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Proposed Updates to the Common Rule: An Overview of the NPRM

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A Bit About Our Speakers

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Agenda

- NPRM Overview
- II.A. Proposed Changes to the Scope and Applicability of the Regulations
- II.B. Proposed Changes to Obtaining, Waiving, and Documenting Informed Consent
- II.C. Proposed Changes to Protect Information and Biospecimens
- II.D. Harmonization of Agency Guidance
- II.E. Cooperative Research
- II.F. Changes to Promote Effectiveness and Efficiency in IRB Operations
- II.G. Proposed Changes to IRB Operational Requirements
- II.H. Other Proposed Changes
- Updates from recent OHRP communications

NPRM Overview

- On September 2, 2015, the Department of Health and Human Services (DHHS) and fifteen other Federal Departments and Agencies announced that a Notice of Proposed Rule Making (NPRM) was put on public display
- The NPRM was published in the Federal Register on September 8, 2015 https://www.federalregister.gov/articles/2015/09/08/2015-21756/federal-policy-for-the-protection-of-human-subjects
- Included within the 519-page NPRM are approximately 45 major proposals to the Common Rule and 88 questions/requests for comment
- Comments are due no later than 5 p.m. on December 7, 2015

II. A. Proposed Changes to the Scope and Applicability of the Regulations

1. Expanding the Definition of Human Subject to Cover Research with Non-identified Biospecimens

§__102(e)(1) Human subject means a living individual about whom an investigator (whether professional or student) conducting research:

(i) Obtains data through intervention or interaction with the individual, and uses, studies, or

analyzes the data;

(ii) Obtains, uses, studies, analyzes, or generates identifiable private information; or

(iii) Obtains, uses, studies, or analyzes biospecimens

1. Expanding the Definition of Human Subject to Cover Research with Non-identified Biospecimens

- Focus on “secondary research use”
- Goal of requiring informed consent for research involving biospecimens in all but a limited number of circumstances
- Response to public demand
- New definition would apply *prospectively*
- Enforcement delayed until three years after publication of final rule
- Not changing: definition of “identifiability”
- Two alternative proposals seek to narrow the types of applicable biospecimens through alternate definitions

2. Explicit Exclusion of Activities from the Common Rule *§__.101(b)*

- Unlike “exempt” research, excluded research is not expected to undergo any type of review to determine this “excluded” status
  - Investigators would independently make these determinations with little to no IRB involvement
- There is no alteration to the fact that activities that do not meet the criteria for being subject to the Common Rule remain outside the scope of the rule (i.e., Not Research, Not Human Subject Research)
- Eleven specific “excluded” activities broken into three subcategories
- “Low-risk” is used to denote research activities that do not entail physical risk, and where both the probability and magnitude of other risks, once required protections are applied, are hypothesized to be low

2. Explicit Exclusion of Activities from the Common Rule *§__.101(b)(1)*

Excluded Category 1: Activities determined not the be research

1. Certain internal program improvement activities
2. Certain oral history, journalism, biography, and historical scholarship activities
3. Criminal investigations
4. Certain quality assurance or improvement activities
5. Public health surveillance
6. Intelligence surveillance

2. Explicit Exclusion of Activities from the Common Rule *§__.101(b)(2)*

Excluded Category 2: Activities that are considered low-risk either in themselves or because appropriate safeguards are already in place independent of the Common Rule

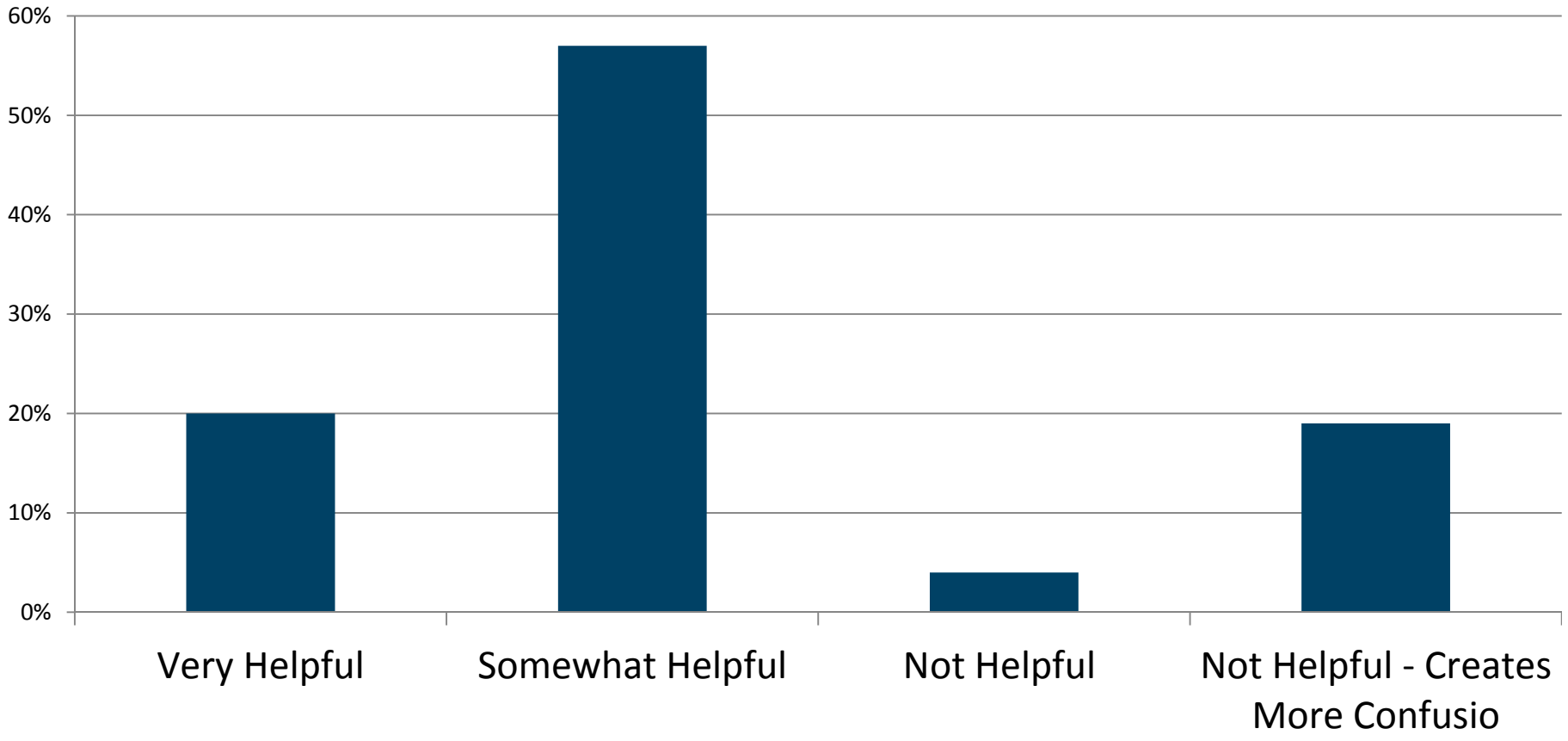
1. Revised version of current Exempt Category 2 (research involving educational, survey procedures, interview procedures or observation of public behavior) – no interventions; similar Subpart D application
2. Revised version of current Exempt Category 4 (Research involving the collection or study of existing data, documents, records, pathological specimens, etc.)
3. Certain federal government-conducted research using government generated/collected information obtained for non-research purposes
4. Certain research involving the use of protected health information regulated elsewhere under HIPAA

2. Explicit Exclusion of Activities from the Common Rule *§__.101(b)(3)*

Excluded Category 3: Low-risk human subjects research activities that do not meaningfully diminish subject autonomy

