Overview and Discussion of the NPRM and Its Implications

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Broad Overview

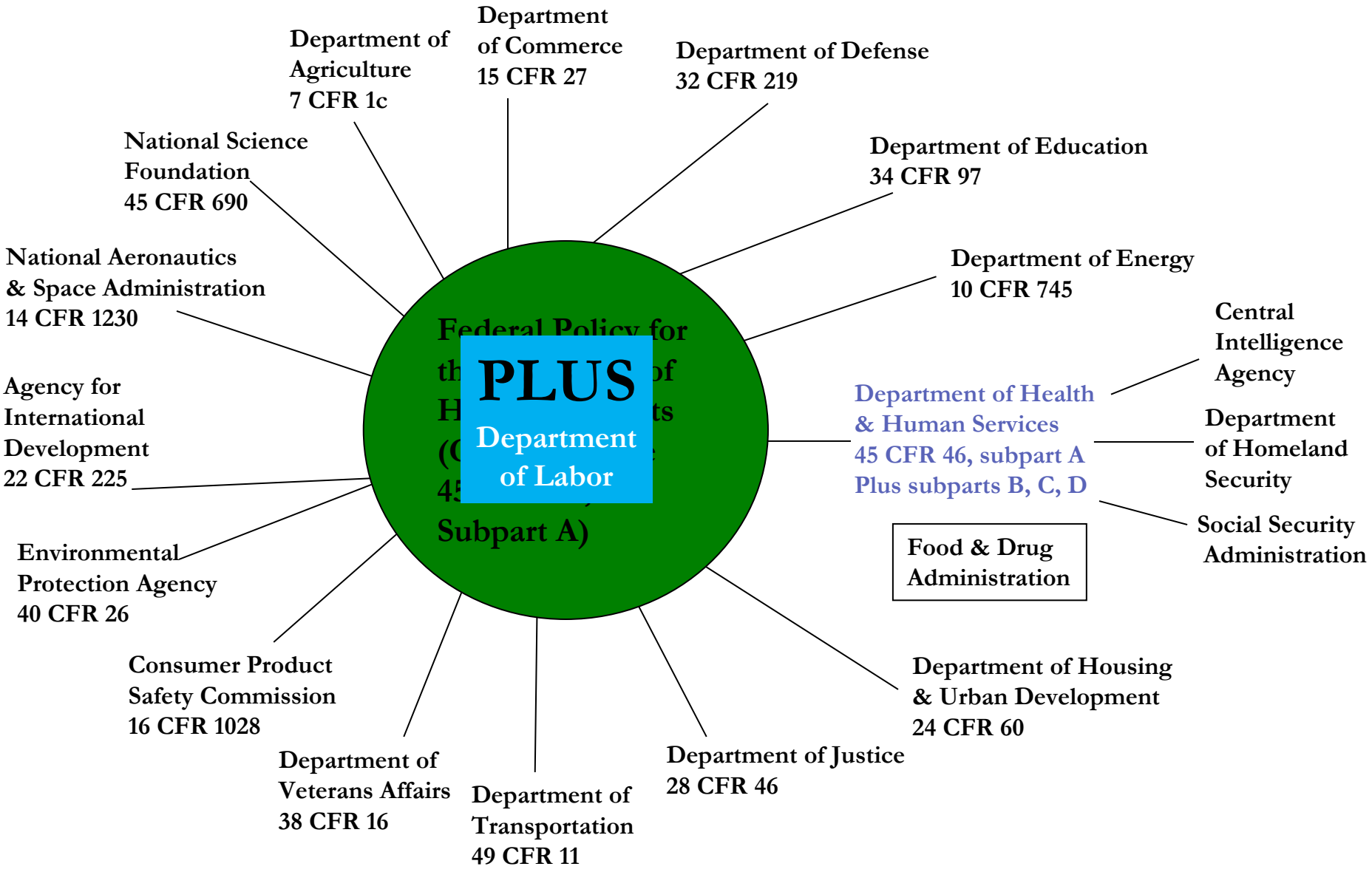
- Background
- Goals of the NPRM
- Summary of major changes

Why Revise the Common Rule?

