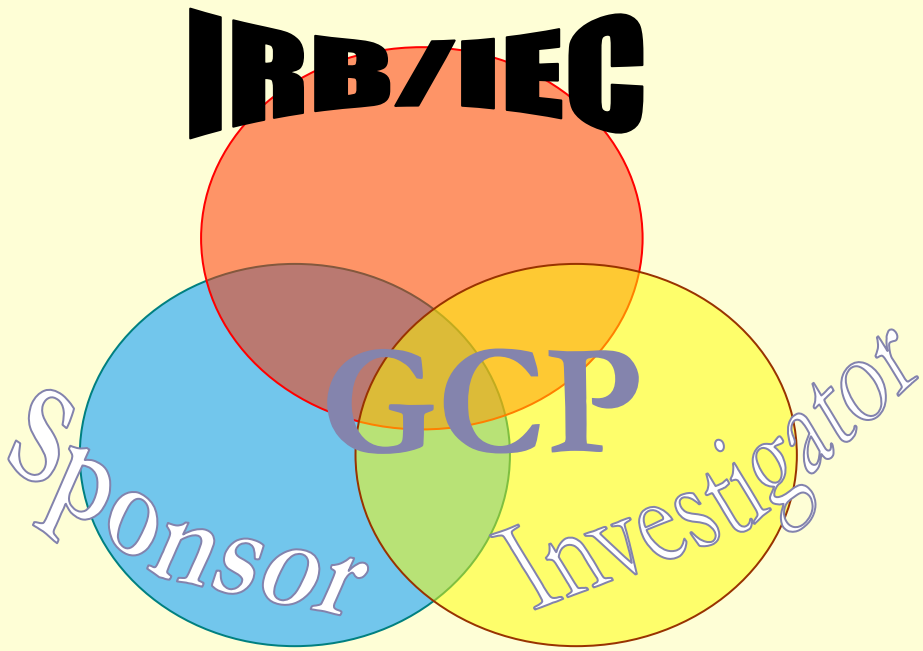
Role of IRB/IEC in GCP

Cristina E. Torres, Ph.D.

Stakeholder Responsibilities in Research

Regulatory/Ethical Framework



Protection of Human Subjects and Credible Data

Common Good

Institutional Review Board (IRB)

- An independent body constituted of medical, scientific and non scientific members
- Responsible for ensuring protection of rights, safety and well being of human subjects
- Responsible for reviewing, approving and providing continuing review of protocol and obtaining and documenting informed consent of trial subjects

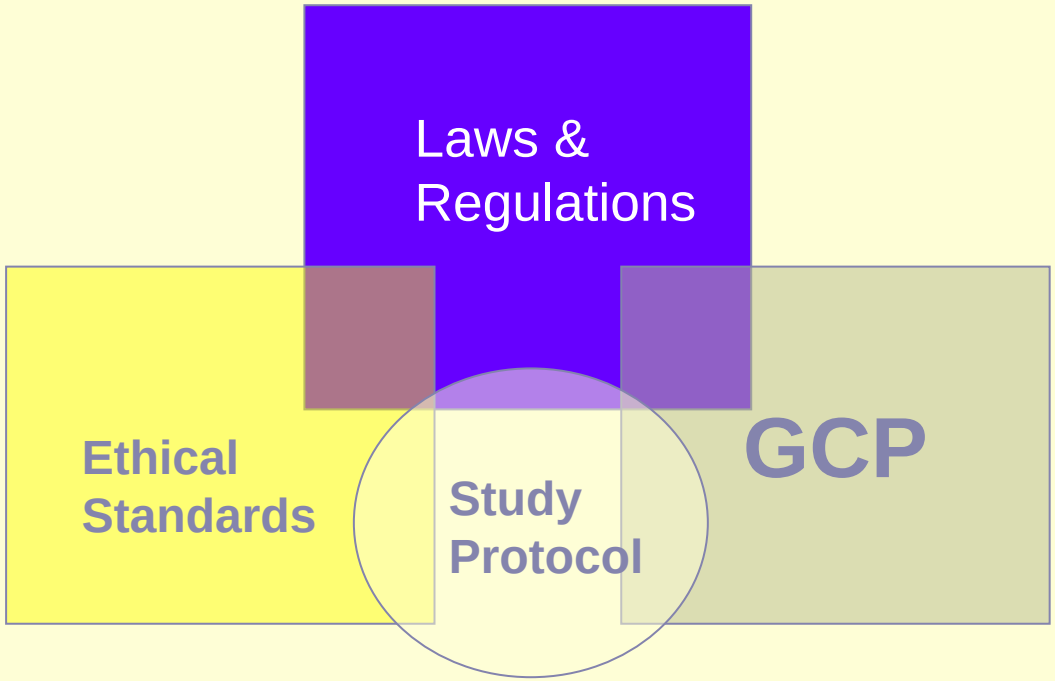
Independent Ethics Committee (IEC)