1. The secondary research use of non-identified biospecimens that is designed only to generate information about an individual that already is known
    - Applies to research subjects to this policy and to research subject to the additional requirements of 45 CFR part 46, subparts B, C, or D

Survey Question: Do you believe the addition of excused research categories is helpful to have in the regulations? *(201 Responses)*



3. Proposed Exemptions
§__.104(c) Making Exempt Research Determinations

- Federal departments and agencies shall develop a "decision tool" to assist in exemption determinations. If the decision tool is used, further assessment or evaluation of the exemption determination is not required. Decision tool could be used by a knowledgeable individual or by the investigator or another individual at the institution who enters accurate information about the proposed research into the decision tool
- An institution or, when appropriate, the IRB, must maintain records of exemption determinations made for research subject to the requirements of this policy for which the institution or IRB exercises oversight responsibility.
- Note that for FDA-regulated device studies IRB review is required by statute
- Eight new exemptions divided into three groupings according to the kind of risk and what protections are called for

3. Proposed Exemptions
Low Risk Interventions

Exemptions for low-risk interventions that do not require application of standards for information and biospecimen protection:

- One new exemption – Research involving benign interventions in conjunction with the collection of data from an adult subject (NPRM at §__.104(d)(3))
- Revised version of exemption category 1 in the current Common Rule (research conducted in established or commonly accepted educational settings)
- Revised version of the current exemption category 5 (research and demonstration projects)
- Not changing: Exemption category 6 in the current Common Rule (taste and food quality evaluation)

3. Proposed Exemptions

Research That May Involve Sensitive Information

Exemptions for research that may involve sensitive information that requires application of standards for information and biospecimen protection described in proposed §__.105

- Research Involving Educational Tests, Surveys, Interviews, or Observation of Public Behavior if the Information is Recorded with Identifiers and even if the Information is Sensitive (NPRM at §__.104(e)(1))
  - Does not include interventions
- Secondary Research Use of Identifiable Private Information (NPRM at §__.104(e)(2))
  - Previously collected for non-research purposes
  - Only for purposes of the specific research proposed in exemption request, not for any further secondary research use

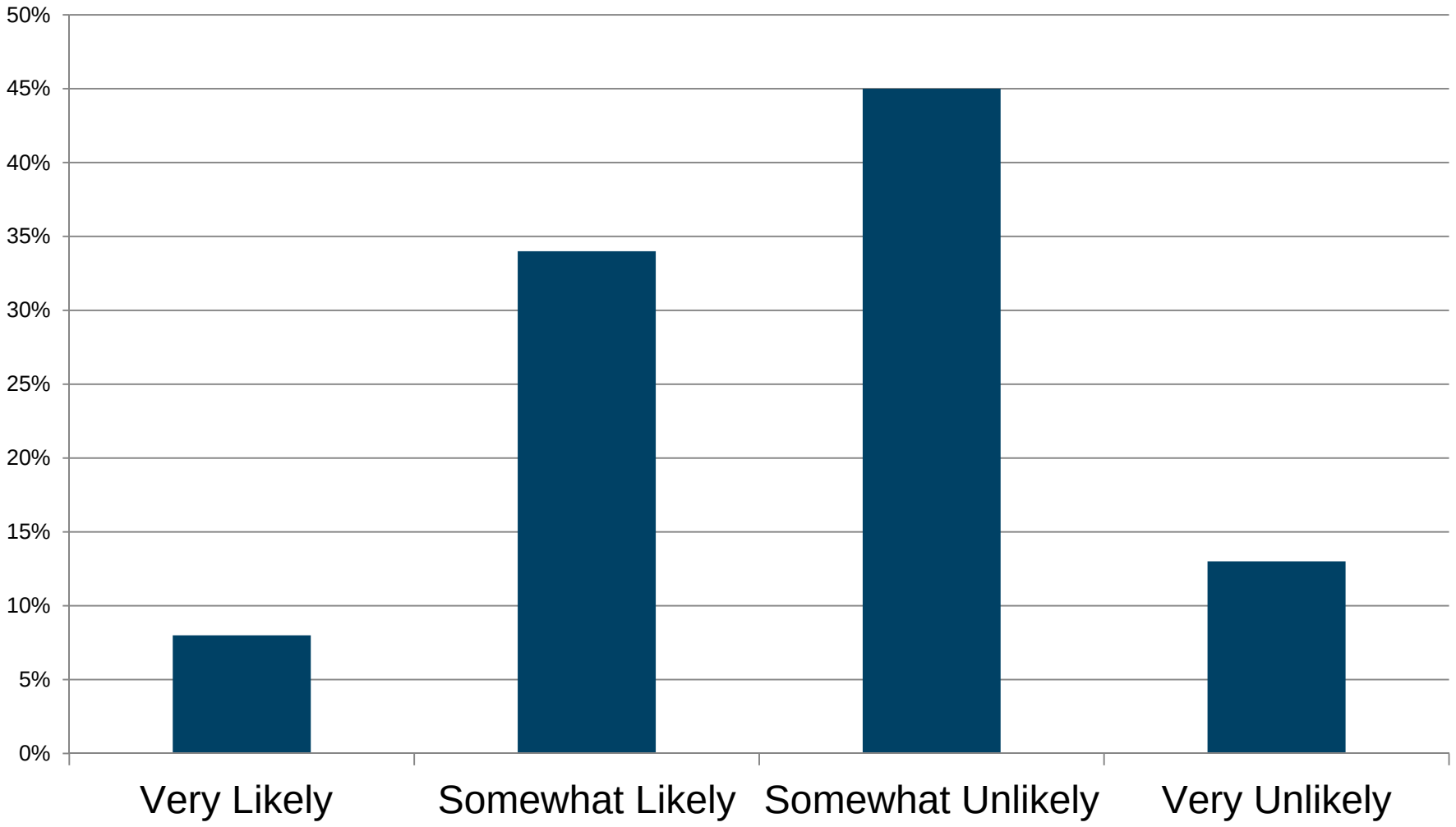
3. Proposed Exemptions

Secondary Research With Biospecimens & Identifiable Private Information

Exemptions for secondary research involving biospecimens and identifiable private information that requires application of privacy safeguards, broad consent, and limited IRB review (§__.105, §__.116(c), §__.111(a)(9))

- Exemption for the Storage or Maintenance of Biospecimens or Identifiable Private Information for Secondary Research Use (§__.104(f)(1))
  - Applies to biospecimens and identifiable private information that were initially collected for purposes other than the proposed research activity
  - Must obtain consent (can be oral for data)
- Exemption for Secondary Research Use of Biospecimens or Identifiable Private Information where Broad Consent has been Sought and Obtained (§__.104(f)(2))
  - For the actual secondary research studies that will be conducted using biospecimens or identifiable private information that have been stored for unspecified secondary research studies

Survey Question #2: As proposed in the NPRM, how likely is it that your institution will allow investigators to use a published exemption tool to make their own exemption determinations? *(202 Responses)*



II. B. Proposed Changes to Obtaining, Waiving, and Documenting Informed Consent

II.B. Proposed Changes to Obtaining, Waiving, and Documenting Informed Consent

- Consent form information to be presented not merely as a list of facts, but rather as meaningful for the potential subject to decide whether or not to participate
- Elements of consent must be presented first; any additional information must be included in appendices
- New required element when collecting identifiable private information
- New additional elements of informed consent
- Additional considerations and criteria when waiving the informed consent process or documentation of informed consent
- New category of “broad consent” for storage, maintenance, and secondary research use of biospecimens or identifiable private information
- Required posting of consent forms

1. Required Elements of Informed Consent
New Basic Element

§__.116(a)(9) One of the following statements about any research that involves the collection of identifiable private information:

(i) A statement that identifiers might be removed from the data and the data that is not identifiable 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 representative, if this might be a possibility; or

