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PUBLIC RESPONSIBILITY IN MEDICINE AND RESEARCH

## Proposed Changes to the "Common Rule"

On September 8, 2015, the Department of Health and Human Services (DHHS) released a notice of proposed rulemaking (NPRM), which proposes significant changes to the Federal Policy for the Protection of Human Subjects. The table below summarizes the changes put forward in the proposed rule, including how those changes compare with the current regulations at 45 CFR 46.

Please note that the regulatory text below is summarized and shortened for the purposes of this chart. For further clarification and additional information, please make sure to refer to the complete text of 45 CFR 46 and DHHS' September 2015 NPRM. We welcome your feedback on this chart, including corrections or suggestions for further clarification.

| Current Regulations[1] | Notice of Proposed Rulemaking[2] |
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| **__.101 – To what does this policy apply?** | |
| ▪ **46.101(a)** – This policy applies to all research involving human subjects conducted, supported, or otherwise subject to regulation by any Federal department or agency, including such research that is conducted outside the US. | ▪ **__.101(a)** – Language added to reflect that, with the exception of excluded activities or exempt research, all clinical trials (i) being conducted at an institution that receives Federal funding; (ii) that are not subject to regulation by the FDA; and (iii) that are conducted at an institution within the US, are subject to the policy. In addition, makes clear that institutions engaged in, and IRBs reviewing, research involving human subjects are the entities charged with complying with the policy. The other provisions at __.101(a) remain the same. |
| ▪ **46.101(b)** – Research activities in which the only involvement of human subjects is in one of the following categories are exempt from this policy:<br>(1) Research conducted in educational settings involving normal | ▪ **__.101(b)** – This section has been modified significantly with, what are now referred to as, excluded activities, broken into three categories:<br>(1) The following activities are excluded because they are not |

[1] The regulatory text below is summarized and shortened for the purposes of this chart. For further clarification and additional information, please make sure to refer to the complete text of 45 CFR 46.

[2] The regulatory text below is summarized and shortened for the purposes of this chart. For further clarification and additional information, please make sure to refer to the complete text of the DHHS' September 2015 NPRM.

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| educational practices;<br>(2) Research involving the use of educational tests, surveys, interviews, or public behavior observation (unless research is identifiable or disclosure of responses could reasonably place subjects at risk);<br>(3) Research involving the use of educational tests, surveys, interviews, or public behavior observation not exempt under 46.101(b)(2) if the subjects are appointed public officials or candidates for public office or Federal statues require without exception the confidentiality of any identifiable information;<br>(4) Research involving the collection or study of publicly available or existing data, documents, records, pathological specimens, or diagnostic specimens that is not identifiable;<br>(5) Research and demonstration projects which are conducted by or subject to the approval of government department or agency heads that evaluate public benefit service programs;<br>(6) Taste and food quality evaluation and consumer acceptance studies. | deemed to be research for the purposes of this regulation:<br>(i) Data collection and analysis, including the use of biospecimens, for an institution's operational monitoring or program improvement purposes if data was originally collected for another purpose or is obtained through oral or written communications with individuals (e.g., surveys, interviews);<br>(ii) Oral history, journalism, biography, and historical scholarship activities that focus directly on the specific individuals;<br>(iii) Collection and analysis of data, biospecimens, or records by or for a criminal justice agency as authorized by law or court order;<br>(iv) Quality assurance or improvement activities involving the implementation of an accepted practice to improve the delivery or quality of care or services if purposes are limited to altering the utilization of the accepted practice and collecting data or biospecimens to evaluate the effects on the utilization of the practice;<br>(v) Public health surveillance activities;<br>(vi) Surveys, interviews, surveillance activities and related analyses, or the collection and use of biospecimens conducted by a defense, national security, or homeland security authority solely for authorized intelligence.<br>(2) With the exception of research that involves the collection or analysis of biospecimens, the following activities are excluded because they are considered to be *low-risk* human subjects research:<br>(i) Research, not including interventions, that involves the use of educational tests, survey procedures, interview procedures, or public behavior observation (unless the information is identifiable; disclosure of responses could reasonably place subjects at risk; *or* the research involves a collection of information subject to the Paperwork Reduction Act of 1995, which will be maintained in accordance with the E-Government Act of 2002 and the Privacy Act of 1974);<br>(ii) Research involving the collection or study of information that has been or will be acquired solely for non-research activities or were acquired for research studies other than the proposed research study, if the sources are publicly available *or* the information is not identifiable, the investigator does not contact subjects, or re-identify or |

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| | conduct an analysis that could create identifiable private information;<br>(iii) Research conducted by a Federal department or agency using government-generated or government-collected information obtained for non-research purposes, if the information involved a collection of information subject to the Paperwork Reduction Act of 1995, which is maintained in accordance with the E-Government Act of 2002 and the Privacy Act of 1974;<br>(iv) Research that involves only data collection and analysis involving the recipient's use of identifiable health information when such use is regulated under 45 CFR parts 160 and 164, subparts A and E;<br>(3) The following activities are excluded because they are considered to be *low-risk* human subjects research activities that *do not meaningfully diminish subject autonomy:*<br>(i) The secondary research use of a non-identified biospecimen that is designed only to generate information about an individual that already is known, including but not limited to the development and validation of certain tests and assays, quality assurance and control activities, and proficiency testing. |
| ▪ **46.101(c)** - Department or agency heads retain final judgment as to whether a particular activity is covered by this policy. | ▪ **__.101(c)** – This provision has been modified to indicate that such determinations should be consistent with the ethical principles of the Belmont Report. |
| ▪ **46.101(d) –** Department or agencies heads may require that specific research or classes of research activities conducted, supported, or otherwise subject to regulation by the department or agency that not covered by this policy comply with some or all of the requirements of this policy. | ▪ **__.101(d) –** This provision has been modified to indicate that department or agency heads may require additional protections for specific research or classes of research activities and that advance public notice will be required if the requirements are to apply to entities outside of the department or agency itself. |
| ▪ **46.101(e) -** Compliance with this policy requires compliance with pertinent federal laws or regulations which provide additional protections for human subjects. | ▪ **__.101(e) –** No substantive[3] changes. |
| ▪ **46.101(f) -** This policy does not affect any state or local laws or regulations which may otherwise be applicable and which provide additional protections for human subjects. | ▪ **__.101(f) –** No substantive changes. |

[3] Changes limited to grammar, capitalization, format, or some other element that does not change meaning.

