OTICE OF PROPOSED RULEMAKING (NPRM) FOR EVISIONS TO THE COMMON RULE

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NE 21, 2016

SCLAIMER

SACHRP members and SACHRP subcommittee members represent some of the most knowledgeable and experienced individuals in the nation with respect to the human subjects regulations. Despite extensive study the NPRM in collaboration with numerous colleagues, the universal assessment is that the proposals are virtua impenetrable due to opaque language, unclear concepts, the overlapping nature of various elements, and the intricate relationships to elements to another. A common refrain is, 'If we cannot understand this, where will th leave the average IRB administrator, and investigator?'"

- Secretary's Advisory Committee on Human Research Protections (SACHRP)
- **SACHRP Charter**: provide expert advice and recommendations to the DHHS secretary on issues associated with the protection of human research subjects

"This proposed rule has confused and frustrated a very engaged and thoughtful community of investigators, institutions, and ethicists."

- AAMC

VERVIEW

History of federal research regulations

The rulemaking process

Overview of proposed changes

Critiques: Public comments and my own

What's next/timeline

Discussion

ISTORY OF FEDERAL RESEARCH REGULATIONS

OM MY DISSERTATION ☺

HAT LED TO FEDERAL REGULATIONS FOR RESEARCH?

Pre- 1950 Informal rules; 1950s rules at NIH for intramural research

940s-1980s: Scandals

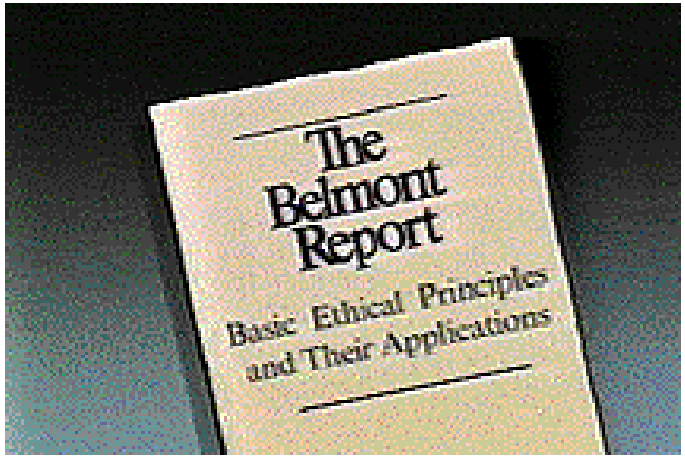
970s: Congressional investigations, Presidential Commissions (first one in 1974)

Belmont Report (1979)

Federal Regulations (1981)

HE BELMONT REPORT

Ethical Principles and Guidelines for the Protection of Human Subjects of Research



The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

April 18, 1979

HE BELMONT REPORT (1979)

- **Respect for Persons**
  - Promote individual autonomy
  - Protection of individuals with reduced autonomy
- **Beneficence**
  - Don't harm; maximize benefits and minimize harms
  - Obligations on investigators (consider benefit/risk of specific project)and society (consider long-term benefits/risks of improving knowledge and advancing science)
- **Justice**
  - Equitable distribution of research costs and benefits

HS PROTECTION OF HUMAN SUBJECTS REGULATIONS

45 CFR part 46 – HHS Protection of Human Research Subjects

- Subpart A is the Federal Policy for the Protection of Human Subjects "Common Rule" (1991)
  - Applies to 17 other Federal Departments and Agencies
- Subparts B (pregnant women, fetuses and neonates), C (prisoners), D (children), E (IRB registration)

HE REGULATIONS APPLY WHEN:

- Research involving human subjects conducted or supported by HHS that is not otherwise exempt

-OR-

- Non-exempt human subject research covered by Assurance of Compliance

- **Not applicable** to research on de-identified information or biospecimens
- **Not applicable** to HSR that is not federally supported, conducted, or regulated

Slide courtesy of Laura Odwazny, DHHS General Couns

GULATORY REQUIREMENTS

3 basic requirements:

- Assurance of compliance
  - Federalwide Assurance (FWA)
- Institutional review board (IRB) review of non-exempt human subjects research
- Informed consent, unless waived

Slide courtesy of Laura Odwazny, DHHS General Couns

AKEAWAYS

This is a unique system in which federal regulations are enforced by local institutions with heavy reliance on se
eporting

Compared to other industries, scientists have A LOT of autonomy

Local institutions have a fair amount of latitude in interpreting/applying the regulations

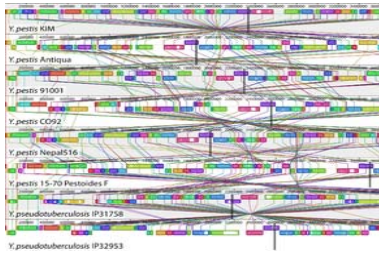
Remember: The federal regulations are an ethical "FLOOR" not a "CEILING"

- Institutions may (for good reasons) require "more" from investigators

HE RULEMAKING PROCESS

E YOU SURE YOU WANT TO KNOW HOW THE SAUSAGE IS MADE?

