Human Subject Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay and Ambiguity for Investigators

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Objectives

- Why is the Department of Health and Human Services proposing changes to the regulations for the protection of human subjects?

- What are the proposed changes and how will they affect investigators and IRBs?

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Changes are being proposed to…

- 45 CFR Part 46
  - ***Subpart A – Common Rule***
  - Subpart B,C,D – Vulnerable Populations
  - Subpart E – IRB Registration

- Office for Human Research Protections (OHRP**)**

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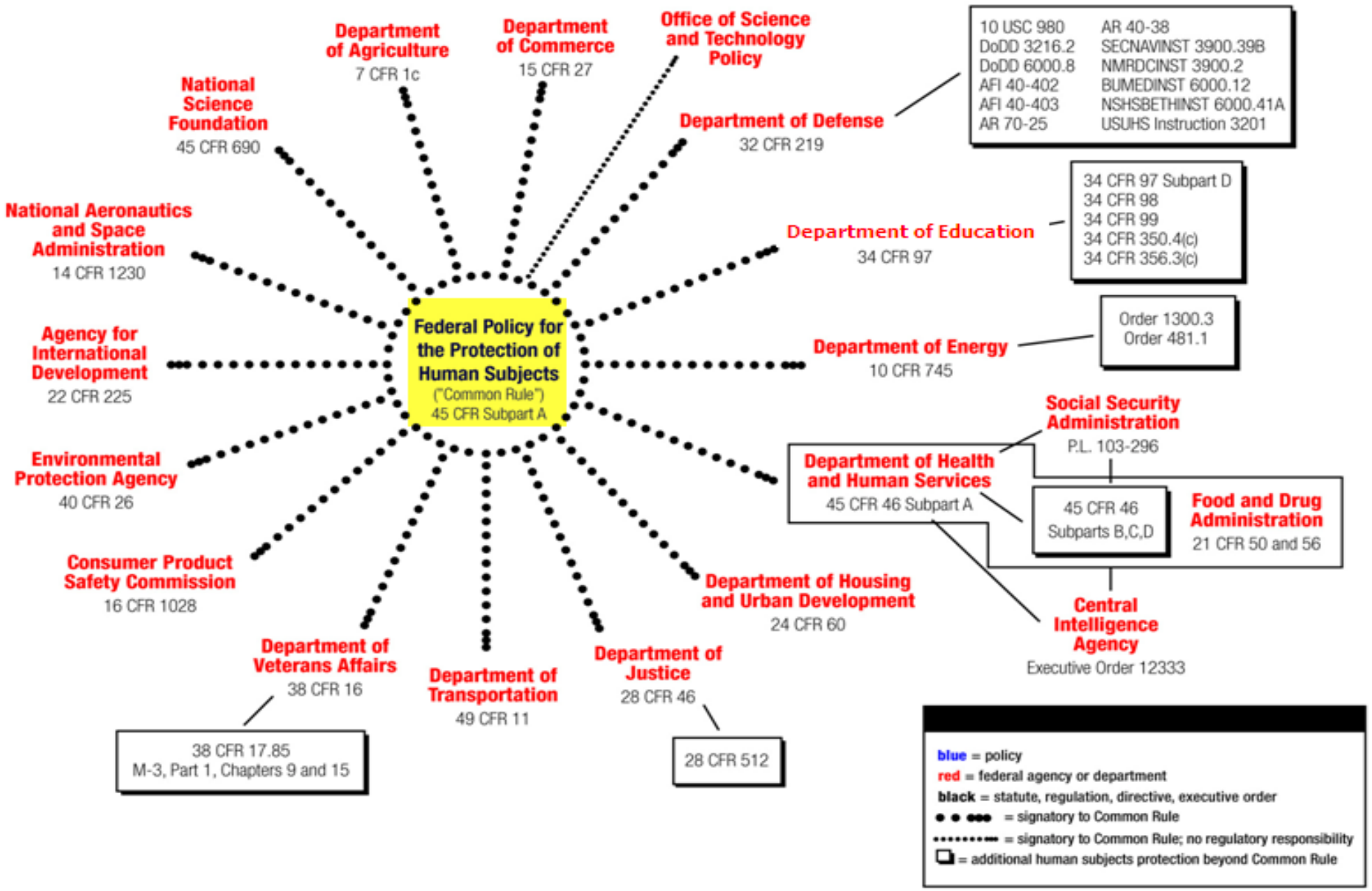
Current Federal HRP Regulatory Structure



Why are changes being proposed?