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| ▪ **46.101(g) -** This policy does not affect any foreign laws or regulations which may otherwise be applicable and which provide additional protections to human subjects of research. | ▪ **__.101(g) –** No substantive changes. |
| ▪ **46.101(h) -** When research covered by this policy takes place in foreign countries, a department or agency head may approve the substitution of foreign procedures in lieu of the procedural requirements provided in this policy if the department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy. Notices of such actions will generally be published as appropriate. | ▪ **__.101(h) –** No substantive changes. |
| ▪ **46.101(i) -** Department or agency heads may waive the applicability of some or all of the provisions of this policy to specific research activities or classes or research activities otherwise covered by this policy. Advance notices of such actions will generally be forwarded to OHRP and published as appropriate. | ▪ **__.101(i) –** This provision has been modified to indicate that any alternate procedures to be followed must be consistent with the Belmont Report. In addition, notices of waivers must identify the conditions under which the waiver will be applied and a justification as to why the waiver is appropriate for the research, including how the decision is consistent with the principles in Belmont Report. Waivers must also be posted on a publicly accessible Federal website. The rest of the provision remains the same. |
| ▪ Not applicable. This is a new sub-section. | ▪ **__.101(j) –** This new provision states that Federal guidance on the requirements of this policy shall be issued only after consultation with other Federal departments and agencies that have adopted this policy, unless such consultation is not feasible. |
| ▪ Not applicable. This is a new sub-section. | ▪ **__.101(k) –** This new section explains that for the purposes of transition: (1) research initiated prior to the compliance dates for cited provisions is not required to apply the additional requirements of the proposed rule; and (2) research involving the use of prior collections of biospecimens that were collected for either research or non-research purposes before the compliance date *and* where the use of the biospecimens occurs only after removal of any individually identifiable information associated with the biospecimens is not required to comply with the requirements of this regulation. |

| __.102 – Definitions for purposes of this policy.[4] | |
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| ▪ **46.102(j) -** *Certification* means the official notification by the institution to the supporting department or agency, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance. | ▪ **__.101(a) -** *Certification* – No substantive changes. |
| ▪ *Clinical trial* - Not defined in 45 CFR 46.102. | ▪ **__.101(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. |
| ▪ **46.102(a) -** *Department or agency head* means the head of any federal department or agency and any other officer or employee of any department or agency to whom authority has been delegated. | ▪ **__.102(c) -** *Department or agency head* – No substantive changes. |
| ▪ *Federal department or agency* - Not defined in 45 CFR 46.102. | ▪ **__.102(d) -** *Federal department or agency* refers to a Federal department or agency (the department or agency itself rather than its bureaus, offices or divisions) that takes appropriate administrative action to make this policy applicable to the research involving human subjects it conducts, supports, or otherwise regulates (*e.g.,* HHS, the Department of Defense, or the Central Intelligence Agency). |
| ▪ **46.102(e) -** *Research subject to regulation*, and similar terms are intended to encompass those research activities for which a federal department or agency has specific responsibility for regulating as a research activity. | ▪ *Research subject to regulation* - Not defined in section __.102 of the NPRM. |
| ▪ **46.102(f) -** *Human subject* means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. *Intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research | ▪ **__.102(e) -**<br>(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 |

[4] For the purposes of this section, the content has been organized by definition, since the order of terms is different in the NPRM versus 45 CFR 46. In addition, definitions have been included in full from their respective sources in order to ensure accuracy.

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| purposes. Interaction includes communication or interpersonal contact between investigator and subject. *Private information* includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. | biospecimens.<br>(2) *Intervention* – No substantive differences.<br>(3) *Interaction* – No substantive differences.<br>(4) *Private information* includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be shared or made public (*e.g.,* a medical record or clinically obtained biospecimen).<br>(5) *Identifiable private information* is private information that is individually identifiable (*i.e.,* the identity of the subject is or may readily be ascertained by the investigator or associated with the information). |
| ▪ **46.102(b) -** *Institution* means any public or private entity or agency (including federal, state, and other agencies). | ▪ __**.102(f) –** *Institution* – No substantive changes. |
| ▪ **46.102(g) -** *IRB* means an institutional review board established in accord with and for the purposes expressed in this policy. | ▪ __**.102(g) –** *IRB* – No changes. |
| ▪ **46.102(h) -** *IRB approval* means the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements. | ▪ __**.102(h) –** *IRB approval* – No changes. |
| ▪ **46.102(c) -** *Legally authorized representative* means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. | ▪ __**.102(i) –** *Legally authorized representative* – No changes. |
| ▪ **46.102(i) -** *Minimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. | ▪ __**.102(j) –** Minimal risk **–** No changes to the core definition, but addition of language indicating that the Secretary of HHS will maintain a list of activities considered to involve no more than minimal risk, which will be updated no less frequently than every eight years. |
| ▪ *Public health authority* - Not defined in 45 CFR 46.102. | ▪ __**.102(k) –** *Public health authority* (consistent with 45 CFR 164.501) means an agency or authority of the United States, a state, a territory, a political subdivision of a state or territory, an Indian tribe, or a foreign government, or a person or entity acting under a grant of authority from or contract with such public agency, |

