Pan American Network
for Drug Regulatory Harmonization

Steering Committee Meeting

Mexico City

May 7-8, 2003

Bioequivalence Working Group

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Pan American Network for Drug Regulatory Harmonization Work Plan 2000 - 2001

- Priorities Approved by the Steering Committee
  - **First:Urgent Issues**
    - GMP
    - **Bioequivalence**
    - GCP
    - Counterfeit
  - **Second:Important Issues**
    - Classification
    - Drug Regulatory Agency
  - **Third: Recommended Issues**
    - Pharmacopoeia

BIOEQUIVALENCE WORKING GROUP WORKPLAN 2000-2001

- Assessment of BE in countries
- Selection of team members
- Consolidation of questionnaire
- Selection of materials
- AAPS Workshop on BA/BE
- Regional seminar
- Evaluation (Pharmacy Congress)
- Pending Possibility:
  - National Seminars
  - Regional Seminars
- Working Group meeting

BIOEQUIVALENCE WORKING GROUP TEAM MEMBERS COORDINATOR: FDA/USA

- **Contact Person:** Justina Molzon (FDA)
- **Topic Lead:** Lizzie Sanchez (FDA)
- **ALIFAR:** Silvia Giarcovich
- **Argentina:** Ricardo Bolaños
- **Brazil:** Silvia Storpitis
- **Canada:** Conrad Pereira
- **Chlie:** Ana Maria Concha
- **Costa Rica:** Lidiette Fonseca
- **FIFARMA**:Amparo de la Peña/ Vivian de Tres Palacios
- **Jamaica:** Eugenie Brown
- **Venezuela:** Mara de Levy/Irene Goncalves
- **USP:** Roger Williams
- **University of Texas:** Salomon Stavchansky

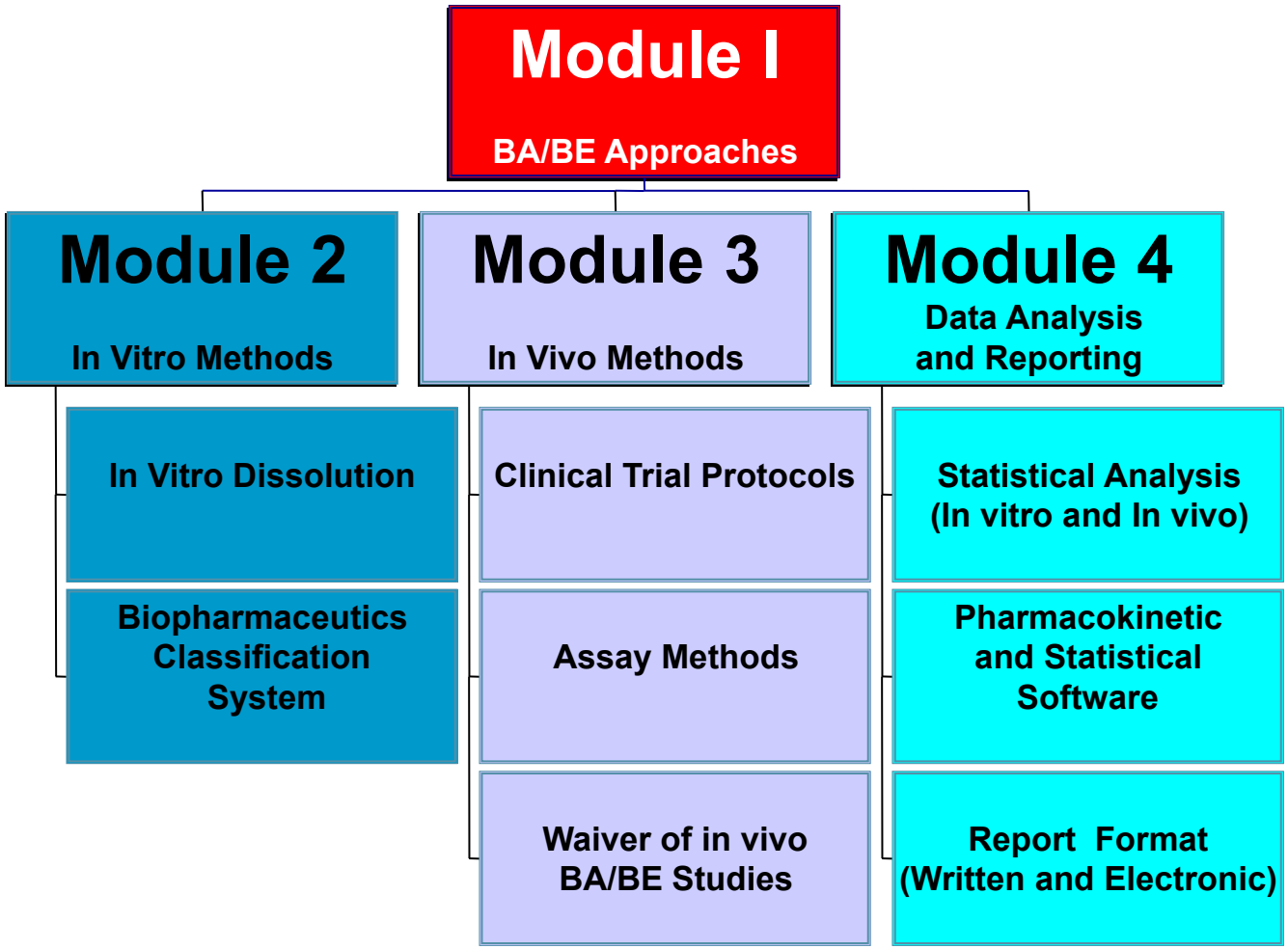
BIOEQUIVALENCE WORKING GROUP
ASSESSMENT OF BA/BE TRAINING NEEDS
Washington, DC
September 14, 2000

