Hands-on in Latin America
Regulations for Clinical Trials

Director: Silvia Zieher
VP Clinical Development,
Latin America Operations
INC Research
The views and opinions expressed in the following PowerPoint slides are those of the individual presenter and should not be attributed to Drug Information Association, Inc. ("DIA"), its directors, officers, employees, volunteers, members, chapters, councils, Special Interest Area Communities or affiliates, or any organization with which the presenter is employed or affiliated.

These PowerPoint slides are the intellectual property of the individual presenter and are protected under the copyright laws of the United States of America and other countries. Used by permission. All rights reserved. Drug Information Association, DIA and DIA logo are registered trademarks or trademarks of Drug Information Association Inc. All other trademarks are the property of their respective owners.
• Learn on:
  – The trends and major challenges in the regulatory environment and current regulations
  – How to obtain regulatory approvals in each of the major LA countries
  – Prepare the regulatory submission package for Ethics Committees and Regulatory Authorities
Introduction: Tutorial Objectives

• Learn on:
  – How to optimize the regulatory process through a defined regulatory strategy implemented
  – The importation process in each selected country
  – Informed consent requirements
  – Recent relevant updates
• Country Regulatory Experts for countries selected: CROs + Pharmaceutical Companies
  – BRAZIL:
    • Felipe Simoes, COVANCE & ABRACRO Head of Regulatory Committee
  – ARGENTINA
    • Carolina Dias Rato, Associate Director Start-up and Regulatory, INC Research
  – MEXICO
    • Jenny Paredes, Operations Manager PRA & ACROM Board of Director
Speakers

– COLOMBIA
  • %22Vivian Yohanna Gomez, Regional Clinical Monitoring Manager, Sanofi-Pasteur Colombia

– CHILE
  • %22Mafalda Gimenez, Manager Regulatory and Start-Up, Integrated Site Services, Quintiles Chile

– PERU
  • %22Stela Lopez, S&C Consultoría Empresarial and Gerente de Investigación Clínica, BMS
• Country Regulatory Experts for countries selected: CROs + Pharmaceutical Companies

  – Informed Consent Process: Ethical and Regulatory requirements
    • Rodrigo Xavier, Country Start-up Specialist, PRA
• A practical approach to the regulatory process in Latin America
• Interactive sessions: Q&A sessions at the end of sections
• Please give us your feedback: to ensure improvements for future courses.
An important force that is moving clinical trials to developing countries is the increasingly bureaucratic and expensive regulatory environment in many wealthy countries. Regulations governing the conduct of clinical research have become more and more complex, placing a greater burden on investigators in terms of compliance, documentation, and training.


Are Latin America regulations less complex?
The regulatory environment is becoming increasingly complex at global level:

“During the past decade, however, increasingly onerous regulation and related bureaucracy have made trials much more difficult and costly to conduct, slowing further improvements. This adverse regulatory environment hinders important research and urgently needs to be changed for the benefit of patients and public health”.

“The approval process is complex, costly, heterogeneous and time consuming”

Randomized Clinical Trials – Removing Unnecessary Obstacles, Christina Reich et al, N Engl J Med 369; 11, September 12, 2013
1) EU Jul 2012 Proposal to replace the Clinical Trials Directive (not approved yet):
   - Single portal for authorizing trials
   - More flexibility for consent in emergency situations
   - Decrease indemnity costs
   - Shorter approval timelines for “Low interventions”

2) EU 2012 - other

   Commission Guideline — Guidance on posting and publication of result-related information on clinical trials in relation to the implementation of Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006 (2012/C 302/03)
Overview of the Global Regulatory Environment - FDA recent Guidances

FDA 2012

- **Dec 2012**: Enrichment Strategies for Clinical Trials to Support Approval of Human Drug and Biological Products
- **Dec 2012**: Safety Reporting Requirements for INDs and BA/BE Studies

FDA 2013

- **Aug 2013**: IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed
- **Aug 2013**: Oversight of Clinical Investigations - A Risk-Based Approach to Monitoring
- **Sep 2013**: Electronic Source Data in Clinical Investigations
• Better readability by reorganising and restructuring the document with sub headings
• More protection for vulnerable groups
• More protection for participants by including the issue of compensation for the first time
• More precise and specific requirements for post-study arrangements
• A more systematic approach to the use of placebos, but no weakening of the ethics of placebo use

A public consultation was completed between April and June 2013.
There are **well established regulations** in main countries with good ICH E6 (GCP) alignment.

Some regulations are **stricter** than some regulations in central countries.

Each country with **separate regulations**

There is an **evolving regulatory environment** with new regulations and updates
Certain levels of unpredictability for timelines and protocol approvals driven by:

- Lack of a well standarized review process by Ethics Committees (EC) and Regulatory Agencies (RA)

- Ongoing regulatory changes in main countries with increasing complexity

- Lack of long term stability of RA (i.e driven by political changes)
What Are The Main Trends in Regulations?

- Continued changes to regulations (Colombia, Peru, Mexico, Brazil, Chile)

- Increasing review and changes requested for the informed consent forms.

- Increasing review of site contracts by Institutions (i.e. legal departments) leading to longer timelines for execution.

- IP supply at the end of the study with more regulations (Brazil, Argentina, Peru)

- Mental health care changes impacting clinical trials in Chile and Argentina
Increasing number of regulatory inspections (and new countries as Mexico began inspections)

Registration of clinical trials, clinical research sites, CROs

Increased oversight of ECs:
- Inspections by ECs

More control on the supplies importations and more requirements for impo/expo, with challenges in Peru, Colombia

Insurance requirements by RA or ECs increasing

Trend to more clinical trials rejected by RA (i.e. Peru).
Local regulatory knowledge is a key successful factor

Early start of the regulatory planning
- Latin America not recommended for rescuing studies
- Contingency plans

Define an effective regulatory strategy
- Use the past experience (i.e. select “target sites” with predictable approval timelines)
- Take into consideration risk areas as upcoming or ongoing regulatory changes

Prevent sponsor/ CRO delays in compiling regulatory packages and respond to EC/RA questions
What are the main areas to focus work?

- Review protocol designs/ use of placebo
- Delegation of responsibilities/ LOAs
- ICF requirements per country
- EC/IRBs compliance
- Label requirements
- Site contract requirements
- Insurance requirements
- Coverage of costs (and contraceptives)
- Additional approvals needs
- Comparators
- Supplies importation requirements
- Regulatory intelligence