG. There is a need to clarify if the issue is still relevant and if the WG should continue the discussion until develop a regional proposal.

### Discussion:

- Salomon: we need to look at ethics of doing drug studies unnecessarily. Commercial interest would be facilitated if one comparator were used regionally. There is sensitive to using human beings as detectors. Are there regulations that would preclude use of non national comparator?
- In past meetings Loreta/ FIFARMA said that they could not guarantee that products in various countries were the same. It is impossible to do so retrospectively.
- CONRAD--In Canada they have evaluated the innovator so know product well. If have not evaluated comparator product what is your experience? Why request a national product if don't know anything about it?. Silvia Giarcovich responded: so product can be interchangeable with product in that country.
- Salomon: the innovator can use bridging study to product in Germany, etc.
- In Argentina ANMAT must show equivalence to a validated reference product which would be anchored.
- In Brazil, the Comparator product be recognized as such and registered in ANVISA

### Decisions:

1. If legislation in countries requires that comparator needs to be approved in their country it would be difficult to have a regional comparator. Selection of a Regional

Comparator may be an obstacle to proceeding with implementation. Let countries decide based on WHO document and risk assessment. Once BE system established may move toward regional comparator.

2. Prospectively DRA can ask for assurance that product registered in country is linked to product on which S/E is established. This will pave the way for a regional comparator.

3. In WHO document need to add link to product on which S/E was established. If innovator makes major changes in formulation need to let DRA know.

4. Recommendation for PANDRH Drug Registration Working Group: To ask for bridging information to S/E study for manufacturing site change especially for Reference product and changes

## 7. **BE Indicators**

The group discussed indicators to be used by the working group to track implementation of bioequivalence studies in the Americas. The WG has conducted two surveys to date but no indicators were developed.

### Comments:

- Countries needs could serve as a diagnostic tool to determine areas needing improvement. Frequency of indicators: Doesn't need to be done prior to each Conference but can be accumulated.
- Lidiette suggested the following indicators: Main areas of evaluations should be Training, Infrastructure and impact.

#### Infrastructure:

- Regulations: prepared and approved
- Number of center that implement BE studies
- Number of studies performed
- Number of Professionals in the NRA working in BE

#### Training:

- Number of persons trained in the national regulatory agency;
- Number of course or training activities

#### Impact:

- Number of BE studies presented to the NRA
- Number of studies approved
- Number of studies rejected
- Number of in vivo studies approved
- Number of in vitro studies approved

### Decision:

1. The indicators should be used to assess the processes, performance and impact. A review and final selection of indicators to use should be done in the near future.

## 8. Glossary of Terms

The PANDRH BE document has a glossary of terms that needs to be updated accordingly with the new definitions of WHO document. On the other hand, considering that all WG are developing their own glossary of terms, the IV Pan American Conference recommended the Secretariat to update the PAHO publication on "Glosario de Medicamentos: Desarrollo , Evaluación y Uso". The Secretariat is reviewing and updating the publication with participation of PANDRH' WGs.

### Decision:

1. Lidiette Fonseca and Regina Pezoa volunteers in reviewing terms related to BE of the aforementioned publication.

## 9. Educational programs

Training issues were discussed. In the first meeting of the Group and after a pre-meeting AAPS conference on BE, the FDA developed a proposed program on BE training which cover three modules. After that, the FDA implemented two sub-regional courses (AA and Central America) on Module 1&2 of the program, as a train the trainer methodology.

### Comments:

- At this stage FDA can not implement training activities on Module 3 & 4. Justina suggested that having the WG developed a scientific document all training activities of the WG should be addressed to disseminate the document focusing the implementation strategy.
- Moreover, the FIP and AAPS are offering courses could have an arrangement with PAHO to teach them on a regular basis. They may work with National Universities. Associations can also work with universities
- DRA have to allocate funds for training programs shows lack of commitment. PAHO can't fund all training activities.
- Silvia Giarcovich pointed out that have complete courses and have them open so they can be replicated in their own country.
- Conrad suggested getting in touch with WHO as they offered a course on BE for reviewer in South Africa.
- Distance learning training programs was also considered. They are generally attended by managers and not staff people. As a result information doesn't filter down to working level.
- Justina explained plans for CDER Forum for DRA offering in spring for countries of the Americas. The training is free but countries must provide their own travel expenses.

