RED PARF: Grupo de Trabajo en Bioequivalencia (GTBE)

MINUTAS DE LA 3ra REUNIÓN

Fecha: Febrero 14-15, 2003

Actividad asociada: Seminario Internacional sobre Medicamentos Genéricos, organizado por ANVISA/Brasil y OPS/OMS

Lugar: Brasilia, Brasil

Asistentes:
Miembros
- Justina Molzon FDA, Coordinadora
- Ricardo Bolaños, ANMAT/Argentina
- Salomon Stavchansky, Texas
- Irene Goncalves, INH Venezuela
- Ana María Concha, Chile
- Lidiette Fonseca (Costa Rica)
- Conrad Pereire (Canada)
- Silvia Storpitis (Brazil)
- Vivian Trespalacios (FIFARMA) por teleconferencia

Secretariado (OPS/OMS): L. Rago, R. D'Alessio, N. Marín
Recursos técnicos: Lizzie Sánchez (FDA)
Observadores:
- Pogány János
- Maz Weber Pereira
- Marcela Rodríguez

Objetivos:
- Discutir Plan de Trabajo a cumplir hasta la próxima Conferencia Panamericana
- Definir responsabilidades y determinar metodología de trabajo
- Definir la misión y objetivo
- Avanzar en la discusión de tópicos de interés en BE

Minutas de la reunión (sólo en inglés)

Day 1 (February 14-15, 2003)

1. Welcome and introductions
   - Dr. Gonzalo Vecina Neto
   - Rosario D'Alessio
   - Justina Molzon

2. Reviewed past meetings and activities (Justina Molzon)

3. Topics discussed:

3.1 To define the working groups mission and prioritized objectives to be presented for approval of the next Conference

To make sure objectives were completed, they were compared to 3rd Conference recommendations to BE/WG

Mission:

The working group should contribute to harmonized bioequivalence criteria for the interchangeability of pharmaceutical products in the Americas.

Prioritized objectives:

- Develop science based criteria for products requiring in vitro and/or in vivo BE studies and those not requiring BE studies.
- Develop prioritized lists (core nucleus and recommended) of those pharmaceutical products where in vivo BE studies are necessary.
- Develop a list of pharmaceutical products where in vivo BE studies are not necessary.
- Develop a list of comparator drug products for use in the Americas region.
- Develop recommendations and guidelines for the interpretation, evaluation and application of science based bioequivalence principles.
- Promote and assist in the education and training in countries of the Americas to implement bioequivalence principles.
- Promote bioequivalence of pharmaceutical products in the countries of the Americas.
- Adjust training programs to share regulatory experience in implementing BE within the framework of the PANDRH.
- Develop indicators to evaluate implementation of BE in the Americas.

3.2 Discussed the expected results of the group and prioritized and defined the plan of work until the next Pan American Conference. The responsibilities for carrying out the plan of work were distributed amongst the members of the working group.

Immediate Activities:

1. **Develop science based criteria for products requiring in vitro and/or in vivo BE studies and those not requiring BE studies.** [Criteria to be used as the basis for discussion of nomenclature (generic drug, multisource, similar) at next meeting of the working group.]

    a. Members: Salomon Stavchansky (lead), FDA, Silvia Storpirtis, Conrad Pereira, FIFARMA

b. Activities:
    1. Consult regulatory agencies to see what is in place
    2. Working group members from regulatory agencies to provide SOL with relevant information electronically (Grad student special project).
    3. Focus on major markets
    4. WHO recommendations in Multisource document.
    5. Data base: BCS, metabolism and literature
    6. Post approval changes
    7. Develop indicators to assess how criteria are being implemented
    8. PAHO to collect various definitions in laws, regulations or guidances in the Region

c. Timeframe:
    1. Group to develop Gant chart
    2. Send to Justina as Coordinator and Rosario as Secretariat
    3. Plan is to develop criteria by the end of April 2003, ideally in time to report at next meeting of the PANDRH Steering Committee

2. **Develop prioritized lists (core nucleus and recommended) of those pharmaceutical products where in vivo BE studies are necessary.**

a. Members: Ricardo Bolanos (lead)
Anna Maria Concha
Irene Goncalves
Lidiette Fonseca

b. Activities:
    1. Clinical concerns
    2. BE Seminar Caracas 1999
    3. DRA to provide information [regulation vs. concern] (Brazil, Venezuela, Argentina, Mexico, Chile, Costa Rica)
    4. WHO recommendations in Multisource document
    5. Start work with preliminary list (top 20) based on the second meeting of the working group and the 3rd Conference and then criteria developed by group 1 to finalize list.
    6. Provide feedback to group 1 on practicality, relevance and completeness of criteria.
    7. Use agreed upon criteria to recommend modification of the list.
    8. Establish mechanisms for maintenance of the list.
    9. Indicate mechanism to disseminate the list to the countries of the Americas
    10. Develop indicators to assess implementation in countries

c. Timeframe:
    1. Gather additional information until April 2003, when group 1 will have developed criteria
    2. Finalize list by end of June 2003
    3. Items 8-10 are to be completed one month before the next meeting of the working group.