(ii) A statement that the subject's data collected as part of the research, from which identifiers are removed, will not be used or distributed for future research studies

- Does not require specification of the future use of those non-identified data
- It is anticipated that very few investigators will elect to offer the option to restrict the future research use of non-identified data [(a)(9)(ii)], in part because of the challenges of marking and tracking such decisions

1. Required Elements of Informed Consent
New Additional Elements

§__.116(b)(7) A statement that the subject's biospecimens may be used for commercial profit and whether the subject will or will not share in this commercial profit

§__.116(b)(8) A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions

§__.116(b)(9) An option for the subject or the representative to consent, or refuse to consent, to investigators re-contacting the subject to seek additional information or biospecimens or to discuss participation in another research study

- Goal is to help ensure that prospective subjects are more consistently provided with this information when appropriate
- The Secretary will publish guidance in the future to explain how consent forms can be written to comply with the regulatory requirements

2. Waiver of Informed Consent or Documentation of Informed Consent

- New consideration and criteria when approving waivers or alterations of informed consent when research involves accessing or using identifiable biospecimens or identifiable information (§__.116(f)(1)(iii)), (§__.116(e)(2) and (f)(2))
- IRB cannot waive consent for storage/maintenance for secondary research use if an individual refused to consent to the "broad consent" form (§__.116(e)(3) and (f)(3))
- Specifies that the consent document should include only the language required by §__.116, with appendices included to cover any additional information (§__.117(b)(1))
- Requirement to obtain a signed consent form may be waived under certain circumstances for research involving members of a distinct cultural group or community for whom signing documents is not the norm (§__.117(c)(1)(iii))

3. Broad Consent to the Storage, Maintenance and Secondary Research Use of Biospecimens and Identifiable Private Information

§__.116(c)(1) Elements of informed consent for broad consent to the storage, maintenance, and secondary research use of biospecimens or identifiable private information

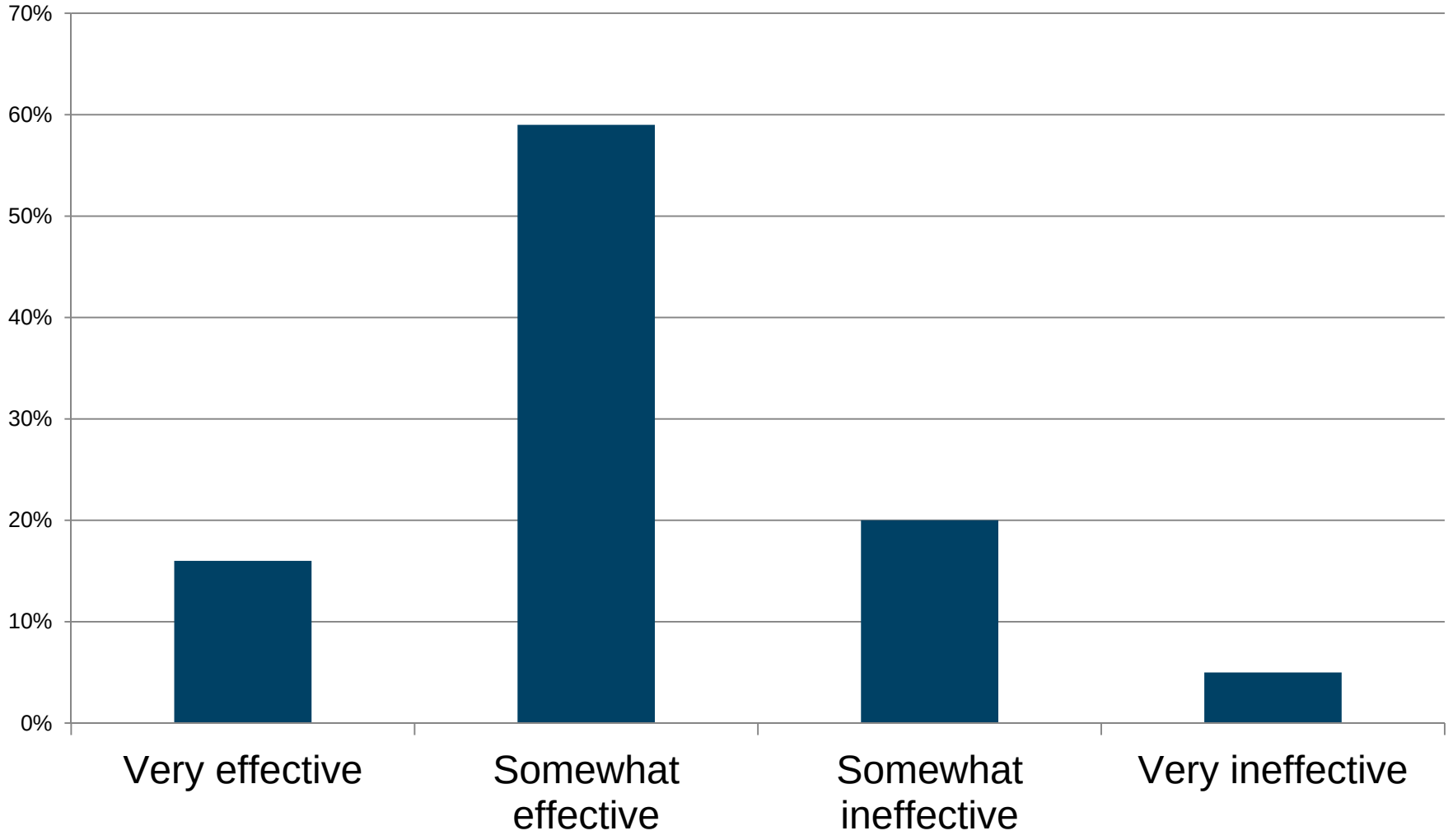
§__.116(d)(1) The Secretary of HHS will establish, and publish in the Federal Register for public comment, templates for consent that will contain all of the required elements of informed consent under paragraph (c) of this section. IRB review of the broad secondary use informed consent form obtained in accordance with paragraph (c) of this section is required unless the consent is obtained using only this template, without any changes

- Note that this is different than the proposed requirement at §__.116(a)(9), which applies only to future use of non-identified data
- Also references written and oral consent for new exemption at §__.104(f)(1)
- If subject declines to consent to research use of biospecimens or identifiable private information, must be documented

4. Posting of Consent Forms
§__.116(h)(1)

- A copy of the final version of the informed consent form for each clinical trial conducted or supported by a Federal department or agency must be posted on a publicly available federal web site that will be established as a repository for such informed consent forms within 60 days after the trial is closed to recruitment. (§__.116(h)(1))
    - Seeks to improve the quality of consent forms in federally funded research by subjecting them to public scrutiny
    - Investigators would only be required to post one consent form (even if changed after posting)
    - Only one posting would be required for each multi-site study

Survey Question #3: Would these consent changes be effective in "strengthening, modernizing, and making the regulations more effective in protecting research subjects?“ *(199 Responses)*



II. C. Proposed Changes to Protect Information and Biospecimens

Protection of biospecimens and identifiable private information §__.105

- Investigators conducting non-exempt human subjects research involving the collection, storage, or use of biospecimens or identifiable private information will need to implement:
  - List of specific safeguards that would be identified by the Secretary
  - If an institution or investigator is currently required to comply with the HIPAA rules, then the specific safeguards required here would be satisfied (§__.105(b))
- IRBs would not be required to review the individual plans for safeguarding information and biospecimens for each research study, so long as investigators will adhere to them (§__.105(a))
- Specific list of limitations on use, release, and disclosure is proposed for the use and disclosure of identifiable private information and biospecimens maintained for research (§__.105(c))

II. D. Harmonization of Agency Guidance

Adding Regulatory Requirement for Consultation Among Common Rule Agencies for New Guidance

§__.101(j) Federal guidance on the requirements of this policy shall be issued only after consultation, for the purpose of harmonization (to the extent appropriate), with other Federal departments and agencies that have adopted this policy, unless such consultation is not feasible

- Although Common Rule agencies attempt to coordinate on guidance for harmonization, there is currently no regulatory requirement to do so
- NPRM acknowledges difficulty of coordination among agencies
- Regulatory requirement includes caveats of “to the extent appropriate” and “unless…not feasible”
- Agencies may voluntarily consult even when the requirement does not apply

II. E. Cooperative Research (NPRM and Current Rule at §__.114) and Proposal to Cover Unaffiliated IRBs Not Operated by an Institution Holding a Federalwide Assurance

Cooperative Research

§__.114 Cooperative research.