- It was also suggested that we should exchange training resources in the Americas and continuing education. It would be helpful to develop a list of BE training. All training shouldn't be by us but we could take advantage of other offerings

Decision:

1. No final decision was made. Dissemination of PANDRH WG/BE document should be a priority. It was recommended to closely follow up courses or other training activities already in the market for possible sponsorship from PAHO, in which PANDRH document should be given special consideration.
2. Countries should continue promoting implementation of training courses jointly with universities and other international agencies.

10. **WG/Plan of work. Tasks & Agreements**

<b>TASKS</b>	<b>Responsible</b>	<b>Dateline</b>
<b>1. To inform WHO</b> a. To send mail to WHO (Sabine) on issues discussed at the 6 <sup>th</sup> meeting	<b>Secretariat</b>	<b>ASAP</b>
<b>2. WHO doc</b> a. To send comment the WHO draft Version#4	<b>All members</b>	<b>30 Aug 05</b>
<b>3. Development of the PANDRH BE document</b>  a. Comments on current version  b. Introduction of the doc  c. Review and complete the parts of the document to be only Referred to WHO and to those parts "As in WHO version 4"  d. Expand parts of document referred as "Expand as in previous WHO version"  e. To update Part II of the doc: Implementation strategy <ul style="list-style-type: none"> <li>• Introduction</li> <li>• Require new list of drug with BE studies</li> <li>• Update Tables for Part II of the document</li> </ul> <ul style="list-style-type: none"> <li>• To add: a decision tree on the whole issue of BE based on sanitary risk of product.</li> </ul> f. To add: review of electronic submissions and analysis of documents to prevent the need to reenter data; and harmonized submission format such as CTD; develop reviewer template for review.  g. In Regional Comparator to add: prospectively DRA ask for assurance that product registered in country is linked to product on which S/E is	<b>ALL Members</b>  <b>Silvia Giarcovich</b>  <b>TBA</b>  <b>Silvia Storpirtis</b>  <b>Ricardo Bolanos (coordinator)</b> <b>Silvia Giarcovich</b> <b>Secretariat</b> <b>Bolanos-Lidiette-Regina &amp; Irene</b> <b>Ricardo Bolanos</b>  <b>TBD</b>  <b>TBD</b>	<b>30 Oct 05</b>  <b>30 Oct 05</b>  <b>30 Oct 05</b>  <b>30 Oct 05</b>  <b>30 Oct 05</b>

established; If innovator makes major changes in formulation need to let DRA know; and to ask for bridging information to S/E study for manufacturing site change especially for Reference product and changes		
h. Definitions of Terms (comments)		
<b>4. Follow up to PAHO Resolution on PANDRH</b> a. To recommend to PANDRH SC to develop a follow up report on Resolution on PANDRH.	<b>Secretariat</b>	<b>ASAP</b>
<b>5. Promotion of exchange of information and experiences among countries</b> a. To include experiences in national seminars	<b>ALL members</b>	<b>Next National Seminar Next meeting</b>
<b>6. Regional Comparator</b> a. To follow up legislation in countries requires that comparator needs to be approved in their country b. Analysis and possible decision	<b>All members WG/BE</b>	<b>Cont. Next meeting</b>
<b>7. Indicators:</b> a. To develop a set of indicators to assess the processes, performance and impact of implementation of BE studies. b. To review and final selection of indicators to use should be done in the near future.	<b>Lidiette Fonseca WG/BE</b>	<b>January 06 Next meeting</b>
<b>8. Up date the PAHO publication Glosario de Medicamentos.</b> a. Review of terms related to BE of the aforementioned publication.	<b>Secretariat</b>  Lidiette Fonseca and Regina Pezoa	
<b>9. Training:</b> a. Closely follow up courses or other training activities already in the market for possible sponsorship from PAHO, in which PANDRH document should be given special consideration.  c. Countries to continue promoting implementation of training courses jointly with universities and other international agencies, and inform the Secretariat on those being implemented	<b>All members/ Secretariat</b>  <b>All members in each country</b>	<b>Cont.  Cont.</b>
<b>10. Next meeting (estimated)</b>	<b>WG/BE</b>	<b>March 06</b>

## 11. Agenda of the National Seminar on BE

A half day national seminar was organized by the Drug Regulatory Authority of Panama. The Minister of Health opened the seminar and representatives from different groups participated. See the agenda. Presentations are also included.