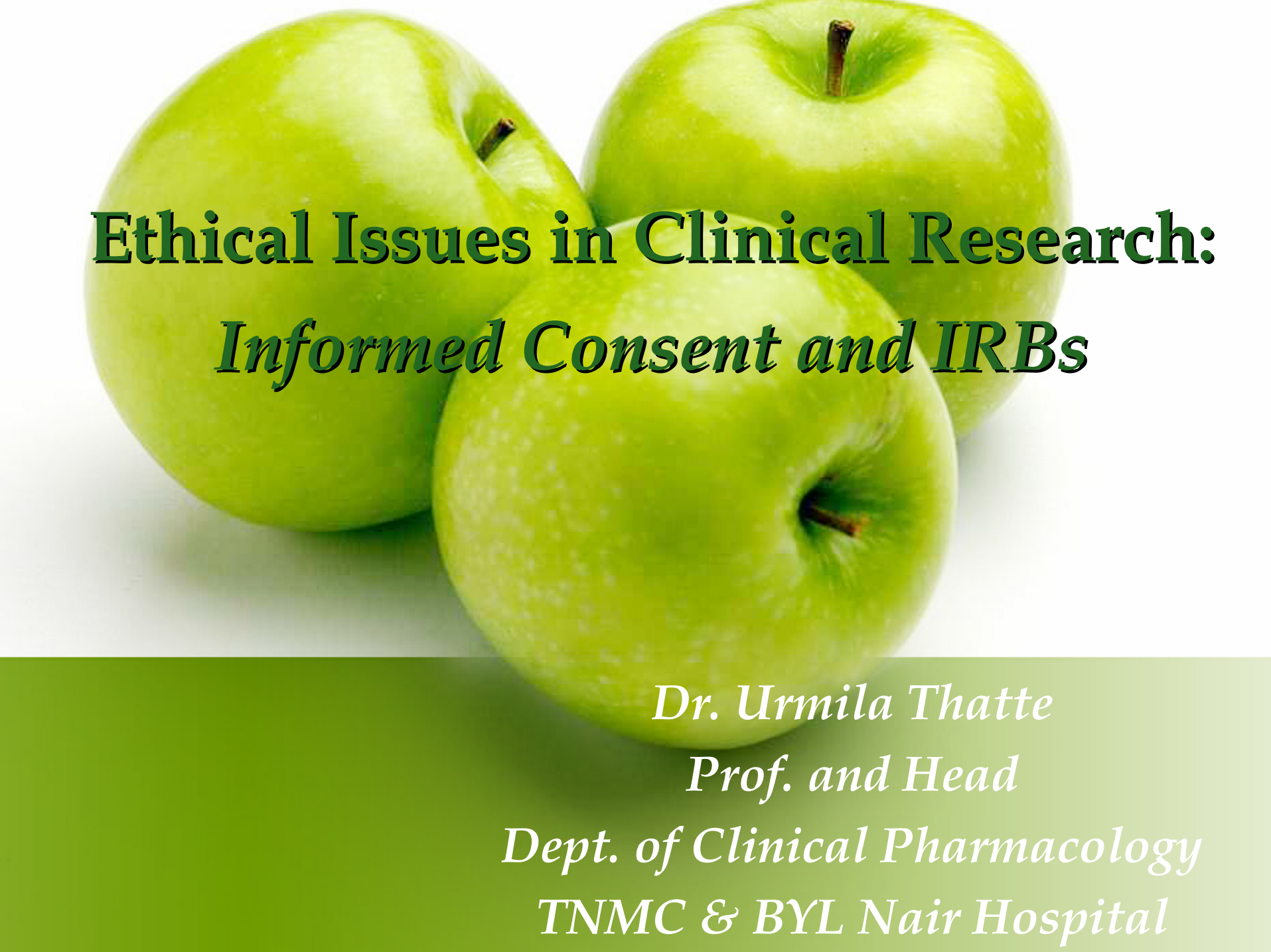


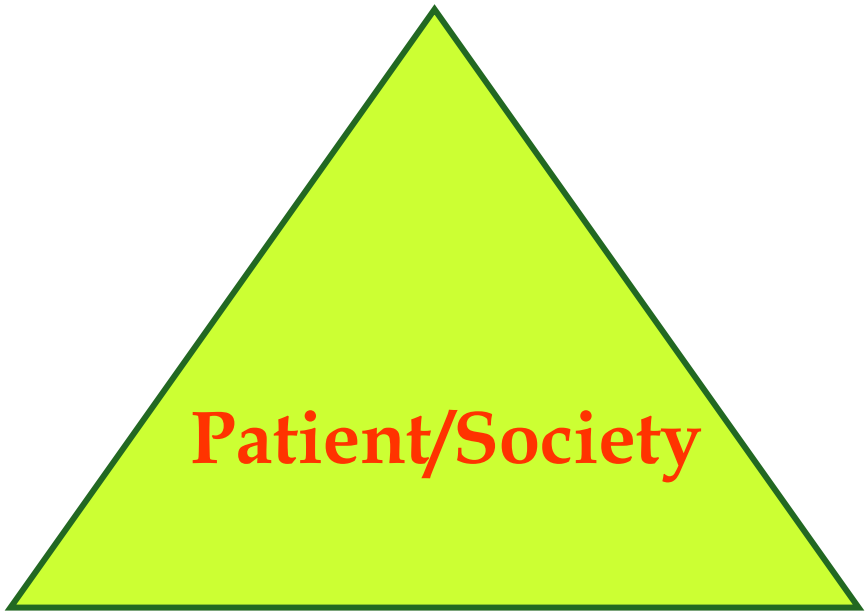
Ethical Issues in Clinical Research:

Informed Consent and IRBs

Dr. Urmila Thatte
Prof. and Head
Dept. of Clinical Pharmacology
TNMC & BYL Nair Hospital

Participants in Clinical Research

Regulators