VHY REVISE THE COMMON RULE?



FR 46 1981; Common Rule 1991 – no substantive revisions since then

ges in volume and landscape of research

ink which protections are appropriate and ought to be afforded to individuals involved in research,
facilitating valuable research (weighing risks to individuals against benefit to society)

ider of how to better calibrate the level of regulatory protections to the risks of particular
rch activities

ce burden, delay, and ambiguity for investigators

iate pressure on HRPPs by streamlining IRB review and reducing administrative burden

Slide courtesy of Laura Odwazny, DHHS General Cou

GULATORY HISTORY: THE A (ADVANCED) NPRM(S)

ANPRM even I didn't know about

Published March 5, 2009, by HHS

Requested comments on whether OHRP should pursue rulemaking to exert compliance directly over IRBs and IRB organizations

Attempt to provide reassurance to regulated institutions re: relying on an external IRB

30 comments received

Common Rule ANPRM

- Published July 26, 2011 by HHS "in coordination w the Office of Science and Technology Policy"
- "Human Subjects Research Protections: Enhanci Protections for Research Subjects and Reducing Burden, Delay and Ambiguity for Investigators"
- Sought comment on possible areas of change
- **1000+ comments received**

Slide courtesy of Laura Odwazny, DHHS General Couns

PRM seeking comment
n proposed changes
the Common Rule

Federal Register / Vol. 80, No. 173 / Tuesday, September 8, 2015 / Proposed Rules 53933

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Department of Energy; National Aeronautics and Space Administration; Department of Commerce; Social Security Administration; Agency for International Development; Department of Justice; Department of Labor; Department of Defense; Department of Education; Department of Veterans Affairs; Environmental Protection Agency; Department of Health and Human Services; National Science Foundation; and Department of Transportation.

ACTION: Notice of proposed rulemaking.

SUMMARY: The departments and agencies listed in this document propose revisions to modernize, strengthen, and make more effective the Federal Policy for the Protection of Human Subjects that was promulgated as a Common Rule in 1991. This NPRM seeks comment on proposals to better protect human subjects involved in research, while facilitating valuable research and reducing burden, delay, and ambiguity for investigators. This proposed rule is an effort to modernize, simplify, and enhance the current system of oversight. The participating departments and agencies propose these revisions to the human subjects regulations because they believe these changes would strengthen protections for research subjects while facilitating important research.

DATES: To be assured consideration, comments must be received at one of the addresses provided below, no later than 5 p.m. on December 7, 2015.

ADDRESSES: You may submit comments, identified by docket ID number HHS–OPHS–2015–0008, by one of the following methods:

- *Federal eRulemaking Portal:http://www.regulations.gov.* Enter the above docket ID number in the "Enter Keyword or ID" field and click on "Search." On the next Web page, click on "Submit a Comment" action and follow the instructions.
- *Mail/Hand delivery/Courier [For paper, disk, or CD–ROM submissions]* for: Jerry Menikoff, M.D., J.D., OHRP, 1101 Wootton Parkway, Suite 200, Rockville, MD 20852.

Comments received, including any personal information, will be posted without change to *http://www.regulations.gov.*

FOR FURTHER INFORMATION CONTACT: Jerry Menikoff, M.D., J.D., Office for Human Research Protections (OHRP), Department of Health and Human Services, 1101 Wootton Parkway, Suite 200, Rockville, MD 20852; telephone: 240–453–6900 or 1–866–447–4777; facsimile: 301–402–2071; email: *jerry.menikoff@hhs.gov.*

SUPPLEMENTARY INFORMATION:

Executive Summary

Human Subjects Protections UPDAT

- Official publication for public comment on September 8, 2015
- 15 Federal Departments and Agencies + HHS
- Only 131 pages in PDF Federal Register format
- 88 numbered questions and many embedded specific solicitations of public comment