- Changes in research
- Attempt to better protect human subjects who are involved in research
- Attempt to reduce burden, delay, and ambiguity for investigators, to facilitate valuable research

Overview of Rulemaking Process

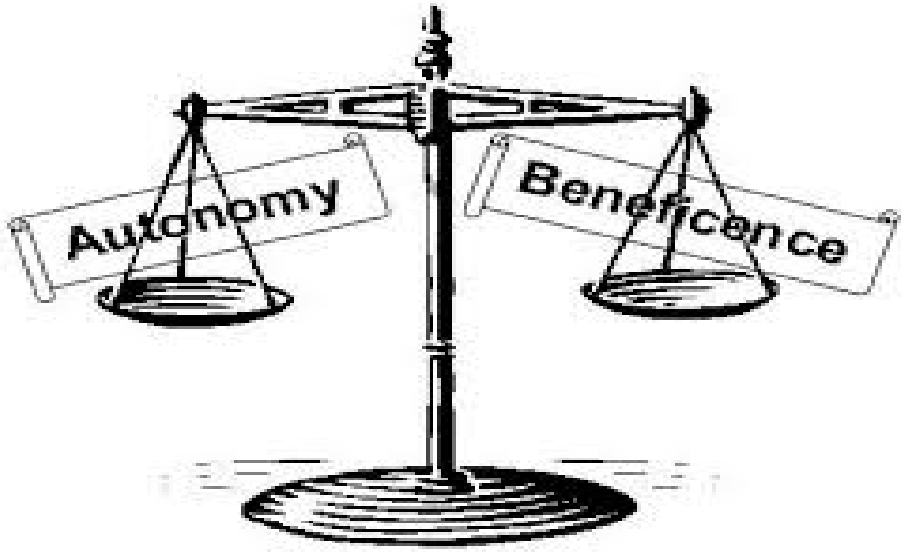
18 Common Rule Departments & Agencies



Goals

- Better protect human subjects involved in research

- Simplify the current oversight system and reduce inappropriate administrative burdens



SUMMARY OF MAJOR CHANGES

Major Changes

1. Improve informed consent – content and organization – to facilitate understanding
2. Almost always require informed consent for secondary use of biospecimens – regardless of identifiability
3. Mandate single IRB review of multi-site research conducted at U.S. institutions
4. Eliminate continuing review for certain minimal risk research

Major Changes (2)

5. Extend the scope of rules to cover clinical trials – regardless of the source of funding
6. Require privacy safeguards
7. Exclude certain activities from coverage
8. Expand the categories of research that are exempt from the rules, better calibrating the level of review to the level of risk

Major Change
1. Improving Informed Consent

Major revision to introduction of §116 does the following:

- Emphasizes need to provide *essential* information a reasonable person would want to know, before providing other supplemental information to the subject

Improving Informed Consent

Major revision to introduction of §116 does the following:

- Information must be presented in sufficient detail, and must be *organized and presented* in a way that facilitates prospective subject's understanding of the reasons why one might or might not want to participate

Posting of Clinical Trial Consent Forms

- For clinical trials: within 60 days of being closed to recruitment, copy of final consent form must be posted on government website
- One-time requirement

Major Change: 2. Requiring Consent for Secondary Research with De-identified Biospecimens

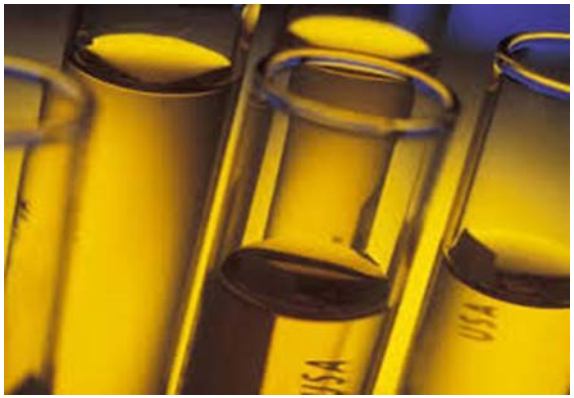
- Consent will almost always be needed to conduct secondary research with a biospecimen (e.g., excess blood collected in clinical care), even if de-identified
- Compare to current rules: de-identified biospecimen not considered a human subject, thus no consent needed
- This change accomplished by expanding definition of human subject

