PANDRH: Working Group on Drug Registration (WG/DR)

2nd meeting

Place: Dominican Republic

Date: 23-26 August 2004

Participants

Members:
Esperanza Briceño, Ministry of Health, Venezuela. Coordinator
Izabella Núñez Chinchilla, Regulatory Authority, ANVISA, Brazil
Pilar Lagos Lagos, Regulatory Authority, MOH, El Salvador
Viviente Lockhart, Regulatory Authority, MOH, Bahamas (arrived a day latter)
Rosa Angela De Sario, FIFARMA (absent)
Miguel Maito, ALIFAR
Jamaica (absent)
Victoria de Urioste, Regulatory Authority, MOH, Bolivia (absent)

Resource Person:
Leopoldo Landaeta: MOH, Venezuela

Observes:
Pamela Milla, Regulatory Authority, Instituto Salud Publica/Chile
ANMAT/Argentina (absent)
Justina Molzon, FDA/USA
Vilma Guerrero. SESPAS, Regulatory Authority, Dominican Republic

Secretariat:
Rosario D'Alessio, PAHO/WHO
Dalia Castillo, PAHO-WHO/Dominican Republic

MINUTES

1. **Update on previous meeting (Mexico, August 2003**)

Esperanza presented the background information on the survey focusing on the level of responses. Up to date, 18 countries answered the questionnaire; 15

from Latin America, two from North America and one from the Caribbean. She emphasized that some of the responses needed to be confirmed, and it was proposed to send the survey again to the countries (along with other PANDRH surveys) for confirmation.

The results of the questionnaire will be presented at the IV Conference. It is necessary to validate data and to try again to get responses from those countries that have not done that yet. It is also recommended to include the name of the person responsible of answering the questionnaire.

The working group should identify critical requirements for each type (modality) of registration. To begin with, new entity, generic and similar should be defined. It is assumed that in the case of renewals, there will not be technical changes but of administrative nature only.

2. **Preliminary Results of the survey**

The consolidated results of the three sections of the survey were presented (Annex 1): 1-Product Information; 2-Technical Information; and 3-Legal Documents.

The difficulties of the survey identified by some countries were:

1. The questionnaire was the most complex within PANDRH and requires participation from several units within the drug regulatory authority.
2. Some of persons who answered the survey did not understand categories. Some countries answered that phase studies 1, 2 and 3 were conducted for generic drugs, which is not acceptable. It was not clear and there was a confusion in the subsection “pharmacological aspect—pK, pD”, answered by the countries.
3. There were also some confusion with terminology—product conservation is storage conditions----

3. Developing of a harmonized proposal on Drug Registration Requirements. *Esperanza Briceño.*

The working group considered the different modalities of drug registration covered by the survey:

- New Entity
- Generic
- Similar
- Renewals
- New Strength
- New Dosage Form
- Biologicals

The working group recognized that the issue of generics, similars and interchangeability is seen differently in the Region, and mainly, among Latin American countries. The representative from ALIFAR explained that "similar" drug products were never meant to be interchangeable by the time of their registration; however, nowadays, both generics and similars could eventually meet bioequivalence requirements. In relation to this, the drug regulatory authority of Chile said that generics and similars are the same from a practical point of view.

Equally important is the fact that there are many definitions for generic medicine. Each country may even have its own definition, which causes more confusion. The need for a harmonized definition was highlighted by the II and III Pan American Conference. The main products / definitions are:

* WHO definition—multisource—includes the concept of interchangeability
* Generic
* Similar with trademark
* Similar without trademark

Several studies that address the concept of generic drugs are undergoing: WB, Parlatino, ALADI, and PAHO/WHO. The working group decided that if we do not have harmonized definitions, we can focus on pharmaceutical equivalents and therapeutic equivalents.

The most important and controversial part for a harmonized proposal for drug registration requirements are those referred to the recommendations of the working group on "similars" and "generics". Some members expressed their concern about if a therapeutic category could imply a third category of products on the market that do not meet standard. From the pubic health point of view, quality requirements should be the same.

After a discussion, the group decided that there should be no difference in requirements for registration of generic and similar drugs. The main concerns for discussion were: requirements for drug registration of dissolution test, dissolution profile and BE studies. After discussion, the group considered necessary to set a criteria for countries to prioritize requirements for BE studies. However, it was accepted to rely on the work of the WG/BE, which is developing a document on Proposed criteria for bioequivalence testing (*in vitro* and *in vivo*) and for waivers of *in vivo* testing of generic drug products.