2000+ comments received

Slide courtesy of Laura Odwazny, DHHS General Coun

RITICISMS OF PROCESS

- Bias, conflicts of interest
- Lack of involvement from experts (SACHRP, President's Commission for the Study of Bioethical Issues)
- Unclear/changing goals from ANPRM to NPRM
- Lack of response to/incorporation of comments to ANPRM in NPRM

RIEF OVERVIEW OF PROPOSED CHANGES

Y BRIEF

VERARCHING GOALS

Modernize, strengthen, and make the Common Rule more effective

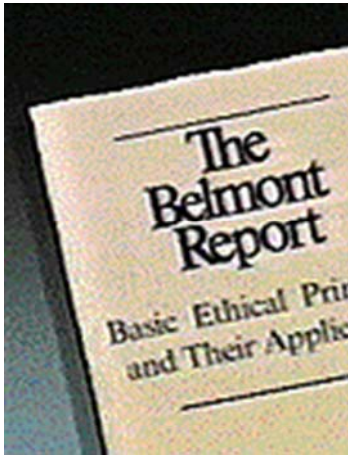
Better protect human subjects involved in research, while facilitating valuable research and reducing burden, de
and ambiguity for investigators

Simplify and enhance the current system of oversight

Remember: these are *proposed* changes – not yet final

Slide courtesy of Laura Odwazny, DHHS General Counsel/C

UIDING PRINCIPLES FOR PROPOSED CHANGES



olying Belmont principles (autonomy/respect for subjects, beneficence, justice) olves value judgments as to the appropriate balance to strike

three principles may not be able to be maximized in every situation

c comment specifically sought as to whether the appropriate balance of elmont principles has been struck by the NPRM proposals

Slide courtesy of Laura Odwazny, DHHS General Counsel/C

MMARY OF MAJOR CHANGES

- Extend scope of what research is covered (including non-federally funded research, biospecimens research)
- Clarify what's excluded (not subject to the regulations)
- Change the meaning of exempt, clarify specific requirements and outline exemption categories
- Changes to informed consent
- Require reliance on single IRB (with some exceptions)
- Harmony across all Common Rule agencies

XPANSION OF WHAT'S COVERED

Extend the scope to all clinical trials, regardless of source of support, conducted at U.S. nstitution that gets Common Rule agency funding for other non-exempt human subjects esearch

- Exception: Clinical trials regulated by FDA

Expand the definition of human subject to include the research use of biospecimens, egardless of identifiability

Extend jurisdiction for Common Rule agencies to enforce regulatory compliance against RBs not affiliated with an FWA-holding institution

Slide courtesy of Laura Odwazny, DHHS General Counsel/C

LARIFYING/RE-DEFINING WHAT'S SUBJECT TO REGS

Current Regs

Exemptions

Eligible for Expedited Review

Requiring Full Board Review

Proposed

- Exclusions
- Exemptions – more categories
- Eligible for Expedited Review – no more continui review*
- Requiring Full Board Review

HANGES TO EXCLUSIONS AND EXEMPTIONS

Net effect: More low-risk research may be exempt or excluded, much research us
of information may be exempt or excluded

Exempt research may have more specific requirements re: data security, consent, ar
documentation

Tools to guide determinations is TBD

- Will it increase consistency across institutions?
- Investigator responsibility, accountability, and consequences for non-adherence?

Slide courtesy of Laura Odwazny, DHHS General Counsel/C

SEARCH USING BIOSPECIMENS

vised definition of "human subject" to include (even de-identified) specimens

pansion to require consent for research use of all biospecimens, whether ntifiable or not

e-time general consent to open-ended future research explicitly allowed road consent"); secondary use studies would be exempt if certain nditions met

quired DHHS template for broad consent (TBD)

Slide courtesy of Laura Odwazny, DHHS General Couns

HANGE (IMPROVE?) INFORMED CONSENT

Require regulatory information to be disclosed first

Add "reasonable person" standard for disclosure of information n a way that facilitates understanding

Require posting of final consent form for clinical trials conducted/supported by Common Rule agency on publicly available Federal website