Institute
Investigator
Ethics Committee
Administrator

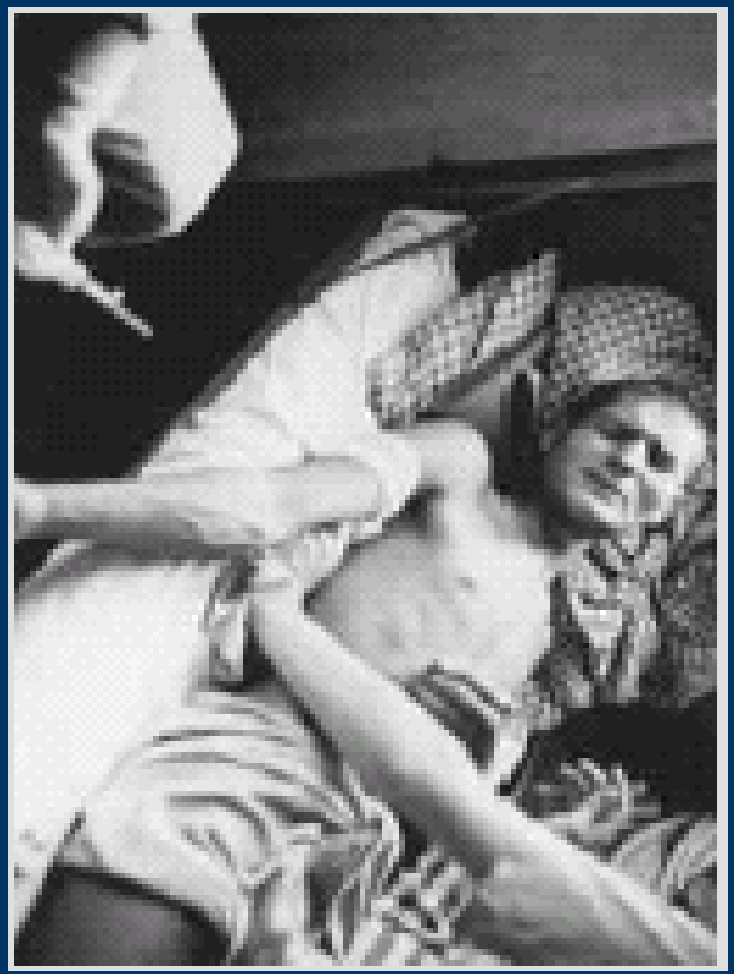
Sponsor
Monitor

Ethics in Biomedical Research

Right of the human subject to understand

- ✓ the nature of research,
- ✓ risks & benefits involved
- ✓ to agree or not agree to participate.

