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Global Harmonization: Latin America Overview and Perspective

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EBF - European Bioanalysis Forum - 3rd Open Symposium
Date: 1 - 3 December 2010

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Introducing ACBio-Br

- Founded in 2006
  - Legally since February, 2007
- Website
  - www.acbio.org.br
- Nowadays ACBio has 12 members
- Board:
  - Dr. Eduardo Abib (Scentryphar) – President
  - Dr. Rafael Barrientos (Magabi) – Vice President
  - BSc. Fabiana Fernandes (ICF) – Secretary
  - BSc. Eunice Suenaga (NuBEC) – Treasurer
- ACBio is the former member of the Latin America Bioavailability and Bioequivlence Network (RLABB)
  - HT for LATAM called as GBC LATAM

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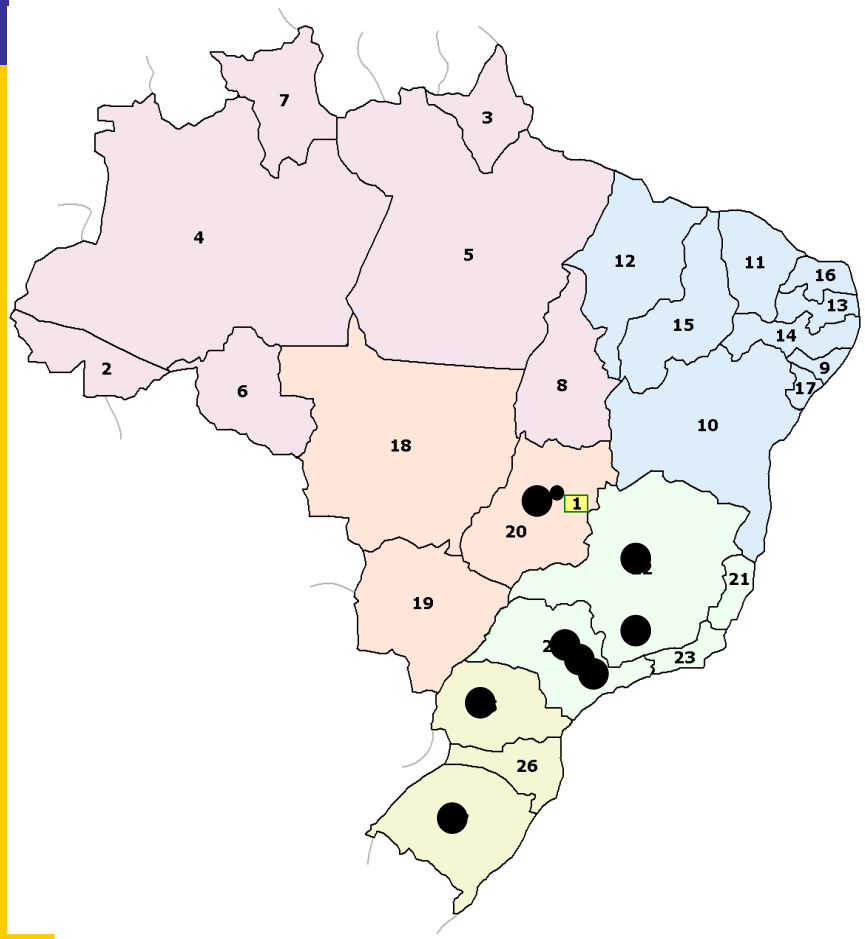
Introducing ACBio-Br



- Members (12)
  - BIOAGRI (Piracicaba/SP)
  - BIOCINESE (Toledo/PR)
  - CAEP (Campinas/SP)
  - CEBIFAR (Santa Maria/RS)
  - CEBIO (Belo Horizonte/MG)
  - CORE (Bragança/SP)
  - ICF (Goiânia/GO)
  - Instituto Claudia Marques (Pouso Alegre/MG)
  - MAGABI (São Paulo/SP)
  - NUBEC (São Paulo/SP)
  - SCENTRYPHAR (Campinas/SP)
  - T&E Analítica (Campinas/SP)
  - UNIFAG (Bragança/SP)

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Introducing ACBio-Br

- Technical forum for the discussion of the analytical part of the BE studies (bioanalysis)
  - Participants:
    - all members of ACBio and other invited CROs
- Philosophy of the discussions
  - Driven by scientific basis
  - Technical rational behind each point to be discussed
  - Universality of the decisions
    - each member should be able to follow the harmonized rule

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Introducing ACBio-Br

- Main achievements
  - Technical discussions using workshops in order to have information exchange
    - I Workshop (Feb. 2nd, 2008)
    - II Workshop (July 22th, 2008)
    - III Workshop (June 8th, 2010) – more than 150 attendees
    - IV Workshop (Nov. 16th, 2010) – capped to 150 attendees
  - Specific discussions together with Coordination of Bioequivalence - ANVISA in order to clarify some points of the Brazilian guidelines
  - Questions are being treated in block rather than individually by each BA lab
  - To harmonize the understanding of the bioanalytical guidelines among the members of ACBio
  - To become member of the SC of GBC

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Brief overview on the present situation of bioanalysis (BA) in LATAM countries

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Where are we?