- Meeting to assess the BA/BE training needs in the Americas
- In preparation for the meeting, a survey on BA/BE status and needs assessment was distributed to all countries in the Americas
- Survey responses facilitated discussion on BA/BE training topics
- 37 participants from 13 countries
- Regulators, Academia, Industry and USP

BIOEQUIVALENCE WORKING GROUP
1st Meeting of the Working Group
Washington, DC
September 14, 2000

- Focused on selection of training topics
- Based on input and comments from attendees at “Assessment” meeting
- Concluded that a modular training program should be developed
- Determined resource materials to support the modules of the training program
- Materials selected for translation into Spanish

BA/BE TRAINING MODULES



Pan American Network for Drug Regulatory Harmonization 2nd Steering Committee Meeting Orlando, Florida

March 23-24, 2001

BIOEQUIVALENCE WORKING GROUP
Regional Seminars

- Based on Steering Committee discussions
- Two courses based on Module 1 and 2
- First course September 2001, Costa Rica (Postponed until February 2002)
- Second course December 2001, Venezuela
- Next courses Mexico and Argentina
- Logistics being worked out

Bioequivalence Working Group
Second Meeting
Caracas, Venezuela
3-4 December 2002

- Analysis of current issues
- Examine existing regulations
- Identify differences or gaps
- Set up action plans
- Collaboration between countries
- Develop harmonized instruments

Bioequivalence Working Group
Second Meeting
Caracas, Venezuela
3-4 December 2002

Topics for Discussion

- Criteria for prioritizing BE studies in countries where they are currently not being done
- Criteria for selecting BE drug comparator
- Indicators to be used by the WG/BE to follow up the implementation of BE in the Americas

Proposal 1
Criteria for Prioritizing Bioequivalence Studies

The working group endorsed recommendations from the *Consultation of Experts on Bioequivalence of Pharmaceutical Products* (Caracas, 13-15 January 1999)

1. *Bioequivalent generic drugs should meet efficacy, safety and quality standards.*
2. *Should establish criteria, standards or guidelines for the selection of in vivo or in vitro methodologies for determining BE.*
3. *Generic drugs should be based on evaluation of the bioequivalence of these products vis-à-vis the reference products in the country.*
4. *In vivo bioequivalence studies of products already on the market that pose a high health risk should be conducted within the strict time limits established by the health authority.*

Proposal 1
Criteria for Prioritizing Bioequivalence Studies

- The working group recognized the efforts of WHO in this area and endorsed WHO documents on the topic
  - Multisource (generic pharmaceutical products: guidelines on registration requirements to establish interchangeability- WHO Technical Report Series, No. 863, 1996 (pp 122-124)

- The working group recommends that the Conference adopt this proposal for the countries of the Americas to adapt these concepts to meet local needs and resources

Proposal 2
Criteria for Selecting a Bioequivalence Drug Comparator

- The working group recognized the ultimate goal of connecting all products in the Americas to the respective “original” innovators product on which safety and efficacy approval was based.
- The working group proposed a process to implement this goal
  - Harmonize the definition of “generic and multisource”
  - Demonstrate that the innovator’s products in Latin America have the same performance characteristics as those of the original innovators product
  - National regulators would select a comparator product at the national level, which could be the same in all countries in the sub-regions and/or the American Region.