"Medical experiments of the 20th Century"



Sea Water Experiments

High Altitude Experiments

The Declaration of Helsinki 1964

Adopted by the 18th World Medical Assembly

Revised 5 times

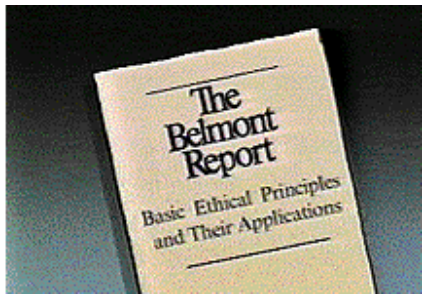
Latest version 2000, Edinburgh, Scotland

32 principles

Para 13: protocols must be submitted to an Ethics Committee for review, which must be independent of the investigator, the sponsor or any other kind of undue influence.

The Belmont Report

Ethical Principles and Guidelines for the Protection of Human Subjects of Research



The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

April 18, 1979

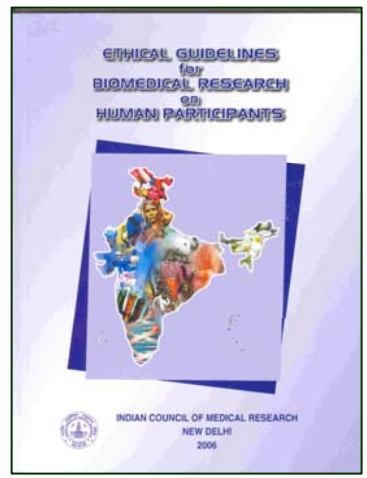
Basic Principles of Ethics

Autonomy	Informed Consent
Justice	Equitable Selection
Beneficence	Protocol
Non-malfeasance	Protocol

Ethics Committee Oversight

ICMR Ethics Guidelines

- Released in 2000; second version 2006-07
- Guidelines on website http://www.icmr.nic.in
- To be legislated - **The Biomedical Research on Human Subjects (Promotion and Regulation) Bill, 2007**