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Overview in LATAM

- Countries with implemented BA guidelines
  - México
  - Chile
  - Uruguay
  - Brazil
  - Argentina
- Countries with *under discussion* how to implement guidelines
  - Peru
  - Colombia
- Countries with no guidelines
  - Ecuador
  - Bolivia
  - Paraguay
  - Venezuela
  - Costa Rica
  - Most of the countries in Central America and Caribbean

BA Guidelines in LATAM

- The implemented BA guidelines are more related to BE studies
  - Most of them are based on ICH, FDA and/or EMEA ones
- PAHO (PanAmerican Health Organization) support projects for harmonization of requirements in LATAM countries
- The guidelines highlight the requirements for following the GLP
  - QA unit
  - Documentation (traceability)
  - Report

BA Guidelines in LATAM

- In a general perspective, the requirements for Bioanalytical Method Validation in Latin America are aligned to the FDA and EMEA guidelines
  - Selectivity/specificity
  - Linearity
  - Accuracy and precision
  - Recovery
  - Stability in biological matrix
    - Freeze-and-thaw
    - Short-term
    - Long-term
    - Post-processing (autosampler)
  - Stock solution stability
  - Use of a validated bioanalytical into the routine
    - Run acceptance criteria
    - Use of QCs samples

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Brazil

- Regulatory agency:
  - ANVISA (National Health Surveillance Agency)
    - Coordination of Bioequivalence (COBIO)
- Bioanalytical laboratories are certified by COBIO/ANVISA (called Bioequivalence Centres)
  - Annually inspected
  - BA/BE Studies conducted into a not certified CROs are not accepted by ANVISA
  - The list of BE centers are into the web site www.anvisa.gov.br
- Guidelines regarding bioanalysis
  - RE899/03 – Guideline for Analytical and Bioanalytical Method Validation
  - Official Documents: Clarifications on RE899
  - RE 1170/06 – Guideline for BE Studies (include bioanalysis)
  - RE 895/03 – Guideline for reporting data
  - RDC 103/03 – Inspection check-list and certification for Good BE Practices

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Brazil

- Focus of the Guidance are related to BD/BE Studies
  - PK studies, TDM or LBA are incipient yet
  - LBA are expected to be included into the next revision of the guideline on BMV
  - The 1st guideline has been published in 1999
- The bioanalytical guideline have been reviewed 3 times
  - The actual guideline (RE899) is under revision since the Q3 of this year and a draft is expected to be published by the Q1/Q2 of 2011
- 30 Bioequivalence Centers certified by ANVISA
- +400 BE studies conducted in Brazil last year (2009)
  - ACBio members are responsible for 70-75% of the total amount of BD/BE studies
- All the BE centers which conduct BA are equipped with LC-MS/MS systems

México

- Regulatory agency:
  - COFEPRIS (Federal Commission for the Protection against Sanitary Risk)
- Bioanalytical labs (called *Terceros Autorizados*) are inspected every 2 years by COFEPRIS
  - The list is available at the website www.cofepris.gob.mex
- Guidelines regarding BA
  - NOM-177-SSA1-1998
  - It is not up to date and no harmonized to FDA/EMEA guidances
  - It is under revision but it is not expected to cover the specificity of the LC-MS/MS technique

México

- There are not BA forums or either a representative organization in this country
- Guidelines are also focused on BE studies
  - 100% of the BE study should be conducted in México
    - It is likely a “restraint of trade”
- LC-MS/MS technique is still growing
  - 3-4 BA labs are equipped with LC-MS/MS systems

Argentina

- Regulatory agency:
  - ANMAT (National Administration of Food, Medicines and Medicinal Technology)
  - www.anmat.gov.ar
- There is no a certification program for BA labs
  - ANMAT use to make inspection
  - BA labs are mostly focused on academic issues
  - There is not a list of BA labs available
- Guidelines
  - ANMAT Resolution 6677/10 – BPC for Clinical Assays including BE studies
  - Resolution 4844/10 – Guidaline for the analytical part of Bioavailability and Bioequivalence studies
- Fews labs using LC-MS/MS systems
  - 3-4 at all

Chile and Uruguay

- Chile
  - Regulatory agency:
    - ISP (Public Health Institute)
    - Resol. 727/05
    - Technical guide G-BIOF 01/2007
  - Guideline harmonized with FDA
  - ISP certifies BA labs
    - Just 1 lab certified
      - IFT – Medicine Shcool – University of Chile
- Uruguay
  - Regulatory agency
    - M.S.P. (Ministry of Public Health). www.msp.gob.uy
    - Decree Nº 12/007
      - Regulates the quality and control of medicines for health care. “Interchangeability of Products”
      - MSP perform inspections and certifies BA labs
    - There is only one BA lab certified
      - Private area

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Perspectives on bioanalysis in LATAM countries

Perspective

- Regulatory agencies are in general open for harmonization
  - ANVISA is becoming an important “player” and might lead this process influencing other regional agencies (ANMAT, ISP, etc.)
- Definitely Brazil is in a step forward when compared to the rest of LATAM countries in terms of
  - number of assays conducted
  - technology already implemented
  - size of the market
- Issues that would be more thoroughly discussed
  - QA processes
  - How to report data (documentation)
- GBC and other harmonization initiatives can help LATAM countries to better set up their guidelines and to move forward in a more rational way

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- V Workshop on BE studies
  - June 5-8th, 2011
  - Novotel Center Norte - São Paulo/SP
- For more information, visit our web site: www.acbio.org.br