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| | including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its official mandate. |
| ▪ **46.102(d) -** *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. | ▪ **__.102(l) –** *Research* – No substantive changes. |
| **__.103 Assuring compliance with this policy—research conducted or supported by any Federal department or agency.** | |
| ▪ **46.103(a) -** Each institution engaged in research which is covered by this policy and which is conducted or supported by a federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in this policy. In lieu of requiring submission of an assurance, individual department or agency heads shall accept the existence of a current assurance, appropriate for the research in question, on file with OHRP, HHS, or any successor office, and approved for federalwide use by that office. When the existence of an HHS-approved assurance is accepted in lieu of requiring submission of an assurance, reports (except certification) required by this policy to be made to department and agency heads shall also be made to the OHRP, HHS, or any successor office. | ▪ **__.103(a) –** This section has been combined with elements from what was previously 46.103(b). Language has been added to note that these provisions do not apply to exempt or excluded research. |
| ▪ **46.103(b) -** Departments and agencies will conduct or support research covered by this policy only if the institution has an assurance, and only if the institution has certified to the department or agency head that the research has been reviewed and approved by an IRB provided for in the assurance, and will be subject to continuing review by the IRB. Assurances shall at a minimum include:<br>(1) A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution, regardless of whether the research is subject to Federal regulation. | ▪ **__.103(a) –** The requirement that an institutions provide an assurance, which was previously found in section 46.103(b), has been combined with the requirements in 46.103(a) and the term “approved” has been eliminated in relation to assurance.<br><br>The elements of an assurance, which were previously listed in section 46.103(b) have also been modified. The requirement to include a statement of principles governing the institution in its discharge of its responsibilities for protecting the rights and welfare of subjects has been eliminated, as has the requirement to designate one or more IRB. The other elements that were outlined at 46.103(b) are now found in section __.108(a), which describes |

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| (2) Designation of one or more IRBs established in accordance with the requirements of this policy, and for which appropriate provisions exist.<br>(3) A list of IRB members with details sufficient to describe each member's chief anticipated contributions to IRB deliberations; as well as information on employment or other relationship between each member and the institution, with changes in IRB membership reported as appropriate.<br>(4) Written procedures which the IRB will follow (i) for conducting its initial and continuing review of research and for reporting its findings and actions; (ii) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators; and (iii) for ensuring prompt reporting to the IRB, and for ensuring that changes in approved research may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.<br>(5) Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance; and (ii) any suspension or termination of IRB approval. | IRB functions and operations. |
| ▪ **46.103(c) -** The assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this policy and shall be filed in such form and manner as the department or agency head prescribes. | ▪ **__.103(b) –** The requirements at 46.103(c) are now located at __.103(b). There are no changes in the content. |
| ▪ **46.103(d) -** The department or agency head will evaluate all assurances submitted in accordance with this policy as appropriate. The department or agency head's evaluation will take into consideration the adequacy of the proposed IRB in light of the anticipated scope of the institution's research activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution. | ▪ This provision has been eliminated in the NPRM. |
| ▪ **46.103(e) -** The department or agency head may approve or disapprove the assurance, or enter into negotiations to develop an approvable one. The department or agency head may limit the period during which any particular approved assurance or class of approved assurances shall remain effective or otherwise condition or | ▪ **__.103(c) -** The requirements at 46.103(e) are now located at __.103(c). References to approved assurances have been removed, but the other provisions remain the same. |

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| restrict approval. | |
| ▪ **46.103(f) -** Certification is required when the research is supported by a federal department or agency and not otherwise exempted or waived. An institution with an approved assurance shall certify that each application or proposal for research covered by the assurance and by §46.103 has been reviewed and approved by the IRB. Such certification must be submitted with the application or proposal or by such later date as may be prescribed by the department or agency to which the application or proposal is submitted. Under no condition shall research covered by §46.103 be supported prior to receipt of the certification that the research has been reviewed and approved. Institutions without an approved assurance covering the research shall certify within 30 days after receipt of a request for such a certification from the department or agency, that the application or proposal has been approved by the IRB. If the certification is not submitted within these time limits, the application or proposal may be returned to the institution. | ▪ **__.103(d) -** The requirements at 46.103(f) are now located at __.103(d). Language has been added to note certification is not required for exempt, excluded, or waived research. In addition, language indicating that certification must be submitted with IRB applications or proposals has been removed. Requirements relating to certification by institutions without an approved assurance have also been eliminated. |
| ▪ Not applicable. This is a new sub-section. | ▪ **__.103(e) –** This new section indicates that for non-exempt research involving human subjects covered by this policy that takes place at an institution in which IRB oversight is conducted by an IRB that is not operated by the institution, the institution and the organization operating the IRB shall establish and follow procedures for documenting the institution's reliance on the IRB for oversight of the research and the responsibilities that each entity will undertake to ensure compliance with the requirements of this policy. |
| **__.104 Exempt research.** | |
| ▪ Not applicable. This is largely a new section. Some elements do, however, reflect what was previously found at 46.101(b). | ▪ **__.104(a) –** This section states that unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the categories in paragraphs (d) through (f) of this section are not subject to the requirements of this policy, other than those specified in the category. |
| | ▪ **__.104(b)** – This section provides information on the use of the exemption categories for research subject to the requirements of subparts B, C, and D. Specifically, application of the exemption |