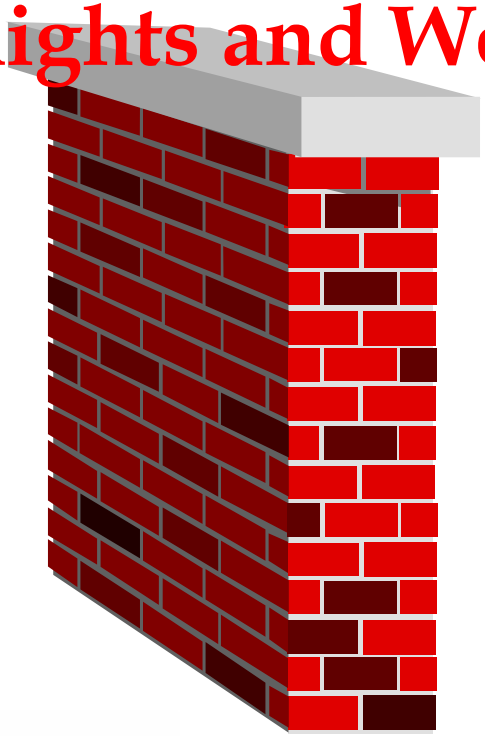


India

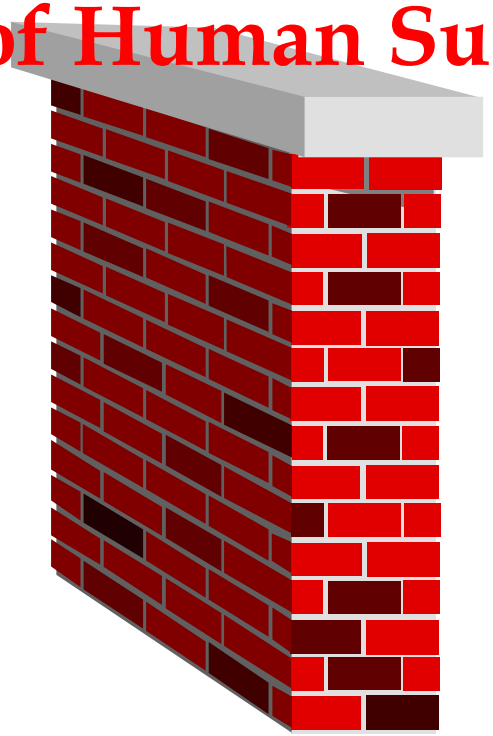
- 2001 Indian GCP
- 2005 Schedule Y of Drugs and Cosmetics Act Amendment: pertinent to clinical trials

"The Twin Pillars of Protection"

Rights and Welfare of Human Subjects



Independent Review



Informed Consent

Informed consent

- Consent given by a competent individual who
- Has received the necessary information
- Has understood the information
- And having understood the information has arrived at a decision without having been under any coercion, undue influence or inducement or intimidation

Informed consent

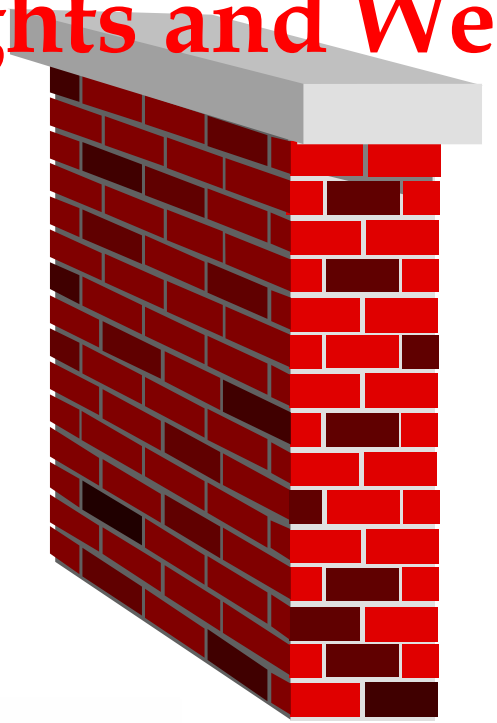
- **Written**
- **Voluntary**
- from **every** subject
- **before** any study related procedure
- and **documented** on EC approved form
- adhere to GCP, based on Helsinki Declaration

Informed Consent: Children

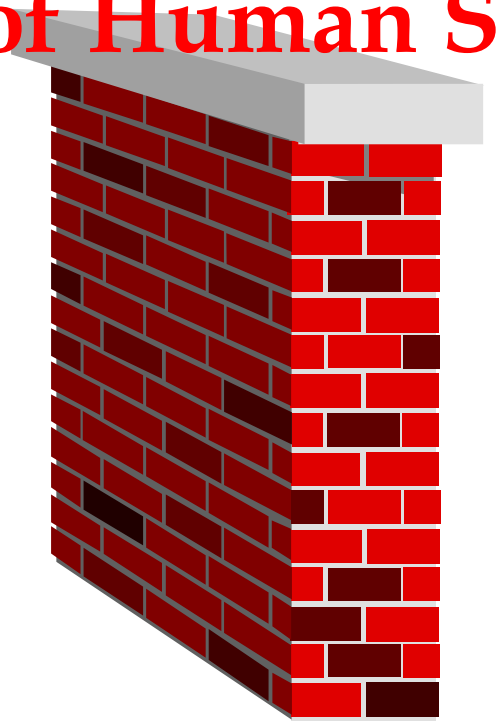
- Approval of older children: understand the concepts: **assent**
- Consent from parents/legally acceptable representative

"The Twin Pillars of Protection"

Rights and Welfare of Human Subjects



Independent Review



Informed Consent

Composition of the EC

A **reasonable** number of members who **collectively** have the qualifications and experience to review and evaluate the **science, medical aspects and ethics** of the proposed trial

What does an EC do for Clinical Research?