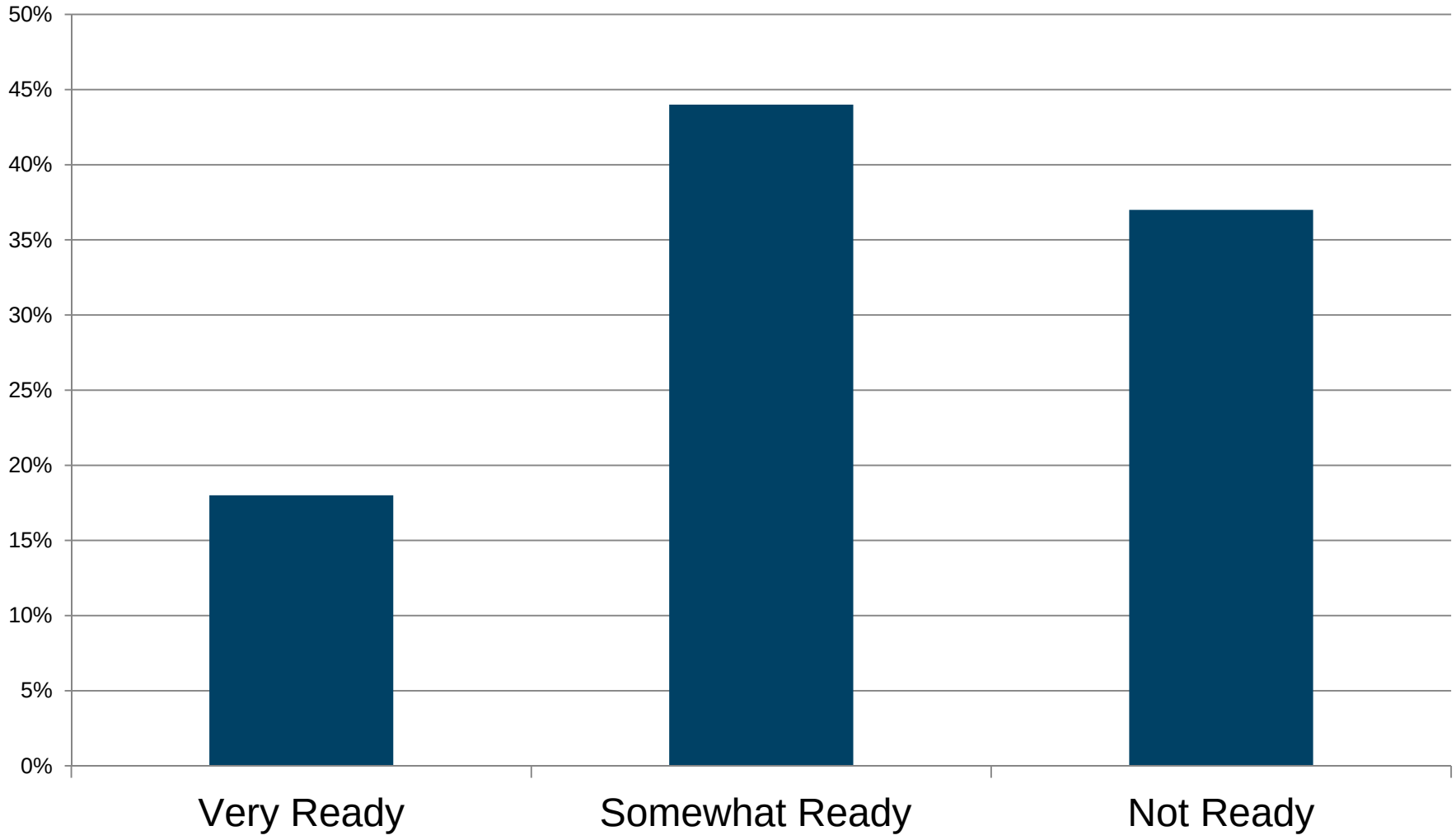
(b)(1) Any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be selected by the Federal department or agency supporting or conducting the research or, if there is no funding agency, by the lead institution conducting the research

- Would not apply:
  1. When more than single IRB review is required by law (e.g., FDA-regulated devices); or
  2. If the Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate

Cooperative Research

- New provision at §__.101(a) that would explicitly give Common Rule departments and agencies the authority to enforce compliance directly against unaffiliated IRBs that are not operated by an assured institution
- New provision at §__.103(e) that the institution and the IRB of record should establish and follow written procedures identifying the compliance responsibilities of each entity (applies to US only)
- Relevant local contextual issues (e.g., investigator competence, site suitability) pertinent to most studies can be addressed through mechanisms other than local IRB review
- See Huron April 2015 Webinar for additional considerations on single IRB review of multi-site research

Survey Question #4: Would your institution be ready operationally if chosen to serve as the singe IRB of record for multi-site research? *(198 Responses)*