Major Change: 2. Requiring Consent for Secondary Research with De-identified Biospecimens

- However, one major category of biospecimens will be excluded from this new requirement – could still conduct research, if de-identified, without consent
- Exclusion: research designed to generate information already known about a person
- Example: evaluating a new in vitro test for a particular genetic mutation

Major Change: 2. Requiring Consent for Secondary Research with De-identified Biospecimens

- The new consent requirement could be met by using a new "broad consent" form to be released by federal government
- Would allow biospecimen to be stored and used for *unspecified future research* – in contrast with consent for a specific study
- Storage and use would be exempt if form used



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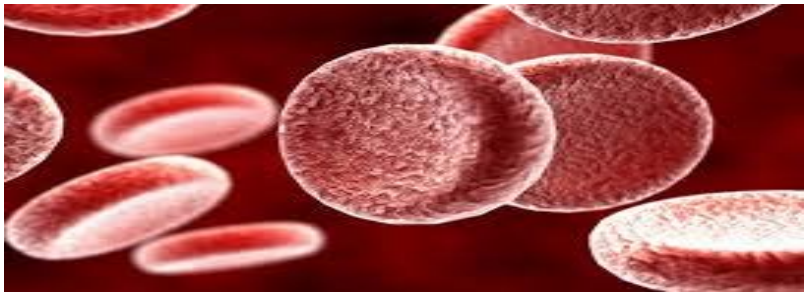
Waiver of Consent Requirements More Stringent for Biospecimens

- Compelling scientific reasons for the use of biospecimens
- Research could not be conducted with other biospecimens from which informed consent was/could be obtained
- IRBs would not be permitted to waive consent if individuals were asked to provide broad consent and declined



Waiver intended to be **rare!**

How Do these Proposals Affect Secondary Research with ***Data***?

- No change to definition of what constitutes "identifiable private information" – it would not be expanded
- Proposal from ANPRM to implement HIPAA standards is no longer being proposed

How Do these Proposals Affect Secondary Research with ***Data***?

- Core rules relating to secondary research with de-identified data are unchanged: it would still not constitute a human subject, and not be under the regulations
- Furthermore, new rules relating to biospecimens do not alter rules relating to secondary research with data, regardless of whether data had been obtained from a biospecimen or some other way
- All data, regardless of source, treated same way

How Do these Proposals Affect Secondary Research with ***Data***?

- In several ways, proposals increase ability to conduct research with identified data without consent, assuming appropriate protections in place
- While new broad consent forms can be used by researchers to obtain consent for secondary use of identifiable data, that is merely a new option
- Unlike for biospecimens, there are many other options for data researchers apart from obtaining broad consent

How Do these Proposals Affect Secondary Research with ***Data***?

- Researchers could
  - Use data stripped of identifiers
  - Keep a one-way link to identifiers
  - Obtain IRB waiver allowing use of identifiers
  - Use new exemption allowing use of identifiable data with notice instead of consent
- Any one of these might be preferable to obtaining broad consent (in contrast to few options for research with biospecimens)

Major Change
3. Single IRB Review of Multi-site Research

- Require single IRB review for multi-site research conducted in U.S. institutions – unless:
  - More than single IRB review required by law; or
  - Federal department or agency determines single IRB review is not appropriate
- Hold independent IRBs directly responsible for compliance with the Common Rule

Major Change
3. Single IRB Review of Multi-site Research

- Note that this change does not prevent any site from conducting whatever additional review it wants, nor does this bind any site to participate in a particular study
- Can be viewed as making the system more flexible – instead of each site needing formal IRB review, they can now decide what review works best for them

Major Change
4. Eliminate Some Continuing Review

- No continuing review required if study undergoes expedited review
- No continuing review required if study has completed interventions and only involves analyzing data, including newly collected clinical data
- Annual confirmation that research is ongoing without changes requiring continuing review
- IRB can override this default and require continuing review – but this must be documented