- ***It's about time…***
  - 1981 – Regs. revised and expanded based on National Commission/Belmont Report recommendations
  - 1991 - Subpart A adopted by 14 other federal agencies; became known as the "Common Rule"
  - No significant changes in 30 years
- ***Yet, Human Subjects Research has changed…***
  - Increase in Human Subjects Research
    - Domestic and International
    - Multi-site research
    - Biospecimens and Repositories
  - Social and Behavioral Scientists
    - Concern that S&B research is over-regulated
    - Common Rule does not apply; imposes a biomedical model

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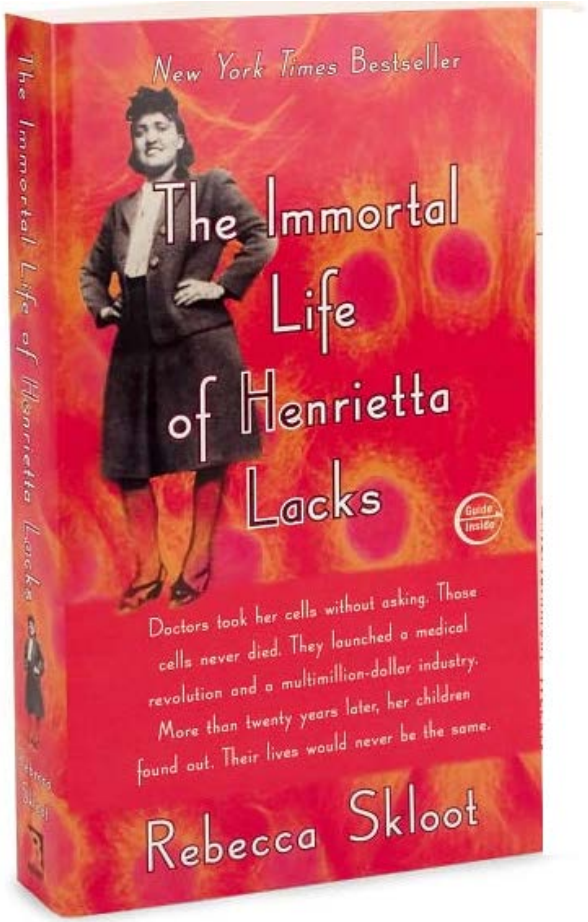
Henrietta Lacks – HeLa Cells

In culture, cancer cells can go on dividing indefinitely, if they have a continual supply of nutrients, and thus are said to be "immortal." A striking example is a cell line that has been reproducing in culture since 1951. (Cells of this line are called HeLa cells because their original source was a tumor removed from a woman named Henrietta Lacks.)



Havasupai Indians and Arizona State Univ

The New York Times

Indian Tribe Wins Fight to Limit Research of Its DNA

The NEW ENGLAND JOURNAL of MEDICINE

The Havasupai Indian Tribe Case — Lessons for Research Involving Stored Biologic Samples

Michelle M. Mello, J.D., Ph.D., and Leslie E. Wolf, J.D., M.P.H.

N Engl J Med 2010; 363:204-207 | July 15, 2010

PHOENIX New Times

News

Havasupai Tribe Win Nice Settlement From ASU In Scandalous Blood-Sample Case

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Unpublished Guatemala Syphilis Research

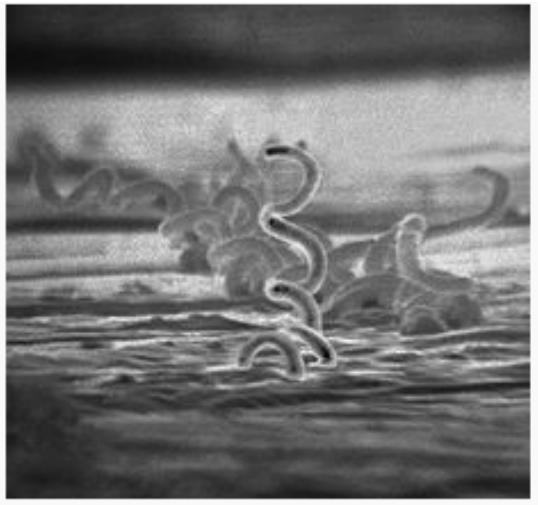
USA TODAY

Guatemala revelation recalls era of research abuses

U.S. Secretary of State Hillary Clinton, seen earlier this week, apologized to Guatemala about U.S. government researchers using prostitutes to deliberately infect prison inmates in Guatemala with syphilis in the 1940s. (J. Scott Applewhite/Associated Press)

The New York Times

U.S. Apologizes for Syphilis Tests in Guatemala



REUTERS EDITION: U.S.

