UNIVERSITY OF BERGEN

Department of Philosophy

U N I V E R S I T Y O F B E R G E N

Department of Philosophy

Ethics review – quality control

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Positive developments

- Primary justification for requiring ethics review is to have an independent assessment of acceptability of research
- On a macro level, system works well: Very few cases of documented abuse
- Research protocols have improved
- But
  - What specifically has the IRB/ERC system contributed to that?

Common complaints

- Long turnover times
- Too much attention to irrelevant details
- Unerresourced and overworked committees
- Inconsistencies between different committees
- Lack of competence, both about science, regulations and ethics
- Conflicts of interests

Abbott & Grady, 2011

- Multiple studies evaluating the structure, process, and outcome of IRB review in the United States have documented inconsistencies and inefficiencies.
- Additional research is needed to understand how
  - IRBs accomplish their objectives
  - what issues they find important
  - what quality IRB review is
  - how effective IRBs are at protecting human research participants.

Variations

- Compensation and assent
- Minimal risk level
- Requests for changes in consent forms
- Expedited versus full review
- Exempt research
- Variations in compliance with consent requirements in US federal regulations

Remedies

- Centralized IRBs
  - NIH requirement
  - New US federal regulations
  - EU drug approval process
- Accreditation and certification
  - AAHRPP
    - Association for the Accreditation of Human Research Protection Programs
  - FERCAP/SIDCER
    - Forum for Ethics Review Committees in Asia Pacific
    - Strategic Initiative for Developing Capacity in Ethics Review

Central IRB

- NIH requirement for multi-site research
- Introduced in new OHRP regulations
- Required in new EU drug regulations

Multi-site trials, EU

- Ethics review carried out according to national regulations
- One reporting member state, chosen by the sponsor
- Requirement that this member state carries out an evaluation of the protocol within a specified time period, taking into accounts comments by all participating states
- Each individual member state evaluates, for their own territory,
  - Informed consent requirements
  - Compensation requirements
  - Arrangements for recruiting of subjects
  - Procedures for collection, storage and future use of samples

Issues

- Supposed to shorten approval times and solve issues of inconsistent requirements from different IRBs
- Less thorough review?
- Reluctance by institutions to give up control?

FERCAP

- Structure and Composition, office facilities, training, availability of SOPs, meeting and quorom requirements
- Submission of protocols, specification of what documents are needed (compensation for injury, CV, previous decisions)
- Criteria for expedited, full review, use of experts and consultants
- Elements
  - Scientific design
  - Justification for use of control arm
  - Criteria for withdrawal of participants
  - Criteria for suspending or terminating research

FERCAP

- Does the EC review the impact and relevance of research on the local community from which the research participants are drawn?
- Does the EC review a description of the availability and affordability of any successful study product?
- Does the EC review the standard of care and other post-trial benefits offered to participants?

FERCAP

- Continuing review procedures
- Completeness of minutes
- Decision making procedure
- Elements of decision letter
  - Title of protocol, name of applicants, date
- Clearly state reasons for modification/termination

FERCAP

- Most of the elements highlighted in the self-evaluation are important, and even essential, but they do not really address the problems identified with the IRB review process.
- Fercap recognition is therefore neither necessary nor sufficient for ensuring high quality review

AAHRPP

- Element II.3.A. The IRB or EC has and follows written policies and procedures for identifying and analyzing risks and identifying measures to minimize such risks. The analysis of risk includes a determination that the risks to participants are reasonable in relation to the potential benefits to participants and to society.

- Another criterion for approval of research is that risks to participants are reasonable in relation to potential benefits, if any, to participants, and the importance of the knowledge that may reasonably be expected to result. The IRB or EC should evaluate whether research submitted for review satisfies this criterion. The IRB or EC should be able to recognize the likelihood and magnitude of harms and benefits, and understand the importance of the knowledge reasonably expected to result. The IRB or EC should be cognizant of the range of harms, including physical, social, economic, psychological, and legal harm. The IRB or EC should also be cognizant of the range of benefits. Direct benefits to participants can take the form of therapy, education, information, resources, or empowerment.

AAHRPP – how to determine compliance

- Application materials require description of procedures, their risks and benefits
- The IRB has a policy that requires that IRB determines that
  - risks are reasonable in relationship to benefits
  - The researchers have sufficient resources available

OHRP self assessment

- https://www.hhs.gov/ohrp/sites/default/files/ohrp/education/qip/ohrpqatool.pdf.pdf

Self-assessment - Mahidol

- Days in review against some benchmark
- Staffing
- Reasons for deferral or non-approval
  - Clarification of research objectives and study designs (80-90%)
  - Balancing risks and benefits
  - Confidentiality/privacy (20-40%)
  - Recruitments issues (30-60%)
  - Informed consent process (50-90%)
  - Additional documentation (40%)

Self-assessment, VA Pittsburgh

- Series of questions regarding quality addressed to IRB members and researchers
- Assess degrees of agreement and differences in judgements between the two groups
- On the basis of that identify problem areas
- Example
  - An IRB that gives a complete explanation for any required changes to or disapproval of protocols
    - Difference between ideal IRB and actual IRB. Difference between IRB members and researchers

Self-assessments

- Self assessments are better quality control activities than accrediation
  - Mahidol
  - VA
  - OHRP
- Why?
  - Cost issue
  - Accreditation not officially recognized anyway
  - Gets the IRB involved in the process

Problems with current accreditation procedures

- Does not go much beyond conscientious self-assessment
- Does not address the issues that have raised concerned
  - Does IRB review contribute to the protection of research subjects?
  - Delays and irrelevant & arbitrary modifications of protocol
  - Variability in substantive judgments
    - Exemption and expedited review
    - Risk judgments
    - Requirements for informed consent forms
- Special concerns for research outside the US

Models of IRB review

- US
  - Institution based. Institutions are responsible for human subjects protection programs
    - As a condition for receiving US federal funds
    - As a condition for approval of drugs by FDA
    - One requirement is IRB review and approval
- Internationally
  - Many countries have national laws or regulations
    - Indonesia: Health Act o 23/1992; Regulation no 39/1995
    - Exceptions: India, Thailand. Laws still being drafted
      - ICMR guidelines, NRC Guidelines
    - Indirect: Medical Council Thailand, Physician Act

Institutional responsibility

- In the US it is the institution that carries out the research that is responsible for the protection program. IRB is just one element of that.
  - Training of researchers
  - Office that oversees compliance in general, including the IRB
- Other countries may not have this explicit focus on institutional responsibility, but has en research ethics review committee with an independent, legal basis.
- This also complicates use of US based accreditation procedures

Misperceptions

- Accreditation provides some sort of official endorsement or recognition or is a regulatory requirement
  - WHO/Fercap
  - AAHRPP/US regulatory authorities
- Accreditation will make it easier to attract outside funding
- Accreditation means that the institutions are better at protecting human subjects
  - No empirical data

Recommendations for control control of ethics review

- Government endorsed/mandated system
  - Organizational and record keeping requirements
  - Training requirements
  - Focus BOTH on institutional requirements and REC requirements
- Process at the National/Regional level to reach common understanding/practice regarding key substantive issues
  - Exempt research
  - Expedited review procedures
  - Risk judgments
  - Informed consent requirements