- **Before the study begins:**
  - Submission of research proposal
  - Review of proposal
  - Decision making process
  - Issuing an approval
  - Record keeping

What does an EC do for Clinical Research?

- **During the study:**
  - Review of amendments (Protocol, ICD)
  - Review of Serious Adverse Events
  - Protocol deviations
  - Progress (study status)
  - Record keeping

What does an EC do for Clinical Research?

- **After the study:**
  - Study report,
  - Post trial management
  - Publishing
  - Record keeping

Criteria For Approval

- Suitability of Investigator
- Suitability of Protocol
- Equitable Selection Of Subjects
- Time management
- Confidentiality of subjects and data
- Informed consent process

Some Issues …..

What requires Ethical Clearance?

- ? Retrospective studies
- ? Studies on
- ✓ **Drug studies sponsored by pharmaceutical companies**
- ? Devices, radiation and imaging
- ? Student's thesis
- ? Phase IV studies
- ? Medical records/HP slides
- ? Embryos, stem cells
- ? Epidemiological, social and psychological studies

What studies to submit to the Ethics Committee?

WHO is a research participant?

The human participant is **a living individual about** whom a researcher obtains either:

1. data through intervention or interaction with the individual; or
2. identifiable private information.

What studies require Ethics Committee Clearance?

Research involving

1. tissue specimens, medical records, genetic material, behavioral and/or biomedical assessments, and treatments.
2. cells, blood or urine, tissues, organs, and hair or nail clippings, **even if the researcher did not collect these materials.**
3. **residual diagnostic specimens**, including specimens obtained for routine patient care that would have been discarded if not used for research.

What studies require Ethics Committee Clearance?

Research involving

4. Private information, such as **medical data,** that can be readily identified with individuals, even if the information was not specifically collected for the study in question.
5. Research on cell lines or DNA samples that can be associated with individuals falls into this category.

Regulatory Clearance?

- DCGI permission for Phase 1-3 studies
- Definition of a "new drug" – new indication/new route of administration/new dosage form
- Sending samples abroad: DGFT, MOH (ambiguity: "collaborative")
- Biotech products: multiple agency approvals
- Devices?????

WHY are you looking at the science?

- Incomplete protocols only CRF submitted
- Safety emphasis is low: interim analysis, lab tests
- No controls: level of evidence very low
- “Me-too” studies
- Efficacy and failure end points not specified

Poor science is poor ethics

Special Considerations

- Vulnerable populations
- Commercialization of research results
- International collaborations: protection of IPR, rights of patients and investigators
- Multi-centric studies
- Standard of care for controls
- Use of Placebo

Investigator

- Multiple studies: conflict of interest and bias in allocation
- Qualifications and expertise
- Communication between Investigator and EC: Skills of the Secretary!
- Continued communication during trial

Subjects in Study

- *Incentives?*
- *Management of trial related injury*
- Advertisements/recruitment methods
- How will the patient be looked after the end of study?
- Methods for retention of patients

