The ANPRM and Work of the Presidential Commission

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History of the Current Regulations

- 1966 Beecher article published in NEJM
- 1972 Tuskegee Study exposed in the press
- 1974 National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research created.
- 1979 Belmont Report published
- 1981 HHS adopts 45 CFR 46
- 1991 14 Federal agencies adopt Part A of 45 CFR 46—the Common Rule

Problems with the Current Regulations

- Commentators have identified numerous problems with Common Rule protections:
  - Inadequate IRB time devoted to review of high risk research studies.
  - Time consuming IRB reviews and continuing review of low- or no-risk research, such as surveys.
  - Inconsistent IRB practices regarding research with bio-specimens, claims data, and medical records data.

Problems with the Current Regulations

- Multiple reviews of multi-centered trials with no evidence of reduced risks or enhanced protections.
- Informed consent documents that have become excessively long and written at a high grade level.
- Lack of data on risks of research and value of IRB protections.
- Attempts at evading IRB review by claiming QI or QA “work” is not research.

Goals of Regulatory Reform

- Two main goals for reforming the research regulations

  1) Enhance the protections of research participants.

  2) Improve efficiency of the review process.

  By reducing unnecessary paperwork, multiple reviews of studies, and IRB reviews of very low-risk research, resources could be focused on review of truly high-risk studies.

Specific Reforms

- **Risk-based Research Review Process.**

  Three pronged review process:

Greater than Minimal Risk	Full IRB review and annual review (Current protections). No annual review when analyzing data or the only remaining interventions are standard clinical follow-up.
Minimal Risk	Expedited review by 1 trained person with option to send for full IRB review. No annual review unless explicitly justified by reviewer.
Information Risks Only (surveys or record review)	No IRB review but register research project with IRB office. IRB office could require an IRB review. Adherence to HIPAA-based data security measures.

Specific Reforms

- Surveys, focus groups, interviews, maybe economic and psychology studies with mentally competent adults **excused** from IRB review but register with IRB office. Must adhere to data security standards.

- Research based on secondary use of existing data and biospecimens also qualify for **excused** status.

Specific Reforms

- Written consent would be required for all uses of biospecimens whether with identifiers or not.
  - Presumption is that all biospecimens are identifiable. Either today or in near future it will be possible to identify a person from their biospecimen. Distinction between identifiable and anonymized biospecimen is no longer tenable.
  - Consent would be a standard, general, open-ended consent obtained at the time of admission to hospital or clinic.

Specific Reforms

- **Multi-site research.**

  Require only one IRB of record for domestic research sites. Separate IRB review for international studies. No requirement for each institution to review a protocol.

- **Up-dating minimal risk interventions.**

  Standing federal committee to regularly update list of minimal risk interventions based on data from literature or researchers.

Specific Reforms

- **Extend federal protections.**

  Require all research—including non-federally funded research— conducted at institutions subject to the Common Rule be subject to the new federal research regulations.

Specific Reforms

- **Electronic adverse event reporting system.**

  Develop a web-based reporting system that would permit systematic and comprehensive data on adverse events from research to facilitate the identification of low risk research and “hot spots” of research risk.

Specific Reforms

- **Improve informed consent documents.**

  Explicit delineation of information that must be in the documents.

  Creating standardized consent templates. Oral consent for adults participating in surveys, focus groups and similar types of research.

Specific Reforms

- **Standardize protections for information risks.**

  Require institutions to implement HIPAA-based data security standards for research posing informational risks.

What Can the Presidential Commission Add?

Zeke's Recommendations

- **Warning:** Whenever there is a response to a problem or scandal, there is a tendency to just add more and more regulation and oversight. This is how we get burdensome inefficient regulations that do not protect people.

- The correct response is to re-evaluate the package of protections to see what is helpful and what is unnecessarily burdensome and what there is good reason to believe changes will enhance protections.

Zeke's Recommendations

- Endorse the need to re-evaluate the existing regulations governing human subjects research and to establish mechanisms to constantly up-date provisions that are likely to change with more data or other changes, eg what interventions are minimal risk.

- Examine the ANPRM and see what the Commission wants to endorse and what it thinks might need changing.

Zeke's Recommentaions

- The Inter-agency working group I chaired recognized it could not address all issues in need of reform.

- The group explicitly set aside issues related to international research.

Zeke's Recommentaions

- One issue explicitly set aside that needs attention is: Equivalent Protections.

Zeke's Recommendations

- Don't kick the ball to a future committee.
- The Presidential Commission should **not** simply identify equivalent protections as an important issue.
- The Commission should not do what an IOM committee once did and say there should be risk-based IRB review but never specified how that should work. Don't just identify issues in need of study and resolution. Do the work.

Zeke's Recommendations

- The Presidential Commission should actually "solve the problem."
  - Delineate a principle(s) for determining what should qualify as equivalent protections.
  - Specify what differences in regulations are not ethically significant—e.g. whether different continuing review timelines or processes are important.
  - Evaluate whether current international regulations—e.g.ICH, European Union regulations—offer equivalent protections.

Zeke's Recommendations

- A second issue that needs attention: How much oversight should U.S. regulators have over actual research oversight being conducted in other countries—China, Mali, etc?
  - Knowing that OHRP is a very small office and not likely to grow and that we want assurance ethical standards are being adhered to, how much effort should OHRP place on actually investigating adherence.
  - What would qualify as adequate adherence efforts?