II. F. Changes to Promote Effectiveness and Efficiency in IRB Operations

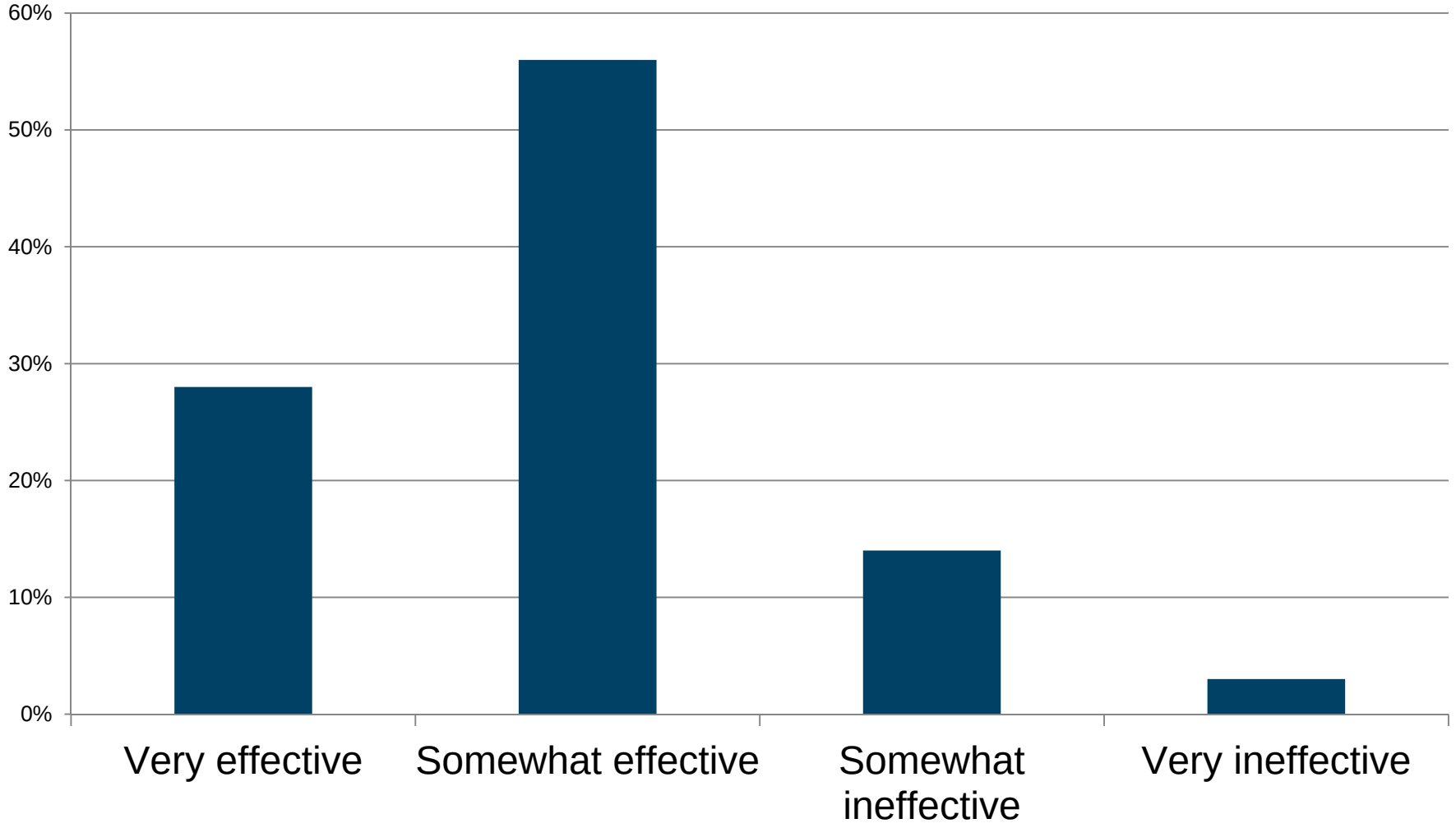
1. Continuing Review of Research
§__.109(f)

- Eliminated for all studies that undergo expedited review, unless the reviewer explicitly justifies why continuing review would enhance protection of research subjects.
- Eliminated for certain studies initially reviewed by a convened IRB, once certain specified procedures are all that remain for the study, unless specifically mandated by the IRB
    - Annual confirmation to the IRB by investigator would be required
- Not required for secondary research using information and biospecimens that requires limited IRB review under new exemption §__.104(f)(1)

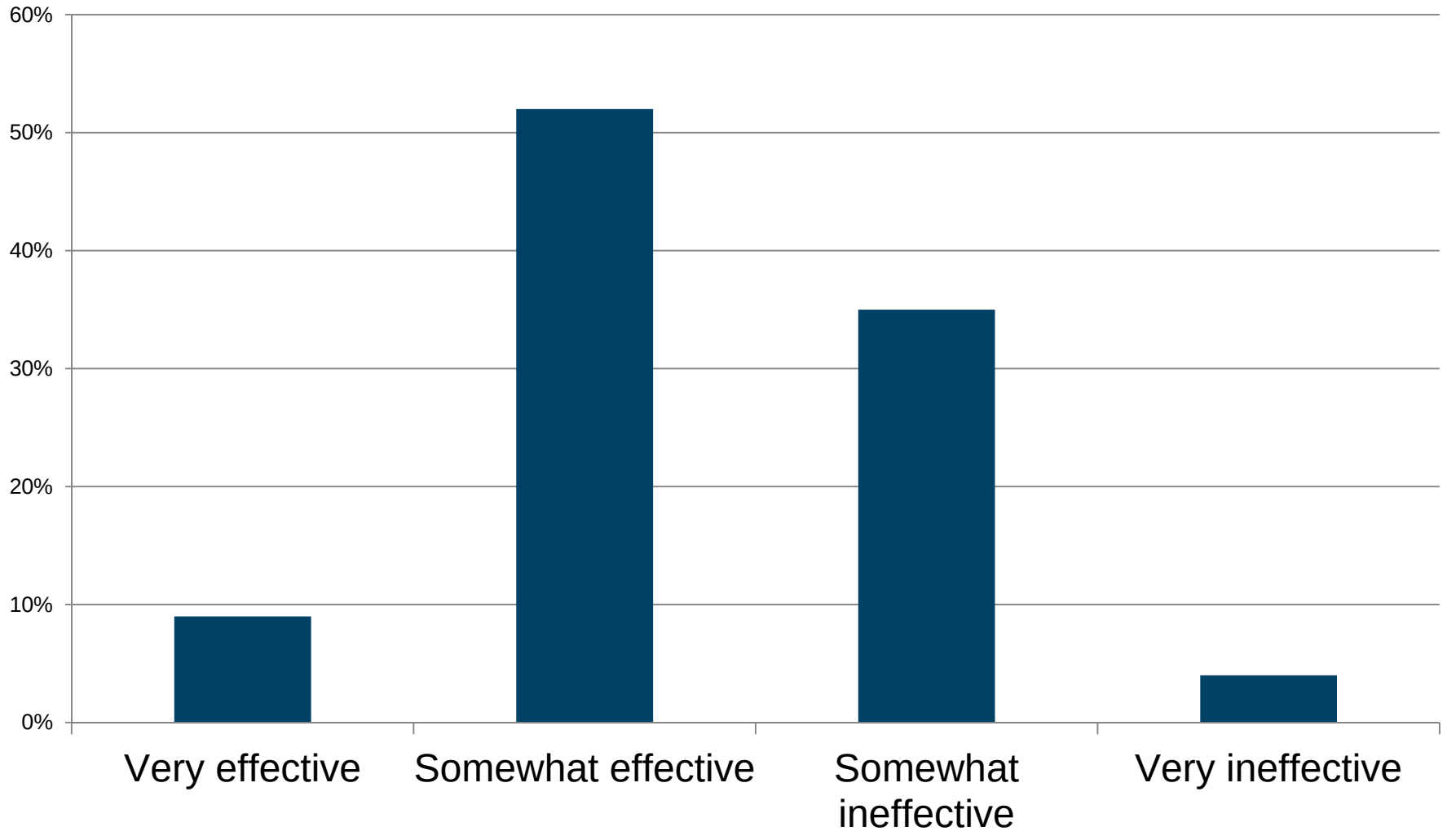
2. Expedited Review Procedures and the Definition of "Minimal Risk" §§__.110 and __.102(j))

- Expedited review categories on the Secretary's list qualify for Expedited Review *unless* the reviewer(s) determine(s) that the study involves more than minimal risk.
    - IRBs will be required to document their rationale when they override this presumption that studies on the Secretary's expedited review list involve greater than minimal risk.
- Re-evaluation of the published list of expedited review categories would occur every 8 years
- The Secretary of HHS will create and publish a list of activities that should be considered minimal risk no less than every 8 years.