U.S. researchers broke rules in Guatemala syphilis study

President Obama

- November 24, 2010 - Asked the Commission for the Study of Bioethical Issues to conduct a thorough review of human subjects protections to determine if Federal regulations and international standards adequately guard the health and well-being of research participants

- January 18, 2011 - Issued an Executive Order requiring all federal agencies to streamline the regulatory process while continuing to protect public health and safety

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ANPRM to Common Rule

- July 26, 2011, the Department of Health and Human Services (DHHS) announced an ambitious plan to update the regulations regarding the protection of human subjects in research.

- The changes can be found in the Advance Notice of Proposed Rulemaking (ANPRM), Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators.

- The government sought the public's input on several issues related to the oversight of human research. The DHHS summary table of all 19 proposed revisions is also available.

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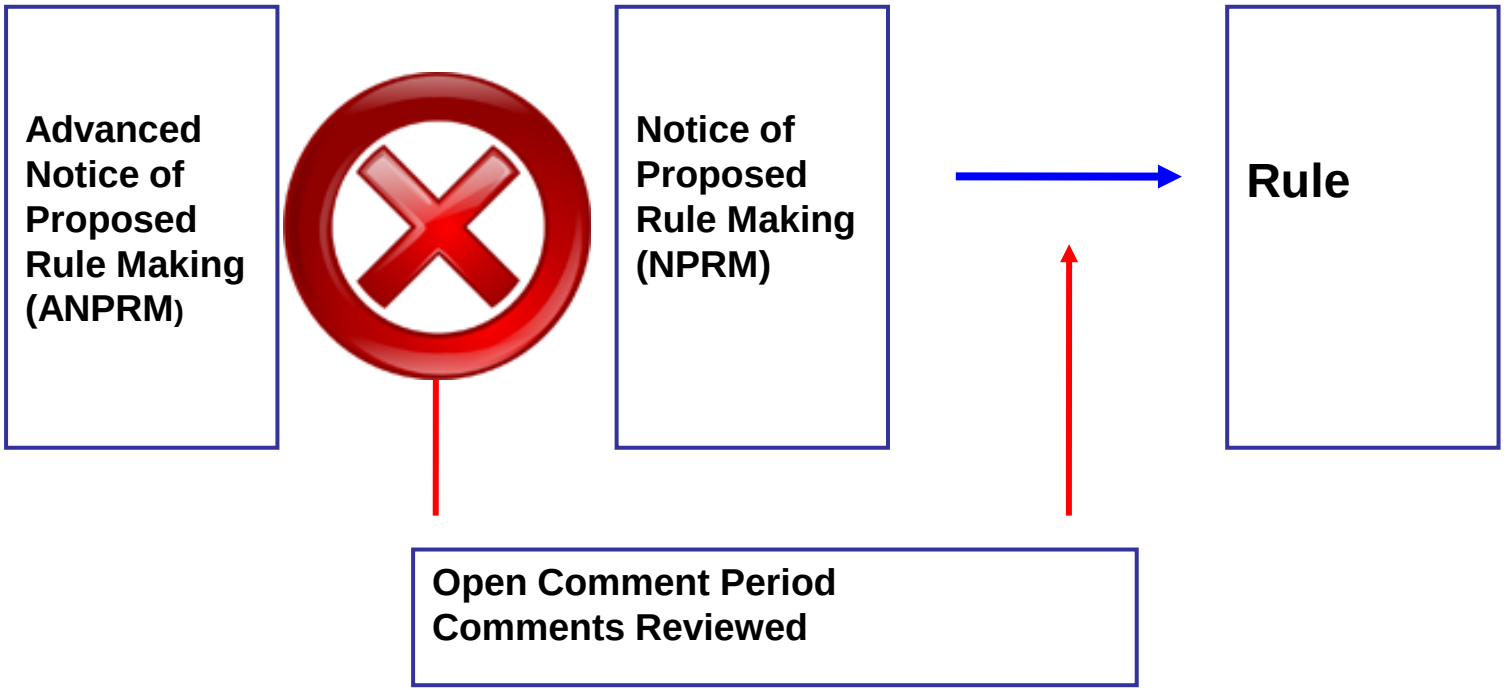
The Process



NOTE: All comments will be posted without change to http://www.regulations.gov

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Summary of Proposed changes

1. Refinement of the existing **risk-based regulatory framework** (Section II);
2. Utilization of a single IRB review of record for domestic sites of **multi-site studies** (Section III);
3. Improvement of consent forms and the **consent process** (Section IV);
4. Establishment of mandatory data security and **information protection standards** for all studies that involve identifiable or potentially identifiable data (Section V);

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Summary of Proposed changes (cont'd)

5. Establishment of an improved, more systematic approach for the collection and analysis of data on **unanticipated problems and adverse events** (Section VI);
6. Extension of Federal regulatory protections to **all research**, regardless of funding source, conducted **at institutions** in the U.S. that receive some Federal funding from a Common Rule agency for research with human subjects (Section VII); and
7. Improvement in the **harmonization of regulations** and related agency guidance (Section VIII).

