

Harmonizing
Regulations and Standards
That Guide
Clinical Investigation
of Medical Devices

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Clinical Studies Are Essential to Evaluate and Assure the Safety and Performance of Many Devices

- During Development
- For Market Approval
- For New Claims
- For Product Changes
- Post-Market Surveillance

The Basics of Good Clinical Studies are the Same Worldwide



Careful Planning and Conduct
are Key to Obtaining Useful Data
and Assuring Human Subject
Protections

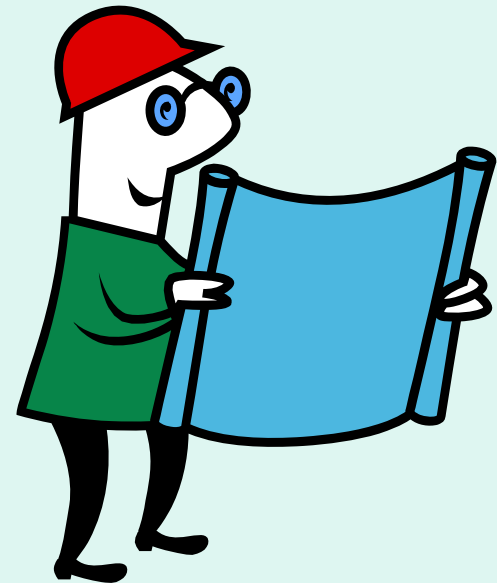
Standardizing Processes Will Benefit Everyone

- New devices to market faster
- Keeps poor products off market
- Saves industry resources
- Less work for Regulators
- Fosters business opportunities
- Improves public health worldwide

Standardizing Poses Challenges:

- ❖ Specialized Medical, Ethical and Regulatory Knowledge Required
- ❖ Regulations Around the World Are Rapidly Evolving

Roles of Sponsor, Monitor and Investigator Have Varied in Different Countries



More Challenges:

- ❖ Medical Devices are Increasingly Complex
- ❖ Scientific Sophistication of Clinical Investigations is Increasing
- ❖ Use of Electronic Data Capture is Growing

A Special Challenge:

- ❖ Regulations and Standards Related to Clinical Investigation of Devices Tend to Overlap in Broad Areas.

GHTF and ISO TC 194 Have an MOU
to Assure Useful Guidance and Prevent
Major Gaps or Inconsistencies

A Harmonizing Challenge

- ❖ Different Areas of Government Oversee Different Policy Areas for Clinical Studies, Making it Difficult to Staff One GHTF / ISO Group to Address All Issues



Quality Systems and Risk Management

- Concepts are Beginning to be Applied to Clinical Investigations of Devices
- Need to Become Integrated into Routine Planning / Conduct of Studies
- Regulations and Standards Must Provide Clear Guidance in Future

Regulations –
Data Needed Before Marketing
Basic Assurance of Public Safety

Standards –
How To Obtain and Document It

Global Harmonization Task Force (GHTF)

Harmonizes Regulations



Study Group 1

- Worldwide Essential Principles of Safety and Performance
- What Must be Demonstrated Before Devices of Different Classes Can Be Marketed – Conformity Assessment
- Worldwide format for submissions

Study Group 5

- When is Clinical Data Needed To Assure That Essential Principles are Met?
 - Clinical Evaluation Process
 - Justification for Clinical Investigation
- What Type / Design of Clinical Investigation is Appropriate?

Study Groups 2, 3, 4

For Clinical Investigations

- Adverse Event Reporting
- Quality Systems
- Audits
- Risk Assessment / Management

Should Take into Account the Work of
These Study Groups

Standards are Developed By Organizations That Coordinate International Scientific Working Groups



The Standard – ISO 14155:

- How to design a clinical study
- How to plan and conduct the study
- How to document, monitor and report
- Use of terms for international consistency
- Roles & responsibilities of participants
- All devices except in vitro diagnostics

Revision In Progress

- Fall 2007 - Complete Draft
- Spring 2008 – Issue DIS for Review?
- Fall 2008 – Incorporate Comments?
- 2009 - Issue FDIS for Vote?

