WORKING GROUP ON GMP
VI Meeting
3-5 March, 2006
Washington D.C.[1]

Participants
Members:

- Justina Molzon, FDA, Coordinator
- Rodolfo Mocchetto, ANMAT/Argentina
- Elsa Castejón, MSDS Venezuela
- Magdalena Reyes, ISP-Chile
- Louise Jodoin, Health Canada
- Marcelo Vogler de Moraes, ANVISA/Brazil
- Sonia Zamudio Alonso, COFEPRIS-SSA, México
- Marisela Benaim, ALIFAR
- Anthony Ventura FIFARMA **Unable to attend**
- Norma de Pinto, MOH, Guatemala

Secretariat (PAHO/WHO):
Rosario D'Alessio PAHO/WHO HQ

Technical Resources:
Mildred Barber, FDA **Unable to attend**
Arlene Badillo, FDA (**only by phone)**

WHO:
Alain Pratt

Observers:
Nathalie Levesque, Office of Regulatory and International Affairs, Canada
Gina Buendia, INVIMA Colombia

Related activity:
CEDER Forum for International Drug Regulatory Authorities (6-9 March)

This activity is organized by the FDA twice a year, generally March and September. This time the activity had simultaneous translation into Spanish to promote participation from the Americas. During the Forum, CIDER/FDA staff presented the regulatory review processes, tools and guidelines currently used by the FDA, including GMP and the use of the WHO Certificate scheme. Members from COFEPRIS and from Health Canada participated in several panels presenting the Mexico and Canada experience on the same area of work. Presentations of this event can be accessed in FDA web page. Regulators form all countries in the Region were invited to participate.

[1] The meeting was financed by PAHO and FDA. It took place at FDA premises.

Due to relevance of this event to the subject of the WG/GMP members representing regulatory offices in the WG were also invited to participate at the FDA Forum. To facilitate their participation, the meeting was organized just before the Forum.

AGENDA & MINUTES

1. **Welcome, Review of the proposed Agenda and Review the WG/GMP Plan of Work.**
   Justina Molzon

Justina pointed out that this is our fourth anniversary of the WG/GMP. Our first meeting was 4 years ago in Caracas, Venezuela. She went over the WG accomplishments.

2. Review of the activities on GMP approved by NRA.
Rosario D'Alessio

The WG reviewed the agreement on GMP of NRA in their sub-regional meetings (August and November 2005).

3. Educational Activities on GMP

The Group was informed about the Plan for implementing Educational workshops on the use of the GMP Guideline adopted by PANDRH:

- The pilot was successfully implemented in January in Guatemala and 12 facilitators participated along with the 50 participants. The pilot was finance by registration fees and PAHO;
- Instructors have updated pp presentation for next course;
- Instructors prepared a proposed plan to replicate the activities in all Spanish speaking countries during 2006. to date only few countries have confirmed their interest in having the activity;
- An orientation doc to plan national seminars was developed to assist NRA, universities and PAHO Offices to organize GMP seminars;
- It is expected that during 2006 most national seminars will take place.

4. Update on WHO activities in GMP

a. NEW WHO GMP and related guidances

The following **new GMP texts adopted by the 39th WHO Expert Committee** held in 2004 are available on the web (http://www.who.int/medicines/areas/quality_safety/quality_assurance/production/en/index.html
as well as in full report, TRS 929:
http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf)

It is also available in printed form:

- Good manufacturing practices: requirement for the sampling of starting materials (amendment to current text, Annex 2)
- Good manufacturing practices: water for pharmaceutical use (new, Annex 3)
- Guideline for sampling of pharmaceuticals and related materials (revision Annex 4)

During the **40th WHO Expert Committee** meeting, held 24-28 October 2005 the following texts (inter alia) have been revised, or newly adopted:

- Supplementary guidelines on GMP for heating, ventilation and air-conditioning systems (new, Annex 2);
- Good manufacturing practices: supplementary guidelines on GMP for the manufacture of herbal medicines (revision, Annex 3);
- Good manufacturing practices: Validation (new, Annex 4)
- Good distribution practices (GDP) for pharmaceutical products (new, Annex 5);
- Guidelines for organizations performing in vivo bioequivalence studies (Annex 9)