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| | categories to research subject to the requirements of 45 CFR 46 subparts B, C, and D, is as follows:<br>(1) *Subpart B.* Each of the exemptions at this § __.104 may be applied to research conducted under subpart B.<br>(2) *Subpart C*. The exemptions at this § __.104 do not apply to research conducted under subpart C, except for research aimed at a broader population that consists mostly of non-prisoners.<br>(3) *Subpart D.* Only the exemptions at paragraphs (d)(1), (2), (4), (e)(2), and (f)(1) and (2) of this section may be applied to research conducted under subpart D. |
| | ▪ __**.104(c) –** This section states that Federal departments and agencies shall develop a decision tool to assist in exemption determinations. Exemption determinations are to be made by an individual who is knowledgeable about the exemption categories and who has access to sufficient information to make an informed and reasonable determination, or by the investigator or another individual at the institution who enters accurate information about the proposed research into the decision tool. The use of the decision tool will eliminate the need for further assessment or evaluation of the exemption determination. 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. Records must include, at a minimum, the name of the study, the name of the investigator, and the exemption category applied. Maintenance of the completed decision tool shall fulfill this recordkeeping requirement.<br>(1) For studies exempted pursuant to paragraph (d)(2) of this section, the recordkeeping requirement will be deemed satisfied by the published list required at paragraph (d)(2)(i). |
| | ▪ __**.104(d) –** This section lists categories of exempt human subjects research that generally involve a low-risk intervention with human subjects, must be recorded as required in paragraph (c) of this section, and do not require application of standards for information and biospecimen protection provided in § __.105 or informed consent, as only paragraph (d)(2) of this section allows for the collection and use of biospecimens. The categories are:<br>(1) Research conducted in established or commonly accepted educational settings when it specifically involves normal educational practices. |

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| | (2) Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads, and that are designed to study, evaluate, or otherwise examine public benefit or service programs.<br>(i) Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible federal Web site or in a similar manner, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to or upon commencement of the research.<br>(3)<br>(i) Research involving benign interventions in conjunction with the collection of data from an adult subject through verbal or written responses or video recording if the subject prospectively agrees and at least one of the following criteria is met: (A) the information obtained is recorded in such a manner that human subjects cannot be identified; or (B) any disclosure of the subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation.<br>(ii) For the purpose of this provision, benign interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing.<br>(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception below.<br>(iv) Authorized deception is prospective agreement by the subject to participate in research where the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.<br>(4) Taste and food quality evaluation and consumer acceptance studies (i) if wholesome foods without additives are consumed, or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural |

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| | chemical or environmental contaminant at or below the level found to be safe. |
| | ▪ __**.104(e) –** The section lists categories of exempt human subjects research that allow for the collection of sensitive information about human subjects, must not involve biospecimens, must be recorded as required in paragraph (c) of this section, and require application of standards for information and biospecimen protection provided in __.105:<br>(1) Research, not including interventions, involving the use of educational tests, survey procedures, interview procedures, or observation of public behavior, if the information obtained is recorded in such a manner that human subjects can be identified directly or through identifiers linked to the subjects.<br>(2) Secondary research use of identifiable private information that has been or will be acquired for non-research purposes, if the following criteria are met: (i) prior notice has been given to the individuals to whom the identifiable private information pertains that such information may be used in research; and (ii) the identifiable private information is used only for purposes of the specific research for which the investigator or recipient entity requested access to the information. |
| | ▪ __**.104(f) –** The section details categories of exempt human subjects research that involve biospecimens or identifiable private information, must be recorded as required in paragraph (c) of this section, require application of standards for information and biospecimen protection as described in § __.105, and require informed consent and limited IRB review to the extent described in each category or otherwise required by law:<br>(1)<br>(i) Storage or maintenance for secondary research use of biospecimens or identifiable private information that have been or will be acquired for research studies other than for the proposed research study, or for non-research purposes, if the following criteria are met: (A) written consent for the storage, maintenance, and secondary research use of the information or biospecimens is obtained in accordance with __.116(c) and (d)(2), and the template published by the Secretary of HHS is used. Oral consent, if obtained during the original data collection and in accordance with __.116(c) and (d)(3), would be satisfactory for the research use of identifiable private information initially acquired in accordance with activities |

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| | excluded from this policy under __.101(b)(2)(i) or exempt from this policy in accordance with __.104(d)(3) or (4), or __.104(e)(1); (B) the reviewing IRB makes the determinations required by __.111(a)(9).<br>(2)<br>(i) Research involving the use of biospecimens or identifiable private information that have been stored or maintained for secondary research use, if consent for the storage, maintenance, and secondary research use of the information and biospecimens was obtained as detailed in paragraph (f)(1)(i)(A) of this section.<br>(ii) If the investigator anticipates that individual research results will be provided to a research subject, the research may not be exempted under this provision and must be reviewed by the IRB and informed consent for the research must be obtained to the extent required by __.116(a) and (b). |
| **__.105 Protection of biospecimens and identifiable information.** | |
| ▪ Not applicable. This is a new section. | **__.105(a) –** This section indicates that institutions and investigators conducting research that is subject to this policy, or exempt from this policy, involving the collection, storage, or use of biospecimens or identifiable private information, shall implement and maintain reasonable and appropriate safeguards to protect biospecimens or identifiable private information. The safeguards shall reasonably protect against anticipated threats or hazards to the security or integrity of the information or biospecimens, as well as any intentional or unintentional use, release, or disclosure that is in violation of paragraph (c) of this section. IRB review of the safeguards required by this section is not required, except to the extent required by § __.104(f)(1). |
| | **__.105(b) –** This section describes the process by which the Secretary of HHS shall establish and publish for public comment a list of specific measures deemed to satisfy the requirement for reasonable and appropriate safeguards. The list will be evaluated as needed, but at least every 8 years, and amended, as appropriate. Institutions and investigators shall choose either to apply the safeguards identified by the Secretary, or to apply safeguards that meet the standards in 45 CFR 164.308, 164.310, 164.312, and 45 CFR 164.530(c). Certain activities conducted by |