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Proposed Changes include…

- ***Improving Efficiency***
  - No Annual Review of Minimal Risk (expedited) Research
  - No Annual Review of Greater than Minimal Research if activities limited to Long-term Follow-up or Data Analysis

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Proposed Changes include…

Improving Efficiency…

- Renaming “exempt” research as “excused”
- Expand categories to include more social/behavioral methods for example interviews, focus groups, and surveys with competent adults even if identifiable information retained
- Primarily risk is informational; must meet standards to protect privacy/confidentiality (HIPAA)
- Requiring researchers to register “excused” research
- IRB review not required to commence research
- Requiring mandatory auditing of “excused” research

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Proposed Changes include…

- ***Improving Efficiency*** (cont.)
  - Minimal Risk Categories would be regularly updated; include research procedures currently reviewed by full board
    - Dexa Scan
    - Skin Biopsy
  - Mandate that a single IRB conduct the review of domestic multi-site studies
    - Would not apply to international research
    - Would not apply to FDA regulated device trials
  - Coordinate and harmonize, where possible, with other federal agencies
    - Department of Defense
    - Department of Education
    - FDA

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Proposed Changes include…

- ***Enhancing Protections***
  - Use of biospecimens would require written informed consent, even if specimens are derived from a non-research procedure (i.e., discarded tissue) and will be de-identified
    - Could use a standardized form allowing open-ended use in future research
  - Mandate new, HIPAA-like data security and information protection standards that would apply to all research data
    - Use of encryption
    - Audit trails for repositories

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Proposed Changes include…

- ***Enhancing Protections*** (cont.)
  - Standardize Informed Consent Documentation
    - Revise required elements of informed consent
    - Limit length of document
    - Standardize templates
  - Changes to informed consent process
    - Clarification of the waiver criteria
    - Allowing more oral consent
    - Requiring consent for use of pre-existing biospecimens regardless of identifiability

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Proposed Changes include…

Strengthening data protections….

- Extend federal oversight to non-federally funded studies if institution receives any funding from Common Rule agencies
- Aligning Common Rule and HIPAA standards for de-identified data
- Classifying all biospecimens as identifiable and requiring consent for use
- Enhancing data security standards
- Data can still be considered de-identified if investigators see the identifiers but don’t record them
- Require periodic random audits for enforcement

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Proposed Changes include…

Strengthening data protections….

- Harmonize safety reporting guidance across all federal agencies
- Adverse events and unanticipated problems would be submitted to and stored in a central database
- Standardize data elements for reporting
- Implementing a web-based Federal-wide portal for safety reporting

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Summary of proposed changes

Improving effectiveness	Enhancing protections
Distinction between types of risk – note informational risk	Federal oversight expanded
Eliminating some required continuing review	Central database for adverse events
Improved application of expedited review for research posing minimal risk	Informed consent improvements
Single IRB review of multisite studies	Written consent for use of biospecimens
Harmonization of guidance	Confidentiality protections

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Emanuel and Menikoff: 10.1056/NEJMsb1106942 published July 25, 2011 at NEJM.org - taken from PRIM&R webinar – Pearl O'Rourke

Comments on ANPRM

- Requiring all US Institutions that receive some federal funding from Common Rule agencies to apply the regulations to all research is problematic
- HIPAA criteria should not be applied to all research
- With single IRB review of multi-center studies, guidance must be written to clarify the role of the local IRB, if any
- Need to address inconsistencies between FDA, HHS, PHS regarding financial conflicts of interest

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Comments on ANPRM

- How does permitting researchers to make their own determinations about an “exempt” or “excused” study enhance human subject research protections?
- Mandatory auditing of “excused” studies will increase burden on IRB’s and Investigators
- Eliminate expedited review categories – declare all research involving minimal risk as eligible for expedited review and define procedures which involve no more than minimal risk

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Comments on ANPRM

- Documentation of consent should be permitted in ways other than signed, written forms
- Criteria for waiving or altering consent should be refined
- Give investigators flexibility in deciding what information should be provided during the consent process – eliminate excessive boilerplate language

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Comments on ANPRM

- Further definition is needed to define vulnerable populations
  - Current definition is narrow and does not take into account different types of vulnerability and how to provide best protections

- Guidance is needed to address which individuals may serve as legally authorized representatives

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Thank you

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