The latter are being edited. It is anticipated that the report be presented to the Executive board meeting in May this year and to be available thereafter.

b. Updated WHO GMP training modules

The update of the basic modules has been progressing well. They will be all soon available in the WHO style in updated form. The rest (i.e. "sterile products, HVAC, validation, water" modules) is being revised and will be made conform to the new GMP texts, which have just been adopted.

c. Planned information materials

In addition to be published in the **TRS report**,, all the above new texts are planned to be available in a revised versions of the **Quality Assurance Volume 2** later this year, once we have got all texts in final from and note by the WHO Executive Board, planned for this May 2006.

All the above (training modules and GMP texts) will, once completed, be made available in **CD-ROM format** together with the video.

All the above will also be updated, and/or newly published on the **web**.

5. Comparative study of implementation WHO report 32 on GMP

The document is to intend to verify that the national regulation on GMP considers, although not limited to, what is expected in the Guideline of Verification of GMP for the pharmaceutical Industry. The preparation of the doc initiated before the IV Conference by the member representing FIFARMA.

In last meeting, it was agreed that this study on "Comparative Analysis between the Requirements for PANDRH WHO Guideline, the WHO Report 32 and national legal requirements" would be redesigned. However, since Anthony, member representing FIFARMA was unable to participate and no new version was proposed (as agreed in previous meeting), this issue was postponed.

However, the Group also considered the possibility of obtaining the information as part of the national seminars that are to take place in all countries. It could be an opportunity since every country has to analyze the feasibility to implement the Guideline.

5. Indicators to follow up Impact of Educational Activities

This subject is being discussed from previous meetings. Rodolfo confirm his interest in preparing a proposal of indicators to be used in evaluating the impact of educational activities in GMP. :

A proposal will be prepared by Rodolfo and the WG will discuss it before the next meeting takes place.

6. Document "NRA Strategies to lead GMP implementation and management in the American Region".

In previous meeting (by phone) Elsa suggested the use of WHO as well as the ISO document and recommended the consideration of existing experiences in the Region such as Mexico and Brazil. Norma (Guatemala) offered also to contribute to the doc.

Elsa prepared a new version of the document and all members had the opportunity to comment on it before the meeting. The doc is available in English and Spanish.

During the meeting, the discussion reflected that the objective of the document and the outline was not clear. A special group was formed with Nathalie and Louise (Canada) to develop a new proposal for the document content, which was presented the following day.

The WG decided to continue the preparation of a proposed draft based upon the outline presented by Louise / Nathalie. Elsa will continue to be in charge of the document with participation of Louise / Nathalie and from Judith Mestre (from Colombia). Participation of Judith was proposed by Gina Buendia who was participating as Observer. Judith has to confirm her participation.

7. Decision Tree for implementing the Guideline for GMP Inspections

In previous meeting the WG decided to prepare a decision tree to help the development of a national plan of implementation of the Guideline for GMP Inspections approved by PANDRH. This DT would help not only national regulators but also the pharmaceutical industry since the industrial sector will be the sector that will implement the guide (and all requirements).

Based upon a model being used in Venezuela and Colombia a proposed Decision tree was prepared by Marisela and Elsa. All members had the opportunity to comments and all comments were incorporated by Elsa to prepare a final draft.

For the meeting the document was available in English and Spanish and a introductory section was included. The Decision Tree (DT) pretends to help NRA and the national industries in their decision making process for implementing the PANDRH WHO Guideline. The proposed Decision Tree may be built on three parts: 1) Quality Assurance; 2) Critical Supporting System; and 3) Validation and facilities. New PLANTS must begin with Facilities, water and air.

The Decision Tree was reviewed and approved the WG as final draft and both versions (English and Spanish) will be incorporated in the PANDRH web page for public opinions before the final version can be presented at the next Conference.

8. Glossary of Terms

Based upon the IV Pan American Conference recommendation to update the PAHO publication: Glossary of Terms for Drug Evaluation, in previous meeting of the WG Magdalena volunteers to prepare a draft version of terms to be included in the Glossary with a clearly identification of their source.

Magdalena sent the first version of terms and Louise sent comments. All members had the opportunity to review both docs before the meeting.

