Hands-on the Regulations in Colombia

Main regulations & features

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• **Regulatory Framework:** 1990/2000
  – 1990/2000… up to date

• **Resolution 2378, Turning Point:**
  – Sites changes
  – Protocol evaluation
  – Safety Reports

• **Local Special Requirements**
  – Inform Consent Process
  – IP Labelling
  – Deviation Reports
  – Contracts
  – Placebo
  – Extension treatment
  – INVIMA FU visits
  – Ethics Committee
Agenda

- Other Requirements
- What we have to date
- Regulatory timelines and Pathway
- Conclusions
  - Advantages
  - Opportunities
- Resources
Regulatory Framework Clinical Research 1990- up to date
Regulatory Framework 1990

- **Laws**
  - Congress
  - Promotion of research in the Country
  - Creation of Social Security system / IPS*

- **Decrees**
  - Presidential
  - INVIMA** Functions

- **Resolutions**
  - Min. of Health
  - 13437 Hospitalary EC, Patients Rights, ICF
  - 8430 Requirements Clinical Research

- **Agreements**
  - INVIMA
  - # 8 Creation of Commissions and SEMPB***

- **1990**
  - Laws
  - Decrees
  - Resolutions
  - Agreements

- **1991**
  - Laws
  - Decrees
  - Resolutions
  - Agreements

- **1993**
  - Laws
  - Decrees
  - Resolutions
  - Agreements

- **1994**
  - Laws
  - Decrees
  - Resolutions
  - Agreements

- **1995**
  - Laws
  - Decrees
  - Resolutions
  - Agreements

- **1997**
  - Laws
  - Decrees
  - Resolutions
  - Agreements

- **1999**
  - Laws
  - Decrees
  - Resolutions
  - Agreements

* IPS: Service Health Institution
**INVIMA: National Institute for Drugs and Food Vigilance
***SEMPB: Specialized Board of Drugs and Biological Products
Regulatory Framework 2000

Decrees
Presidential

Resolutions
Min. of Health

2200
Pharmaceutical Services / IPS*

9455
SAEs report of registered medications

1043
IPS* requirements (Basic standards) to get the Certification of Local Secretary of Health for work

1403
Pharmaceutical Services procedures admon and technical criteria

2378
Functions/Responsabilities of actors (Sponsor, site EC and labs) in Clinical Research GCP Certifications/IPS*

Turning Point

* IPS: Service Health Institution
Regulatory Framework 2011…..Up to date

Resolutions
Min. of Health

Guidelines and Forms
INVIMA

Circular
INVIMA

Presentation of:

- New protocol
- Sites/IPS
- Investigators
- Blood sample exportation
- Supplies importation
- Amendments of protocol and ICF
- Trial Close out

2011020764
SAEs and AEs report of investigational products

SEMP 600-156-12B
Investigational products re-labeling and due date extension

Evaluation of EC specialized in clinical research

Protocol evaluation and FU by INVIMA

Supplies and investigational products

Update of the guidelines issued in 2011

* IPS: Service Health Institution

www.diahome.org
Resolution 2378, Turning Point

- Sites: IPS and certified services
- Site staff: Health care professionals (nurses, doctors, pharmaceutical chemist and bacteriologist)
- Protocol submission/evaluation: INVIMA forms (F) and guidelines (PM)
- GCP certification/inspections (Sites, EC and Labs)
- EC: responsibilities, administrative and operative organization for clinical research
- Laboratories: requirements for clinical research
- Safety information reports for clinical research
- Investigational product management and labelling
SITES / LABS/ Ethics Committe: Sponsors/CRO support

1) 6 months of timeline to present the gradual plan to get the certification in GCP (2008)
2) 2 Years for the implementation of the gradual plan
3) Sites become an IPS (facilities, procedures, staff changes) and get the IPS certification
4) INVIMA visits to provide certifications for 5 year (2010… up to date).

