An Investigator's Responsibility for Protection of Human Subjects: Ethics & Good Clinical Practice

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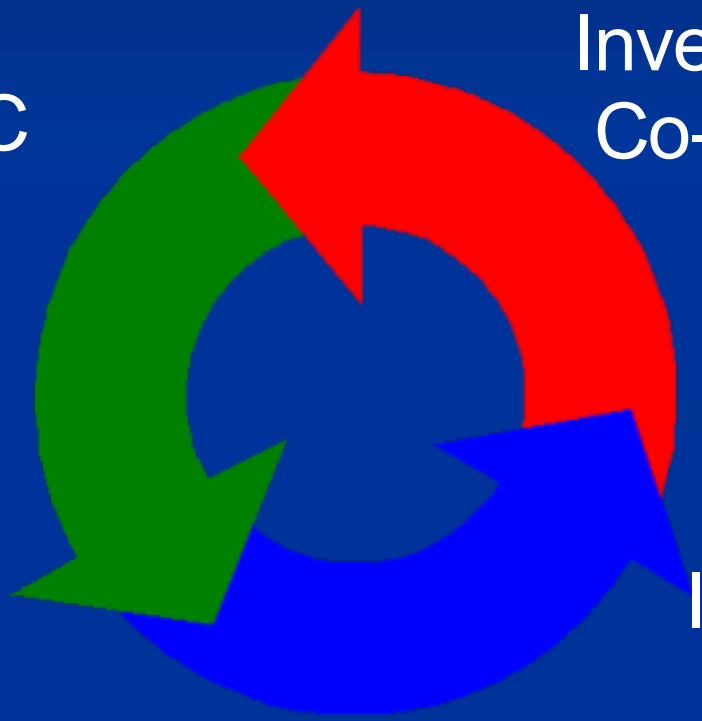
Human Research Protection Program Components

- IRB/REC
- Investigators and Research Staff
- Your Institution
- Others (Radiation Safety Officer, Data and Safety Monitoring Boards, Investigational Drug Services, Clinical Trials Units, General Clinical Research Centers. Legal, Quality Improvement/Safety)
- External (Sponsors, Clinical Research Organizations, Regulatory Agency)
- Participants/the community

Human Subjects Protection is a Shared Responsibility



Institution Responsible For:

- Setting tone for culture
- Complying with regulations
- Ensuring investigators fulfill responsibilities
- Ensuring institution-wide communication
- Establishing IRB/REC
- Developing Policies/Procedures
- Supporting IRB authority/ decisions
- Providing sufficient resources
- Implementing oversight mechanism
- Providing educational opportunities

IRB/REC

- Experience and expertise
- Diversity of backgrounds
- Sensitivity to community attitudes
- Knowledge of Institution, Regulations, Applicable Laws, Standards of Professional Conduct
- Knowledgeable & experienced with vulnerable subjects
- Consultants as needed
- Conducts initial and continuing review

Investigator

- Design & Implement Ethical Research
- Comply with Regulations/Policies
- Obtain IRB/REC Approval
- Comply with IRB/REC Requirements
- Implement Research as Approved and Obtain Prior Approval for Changes
- Obtain Informed Consent/Assent
- Document Informed Consent/Assent
- Submit Progress Reports
- Report Problems
- Retain Records & Document Activities

ICH-GCP

- International Conference on Harmonisation (ICH) / WHO Good Clinical Practice standards.
  - Produced in May 1996
  - Accepted by EU, Japan, USA since 1997
  - EU, Japan, United States, Australia, Canada, Nordic countries and World Health Organization (WHO)
  - Detailed guidelines
- The principles of good clinical practice are referred to in European Law
  - –GCP Directive 2005
  - –Clinical Trials Directive 2001

Good Clinical Practices

- Derived from the International Conference on Harmonization (ICH)
- Based on the Declaration of Helsinki
- Assures protection of human subjects
- Assures unified, high standards for designing, conducting, recording and reporting monitoring, auditing, analysis and reporting of clinical trials or studies
- Provides *public assurance* that the:
  - Rights, safety and well-being are protected and consistent with the Declaration of Helsinki
- Ensures that *clinical trial data* and *reported results* are:
  - Accurate
  - Credible

What are the 13 principles of ICH-GCP?