The working group decided to start with the requirements for new entity, similar drugs, generic drugs and renewals. A separate chart with these four categories was created, and the group discussed the response for each category. English and Spanish versions were created simultaneously, improving translation when needed (Annex 2.)

After this phase was completed, the working group followed with the requirements for other registration modalities (new formulation, new indications, combinations, etc.).

It was decided that requirements for biologicals be selected by experts at PAHO/ HQ, and that their recommendations be reviewed by experts in the countries represented at the working group. This survey will be discussed via e-mail.

Some topics of discussion:

a) Discussion on GMPs for APIs need proof in registration and should also be looked at during GMP inspection.

b) Purpose of renewal –fees-- for updating regulations since registration date. Renewal is also a way of cleaning up products that are not longer on the market and products that were never marketed.

c) Many Latin American countries test each batch before release. Since this represents a lot of work, the use of a random sampling process could be helpful. The quality monitoring of the first batch of marketed product should be strengthen.

d) Labeling discussions: the United States is one of the few countries requiring R.Ph. to dispense Rx drugs via vials. Most Latin American countries use prepackaged containers which must be labeled with indication, etc.

e) It was pointed out that the use of a no harmonized label causes confusion in a globalize market.

f) The need to add expiration date to the packaging was noted since it was not included in list. Manufacture date was listed but not the expiration date.

4. Update on PANDRH Activities. *Rosario D'Alessio*

After presenting an updated version of PANDRH activities (Annex 3), followed a discussion about access issues. It was pointed out that the mission of the conference included the concept of access: *The Conference should promote drug regulatory harmonization for all aspects of quality, safety and efficacy of pharmaceutical products as a contribution to the quality of life and health care of the citizens of the Member Countries of the Americas.*

It was also emphasized that, until now, PANDRH's working groups have been developing regional studies and harmonized proposals in their area to be adopted or approved by the Conference. However, from the next Conference on,

the challenges of PANDRH will focus on the implementation of the adopted proposals, and the impact of the Network should be measured through selected indicators such as:

- Number of countries that adopt instruments produced by the working groups
- Number of countries that integrate these changes in their legislation
- Proposals from PANDRH that are integrated into the country's economy
- Proposals that are applied at a regional level
- Impact of the implemented proposals on quality, safety and efficacy of medicines
- Impact of not applying the proposals of PANDRH

It was reminded that the 42nd PAHO/WHO Directing Council (September 2000) approved a Resolution in support to PANDRH.

It was informed that training programs should be self-financed. For example, for GMP-Validation courses, it was necessary: a) to increase the registration fee from US$200 to $ 350 and to increase the number of participants in order to cover all related cost of each activity. It was also noted that registration fees will be waived for selected representatives of the drug regulatory authorities.

It has been difficult to provide BE training as programmed (four sub-regional educational seminars in each of the four modules) for a variety of reasons. It was proposed to change the time of the course and to focus on the implementation of document developed by the working group which was approved by the Conference. The topics in the modules will be covered with this approach, being then more focused and not abstract.

On BE issues: Until now, there has not been an agreement on a regional reference product.

The importance of the topic of counterfeit was stressed. There was a pre-meeting on this topic at the ICDRA in Spain. It is important that drug regulatory authorities discuss topic before lawyers do. There will be a framework document reviewed by the working group on Counterfeit. It was noted that the working group is concerned that the document (presented at the pre-ICDRA) ignores all the work done in the Region (PANDRH, ANVISA, ANMAT, FDA.) Some aspects of it need more discussion as document makes assumptions that are not correct. It was considered to be written from a narrow point of view.

5. Conclusions:

1) To request the working group on Good Clinical Practices to develop a proposed guideline for accreditation of CRO for BE studies.

2) Izabela (ANVISA) will work on the draft of indicators to measure the implementation and the impact of having common requirements for drug registration (By Sep 30).

3) Esperanza will edit the last version of the common requirements by 30 September. Then, it will be sent to group and to PAHO country representatives by 30 October for distribution to the drug regulatory authorities.

4) Esperanza will work on the proposed recommendations of the working group to the Conference. This will be discussed among the members of the group before the Secretariat presents it to the Steering Committee. The proposed recommendations should include: work plan to change regulations, promotion of a database and training.

5) The analysis of the survey will be published as a PANDRH document. The Member States will have the opportunity to make comments before it is published.

6) Registration requirements for biologicals will be developed by experts at PAHO/HQ, and the members of the working group will discussed them via e-mail.

7) To recommend the Steering Committee to set a structure format for sub-regional presentations of CARICOM, MERCOSUR, NAFTA, SICA and AA at the Conference.

8) The validation of the survey for registration should be extensive to all other PANDRH questionnaires.