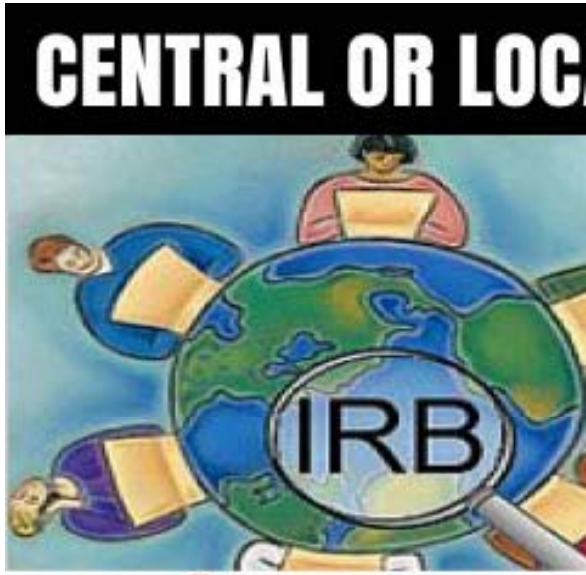
Specific required info

- Future use?
- Biospecimens may be used for future commercial profit and whether subject will benefit or not
- Whether clinically relevant research results will be disclosed to individual subjects
- Specific opt-in or out of re-contact for future research

Slide courtesy of Laura Odwazny, DHHS General Counsel/OH

B REVIEW AND OPERATIONS/SINGLE IRB RELIANCE

Mandate that U.S. institutions engaged in cooperative research rely on a single IRB (unless required by law or if Federal funding agency finds/documents inappropriate for particular study)



Slide courtesy of Laura Odwazny, DHHS General Counsel/OHRP

ARMONY/UNIFORMITY

Guidance on Common Rule will be issued only after consultation for harmonization (to the extent appropriate) with other Common Rule departments and agencies "unless such consultation is not feasible"

Slide courtesy of Laura Odwazny, DHHS General Coun

USE AND TAKE A BREATH!

Don't concern yourself with learning the details re: exclusions and exemptions right now – they are not final a even if these become the final regulations they will not be effective immediately

I suggest you worry more about whether/who will be appointed to replace Scalia… and who will be elected President….

I'll review the timeline for what's next after I discuss some of the public comments

UBLIC COMMENTS ON PROPOSED CHANGES

VERVIEW OF PUBLIC COMMENTS

ANPRM (2011) – 1100+ comments

NPRM (2015) – 2100 + comments

- General concerns about:
  - Hurriedness of the process (not enough time for pu comment)
  - Giving investigators too much leeway to determine whether their research is subject to rule
- Top four areas of focus of comments:
  - Biospecimens
  - Exclusions/exemptions
  - Single IRB mandate
  - Informed consent

OMMENTS ON NPRM

Summary by Julie Kaneshiro (OHRP)

Specific comments from:

- AAMC
  - Broad consent
  - Mandate for single IRB
- PRIM&R
- SACHRP

Comprehensive analysis by Council on Governmental Relations (COGR) with support from the Association o
Public and Land-grant Universities (APLU)

OGR SUMMARY OF PUBLIC COMMENTS

ignificant opposition to most major proposals

Mixed support for

- Mandated use of a single IRB
- Mixed support for extending the Common Rule to non-federally funded research

upport for "the concept of" standard security safeguards

NPRM is overly complex, poorly written, and **not supported by data**

Too many "TBDs"

- Security safeguards
- Consent template
- Decision tool for (or list of) minimal risk studies

Concern that some proposals will adversely affect human health with little perceived benefit (and significant administrative burden)

VERARCHING THEME: SHOW ME THE DATA?!

My hypothesis: Researchers will more willingly accept **and trust** regulations (and changes to regulations) that
based on good evidence

Very few of the proposed changes are rooted in evidence

No proposal for systematic data collection to assess whether changes improve protections or meet other stat
goals

Challenges:

- What are the benchmarks of success?
- How do we measure?

OMMENTS ON BIOSPECIMENS

Major concerns that restricting access to biospecimens will slow research

Public education is needed before public opinion given such weight

General agreement that "broad consent" does not demonstrate respect for autonomy

- Public education and more transparency/ "robust notice" would be better
- Moves IC process to clinical environment, done by people not knowledgeable about research

Resource intensive requirements especially detrimental to smaller institutions (justice)

Unjustified differential treatment of specimens and data (PRIM&R/SACHRP)

Risk of re-identification should be the driver of changes – and as written NPRM poses more privacy risks because of
racking and because it encourages retention of identifiers

and btw, there was overwhelming opposition to this in response to the ANPRM and NPRM didn't even acknowledg

OMMENTS ON EXCLUSIONS/EXEMPTIONS

Very confusing, hard to interpret

Concerns about the exclusion of some social science research

People want to see the tool in order to be able to comment!