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| | Federal departments and agencies that are in compliance with standards set forth in the E-Government Act of 2002, the Privacy Act of 1974, and the Paperwork Reduction Act of 1995 will automatically be considered in compliance with the Secretary's reasonable and appropriate safeguards standards, unless or until any additional safeguards are identified by the Secretary of HHS. |
| | **__.105(c) –** This section indicates that institutions and investigators shall use or release biospecimens or identifiable private information collected or maintained for research only:<br>(3) For human subjects research regulated by this policy;<br>(4) For public health purposes;<br>(5) For any lawful purpose with the consent of the subject; or<br>(6) For other research purposes if the institution or investigator has obtained adequate assurances from the recipient that:<br>(i) The recipient will implement and maintain the level of required safeguards;<br>(ii) The research has been approved before releasing biospecimens or disclosing identifiable private information (this does not apply for excluded or exempt research). The disclosing or releasing institution or investigator must obtain documentation of this; and<br>(iii) The recipient shall not further release the biospecimens or disclose identifiable private information except for human subjects research regulated by this policy, or for other purposes permitted by this paragraph. This is to be done through the use of a written agreement with the recipient. |
| | **__.105(d) –** The section notes that the provisions of this section do not amend or repeal, and shall not be construed to amend or repeal, requirements related to the HIPAA Privacy Rule for the institutions or investigators, including Federal departments or agencies, to which these regulations are applicable pursuant to 45 CFR 160.102. |
| **__.107 IRB membership.** | |
| ▪ **46.107(a) –** Each IRB must have at least five members with varying backgrounds. The IRB shall be sufficiently qualified through the experience, expertise, and diversity of its members, with respect to race, gender, cultural backgrounds, and sensitivity to community | ▪ **__.107(a) –** This section includes some modifications, including limiting the consideration of vulnerability of a subject population to vulnerability to coercion and undue influence, and adding economically or educationally disadvantaged persons to the list of |

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| attitudes, to safeguard the rights and welfare of human subjects. The IRB shall determine the acceptability of proposed research in light of institutional commitments and regulations, applicable laws, and standards of professional conduct and practice, and, as such, include individuals knowledgeable in those areas. IRBs that regularly review research involving a vulnerable category of subjects shall include one or more individuals who are knowledgeable about and experienced in working with these subjects. | examples of categories of subjects that are potentially vulnerable to coercion or undue influence. |
| ▪ **46.107(b) -** Efforts will be made to ensure that no IRB consists entirely of men or entirely of women or entirely of members of one profession. | ▪ This provision has been eliminated in the NPRM. |
| ▪ **46.107(c) -** Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. | ▪ **__.107(b) –** Except for numbering, no changes. |
| ▪ **46.107(d) -** Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. | ▪ **__.107(c) –** Except for numbering, no changes. |
| ▪ **46.107(e) -** No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB. | ▪ **__.107(d) –** Except for numbering, no changes. |
| ▪ **46.107(f) -** An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB. | ▪ **__.107(e) –** Except for numbering, no substantive changes. |
| **__.108 IRB functions and operations.** | |
| ▪ **46.108(a)** - Follow written procedures in the same detail as described in §46.103(b)(4) and, to the extent required by, §46.103(b)(5). | ▪ **__.108(a) –** This section now contains the requirements that were previously listed in section 46.103(b)(2) - 46.103(b)(5). Specifically, that an IRB shall:<br>(7) Have access to meeting space and sufficient staff to support its review and recordkeeping duties;<br>(8) Prepare and maintain a current list of the IRB members;<br>(9) Establish and follow written procedures for: (i) initial and continuing review; (ii) determining which projects require review |

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| | more often than annually and which projects need verification that no material changes have occurred since previous IRB review; and; (iii) ensuring prompt reporting to the IRB of proposed changes and for ensuring that changes in approved research may not be initiated without IRB review;<br>(10) Establish and follow written procedures for ensuring prompt reporting of: (i) unanticipated problems involving risks to subjects or others or serious or continuing noncompliance; and (ii) any suspension or termination of IRB approval.<br>The only substantive difference between the current rule and the proposed rule with respect to these requirements is the elimination of the language requiring that changes in IRB membership be reported to the department or agency head or OHRP, as appropriate. |
| ▪ **46.108(b)** - Except when an expedited review procedure is used (see §46.110), review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting. | ▪ **__.108(b) –** No substantive changes. |
| **__.109 IRB review of research.** | |
| ▪ **46.109(a) –** An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy. | ▪ **__.109(a) –** This section has been modified to indicate that this does not include activities that qualify for an exemption. |
| ▪ **46.109(b) –** An IRB shall require that information given to subjects is in accordance with §46.116. An IRB may also require additional information be given to subjects if the IRB determines the information would meaningfully add to the protection of the rights and welfare of subjects. | ▪ **__.109(b) –** No changes. |
| ▪ **46.109(c) –** An IRB shall require documentation of informed consent or may waive documentation in accordance with §46.117. | ▪ **__.109(c) –** No changes. |
| ▪ **46.109(d) –** An IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of required modifications. If the IRB disapproves a research activity, it shall include a statement of the reasons for its decision and give the investigator an opportunity to respond. | ▪ **__.109(d) –** No changes. |

