

Possible Regulatory Changes in
Oversight of Human Subjects
Research
(Otherwise known as the NPRM)

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Notice of Proposed Rulemaking (NPRM)

Issued

- September 8, 2015
- Department of Health and Human Services

Federal Policy for the Protection of Human
Subjects (known as the Common Rule)

*But First, Some
Background*

Advance Notice of Proposed RuleMaking (ANPRM)

- ANPRM
 - Precedes an NPRM if the government needs public input on various issues before proposing a rule
- Published in the Federal Register: July 25, 2011
 - *Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators*

Rulemaking Under the Administrative Procedure Act (APA)

- The APA (1946) established basic framework of administrative law governing federal agencies, including rulemaking. 5 U.S.C. § 553, *et seq.*

Rulemaking Under the APA

- APA adopted “formal rulemaking” and “informal rulemaking” procedures
- “Formal rulemaking” occurs only when a statute other than APA requires rulemaking on the record after an agency hearing
- The human subjects protection regulation (45 C.F.R. Part 46) is a product of “informal rulemaking” procedures

Informal Rulemaking Procedures--1

- Referred to as “notice-and-comment” rulemaking
- Basic 3-step process, or procedural “floor”
 - Publication of Notice of Proposed Rulemaking (“NPRM”) in the *Federal Register*
 - Public Participation through written comments
 - Publication of a “final rule” not less than 30 days before rule’s effective date

Informal Rulemaking--2

- NPRM components: preamble, rule text, and analyses required by statute or executive order
- Draft NPRM usually prepared by agency program office (OHRP)
- NPRM submitted to internal agency clearance process
- After internal clearance, submitted to OMB, for review and comment by affected agencies

Informal Rulemaking--3

- After notice-and-comment period agency reviews comments and prepares response; revises text of final rule and analyses as appropriate
- Proposed “final rule” then submitted for internal agency and OMB review as with NPRM
- Published as final rule in the *Federal Register*
- Final rules have the force and effect of law

Common Rule Promulgation

- Regulations are typically promulgated by individual agencies
- For a regulation to have federalwide effect, the regulation will go through a process of joint agency promulgation to become a “common rule”
- Part 46 was promulgated as a common rule

Timing Issues-1

- Often 1 year or more (sometimes substantially more) between publication of NPRM and the final rule

Timing Issues-2

- Subpart B—NPRM 5/20/98
 - Final Rule 1/17/01
- Subpart C—NPRM 1/5/78
 - Final Rule 11/16/78
- Subpart D—NPRM 7/21/78
 - Final Rule 3/8/83

*The Human Subjects
Research Common Rule
and its
NPRM*

What is the Common Rule?

- Published in 1991
- Codified in separate regulations by 15 Federal departments and agencies
 - 3 other departments/agencies did not codify - but follow them
 - Each agency includes in its chapter of the Code of Federal Regulations [CFR] section numbers and language that are identical to those of the HHS codification at 45 CFR part 46, subpart A

Five Subparts of 45 CFR 46

Subpart A “Common Rule” (Federal Policy for the Protection of Human Subjects) (1991)

Subpart B Additional protections for pregnant women, human fetuses, and neonates (2001)

Subpart C Additional protections for prisoners (1978)

Subpart D Additional protections for children (1983)

Subpart E Registration of IRBs (2009)

Common Rule and the Current NPRM

- Significant changes
 - Scope
 - Applicability
- Published in Federal Register September 8, 2015
- 131 pages
- 88 questions/requests for comment
 - ??NPRM v. ANPRM
- Comments were due on January 6, 2016
(extended from December 7, 2015)

Major Themes

- Modernize, strengthen and make the regulations more effective
- Reduce burdens, delay, and ambiguity for investigators

The following slides represent only selected,
summary elements of the NPRM

Exclusions from the Common Rule

(new terminology)

Exclude from the Common Rule certain categories of activities that

- Are deemed not to be research
 - Are inherently low risk
 - Protections similar to those usually provided by IRB review are separately mandated
-
- No IRB review needed to determine this status
 - Investigators could make the determinations

Exemptions in the Common Rule

Extensive and Complex Coverage in the NPRM

- New categories added
- Intended to accommodate changes in the scientific landscape
- Better calibrate the level of review to the level of participant risk
- Most studies would not require administrative or IRB review
- Introduction of privacy safeguards for biospecimens and identifiable private information
- A decision tool will be created to assist with exempt determinations
- Determinations can be made by the PI (or others)
- The IRB or the institution must maintain records of exempt determinations

Exemptions – Biospecimens and Identifiable Private Information

Allan Loup will address in his presentation

Expand the Definition of Human Subjects

- Human subject means any living individual about whom an investigator...conducting research
 - (i) Obtains data through intervention...
 - (ii) Obtains, uses...identifiable private information
 - (iii) Obtains, uses studies, or analyzes biospecimens (NEW)

Informed Consent - Facilitate Understandability

- New requirements regarding the information given to prospective subjects - suggests a more evidence based approach.
- Consents must be organized and presented in a way that does not just provide facts, it must facilitate the prospective subject's understanding of the reasons why one might or might not want to participate.