Will it actually increase consistency?

Concerns about investigators using the tool themselves because proposed exemption categories very nuanced

- Mandated investigator education?
- Investigator responsibilities/accountability for overseeing excluded or exempt research
- Consequences for non-adherence?

OMMENTS ON SINGLE IRB MANDATE

More evenly split between supporting and dividing comments?

"Institutions" who oppose cite

- Vague criteria re: selection
- Value of local IRB review
- Maintains institutional accountability
- Increased burden due to more agreements between institutions and IRBs?
- **NEED FOR MORE DATA AND STUDIES (which NIH funded…)**

"Individuals" support

- Favor concept; oppose the mandate

OMMENTS ON INFORMED CONSENT

General support for idea of "core" consent form BUT … **Concerns that**

- Proposed minor changes will not improve understanding
- Length/complexity of forms will not be reduced
- Guidance, not regulations, is what's needed
- Comments on required posting of forms mixed – questionable value
- Proposed changes to not encourage innovation

SSED OPPORTUNITIES (AAMC)

- Revise definitions of research, minimal risk, and legally authorized representative
- nformed consent PROCESS
- nvestigator responsibilities/education
- Delineate research vs. QI/QA
- Evaluation metrics

AKE A DIFFERENT APPROACH!

PRIM&R

- Timeframe is insane
- Too much bias
- Lack of input from expertise
- Lack of transparency
- You're simply replacing old burdens/problems with new ones
- There are too many TBDs which make this impossible to evaluate
- **Take an issue-by-issue approach**

SACHRP

- Start over with a comprehensive re-write

HAT ABOUT…? (EA)

Mandate real-time monitoring of high(er) risk studies (or other safeguards)

Changes to IRB structure and function

- E.g., increase required % of lay and non-affiliated members, requirement for someone with ethics expertise?

More radical changes to the informed consent process

- E.g., limit to max 2 pages?, require tests of comprehension for risky studies

WHAT'S NEXT?

DON'T PANIC! IT WILL BE AWHILE…

OPOSED TRANSITION PROVISIONS

Grandfather clause:

- Human subjects research initiated prior to the effective date of the final rule would not need to comply, could take advantage of added flexibilities
- Biospecimens collected prior to the effective date of the final rule: regulations will not apply to research use if not identifiable – maintenance of status quo