Consent Forms

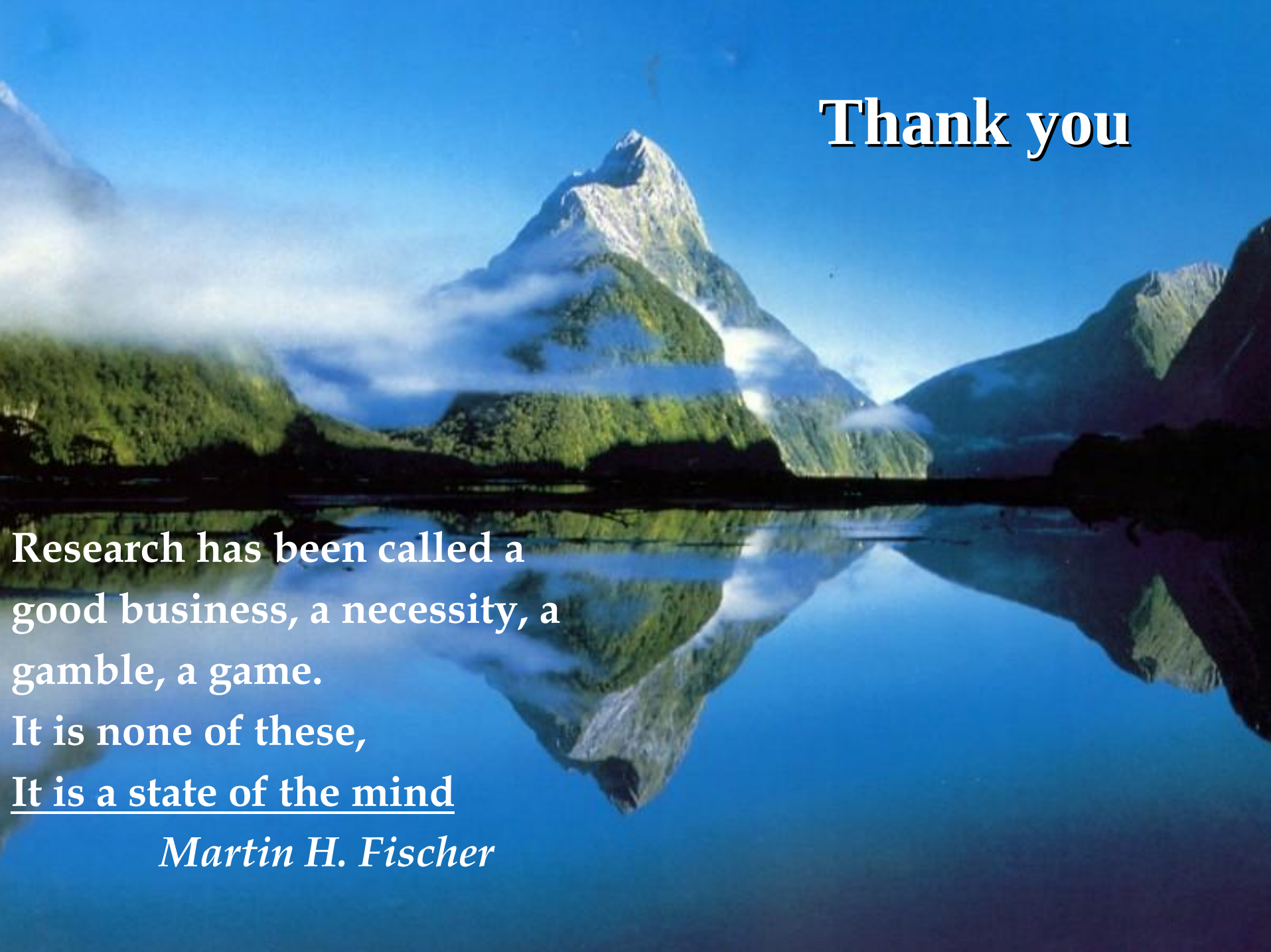
- Generic forms used
- Size of the consent forms, vernacular – meaning
- Language
- Is the modified, approved version being administered?
- Incorrect documentation

Permissions

- Retrospective permissions!!!!
- Expedited reviews
- Content of the permission letter

Herbal/Traditional Medicines

- Need for Ayurveda specialist as co-investigator
- Regulatory clearances: confusions


Thank you
Research has been called a
good business, a necessity, a
gamble, a game.
It is none of these,
It is a state of the mind
Martin H. Fischer