Informed Consent - Format

- Provide the Common Rule-required information, before providing other information to the subject
 - The consent document would include only the elements required by the Common Rule
 - All other information included in an appendix
- The NPRM intends for this scheme to
 - Substantially shorten consent forms
 - Avoid burying key information in long and overly complex documents

Informed Consent - HIPAA Authorization

- HIPAA authorization combined with informed consent
 - Already standard practice for IRBMED
- The required HIPAA authorization elements must be included in the consent document and not the appendix

Informed Consent – New Basic Element – Future Use

Based on study design, the consent form will need to inform subjects either that:

- Identifiers might be removed from the data and that the non-identified data could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject; or
- The subject's data collected as part of the research would not be used or distributed for future research studies, even in a non-identified form*

*NPRM anticipates that few investigators would elect to offer this option in part because of the challenges of marking and tracking such decisions.

Informed Consent – Additional New Elements

- 3 additional elements of consent would require prospective subjects to be
 - Informed that their biospecimens may be used for commercial profit and whether the subject will or will not share in this commercial profit;
 - Informed whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and
 - Provided with an option to consent, or refuse to consent, to recontact by investigators to seek additional information or biospecimens or to discuss participation in another research study.

Clinical Trials- Oversight Expanded

- Estimated that there are 1,399 clinical trials currently not subject to oversight by either the Common Rule or FDA regulations
- Extend the regulations to cover clinical trials conducted at an institution in the United States that receives federal support from a Common Rule department or agency for nonexempt human subjects research, regardless of the funding source of the trial
 - Eliminates any regulatory flexibility
- Extension of the regulations would not apply to clinical trials already regulated by FDA

Eligibility and Recruitment- Waivers Eliminated

- IRBs would be permitted to approve studies in which investigators, for eligibility screening and recruitment purposes only:
 - Obtain identifiable private information from prospective human subjects of research without informed consent
 - If the research proposal includes an assurance that the investigator will implement standards for protecting the obtained information.
- Eliminates the need for IRBs to waive the informed consent requirement required under the current Common Rule
 - NPRM views as burdensome and unnecessary to protect subjects
 - Makes it consistent with FDA's regulations for recruitment, which do not require informed consent or a waiver of informed consent for such activities

Posting of Consent Forms

- For clinical trials conducted or supported by a Common Rule department or agency the entity conducting the clinical trial would need to
 - Post the final document on a public federal website
 - Include the name of the clinical trial and information about whom to contact for additional details about the trial
 - Post within 60 days after the trial closes to recruitment
- Intended to improve the quality of consent forms in federally funded research by assuring that they eventually become subject to public scrutiny

Cooperative Research – Single IRB

- Single IRB review mandated for US institutions engaged in cooperative research
- Reviewing IRB selected by the federal department or agency supporting or conducting the research, or by the lead institution if there is no such funding agency or department.
- Not apply to
 - Cooperative research for which more than single IRB review is required by law (e.g., FDA-regulated devices);
 - Research for which the federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular study.
- Although a local IRB may conduct its own additional internal review, such a review would not be binding on the local site if not adopted by the single IRB, nor would its terms be enforced by OHRP.

Data Security Standards

- Set uniform standards that would help to assure appropriate privacy and confidentiality protections to all subjects
- Require that investigators and institutions implement reasonable and appropriate safeguards for biospecimens or identifiable private information to:
 - Protect the security or integrity
 - Reasonably protect from any intentional or unintentional use, release, or disclosure
- The NPRM would allow investigators and institutions to implement either:
 - A list published by the Secretary of HHS of specific measures that an institution or investigator can use to meet the requirements
 - Safeguards that meet the standards in the HIPAA rules

Continuing Review of Research

- Eliminate continuing review for minimal risk studies that qualify for expedited review, unless the IRB reviewer documents why continuing review should occur
- For studies initially reviewed by a convened IRB, continuing review would not be required (unless specifically mandated by the IRB) when the study reaches the stage when it involves either:
 - Analyzing data (including identifiable private information)
 - or
 - Accessing only follow-up clinical data from procedures that subjects would undergo as part of standard care for their medical condition or disease

Harmonization of Agency Guidance

- The NPRM would require that federal guidance on the requirements of the Common Rule be issued only after consultation, to the extent appropriate, with other Common Rule departments and agencies, if feasible.
- FDA is not a Common Rule agency but the preamble specifies that FDA intends to modify its regulations to the extent appropriate.
- FDA and OHRP will continue to work together in developing guidance on their respective regulatory requirements that are found both in FDA regulations and in the Common Rule, to the extent feasible.

U-M Response

- Signatory on national position statements
 - COGR (Council on Government Relations)
- UMOR submitted robust compiled comments from units comprising the Human Research Protection Program (HRPP)
- Individuals or units submitted comments

QUESTIONS?

(disclaimer: the answer is likely unknown)