Investment: Investigators association, find locations, new facilities (Pharmacy, depot, administrative office, archiving), staff training, new personnel within the site staff (Bacteriologist, pharmaceutical chemist, nurses, pharmacist)

Before 2008

Implementation Res. 2378

Today
Protocol evaluation

*SEMPB*: (Specialized Board of Drugs and Biological Products)
Pharmacological aspects
Concept provided in an act

- Protocol
- Investigator´s Brochure
- Supplies Importation
- Samples Exportation

GCP specialized group:
Administrative and operational aspects
Concept provided INVIMA web page

- Amendments
- ICF
- Site (IPS)
- Investigators/staff
- Other Documents: Diaries, questionaries

*SEMPB*: Specialized Board of Drugs and Biological Products

**Protocol evaluation**

- To submit according to SEMPB calendar (2 months before the meeting)
  - 2 photocopies of the dossier (200 pages per volume)
  - 1CD with all related forms and Documents
- Protocol, related documents, investigators and institution must be approved by EC
  - Payment of 2000USD
Protocol evaluation (SEMPB)

**Protocol**
- F84-PM01-RS
- PM01-RS-G36

- **Part I**: General information /Sponsor
- **Part II**: EC protocol, ICF and IB evaluation
- **List of documents**: Protocol, IB, ICF, recruitment material, diaries, PI CV and certifications including GCP, IRB approval letter, Insurance

**Supplies Importation**
- F81-PM01-RS
- PM01-RS-G42

- Quantities rational / per visit (20% extra)
- Certificate of free sale
- GMP
- Stability evaluation, Lots and CoA (A note can be sent if it is not available at that time)

**Blood Sample Exportation**
- F82-PM01-RS
- PM01-RS-G42

- Contact data of Central laboratory
- Type of sample
- Time and place where samples will be stored
- Exportation propose

**Investigators Brochure**
- F83-PM01-RS,
- PM01-RS-G43

- For new/updated versions
Protocol evaluation (GCP)

**Site / IPS**
- EC approval letter of the institution(s), laboratories and other services where the protocol is going to be conducted
- Site GCP Certification
- IPS Certification (Lab, site and other services)

**Investigators**
- EC approval letter of the PI specifying the time dedicated to the trials number of trials that is participating
- PI and SI: CV, medical license, ID, and professional certifications, GCP training
- PI: at least 3 years of clinical experience and 2 in clinical research

**ICF**
- For new/updated versions
Safety Reports

- **Res. 2010020508**: SAEs, AEs and SUSARs reporting. Annual safety report 2010

Local SAEs
- Initial, First FUP, Close report F38-PM02-IVC

International AEs
- Expected SAEs
  - Anually: Investigator’s Brochure

SUSARs
- PI: 20 days
- EC: 15 days
- INVIMA every 2 months
- F-181-PM02-IVC

Annual Safety Report
- F-180-P02-IVC
Local Special Requirements
Inform Consent Process

Res. 8430

Under 6 years
- Legal Representative signs the ICF
- Documents: copy of the participant´s civil register and representative´s ID
- Witness: 2 independent

6 – 17 years
- Legal Representative signs the ICF
- Psychological evaluation
- Inform Assessment Form
- Documents: copy of the participant´s civil register/ID and representative´s ID
- Witness: 2 independent

> 18 years
- Participant signs the ICF
- Documents: copy of participant´s ID
- Witness: 2 independent
Inform Consent Process
Res. 8430

Mentally disabled/Unconscious*

- Legal Representative  sign the ICF
- Documents: copy of participant ID and representative ID
- Witness: 2 independent
- *Once the participant is recovered they must sign a new ICF

Illiterate

- Participant puts her/his finger print as signature
- Documents: copy of participant’s ID
- Witness: 2 independent +1 who reads the ICF and signs

Subordinate

- In the EC meeting must participate one representative of the population
- Participant signs the ICF
- Documents: copy of participant’s ID
- Witness: 2 independent
Local Special Requirements : Labeling

**IP Labelling**

**PM01-RS-G45**

- Placebo and Comparative
- Spanish
- **Trial code**
- **Product name and concentration: placebo/xxxxx**
- **Pharmaceutical form, route of administration** and number of units (if applicable).
- **Lot number and due date**
- Storage conditions.
- Subject identification code when applicable participant and visit number.
- **Name**, address and telephone number of the **sponsor**.
- The legend "drug for use only in clinical trials."
- The words "Keep out of reach of children"

Minimum requirements if there is not space in the package (vials, Blisters). However in the second package all the information must be written.
Local Special Requirements: Deviations/Contract

**Deviations**
PM01-RS-G45

- Major and Critical reported via e-mail within 15 days after their knowledge

**Contracts**
PM01-RS-G46

- Budget reviewed by EC
- Institution/Investigator
- Evaluated by EC and additional agreements (Labs and other services)
**Local Special Requirements: FU visits/Placebo**