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| ▪ **46.109(e) –** An IRB shall conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research. | ▪ **__.109(e) –** This provision has been modified to make clear it is referring to continuing review by a convened IRB. |
| ▪ **46.109(f) –** Not applicable. This is a new sub-section. | ▪ **__.109(f) –**<br>(1) Unless an IRB decides otherwise, continuing review is not required for: (i) research eligible for expedited review; (ii) research that has progressed to the point that it only involves data analysis of private identifiable information, and/or accessing follow-up clinical data from procedures that subjects would undergo as part of standard care for their medical condition; and research reviewed in accordance with a limited IRB review procedure.<br>(2) An IRB must confirm on an annual basis that the research is still ongoing and no changes have been made to the research that would require the IRB to conduct continuing review. |
| ▪ **46.109(g) –** Not applicable. This is a new sub-section. | ▪ **__.109(g) –** This new section contains provisions that were previously incorporated in section 46.109(e): An IRB shall have authority to observe or have a third party observe the consent process and the research. |
| **__.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.** | |
| ▪ **46.110(a) -** The Secretary of HHS has made available a list of categories of research that may be reviewed by the IRB through an expedited review procedure. The list will be amended, as appropriate, and republished in the Federal Register. A copy of the list is available from OHRP. | ▪ **__.110(a) –** No substantive changes except the addition of language stating that the list will be evaluated at least every eight years. |
| ▪ **46.110(b) -** An IRB may use an expedited review procedure to review: (1) some or all of the research appearing on the list determined to involve no more than minimal risk; and/or<br>(2) minor changes in previously approved research during the study's approval period. Expedited review may be carried out by the IRB chair or by one or more experienced reviewers designated by chair. Reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review at a convened meeting. | ▪ **__.110(b) –** This section now contains a third category of research that may be reviewed by expedited review: Research that is being reviewed to determine whether it qualifies for an exemption in accordance with __.104(f)(1). |

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| ▪ **46.110(c) -** Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure. | ▪ **__.110(c) –** No substantive changes. |
| ▪ **46.110(d) -** The department or agency head may restrict, suspend, terminate, or choose not to authorize an institution's or IRB's use of the expedited review procedure. | ▪ **__.110(d) -** No changes. |
| **__.111 Criteria for IRB approval of research.** | |
| ▪ **46.111(a) -** In order to approve research, an IRB shall determine that:<br>(1) Risks to subjects are minimized: (i) by using procedures consistent with sound research design, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.<br>(2) Risks to subjects are reasonable in relation to anticipated benefits. IRBs should consider only those risks and benefits that may result from the research. IRBs not consider possible long-range effects of applying knowledge gained in the research.<br>(3) Selection of subjects is equitable. IRB should take into account the purposes of the research and the setting and should be particularly cognizant of the special problems of research involving vulnerable populations.<br>(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative.<br>(5) Informed consent will be appropriately documented.<br>(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.<br>(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.<br>(8) Not applicable. This is a new provision. | ▪ **__.111(a) –** The majority of the criteria remain the same, with the exception of __.111(a)(3) and__.111(a)(7), which have been modified. In addition, two new requirements which address the return of clinically relevant results to subjects [__.111(a)(8)] and limited IRB review [__.111(a)(9)], respectively, have been added.<br>(1) No substantive changes<br>(2) No substantive changes<br>(3) No substantive changes except for the addition of physically disabled people to the list of categories of potential vulnerable persons.<br>(4) No substantive changes<br>(5) No substantive changes<br>(6) No substantive changes<br>(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data, in addition to the requirements in § __.105, if the IRB determines that the standards for information and biospecimen protection in § __.105 are not sufficient to protect the privacy of subjects and the confidentiality of data.<br>(8) If the investigator proposes a research plan for returning clinically relevant results to subjects, that the plan is appropriate.<br>(9) For purposes of conducting the limited IRB review, IRBs need not make the determinations at paragraphs (a)(1) through (8) of this section. Instead, IRBs shall determine that: (i) the procedures for obtaining broad consent for storage, maintenance, and secondary research use of biospecimens or identifiable private information will be conducted; and that (ii) if are changes for research purposes in the way the biospecimens or information are stored or maintained, that the privacy and information protection standards at § __.105 are |

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| | satisfied. |
| ▪ **46.111(b) -** When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects. | ▪ **__.111(b) -** No substantive changes except for the addition of physically disabled people to the list of categories of potential vulnerable persons. |
| **__.112 Review by institution.** | |
| ▪ **46.112** - Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB. | ▪ **__.112 –** No substantive changes. |
| **__.113 Suspension or termination of IRB approval.** | |
| ▪ **46.113 -** An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. IRB will provide statement of the reasons for the IRB's action and promptly report actions to the investigator, appropriate institutional officials, and the department or agency head. | ▪ **__.113 –** No substantive changes. |
| **__.114 Cooperative research.** | |
| ▪ **46.114 -** Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the department or agency head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of | ▪ **__.114(a) –** No substantive changes except that the language about when an institution participating in a cooperative project may enter into a joint review arrangement separated and made into section __.114(c). |

