



PANDRH: Working Group on Good Manufacturing Practices (WG/GMP)

4th Meeting

Place: Boca Chica, Dominican Republic

Date: 30 August – 1 September 2004

PARTICIPANTS

Members

- Justina Molzon, FDA, Coordinator
- Rodolfo Mocchetto, ANMAT/Argentina
- Elsa Castejón, MSDS Venezuela
- Magdalena Reyes, ISP-Chile.
- France Dansereau, Health Canada
- Suzana Avila Machado, ANVISA/Brazil
- Saleta García, COFEPRIS-SSA, México (absent)
- Marisela Benaim, ALIFAR (absent)
 - Carman Araujo, ALIFAR
- Marisela G. Poot, FIFARMA (absent)
 - Anthony Ventura, FIFARMA (absent)
- Norma de Pinto, MOH, Guatemala

Secretariat (PAHO/WHO):

Rosario D'Alessio PAHO/WHO HQ

Dalia Castillo Sanchez, PAHO/WHO, Dominican Republic

Technical Resource:

Mildred Barber, FDA

Rebeca Rodriguez, FDA (absent)

Observers:

Vilma Guerrero, Sub Directora de Registro Medicamentos, SESPAS

Luz Ydalia Sasa, Sub Director Drogas y Farmacia, SESPAS

Yoel Baez Almonte, Farmacéutico Industrial, SESPAS

MINUTES

Day 1, Monday

The working group on GMP was welcomed to the Dominican Republic by Dalia Castillo Sanchez, PAHO-Dominican Republic. The working group on GMP initially met with the working group on GCP, so Rosario could provide a general overview of PANDRH and the upcoming PANDRH/PAHO Conference scheduled for March 2005. Both working groups had the privilege to have the participation of the newly appointed head of Dominican Republic's Drug Regulatory Authority, Vilma Guerrero, Sub Directora de Registro de Medicamentos, SESPAS.

During her presentation, Rosario stressed that the documents of the working groups need to be completed to present them for the Conference's approval. Previous to the Conference, the documents will be posted on the PANDRH web page by the end of October for review And will also be widely distributed throughout PAHO country representatives. The working groups will need to develop implementation strategies for their topic. It was noted that different levels of implementation will be necessary for countries of the Region. In order to promote implementation in countries, each country will be requested an action plan on the execution of the proposals of the working groups. It was also noted that countries will need to implement the proposals with resources available.

During discussion on the agenda of the Conference, Justina explained the purpose of the sections of the program entitled Expert Working Group Consultation Sessions. These sessions would allow Conference participants to ask members of the working group attending the meeting more specific questions about the documents proposed. It was expected that allowing more individual discussion on the documents would lead to a better understanding of the proposals and would promote faster implementation.

After these initial discussions, the working groups on GMP and GCP split up and proceeded to discuss their draft documents.

The working group on GMP spent the rest of the afternoon discussing Chapter 5 on Warehouses.

Day 2-Tuesday

The working group started the second day with a discussion on the intent of the GMP document and the need of instructions for the user. The following basic concepts were discussed:

1. The guide will be used to establish the standard for GMP inspections
2. The guide will be used as a training document for GMP inspections
3. The guide will be helpful to countries in educating inspectors with a unified criteria
4. The guide will be more comprehensive than what is in place in the economic blocks (countries) and will send the message that those countries need to work as

a community to meet established standards; and therefore, improve the quality of pharmaceutical products

5. The guide will serve as a work model necessary for common criteria
6. The guide should not be used as a check list, but it should show principles important to consider in association with an inspection.
7. The guide will be a valuable tool to evaluate manufacturing and it would be an important instrument for teaching; thus, it should be more detailed and than general.

It was noted that it may be difficult to have a common guide because of the different level of industry throughout the Region.

It was noted that it was important to show/stress the need for adequate/appropriate training of the inspectors that use the guide. For example, if the guide mentions Good Distribution Practice (GDP), it is necessary to train on GDP. Also, the inspectors need to be trained permanently to help them think and associate finding with GMP principles and not to use the guide just as a checklist. It was noted that the proper use of the guide requires inspectors to consult additional related documents. Otherwise, they will continue to have/follow a check list mentality. Additionally, the guide does not/cannot list everything that needs to be considered. Inspectors need to develop an instinct of finding/uncovering problems instead of going item by item. When they find something significant, they can concentrate on it. The group decided that additional diagnostics can be developed at a later date, as not everything needs to be included in this version of the guide.

Discussion included concerns related to the implementation of the document. It was noted that many countries will benefit from including principles of WHO 32 as the basis of their GMP regulations (includes Report 32 issued in 1992 plus addendums.)

Guatemala has had an inspection guide since 1999. The Guatemalan industry has reached the point where the guide needs to be revised. As a result, Guatemala is updating its GMP regulation as it needs to be in place before implementation of the guideline since the guideline should be based on regulation. Other countries in Central America are using Guatemala's guideline with a different level of interpretation.

Rosario summarized the discussion indicating that the guide will set the standard for quality. It is not intended to establish the minimum standard of quality. For implementation, it should take into consideration different levels of the development of the country. Furthermore, the use of guideline in the countries promotes consistency which is a major benefit for industry. It will also promote consistency from country to country and will be a training tool.