A section of the actual publication was given to Magdalena who from now on will become part of a specific Ad-hoc group to work in the Glossary. The Secretariat will follow up the development of this special group.

9. Mutual Recognition Agreement for GMP Inspections

The objective of a MRA is to promote mechanisms of mutual inspection recognition in GMP inspections between countries. Louise Jodoin sent the doc on MRA being used in Health Canada. She also did a presentation at the meeting.

Members of the WG/GMP reviewed and discussed the document, and agreed on the following recommendations to NRA:

- The objective of the Conference is to reach a mutual recognition among countries; so all countries should work toward that goal;
- Many countries have already similar criteria for MR and as PANDRH continue to harmonize procedures and countries follow the same criteria, information exchange among countries will be strengthened and MR will be a consequence rather than a isolate objective;
- Assessment (evaluation) of national agency is part of the process of MR. NRA should agree on a common criteria for evaluating NRA. Within PANDRH this is a subject to be addressed by the WG on Drug Registration, since they have already started the development of indicators on Basic Functions of NRA and of educational program on this subject;
- Help from other countries is essential, thus participation in join inspections should be promoted. This is necessary even for countries as invitees by those who has more experience;
- All NRA should be notified and invite to participate (even as observers) when in their country there will be a GMP inspection from regulatory authority of another country;
- Multilateral cooperation is a key factor for joint inspections and Reports from inspections and share of information should be clear in MOH among countries;
- In GMP harmonization the use of a common guideline, educational opportunities and performing joint inspections are essentials for MR agreements;
- All countries should have a plan of developed: each country should decide where they want to be in 5 or 10 years and plan ahead to reach that goal;
- The ultimate goal is to build trust among NRA in the Americas.

10. Guideline for Active Pharmaceutical Ingredient

Arlene prepared a draft proposal on Guideline for API. It is in most part a translation into Spanish of the ICH /Q7A Standards. She also reviewed other documents such as WHO, EMEA, FDA, Canada, and all documents use in MERCOSUR provided by Marcelo. All members of the WG had the opportunity to comment on the draft prepared by Arlene before the meeting. The document is available in Spanish, prepared by Arlene and there are two English versions: EMEA & ICH.

Members reviewed and discussed the document, and based on the following:

- ICH document includes all issues included in WHO and MERCOSUR docs.
- ICH doc contains all standards points;
- API has special characteristics and GMP are flexible than GMP for final products;
- The ICH dos is being used by EMEA;
- It will also be used in Canada and USA as well as by other countries;
- It took four years to develop ICH docs;
- It has been analyzed at international level;
- It does contain aspects not in WHO Report 37;
- If is divided in topics as the GMP PANDRH Guideline;

- It is necessary not to reinvent the wheals;
- Mexico has a compromise to legislate accepting Q7A;
- It has been analyzed at international level

The WG/GMP decided: To propose the adoption of the Q7A as a Guideline for API in the Americas. Rodolfo will send the Spanish version done by ANMAT and both (including the one prepared by Arlene) documents will be reviewed by the Secretariat. A final draft will be incorporate in the PANDRH web page for public opinions before the final version can be presented at the next Conference.

11. Code of Ethic

Arlene prepared a first draft and all members had the opportunity to comment on it before the meeting. Arlene reviewed several similar documents including those for internal audits, ISO, Federal Codes USA, ANVISA, EMEA, and Health Canada.

The WG reviewed the draft and based on the following consideration:

- Many aspects are common in all documents;
- Our objective is to establish a model of common requirements for agencies;
- It can be used either for the Agency as a whole or only for inspectors of GMP;
- It can be adopted or adapted by national agencies but the ideal is to have a Code of Ethics for the Region;
- It covers requirements of good conduct, behavior; communications with the industry; loyalty to the agency; anti-discrimination policy; development and conflict of interest;

The WG decided:

Arlene will prepare a new version in which she will incorporate the Canadian version as she will receive it from Louise. A final draft will be incorporate in the PANDRH web page for public opinions before the final version can be presented at the next Conference.

12. UPDATE Of the Plan of Action

See Separate document.

13. Closure

The Group Coordinator and the Secretariat thanked all participants.