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| another qualified IRB, or make similar arrangements for avoiding duplication of effort. | |
| ▪ **46.114(b) -** Not applicable. This is a new sub-section. | ▪ **__.114(b) –**<br>(1) This new section states that 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.<br>(2) This new section indicates that the following research is not subject to the requirements of this provision: (i) cooperative research for which more than single IRB review is required by law; or (ii) 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. |
| ▪ **46.114(c) -** Not applicable. This is a new sub-section. | ▪ **__.114(c) -** This new section contains provisions that were previously incorporated in section 46.116: For research not subject to paragraph (b) of this section, an institution participating in a cooperative project may enter into a joint review arrangement, rely on the review of another IRB, or make similar arrangements for avoiding duplication of effort. In addition, phrase "with the approval of the department or agency head" has been removed. |
| **__.115 IRB records.** | |
| ▪ **46.115(a)** - An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation, including:<br>(1) Copies of all research proposals reviewed; scientific evaluations, if any; approved sample consent documents; progress reports; and reports of injuries to subjects.<br>(2) Minutes of IRB meetings which shall be in sufficient detail to show meeting attendance; actions taken by the IRB; the vote on these actions including the number voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.<br>(3) Records of continuing review activities. | **__.115(a) -** There have been some modifications to the existing IRB documentation requirements, as well as the addition of some new requirements:<br>(1) No substantive changes.<br>(2) No changes<br>(3) Records for continuing review activities, including the rationale for conducting continuing review of research that has progressed to the point that it only involves data analysis and/or accessing follow-up clinical data from procedures that subjects would undergo as part of standard care for their medical condition.<br>(4) No changes |

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| (4) Copies of all correspondence between the IRB and the investigators.<br>(5) A list of IRB members as described previously.<br>(6) Written procedures for the IRB as described previously.<br>(7) Statements of significant new findings provided to subjects.<br>(8) Not applicable. This is a new provision.<br>(9) Not applicable. This is a new provision.<br>(10) Not applicable. This is a new provision.<br>(11) Not applicable. This is a new provision. | (5) No substantive changes.<br>(6) No substantive changes.<br>(7) No substantive changes.<br>(8) Rationale for requiring continuing review for research that otherwise would not require it.<br>(9) Rationale for an expedited reviewer's determination that research appearing on the expedited review list is more than minimal risk.<br>(10) Written agreement between an institution and an organization operating an IRB that outlines the responsibilities of each entity with respect to ensuring compliance with this policy.<br>(11) Records relating to exempt determinations. |
| ▪ **46.115(b)** - The records required by this policy shall be retained for at least 3 years, and records relating to research which is conducted shall be retained for at least 3 years after completion of the research. Records shall be accessible for inspection and copying by authorized representatives of the department or agency at reasonable times and in a reasonable manner. | ▪ **__.115(b) –** No substantive changes except the inclusion of language indicating that records can be maintained in printed form or electronically. |
| **46.115(c) -** Not applicable. This is a new sub-section. | ▪ **__.115(c) –** This section states that the institution or IRB retaining the records shall safeguard identifiable private information contained within these records in compliance with __.105. |
| **__.116 General requirements for informed consent.** | |
| ▪ **46.116 -** Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. Consent must be sought under circumstances that provide the prospective subject or representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. Information must be provided in a language that is understandable to the subject or the representative. No informed consent may include any exculpatory language. | ▪ **46.116 –** In this section, language to the following effect has been added: Prospective subject or representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information. Information must be presented in sufficient detail and organized and presented in a way that facilitates the prospective subject's or representative's understanding. Investigator must present information required by this section first. Any informed consent form must include only the requirements of informed consent under this section, and appendices that include any other information. If an authorization required by 45 CFR parts 160 and 164 is combined with a consent form, the authorization elements must be included in the consent form, not the appendices. |

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| ▪ **46.116(a) -** *Basic elements of informed consent.* Except as provided below, the following information shall be provided to each subject:<br>(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;<br>(2) A description of any reasonably foreseeable risks or discomforts to the subject;<br>(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;<br>(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;<br>(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;<br>(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;<br>(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and<br>(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.<br>(9) Not applicable. This is a new provision. | ▪ **__.116(a) -** This section remain largely unchanged, with the exception of an additional element related to the collection of identifiable private information:<br>(1) No substantive changes.<br>(2) No changes.<br>(3) No substantive changes.<br>(4) No changes.<br>(5) No changes.<br>(6) No changes.<br>(7) No changes.<br>(8) No changes.<br>(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. |
| ▪ **46.116(b) -** *Additional elements of informed consent.* When appropriate, one or more of the following elements of information shall also be provided:<br>(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;<br>(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;<br>(3) Any additional costs to the subject that may result from | ▪ **__.116(b) –**Three additional elements have been added to this section:<br>(1) No substantive changes.<br>(2) Modified to indicate subject’s participating may be terminated without regard to the subject’s or representative’s consent.<br>(3) No changes.<br>(4) No changes.<br>(5) No substantive changes.<br>(6) No changes.<br>(7) A statement that the subject's biospecimens may be used for commercial profit and whether the subject will or will not share |

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| participation in the research;<br>(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;<br>(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and<br>(6) The approximate number of subjects involved in the study.<br>(7) Not applicable. This is a new provision.<br>(8) Not applicable. This is a new provision.<br>(9) Not applicable. This is a new provision. | in this commercial profit;<br>(8) A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and<br>(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. |
| ▪ Not applicable. This is a new sub-section. The provisions that were previously found at 46.111(c) are incorporated into 46.111(e) in the NPRM. | ▪ __**.116(c) –** This new section details the elements of informed consent for broad consent to the storage, maintenance, and secondary research use of biospecimens or identifiable private information. If a subject or their representative will be asked to provide broad consent to the storage or maintenance of biospecimens or identifiable private information and the secondary research use of this stored material, the information required in paragraphs (a)(2), (3), (5), and (7) and, if applicable, (b)(7) through (9) of this section, shall be provided to each subject, as well as:<br>(i) A general description of the types of research that may be conducted and the information that is expected to be generated, the types of information or biospecimens that might be used, and the types of institutions that might the research;<br>(ii) A description of the scope of the informed consent must be provided, including:<br>(A) A clear description of the types of biospecimens or information that were or will be collected and the period of time during which collection will occur. This may include all biospecimens and information from the subject's medical record or other records existing at the institution at the time informed consent is sought; and<br>(B) The period of time during which biospecimen or information collection will occur cannot exceed 10 years from the date of consent. For research involving children, that time period cannot exceed 10 years after parental permission is obtained or until the child reaches the legal age for consent to the treatments or procedures involved, whichever time period is shorter. The time limitations described do not apply to biospecimens or information that initially will be collected for research purposes. |