Survey Question #5: Would these proposed changes be effective in "decreasing administrative burden, delay and ambiguity for investigators, institutions, and IRBs"? *(200 responses)*



Survey Question #6: Would these proposed changes be effective in "strengthening, modernizing, and making the regulations more effective in protecting research subjects"? *(182 Responses)*



II. G. Proposed Changes to IRB Operational Requirements

1. Proposed Criteria for IRB Approval of Research §___.111

- Separate approval criteria for "limited IRB review" of exempt human research involving secondary use of biospecimens or identifiable private information (§__.111(a)(9))
- When considering criteria for approval #3 ((equitable selection of subjects), adds emphasis on issues related to "coercion or undue influence" for research with vulnerable populations
- Adds "physically disabled persons" to list of populations potentially vulnerable to coercion or undue influence (§__.111(a)(3) and §__.111(b))
- Under criterion #7 (privacy and confidentiality), IRBs consider additional provisions only if they find the protections under §___.105 are not sufficiently protective
- IRBs would not be required to determine whether or not research results should be returned to research subjects. ***But*** if such a plan is already included in the protocol, IRBs must determine whether that plan is appropriate

2. Proposed Revisions to IRB Operations, Functions, and Membership Requirements §___.108 and ___.107

- Eliminates the requirement for IRBs to avoid membership that consists entirely of individuals of one gender or profession
- Adds emphasis on issues related to "coercion or undue influence" when considering IRB member expertise in the review of research involving a vulnerable category of subjects
- "Economically or educationally disadvantaged persons" ~~is~~ now included as an example of a vulnerable category of subjects, requiring an IRB to give consideration to membership expertise in this area.
- The term "handicapped" persons is replaced with "physically disabled persons"

II. H. Other Proposed Changes

Proposal to Extend the Common Rule to All Clinical Trials

§__.101 To what does this policy apply?

(a)(2) All clinical trials as defined by this policy, irrespective of funding source, that meet all of the following conditions:

(i) The clinical trials are conducted at an institution that receives support from a federal department or agency for human subjects research that is not excluded from this policy under §__.101(b)(2), and the research does not qualify for exemption in accordance with §__.104;

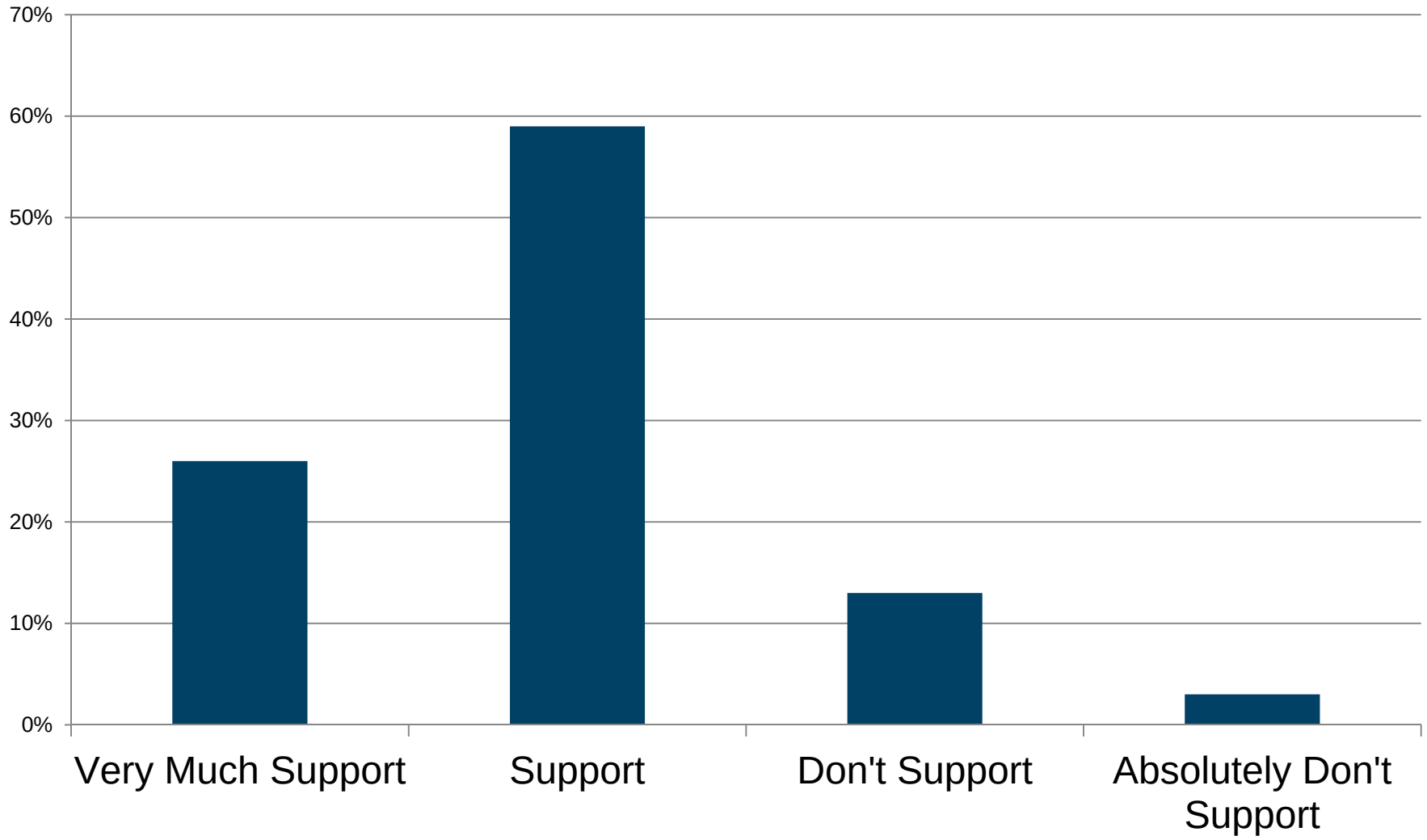
(ii) The clinical trials are not subject to FDA regulation; and

(iii) The clinical trials are conducted at an institution located within the United States

§__.102 Definitions for purposes of this policy

(b) Clinical trial means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes

Survey Question #7: Do you support the NPRM's proposal to apply the Common Rule to all clinical trials within any institution that receives any federal support? *(188 Responses)*



Changes to the Assurance Process

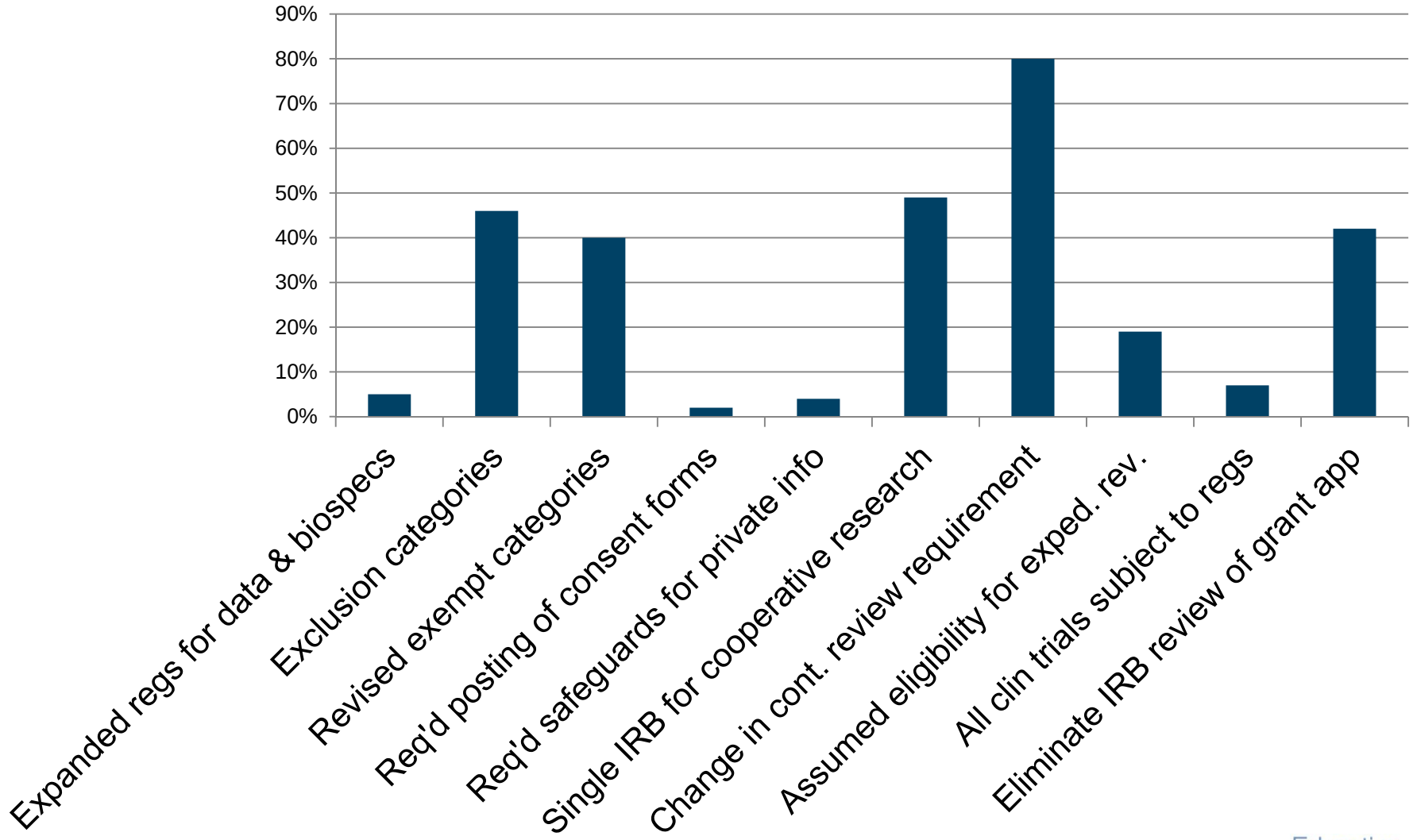
- Eliminate the following requirements:
  - that an institution provide a statement of ethical principles with which it will abide as part of the assurance process
  - that an institution designate one or more IRBs on its FWA established in accordance with the Common Rule
  - that an up-to-date list of the IRB members and their qualifications be included in an institution's assurance
  - the current option of "checking the box" on an FWA
  - that a department or agency head's evaluation of an assurance will take into consideration various factors related to the adequacy of the program
  - that grant applications undergo IRB review for the purposes of certification
- Add requirement for institution to have and follow procedures for documenting the institution's reliance on any unaffiliated IRB and the respective responsibilities of each entity.