**INVIMA FU Visits**
PM01-RS-G45
- No announcement
- To ensure GCP certification maintenance
- To verify correct documentation of SAE’s
- To ensure document management/archiving
- To verify the ICF process
- IP management
- Final report to implement actions plan or not

**Placebo**
(EC)
- It is allowed since there is not a standard treatment available
- Justification letter is NOT Necessary if the protocol has it

**Extension Treatment**
(ICH-GCP)
- INVIMA mention that ICH must be followed and Investigators must sign as a compromise
- However there is not a specific local requirement but some EC request it
Local Special requirements : Ethics Committee

- No Central EC
- GCP certification by INVIMA
- EC has to approve any document before INVIMA submission
- Institution EC for clinical research
- Sites can use EC from other institutions or an independent IRB
**Other requirements**

- **Phase IV trials**
  - They need EC approval
  - IC if there is an intervention (minimal)
  - INVIMA protocol approval is not required
  - If blood samples are going to be sent out of the country, the exportation requires the approval of INVIMA

- **Amendments**
  - Must be approved by IRB to be implemented
  - INVIMA just requires the notification

- **Insurance**
  - It could be global or local policy, it is not specified in the regulation
  - Contractual and extra contractual policy for associated adverse events attributable to the IP or trial procedure
  - It has to be valid until the trial is closed in Colombia
Other requirements

- **Trial FSFV**
  - Protocol approved EC and INVIMA
  - First site approved by INVIMA
  - Additional sites can start with the EC approval and INVIMA notification

- **Import license**
  - Investigational product, comparative and placebo
  - Devices: new or used
  - Laboratory supplies
  - Has a validity period of six months

- **Renewal of protocol approval**
  - Annually
  - EC and INVIMA
What we have
What we have to date

1018 clinical trials
2009 – to date

1999 -2007 : 535 trials
(9 years)

2008 – 2013: 483 trials (6 years)

5000 Direct jobs
Sites/CROs

63 Ethics committees
certified in GCP

118 Sites/IPS
certified in GCP

diabetes, endocrinology,
cardiology, oncology,
pneumology, vaccines,
rheumatology, psychiatry,
transplants, infectology

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(9 years)

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Open communication with INVIMA and collaboration through Clinical research associations such as:

- **AVANZAR** Asociación para el avance de la investigación
- **ACIC** Asociación Colombiana de Centros de investigación Clinica
- **AFIDRO** Asociación de laboratorios farmacéuticos de investigación y desarrollo
Regulatory timelines and Pathway

Dossier preparation

Product Import licence
Submission Pathway

180 Calendar days

EC

- Submission package preparation
- Submission - First local EC approval

INVIMA

- Protocol, ICB, questionnaires, diaries, insurance, EC approval letter
- Investigator product, blood sample, lab information, Investigator CV, GCP Certification
- Submission package preparation and INVIMA forms completion
- Submission - Approval Health Authorities INVIMA

VUCE

- Import Licence
- MoH approval
- Import Licence
- Preference Invoice CoA*
- Import Licence* 15 - 20 days
- 3 days released product from customs
- 20 Days

Documents in Spanish

7 days

50 days

10 days package preparation + 100 days for MoH Submission/Approval
A lesson ...

... in jumping to CONCLUSIONS
Advantages Clinical Research in Colombia

- Support of Regulatory Authorities to promote clinical research in Colombia
- Consolidated regulatory environment that provides legal security to clinical research in Colombia
- Strong relationship between participant and physician that allows high adherence
- Good acceptance by the community to participate in clinical research
- Centers and laboratories with all facilities and certified in GCP capable of delivering data with high quality standards
- Professional personnel trained and with experienced in clinical research
- Significant growth in clinical research in the recent years. Most of the CROs have established legal entities in Colombia.
✓ Enhance the way that INVIMA communicates the updates to the guidelines, forms and other documents related to clinical research

✓ Logistics sufficient of the INVIMA to optimize response times and regulatory processes

✓ Creation of new research centers that will address new population in order to have new alternatives too meet the trials demand for in Colombia.

✓ Support of the pharmaceutical companies, CROs and associations to promote clinical research and motivated new institutions to include clinical research among their services

✓ Postgraduate education in clinical research supported by Universities and the Government
RESOURCES
• Estado de la Investigación Clínica en Colombia relacionado con medicamentos en el desarrollo de nuevas moléculas. Adriana Parra. Tesis de Grado de Maestría, Universidad Nacional de Colombia, 2011