- An independent body (review board or committee, institutional, regional, national, or supranational
- Constituted of medical professionals and non-medical members
- Responsible for ensuring protection of rights, safety and well being of human subjects
- Provide public assurance
- Review, approve protocol, investigators, facilities, ICF

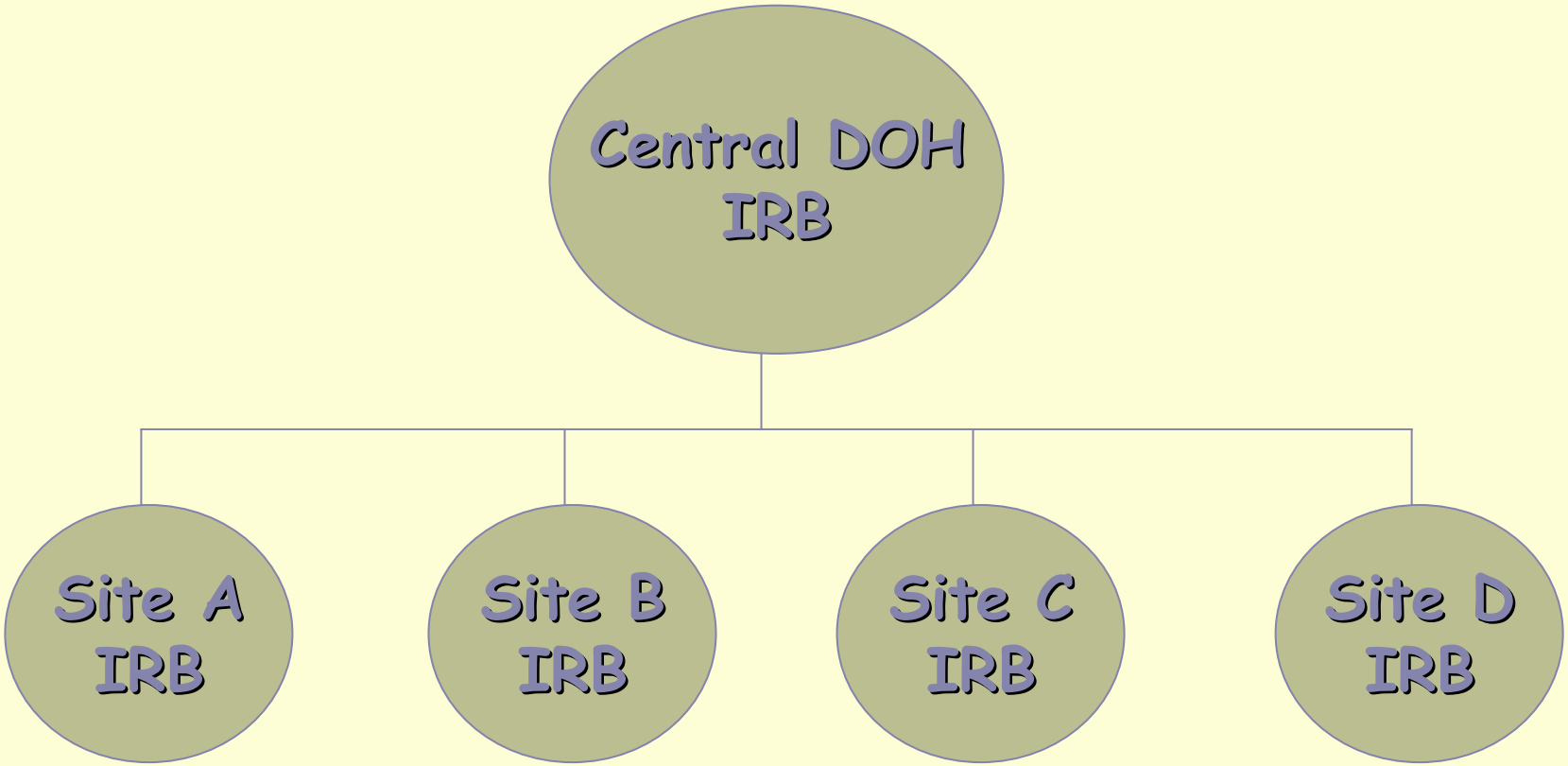
Independent Review

- Address conflicts of interests (COI)
- Individuals not affiliated with the research should review, approve, amend and terminate it.
- Review committee should be made up of competent and properly trained people.
- Review committee should be multidisciplinary.