- Ethics:
  - 1. Ethical conduct of clinical trials
  - 2. Benefits justify risks
  - 3. Rights, safety, and well-being of subjects prevail
- Protocol and science:
  - 4. Nonclinical and clinical information supports the trial
  - 5. Compliance with a scientifically sound, detailed protocol

What are the 13 principles of ICH-GCP?

- Responsibilities:
  - 6. IRB/IEC approval prior to initiation
  - 7. Medical care/decisions by qualified physician
  - 8. Each individual is qualified (education, training, experience) to perform his/her tasks
- Informed Consent:
  - 9. Freely given from every subject prior to participation

What are the 13 principles of ICH-GCP?

- Data quality and integrity:
  - 10. Accurate reporting, interpretation, and verification
  - 11. Protects confidentiality of records
- Investigational Products
  - 12. Conform to GMP's and used per protocol
- Quality Control/Quality Assurance
  - 13. Systems with procedures to ensure quality of every aspect of the trial

Who is responsible for GCP compliance?

- Sponsors
- Clinical Investigators (CIs)
- Independent Ethics Committees (IECs)
- Institutional Review Boards (IRBs)/REC
- Contract Research Organizations (CROs)
- Research nurses
- Clinical Research Coordinators/Associates (CRCs/CRAs)
- Medical monitors
- Data entry personnel
- Others

Informed Consent– ICH - E6 4.8

- Consent forms must be reviewed & approved by IRB/REC
- When new information becomes available and is applicable ,subjects need to be a advised
- No coercion or undue influence
- No waiver of legal rights
- Fully inform subject (or legally authorized representative) of all aspects of the trial
- Language must be understandable
- Provide ample time to review & ask questions

Informed Consent– ICH - E6 4.8

- The consent form must be signed and dated by subject or legal representative
- If subject cannot read, require a witness to process
- Subject should be given a copy

Records and Reports
ICH- E6 4.9

- Accuracy, completeness, legibility & timeliness of data reported
- Data gathering forms are consistent with source documentation (original documents)
- Changes to forms should be dated, initialed & explained
- Maintain trial documents
- Financial aspects noted in contract
- All records need to be available for monitor, IRB/REC, or other regulatory authority

Progress Reports
ICH- E6 4.10

- Written report is submitted to the IRB /REC at least annually but more frequently if IRB/REC requires
- A written report is submitted to the IRB /IEC anytime if the PI notes changes that might significantly impact the conduct of the trial

Safety Reporting
ICH- E6 4.11

- All serious adverse events must be immediately reported to the sponsor and followed up by a written report
- All adverse events critical to the safety evaluation are reported to the sponsor per protocol
- Report death of any subject while on study
- Follow IRB/REC requirements

Investigator Responsibilities ICH - E6 4.13

Final Report(s) by Investigator

- The Investigator is expected to file a written report at the conclusion of a study