Slide courtesy of Laura Odwazny, DHHS General Co

NTICIPATED COMPLIANCE DATES OF FINAL RULE

Effective date: 1 year after publication

Compliance date: generally 1 year after publication

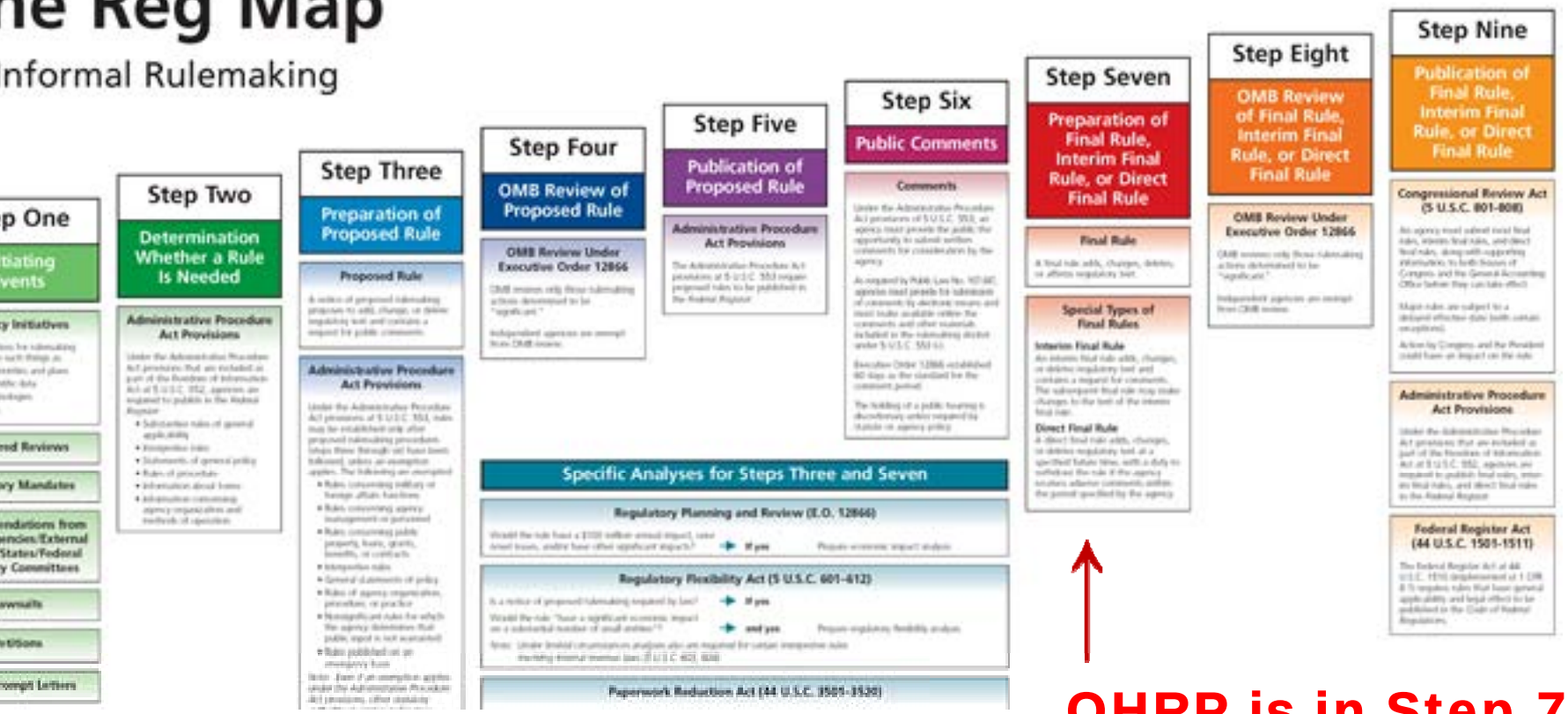
Exceptions:

- Coverage of all biospecimens, regardless of identifiability, by the definition of human subject: 3 years after publication
- Single IRB requirement for cooperative research conducted in US: 3 years after publication
- Extension of regulations to non-funded clinical trials would not occur until institution receives Federal funding for non-exempt research in an award made after effective date of final rule

Slide courtesy of Laura Odwazny, DHHS General Co

EDERAL RULEMAKING PROCESS

TTP://WWW.REGINFO.GOV/PUBLIC/REGINFO/REGMAP/INDEX.JSP



OHRP is in Step 7

Slide courtesy of Laura Odwazny, DHHS General Coun

IMEFRAME FOR FINAL RULE?

OFFICE of INFORMATION and REGULATORY AFFAIRS
OFFICE of MANAGEMENT and BUDGET
EXECUTIVE OFFICE of the PRESIDENT

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iew EO 12866 Meetings Printer-Friendly Version Download RIN Data in XML

HHS/OASH **RIN:** 0937-AA02 **Publication ID:** Fall 2015

itle: Federal Policy for the Protection of Human Subjects

Abstract:

he proposed rule would revise current human subjects regulations in order to strengthen protections for research subjects while facilitating valuable research and reducing urden, delay, and ambiguity for investigators.

Agency: Department of Health and Human Services(HHS)
RIN Status: Previously published in the Unified Agenda
Major: Yes
CFR Citation: 45 CFR 46
Legal Authority: 21 U.S.C. 289
Legal Deadline: None
Priority: Economically Significant
Agenda Stage of Rulemaking: Proposed Rule Stage
Unfunded Mandates: Private Sector

imetable:

Action	Date	FR Cite
ANPRM	07/26/2011	76 FR 44512
ANPRM Comment Period End	10/26/2011	
NPRM	09/08/2015	80 FR 53931
NPRM Comment Period End	12/07/2015	
Final Action	09/00/2016	

Additional Information: Includes Retrospective Review under E.O. 13563.
Regulatory Flexibility Analysis Required: Undetermined
Government Levels Affected: Undetermined

00 Independence Avenue SW.,

Slide courtesy of Laura Oc
DHHS General Counsel/C

ISCUSSION

- General questions or comments?
- Would you be persuaded by proposed changes if there were evidence to support them? Even if burden was ncreased?
- What evidence do you think should inform regulatory changes?
- What changes would you like to see?
- What metrics would you propose using to assess the impact of human research protections regulations?
- Pros and cons of mandated single IRB review?