3. **Develop a list of pharmaceutical products where in vivo BE studies are not necessary**.

a. Member: FDA (Justina Molzon and Lizzie Sanchez)

b. Activities:
   1. Focus on general concepts for list
      a. Regulations
      b. Guidances
      c. RX to OTC switch
      d. Orange book
      e DESI drugs
   2. Intent of list is to help countries focus on priority drugs for BE studies by eliminating those where BE studies are not considered necessary.
   3. Provide general concepts for waiver of BE studies
   4. Consider "grandfather" clause for products that have been on the market for extended periods and have no safety concerns and important to developing countries, such as antimalarials.

c. Timeframe:
   1. General concepts to group 1 by end of March 2003
   2. General concepts for waiver of BE studies
   3. Illustrative list by end of April 2003

4. Develop a list of comparator drug products for use in the Americas region

a. Members: PAHO/WHO, FIFARMA

b. Activities:
   1. Find Comparator drug letter in WHO "files" and/or contact Dr. Heikela and Sabine for background information
   2. FIFARMA to contact PhRMA and IFPMA for background information on comparator
   3. Compare and contrast process for adaptation to Americas region
   4. Use WHO comparator pharmaceutical product decision tree in establishing criteria and apply to high priority products in objective number 2 (Attachment 1).
   5. Use preliminary list from objective number 1 to start work. Consider inclusion of antiretrovirals.
   6. Draft letter to send to innovator companies
   7. BE WG to review draft letter
   8. Submit draft letter to PANDRH Steering Committee for consideration

c. Timeframe:
   1. Draft letter by end of April 2003 considering "top 20" from the 3rd Conference
   2. List by end of June 2003
   3. Because the letter was not supported by the 3rd Conference, the sensitivity of letter to be discussed with the Steering Committee by end of July 2003

3.3 Discussed current training activities and recommendations from 3rd Conference:

1. <u>Update and discussion</u>:

- FDA has offered Modules 1 and 2 in Caracas and Costa Rica and is revising modules based on feedback from attendees. FDA proposed that modules 3 and 4 be taught in English to allow the participation of FDA experts in the specified areas. The working group agreed with the proposal and PAHO will help translate the materials as it has become burdensome on FDA staff. It is anticipated that module 3 will be completed by this fall.

- After the modules are developed the involvement of representatives from the generic and innovator industry, AAPS and FIP will be considered, especially for emerging issues in bioequivalence. It was noted that the intent of the training is to focus on regulatory aspects of bioequivalence with relevant case studies.

- The participants in modules 3 and 4 need to be carefully selected to ensure the proper technical background. Those selected will be responsible for dissemination of the training at the national level.

2. Responses to recommendations from 3rd Conference

a. Implementation of a new diagnostic study with quantitative data and changes from the previous study implemented in 2000 identified.

    - FDA will turn over materials to PAHO for updating and evaluation. Working group members are encouraged to send Rosario their thoughts on additional or revised questions.

b. Training material (Module 1, 2 & 3) finalized by the FDA

    - It is anticipated that the material will be finalized by the fall of 2003

c. Training Seminars (Module 1, 2) in MERCOSUR, Mexico and CARICOM implemented with participation of at least 80 professionals

    - Argentina - Possibilities to offer the course will be discussed with ANMAT
    - Mexico - FDA will discuss possibilities and report back to PAHO and the group for necessary arrangements.
    - CARICOM - A timeframe for offering the course in English will be considered and the logistics need to be worked out.

d. Advance Training Seminar (Module 3) in at least one Sub-region implemented with participation of at least 35 professionals

    - PAHO will solicit volunteers from country/university to host and help with logistics.

e. Nationals seminars in BE/BD implemented in at least three countries with at least 90 professionals

- PAHO to solicit volunteers from attendees of the training courses.

3.4 Discussed advancing technical issues on BE that are under consideration

1. The suggestion to add antiretrovirals to the comparator drug list generated discussion on the importance of bioequivalence principles being applied to this therapeutic category.