Proposal 2
Criteria for Selecting a Bioequivalence Drug Comparator

- The working group recommends that the Conference request all international companies of innovator products included in the LIST provide documentation to the respective DRAs to support that the innovator's products in Latin America have the same performance characteristics as those of the "original" innovator's products

Proposal 3
Indicators to be used by the Working Group to track implementation of the BE studies in the Americas

- The working group recognized the importance of the development of indicators to assess the outcome of all the time, effort and funds expended by PANDRH on the topic of bioequivalence.
- The working group proposed that the 2000 survey be used as a diagnostic tool and serve as a baseline
- The working group will update the survey and request countries not included in the initial survey to submit information.
- The Conference is requested to comment on this proposal

Pan American Network for Drug Regulatory Harmonization

Bioequivalence Working Group Third Meeting

Brasilia, Brazil

February 14-15, 2003

3rd Meeting of the BE WG
Topics for Discussion

- Discuss the plan of work until the next Pan American Conference and prioritize the activities
- Define and distribute responsibilities and determine how to work
- Define Mission and Objectives
- Advance technical issues on BE that are under discussion

3rd Meeting of the BE WG Recommendations--PANDRH III

1. Criteria for prioritizing categories of drugs for BE testing and testing methodology analyzed and a proposal formulated
2. Defined criteria for prioritize BE studies for low risk drugs
3. Definitions of Generic drug and multisource drug in countries of the Americas identified and a harmonization proposal formulated
4. Indicators for BE implementation identified
5. Implementation of a new diagnostic study with quantitative data and changes from the previous study implemented in 2000 identified

3rd Meeting of the BE WG Recommendations--PANDRH III

6. Training material (Module 1, 2 & 3) finalized by the FDA
7. Training Seminars (Module 1, 2) in MERCOSUR, Mexico and Caricom implemented with participation of at least 80 professionals
8. Advance Training Seminar (Module 3) in at least one Subregion implemented with participation of at least 35 professionals
9. Nationals seminars in BE/BA implemented in at least three countries with at least 90 professionals
10. Report of the WG

Bioequivalence Working Group Third Meeting

- **Defined the working groups mission and prioritized objectives**
  - To make sure objectives were complete, the were compared to 3rd Conference recommendations to BE/WG
- **Defined the working groups Mission**
  - The working group should contribute to harmonized bioequivalence criteria for the interchangeability of pharmaceutical products in the Americas.

Third Meeting Bioequivalence Working Group

Prioritized Objectives

1. Develop science based criteria for products requiring in vitro and/or in vivo BE studies and those not requiring BE studies.
2. Develop prioritized lists (core nucleus and recommended) of those pharmaceutical products where in vivo BE studies are necessary.
3. Develop a list of pharmaceutical products where in vivo BE studies are not necessary.
4. Develop a list of comparator drug products for use in the Americas region.

- *PRIORITIZED AS IMMEDIATE ACTIVITIES*

Third Meeting Bioequivalence Working Meeting

Prioritized Objectives

5. Develop recommendations and guidelines for the interpretation, evaluation and application of science based bioequivalence principles.
6. Promote and assist in the education and training in countries of the Americas to implement bioequivalence principles.
7. Promote bioequivalence of pharmaceutical products in the countries of the Americas.
8. Adjust training programs to share regulatory experience in implementing BE within the framework of the PANDRH.
9. Develop indicators to evaluate implementation of BE in the Americas.