Other Changes

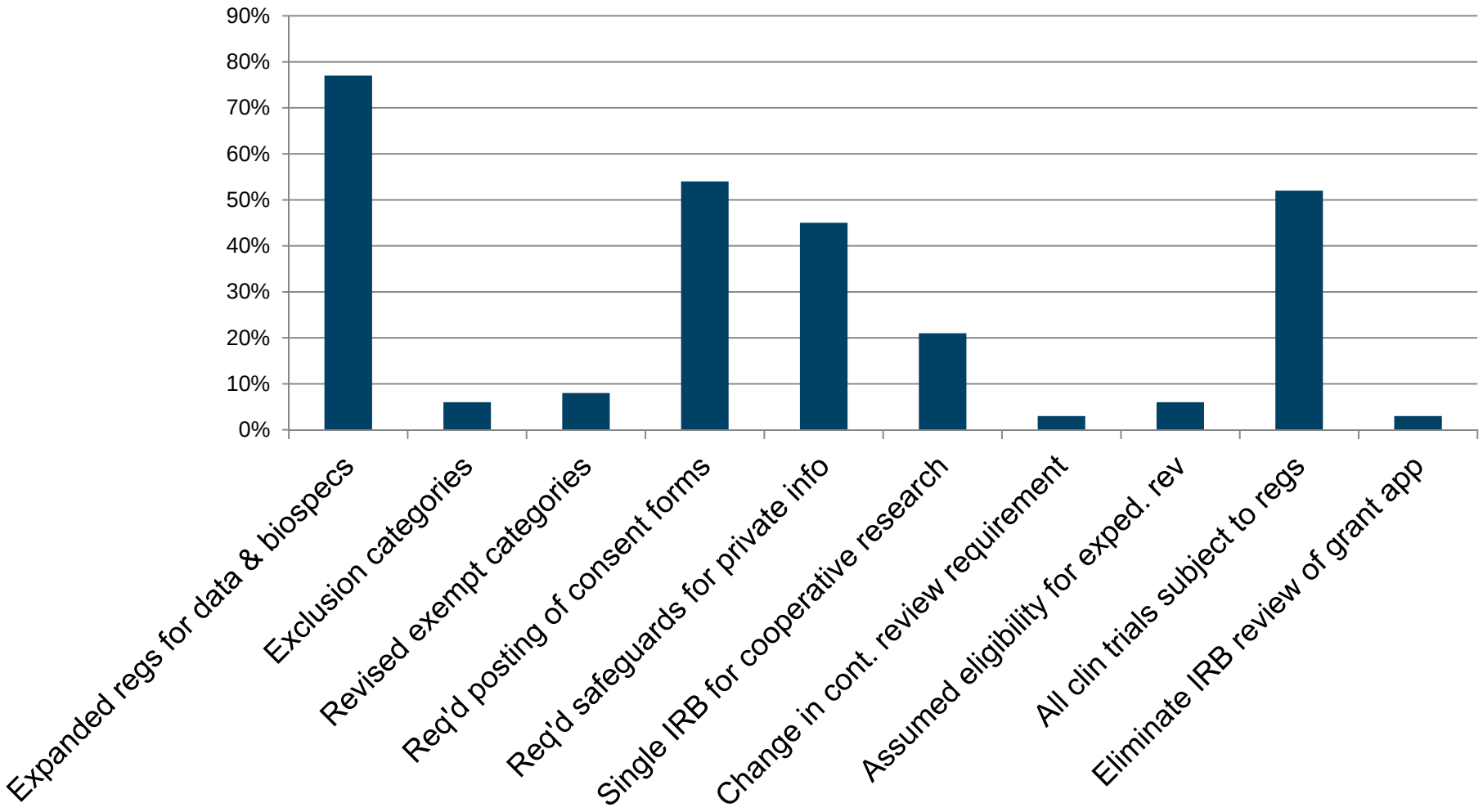
- When exercising final judgment about the coverage of particular research activities under the Common Rule (current policy), Federal department or agency heads must exercise their authority consistent with the principles of the Belmont Report
- When department or agency heads waive the applicability of some or all of the provisions of the policy, the waiver must be supported by an argument that the alternative procedures to be followed are consistent with the principles of the Belmont Report
- For research conducted in foreign countries, revised §__.101(h) to remove Declaration of Helsinki as example of internationally recognized ethical standard