Clinical Research Requirements

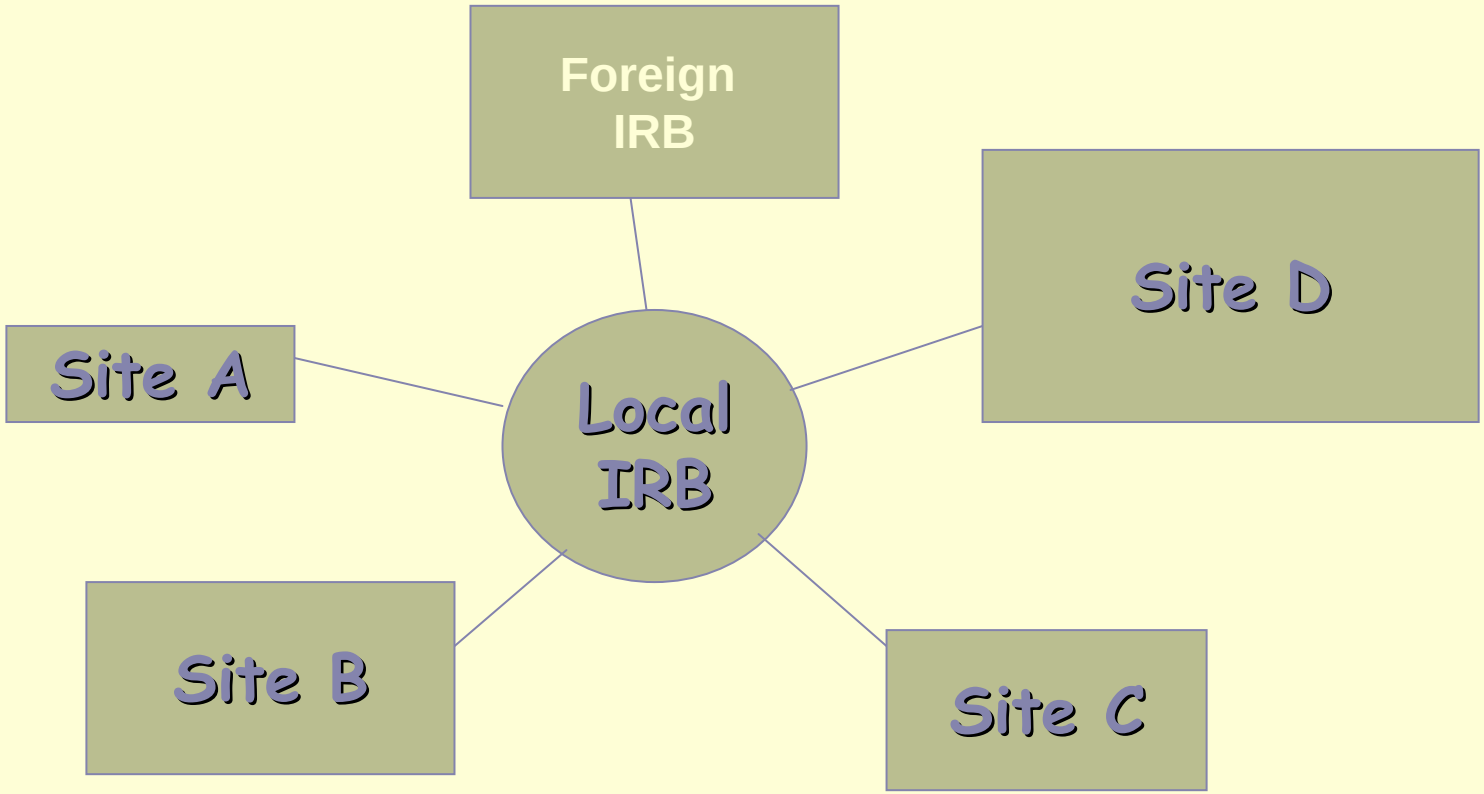


IRB Review Model

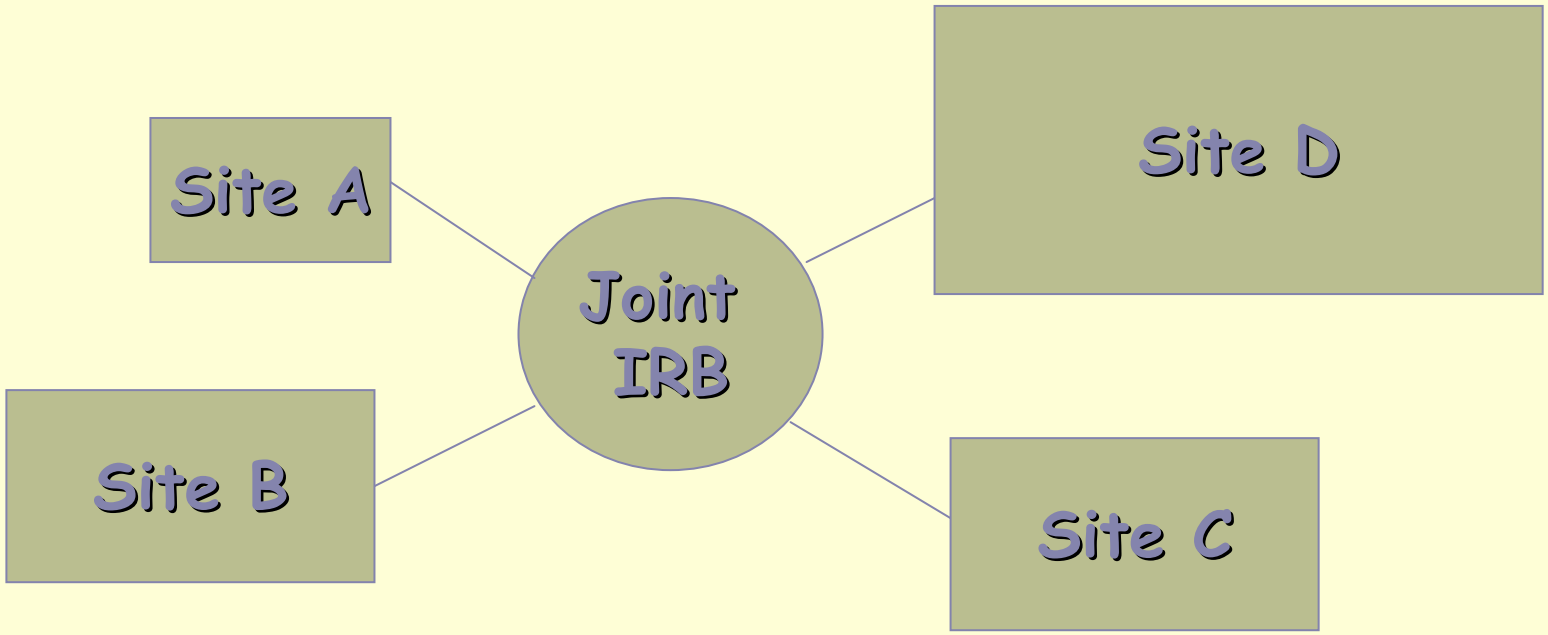


Source: NBAC 2001

Accept the Review of Another IRB Model



Joint IRB Model



A. Defining Scope of IRB/IEC Authority

- Management and balancing of the inherent conflict between the scientific and therapeutic/ humanitarian mission of institutions
- Not an all-purpose mechanism to prevent wrongdoing (malpractice) in hospitals and research institutions (fraud).
- May not cover public health surveillance that helps spread of disease where authority has been given to public health officials
- May not cover ethics issues among institution's constituencies.

Responsibilities of IRB/IEC

- **Safeguard the rights, safety, and well-being of all trial subjects**
- **Review documents**
  - Protocol/ amendments
  - Informed consent forms (ICF)
  - Subject recruitment procedures (advertisement)
  - Patient information sheet
  - Investigator's Brochure
  - Payments for subjects
  - Investigator's cv
  - Others
- **Review protocols within a reasonable time**
- **Document its views in writing**
- **Identify documents reviewed with dates**
- **Conduct continuing review**
- **Implement IC requirements**
  - Request additional information
  - LAR
  - Regulatory requirements (emergency research)
  - Amount and method of payment
  - Documentation and written information

IRB/IEC Composition, Functions and Operations

- Reasonable number of members with necessary qualifications and experience (at least 5, 1 non scientific, 1 non affiliated, independent of the investigator and sponsor)
- Review and evaluate the science, medical aspects, and ethics of the trial
- Maintain list of members and qualifications