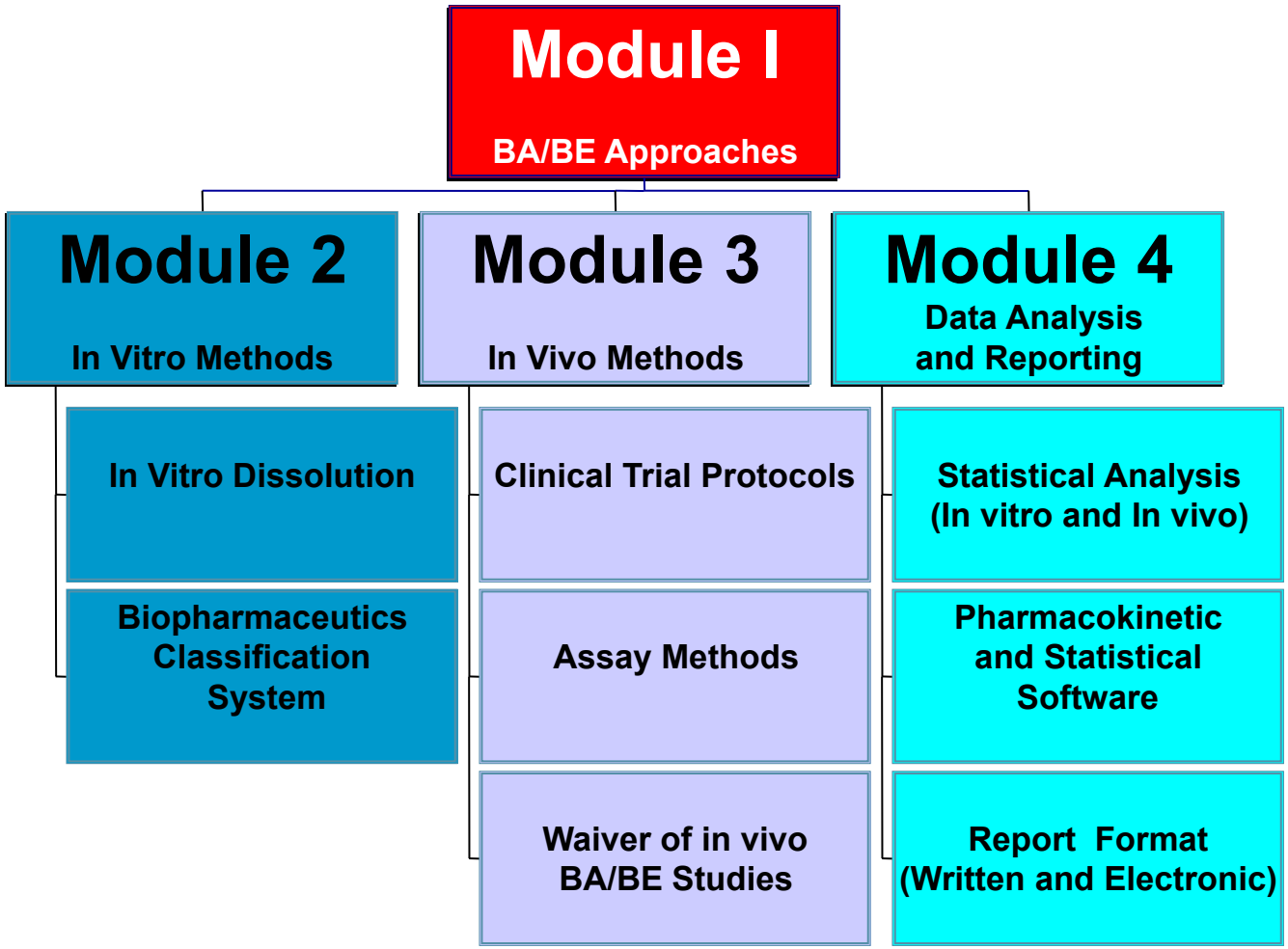
Third Meeting Bioequivalence Working Group

Prioritized Objectives

IMMEDIATE ACTIVITIES

- **Created Subgroups for Priorities 1-4**
  - Lead
  - Members
  - Defined Activities
  - Time frame
- Minutes Provided

UPDATE ON TRAINING



Third Meeting Bioequivalence Working Group
UPDATE OF TRAINING ACTIVITIES

- 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.

Third Meeting Bioequivalence Working Group
UPDATE OF TRAINING ACTIVITIES

- 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.
- 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.

Third Meeting Bioequivalence WG

Responses to recommendations

re: Training from 3rd conference

- 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.
- Training material (Mod 1, 2 & 3) finalized by the FDA
  - It is anticipated that the material will be finalized by the fall of 2003

Third Meeting Bioequivalence WG
Responses to recommendations re: Training from 3rd conference

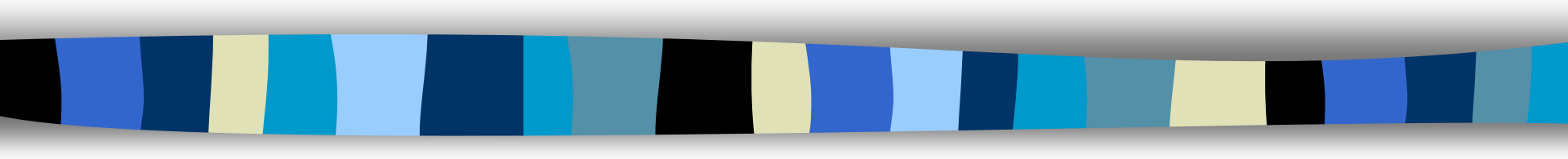
Training Seminars (Module 1, 2) in MERCOSUR, Mexico and Caricom implemented with participation of at least 80 professionals

- 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.

Third Meeting Bioequivalence WG
Responses to recommendations re: Training from 3rd conference

- Advance Training Seminar (Module 3) in at least one Subregion implemented with participation of at least 35 professionals
  - PAHO will solicit volunteers from country/university to host and help with logistics.
- 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.

Muchas gracias
Muito obrigada
Merci



Thank you