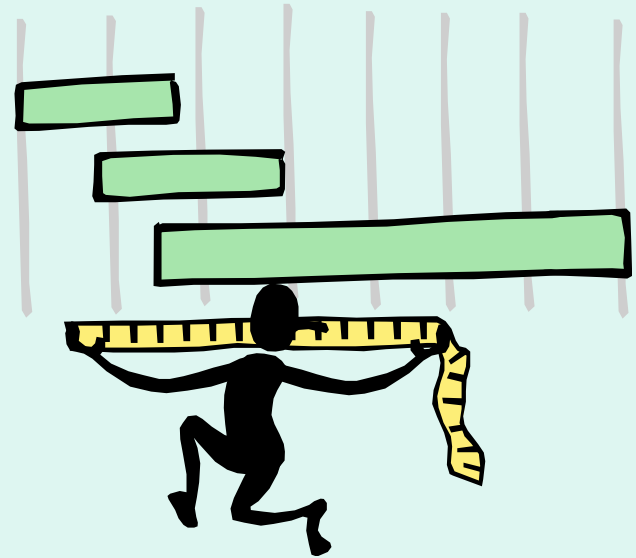
New Format

- Walks through major steps of study planning and execution
- Describes responsibilities of sponsor, investigator and monitor
- Detail in Annexes

Seeking Consistency with GHTF

- Revising Definitions
- Deleted Annex with Literature Review
- Clarifying Adverse Event Reporting
- Harmonizing the “Justification” Section

What Benefit Does ISO 14155 Provide?



It Helps Assure that Data Generated Anywhere in the World Meets Minimum Standards of Quality for Study Design / Planning, Conduct, Documentation and Human Subject Protections.



Multi-National Studies Balance Local & Regional Differences in:

- Medical Practice
- Treatment Practices
- Assessment of Adverse Events

Multi-National Data Is Especially Helpful When:

- Frequency of illness varies
- Treatment method is well known in some countries and novel to others
- Large number of patients are needed

ISO 14155 Is Expected To

- Increase Acceptance of Clinical Data by Regulatory Authorities Across Countries
- Speed Approval of Promising New Technologies



Areas of Future Coordination

Post-Market Studies

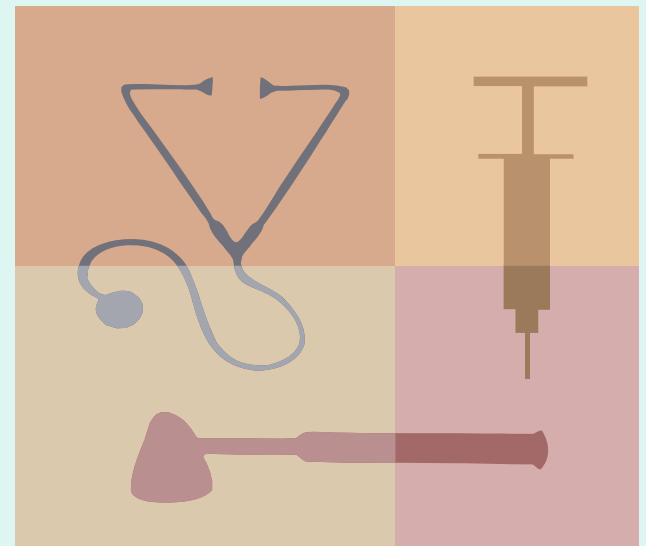
IVD Studies

Study Oversight by Regulators



Future Harmonization by GHTF to Support the Standard

- Adverse Event Reporting in Studies
- IRB Membership and Procedures
- Informed Consent Process
- Insurance Requirements



Examples of Issues the ISO Working Group Is Considering

Sample Questions for the Working Group:

- Does “risk analysis” mean risks of the device or the risks of study participation?
- Is it always necessary to keep records of all the potential subjects screened?
- Must all data be copied into or collected in Case Report Forms vs. hospital records?
- Must marketed products that are studied for new uses have “Investigational” labeling?

Questions (cont.)

- Do IRB's always need to see case report forms?
 - If CRF is electronic do they need a hard copy?
 - What if the CFR asks for information not essential to the study purpose?
- What if local IRB regulations are less strict than standard? Is it enough to document efforts to meet the standard?

Questions (cont.)

- Adverse event reporting to IRB, other investigators, regulatory authorities.
 - Who does the reporting?
 - When is “immediate” reporting necessary?
 - What does “immediate” reporting mean?

Questions (cont.)

- What does “independent” mean regarding IRB’s? Informed Consent Witnesses? Data monitoring boards?
- How much information about pre-clinical testing should be included in the investigation plan vs. Investigators’ brochure?
- How much detail about forms & documentation should be in the investigation plan? In body or appendix?

Questions (cont.)

How to integrate quality assurance for the study into the overall quality system of the Sponsor? Investigator or CRO?

- Retention of files by IRB? Sponsor? Site? As long as device in use?



Questions (cont.)

- When is informed consent needed in native languages?
- Who signs interim & final study reports?
- Should the standard more specifically describe approval needed by regulatory authorities?