IRB/IEC Composition, Functions and Operations

- Perform functions according to written procedures and maintain records
- Decide during announced meetings with required quorum;
  - only members may vote
  - Investigators may provide information but not participate
  - Non members with expertise may be invited

IRB/IEC Procedures

- Establish, document in writing and follow its procedures
  - Determine composition and source of authority
  - Schedule, notify members and conduct meetings
  - Conduct initial and continuing review.
  - Determine frequency of continuing review.
  - Provide expedited review mechanism for minor changes.
  - Specify that no subject may be enrolled and no deviation prior to approval.

IRB/IEC Procedures

- Specify that investigator promptly report protocol changes or deviations, increased risks to subjects, ADRs (serious and unexpected), new information related to subject safety
- Promptly notify in writing the investigator/ institution about its decisions, reasons for its decisions, and procedures for appeal.

IRB/IEC Records

- Maintain all relevant records at least 3 years after completion of the trial
  - SOPs
  - Membership files
  - Submitted documents (protocol related files)
  - Minutes
  - Correspondence

IRB/IEC Records

- Make them available to regulatory authorities
- Make available its SOPs and membership lists to investigators, sponsors and regulatory authorities

Current Global Challenges

- Need to address growing public mistrust
- Need to develop new drugs and interventions to address pandemics and emerging health problems
- Need to harmonize IRB requirements in different parts of the world (developed and developing countries)
- Need to develop ethical review systems that involve research stakeholders (regulatory authorities, industry, academe, patient groups)

Public Perception of Research

Local Challenges in Research

- Need to develop affordable and culturally relevant interventions
- Need to develop evidence based interventions
- Need to regulate commercialization
- Need to develop local research capacity
- Need for capacity building of IRBs/IECs to deal with various types of protocols, of various origins with a wide range of objectives and methodologies

Situation in Asia

- Research is becoming a priority
  - Need for evidence based decision making
  - Need to develop interventions to address health problems
- Advent of globalization
  - Asia as good material for clinical trials
  - Growing number of collaborative researches
- Involvement of industry, GOs, NGOs and international funding agencies in health research

Non Compliance by IRBs

- No written procedures
- Inadequate composition and poor attendance
- Meetings by emails (not face to face)
- Expedited review procedures not defined
- Timelines for submission of ADRs and SAEs not specified

Widler and Johansen"Non Compliance Issues in GCP Audits," Shanghai Presentation 2005

Non Compliance to Review Requirements

- Documents reviewed and/or approved not identified by version, date, etc. (ICH-GCP 3.1.2)
- “Written information” given to patients not adequately reviewed and approved
- Payments and compensation to patients not reviewed and approved
- Qualifications of PI and CV not reviewed

Widler and Johansen“Non Compliance Issues in GCP Audits,” Shanghai Presentation 2005

Common Weaknesses of Asian IRBs

based on FERCAP survey findings

- Weak lay participation in IRB deliberations (board observation)
- Incomplete SOPs and inadequate SOP compliance (document review)
- Poor documentation and archiving procedures (document review)
- Incomplete review of ethical issues (document review and board observation)
  - Inclusion/ exclusion criteria
  - Vulnerability
  - Risk benefit assessment
  - Complete information in consent form

Common Weaknesses of Asian IRBs

based on FERCAP survey findings

- Incomplete review of study design (document review and board observation)
- Inadequate documentation of IRB procedures (document review)
  - Incomplete minutes, incomplete protocol files
- Inadequate implementation of post review procedures (SAE reporting, progress and end of study reports)
- Unclear expedited review procedures

Capacity building of IRBs/IECs

- IRB/IEC need to be developed to fulfill its GCP mandate
- Need to cultivate an ethical infrastructure/system in health research
- Sponsors, institutions, funding agencies need to contribute to training and capacity building of IRB/IEC (not only investigators) to fulfill its GCP mandate
- Regulatory authorities should ensure GCP stakeholder performance of its respective role

SIDCER Recognition Program

Objectives

- To facilitate and support procedures to assist the IRB towards QUALITY and TRANSPARENCY in ethical review
- To conduct an independent evaluation of the IRB and provide feedback on its practices and overall performance
- To ensure its compliance to international, national and local standards
- To determine the availability of IRB written Standard Operating Procedures (SOP) and its adherence to its procedures


11 02 2006


11 02 2006