Representatives from SESPAS were welcomed as observers of the group.

Luz Ydalia Sasa, Sub Director Drogas y Farmacia, SESPAS

Yoel Baez Almonte, Farmaceutico Industrial, SESPAS

After these preliminary discussions, the working group discussed Chapter 11- Production and Chapter 12 –Quality Control

Day 3-Wednesday

Chapter 8– Documentación de la Producción, Formula Maestra, Registro de Proceso de Lote, Envasado, Registro de Envasado de Lote, Documentación General) was reviewed.

Chapter 10-Central de Pesada (Weighting)- was reviewed.

Before discussing Chapter 14 on Validation, the following structure was suggested:

1. General Aspects
2. Qualification (including water systems)
 - IQ
 - OQ
 - PQ
3. Process Validation
 - Manufacturing Process
 - Sterilization
 - Analysis
4. Cleaning

During the discussion of validation, it was noted that the questions in the guide mostly relate to qualification and not to validation. Documentation of the processes should be done consistently in order to do retrospective validations. Validation is difficult and expensive. It was recommended to implement this version of the document, as is; and after equipment and systems are qualified, processes could be validated retrospectively. However, the system for validation of water should be implemented now. It is very important to do so to use it as an example of what needs to be done in other areas of production.

Elsa, Rodolfo y Magdalena volunteered to supplement Chapter 14 with additional information emphasizing validation by 15 September. This will include information on cleaning. Rosario will distribute Chapter 14 to the group, and members will have two weeks to review this chapter.

The resulting version of the guideline will be translated into English by 30 September. Millie and Carmen will review the translation and will compare it with the Spanish version. Justina and France volunteered to review the English version for readability.

Elsa and Marisela (TBC) will complete the reference to the WHO Report 32 of each question of the Guideline.

Day 4, Thursday

Topics of discussion

1. To increase awareness of PANDRH activities, it is intended that documents developed by the working groups of PANDRH be posted on its website for comments and also be distributed to PAHO country representatives, regional drug regulatory authorities and the network of PANDRH WG members.

2. The working group noted the need to include a glossary of terms. The glossary developed will be reviewed to make sure the terms are not already defined in the glossary developed by PAHO. Terms of concern are: sistema de agua abierto, continuo, no continuo, sistema de calidad, garantía de calidad, control de calidad, fabricación, farmacotecnia, produccion, etc. Rodolfo and Norma will prepare a proposed glosary by 15 October. This will be circulated to members of the working group for their comments to the Secretariat within one month.
3. Possible quantitative/qualification (ponderation) of the guideline.

During previous meetings, the WG discussed about assigning quantitative value to most questions in the guideline. During this meeting, the working group decided that this issue should be evaluated after implementation and training, which will influence the values to each question.

4. Plan for implementing GMP courses.

4.1 Modalities:

- 1) Workshops organized by the UPR and the FDA
- 2) Workshops organized by PANDRH based on GMP Modules
- 3) Videotape specific topic presentations
- 4) Videoconference between two or more drug regulatory authorities on specific topics (participants may be observers)

4.2 Next Workshops:

- a) Basic GMP
 - a.1 Chile

- b) Workshop on Validation

- End of October 2004, Chile.
 - It will be based on WHO modules and FDA
 - It will include staff from the FDA, the GMP working group and university professors)
 - Specific presentations will be recorded (DVD/VCD) and will be available for other educational activities
 - Brazil requests to send three participants to the workshop in Validation in CHILE. They will replicate the activity by January 2005
- The workshop on validation will be implemented in Dominican Republic and Costa Rica before the IV Conference.

- As agreed at the previous meeting, the working group requested the training material to be posted on the PAHO/PANDRH website.
- c) A videoconference will be organized between the FDA and ANVISA (or ANMAT). Other countries could participate as observers or it could also be recorded and PAHO/WHO could disseminate it to other countries. This will depend on the availability of infrastructure in each interested country.

4.3 Training for appropriate application of the Guideline for GMP Inspection

- a) Four subregional trainings: AC (Venezuela, Colombia, Peru, Ecuador, Bolivia); CA (Guatemala, El Salvador, Honduras, Panama, Costa Rica, Dominican Republic, Cuba); URU, PAR, CHI; and the Caribbean.
- b) Selection of trainers. The working group agreed that only inspectors and working group members with at least five years of experience can be trainers. Elsa and Rodolfo volunteered for this task.
- c) The training will be based on chapter discussion, site implementation, discussion of findings.
- d) Selection of manufacturing sites (the number will depend on the total of participants for each workshop). The drug regulatory authority in the host country will have the responsibility of selecting the sites.
- e) The number of participants for each workshop is approximately 20 to 25
- f) The number of participants for each visit will vary depending on the chapter of the guideline, the size of the manufacturing plant and the number of participants.
- g) PAHO/WHO will organize the training activity as part of PANDRH overall activities.
- h) Financing: PAHO/WHO will cover the trainers' participation, the host country will cover local costs, and each country will cover the travel expenses of their participants.