Summary: Role of Principal Investigator

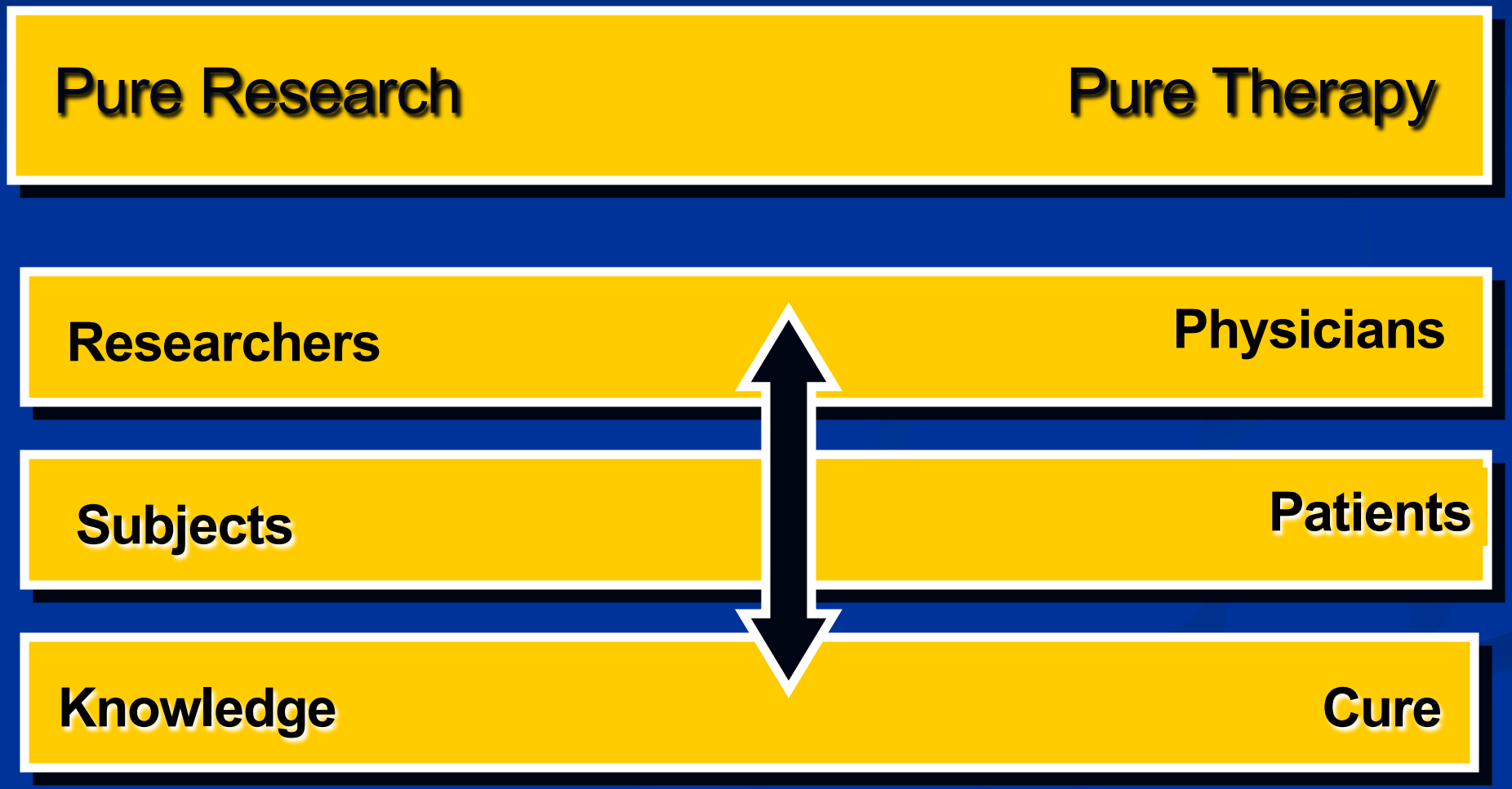
- Is not a just a title, it implies assumption of ethical and oversight responsibilities
- Recognize difference between providing clinical care and performing research
- Ensure that the rights and welfare of subjects are always respected and protected
- Consider the IRB/REC a collaborator

Physician Investigators

It is the duty of the physician to promote and safeguard the health of patients, **including those who are involved in medical research**. The physician's knowledge and conscience are dedicated to the fulfillment of this duty

WMA Declaration of Helsinki

Research/Therapy Spectrum



Summary

Ethical lapses are almost never cases of bad people, doing bad things, for no good reason. Rather, they are good people, doing bad things, for good reasons."

quoting Marcia Angell, MD
(former) Editor-in-Chief, NEJM