Conclusions

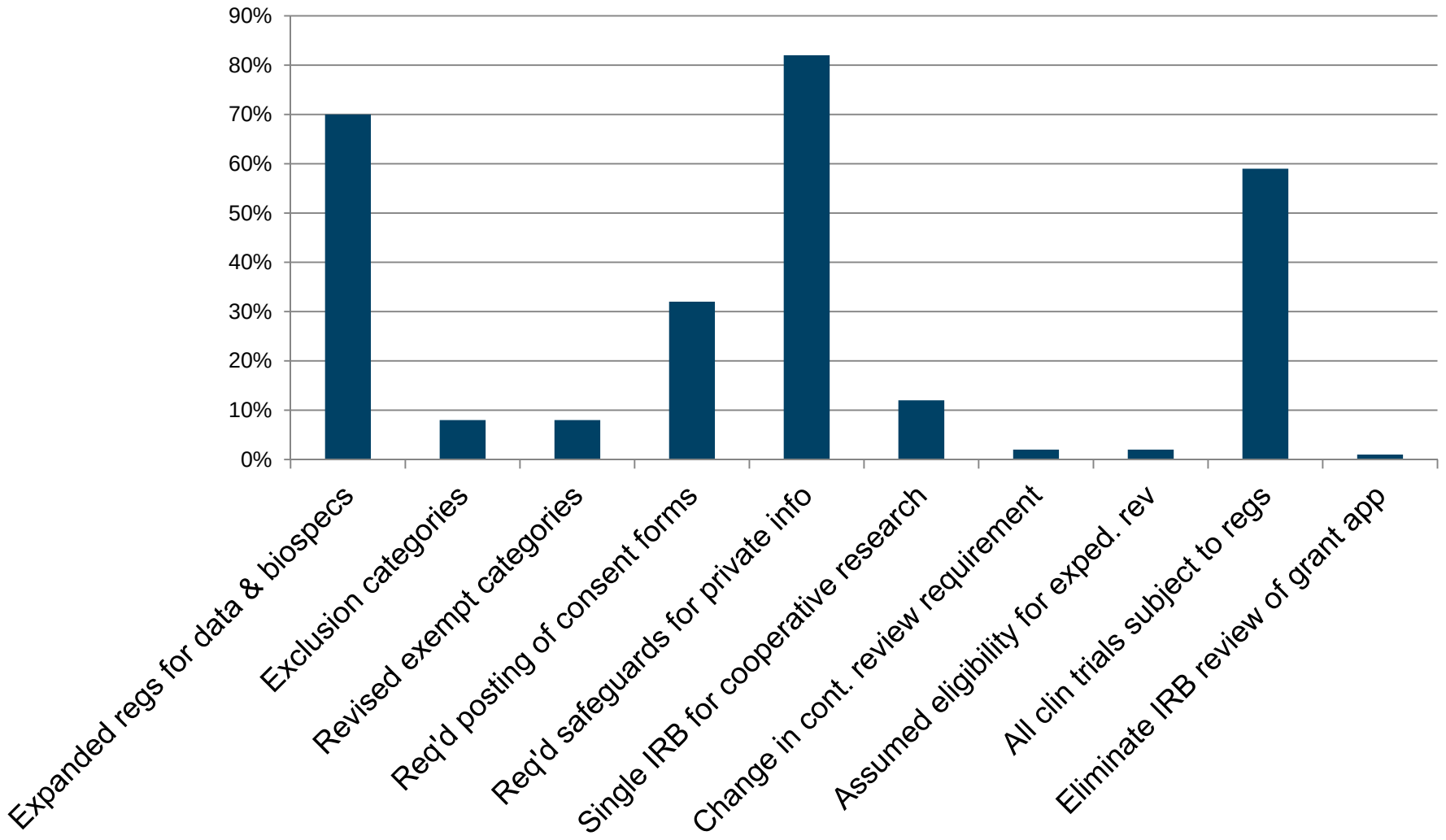
Survey Question #8: Which proposed changes could have greatest impact on reducing administrative burden for IRBs and/or investigators? *(189 Responses)*



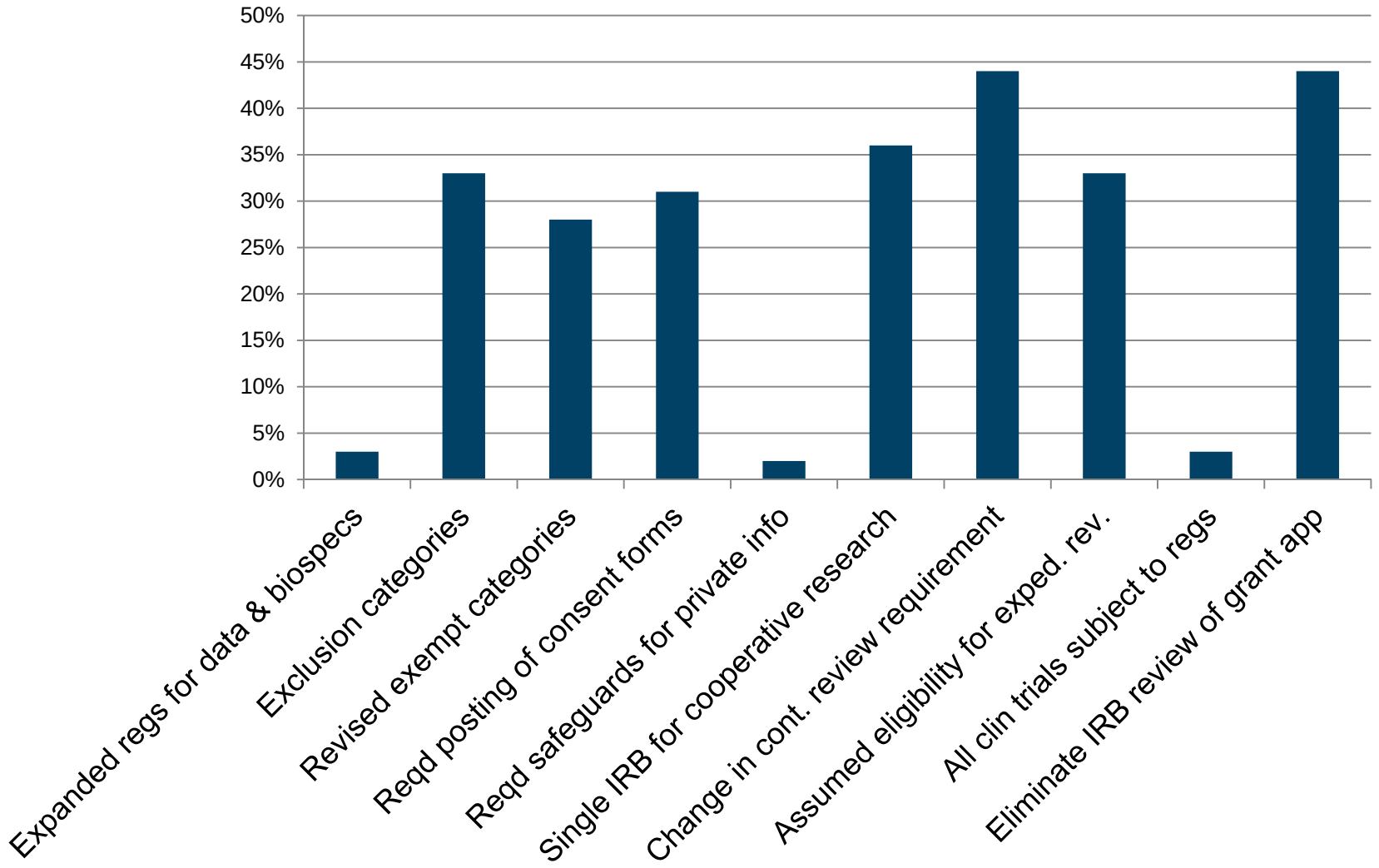
Survey Question #9: Which proposed changes are most likely to increase administrative burden for IRBs and/or investigators? *(191 Responses)*



Survey Question #10: Which proposed changes would be likely to strengthen protections for research subjects? *(186 Responses)*



Survey Question #11: Which proposed changes would be unlikely to strengthen protections for research subjects? *(177 Responses)*



Additional NPRM Resources

- OHRP Website:
  - www.hhs.gov/ohrp/humansubjects/regulations/nprmhome.html
- Federal Register:
  - www.federalregister.gov/articles/2015/09/08/2015-21756/federal-policy-for-the-protection-of-human-subjects
- Huron In-Depth Webinar Series on Key NPRM Topics
  - Overview of NPRM: https://www.huronconsultinggroup.com/Insights/Webinar/Education/Webinar-NPRM-Discussion
  - Biospecimens: http://www.huronconsultinggroup.com/Insights/Webinar/Education/Webinar-NPRM-Biospecs-IPI
  - Reducing Administrative Burden: http://www.nxtmove.com/Company/Media_Center/News_and_Events/Events/NPRM_Proposals_to_Reduce_Administrative_Burden

Thank You!

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