Major Change
5. Extend Common Rule to Cover Clinical Trials

- Scope expanded to cover all clinical trials, regardless of funding source, if:
  - Conducted at a U.S. institution that receives federal funding for non-excluded, non-exempt human subjects research
- Does not include clinical trials subject to regulation by the FDA

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Major Change
6. New Privacy Standards

- New privacy standards would apply to non-exempt research
- Secretary of HHS would promulgate standards that would involve minimal cost and effort for individual investigator to implement

Major Change
6. New Privacy Standards

- Default position that if privacy safeguards at §105 are met, no need for additional IRB review unless those protections are deemed insufficient
- Also required for some exemptions

Major Change
7. Exclusions

- Certain categories of activities are excluded from coverage under the Common Rule
- ***No review required***
- ***Not a new concept*** – merely clarifying line regarding what already currently regularly happens (e.g., determination if activity is research or involves human subjects)

Major Change
7. Exclusions

- Several categories: Activities that should be deemed not to be research, are inherently low risk, or where protections are separately mandated
- Which category an exclusion fits under doesn't affect the conditions of the exclusion – categories are largely merely descriptive headings (contrast with exemptions)
- Thus, e.g., no need for specific definition of "low risk," or how it differs from "minimal risk"

Exclusions – 11 total

- Four involve governmental functions or government-generated information
- Four involve the secondary use of biospecimens or identifiable private information
- One involves interventions
- One involves testing, talking, or watching (like current exemption 2, for surveys, etc.)
- One involves oral history, journalism, biography or historical scholarship

Exclusions – some examples

- Research involving surveys, interviews, etc., where the research is either (i) anonymous, or (ii) disclosure of the information collected will not be harmful to the participants
  - This is very similar to current exemption 2, but now it is an exclusion, not an exemption

Exclusions – some examples

- Quality assurance activities aimed at implementation of an accepted practice
  - Main risk is likely that this activity may not increase the use of that practice, subjects no worse off
  - Does not apply to activities to evaluate the accepted practice (which are less like quality assurance)
  - Example: “checklist” study to reduce infections after inserting central line

Exclusions – some examples

- Research subject to HIPAA rules
  - Only applies to secondary research involving data
  - Purpose is to eliminate duplicative oversight by Common Rule and HIPAA – both are largely designed to protect from risks of breach of confidentiality

Exclusions – some examples

- Secondary research using data where researcher sees but does not record identifying information (e.g., from medical records)
  - Very similar to portion of current exemption 4, but now as an exclusion, not an exemption
  - It also eliminate current exemption 4 limitation that data must all exist before the start of the study

Major Change
8. Revise the Categories of Exempt Research

- To better calibrate the level of review to the level of risk
- New categories would allow exemption of research that currently requires IRB review and approval – an expansion of what is exempt
- While some new categories are subject to conditions (e.g., privacy protections), that is done to enable the expansion to take place

Major Change
8. Revise the Categories of Exempt Research

- Contrast with exclusions: there are procedural requirements for exemptions
- Exemption determination must take place and be documented in some way

Major Change
8. Revise the Categories of Exempt Research

- Exemption determination can be made by researcher using government-produced web-based decision tool
- Researcher would answer questions, and tool would determine if research is exempt, or not exempt, or if review by person who knows the regulations well is needed
- Decision tool would not give researchers any discretion to make their own determinations

Exemptions – 8 total

- One involves governmental functions
- Three involve the secondary use of biospecimens or identifiable private information
- Three involve interventions
- One involves collecting new information by testing, talking, or watching

Exemptions – some examples

- Surveys, interviews, etc., even if sensitive information is collected, so long as appropriate privacy protections are in place
  - This is a version of current exemption 2, expanded to cover collecting sensitive information, but with requirement to follow new privacy safeguards

Exemptions – some examples

- Benign interventions where data collected from adult by verbal or written responses
  - A type of expansion of current exemption 2
  - Examples: Having someone answer questions after reading something; Watching and responding to flashes of light on a computer monitor

Exemptions – some examples

- Secondary use of identifiable private information, if holder of information has given notice this may take place, and appropriate privacy protections in place
  - This is a new category of exemption
  - NPRM asks about what should constitute appropriate notice
  - May be alternative to obtaining broad consent for some researchers, assuming holder of information has given notice

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