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| | (iii) A description of the period of time during which an investigator can continue to conduct research using the subject's biospecimens and information<br>(iv) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits, and that the subject may withdraw consent, if feasible, for research use or distribution of the subject's information or biospecimens at any time without penalty or loss of benefits, and information about whom to contact in order to withdraw consent. The statement must make clear that information or biospecimens that already have been distributed for research use may not be retrieved;<br>(v) If applicable, a statement notifying the subject or the representative that they will not be informed of the details of any specific research studies that might be conducted;<br>(vi) If applicable, a statement notifying the subject or the representative of the expectation that the subject's information and biospecimens are likely to be used by multiple investigators and institutions and shared broadly for many types of research studies in the future, and this information and the biospecimens might be identifiable when shared;<br>(vii) The names of the institution or set of institutions at which the subject's biospecimens or information were or will be collected; and<br>(viii) If relevant, an option for an adult subject or the representative to consent, or refuse to consent, to the inclusion of the subject's data, with removal of the identifiers, in a database that is publicly and openly accessible to anyone. This option must be prominently noted, and must include a description of risks of public access to the data. |

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| ▪ Not applicable. This is a new sub-section. The provisions that were previously found at 46.111(d) are incorporated into 46.111(f) in the NPRM. | ▪ **__.116(d) –**<br>(1) This new provision states that the Secretary of HHS will establish, and publish for public comment, templates for broad consent that will contain all of the required elements 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 the template provided by the Secretary without any changes.<br>(2) If __.104(f)(1) requires written consent, the consent for research use of biospecimens or identifiable private information must be documented by the use of a written consent form signed by the subject or the representative. The template established by the Secretary may serve as the written consent form. A copy shall be given to the person signing the form.<br>(3) If __.104(f)(1) allows for oral consent, a subject's or the representative's oral consent for research use of identifiable private information must be documented such that the consent is associated with the subject's identifiable private information. If this requirement is met through the use of written documentation, the subject or the representative is not required to sign the documentation.<br>(4) If the subject or the representative declines to consent to the research use of biospecimens or identifiable private information, this must be documented appropriately. |
| ▪ **46.116(c) -** An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:<br>(1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine issues related to (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and<br>(2) The research could not practicably be carried out without the waiver or alteration. | ▪ **__.116(e) –**<br>(1) This provision is currently found at 46.116(c). There are no substantive changes from what is found in 46.116(c) with respect to such waivers or alterations of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials.<br>(2) This new provision details the criteria for waivers or alterations of consent for biospecimens. Specifically, for research involving the use of biospecimens, an IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent, or waives the above requirements, provided the IRB finds and documents the criteria in paragraph (e)(1) of this section, and that (i) there are compelling scientific reasons to conduct the research; and that (ii) the research could not be conducted with other biospecimens for which informed consent was obtained or could be obtained.<br>(3) This new provision notes that if an individual was asked to |

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| | consent to the storage or maintenance for secondary research use of biospecimens or identifiable private, and refused to consent, an IRB cannot waive consent for either the storage or maintenance for secondary research use, or for the secondary research use, of those biospecimens or information. |
| ▪ **46.116(d) -** An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:<br>(1) The research involves no more than minimal risk to the subjects;<br>(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;<br>(3) The research could not practicably be carried out without the waiver or alteration; and<br>(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation. | ▪ **__.116(f) –**<br>(1) This provision is currently found at 46.116(d). In addition to the conditions under which an IRB can approve a waiver or alteration of consent currently listed, the proposed rule states that an IRB must also find and document the research could not practicably be carried out without accessing or using identifiers if the research involves accessing or using identifiable biospecimens or identifiable information. There are no other substantive changes to this provision.<br>(2) This new provision lists additional criteria for waiver or alteration of consent for research involving biospecimens. For research involving the use of biospecimens, an IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent, or waive the above requirements, provided the IRB finds and documents the criteria in paragraph (f)(1) of this section, and the following additional criteria: (i) there are compelling scientific reasons for the research use of the biospecimens; and (ii) the research could not be conducted with other biospecimens for which informed consent was obtained or could be obtained.<br>(3) This new provision notes that if an individual was asked to consent to the storage or maintenance for secondary research use of biospecimens or identifiable private information, and refused to consent, an IRB cannot waive consent for either the storage or maintenance for secondary research use, or for the secondary research use, of those biospecimens or information. |

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| ▪ **46.116(e) -** The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective. | ▪ **__.116(i) –** The requirements at 46.116(e) are now listed at __.116(i). There have been no substantive changes to those requirements. |
| ▪ **46.116(f) -** Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law. | ▪ **__.116(f) -** The requirements at 46.116(f) are now listed at __.116(j). There have been no substantive changes to those requirements. |
| ▪ **46.116(g) -** Not applicable. This is a new sub-section. | ▪ **__.116(g) –** This new section explains that an IRB may approve a research proposal in which investigators obtain, through oral or written communication or by accessing records, identifiable private information without individuals' informed consent for the purpose of screening, recruiting, or determining the eligibility of prospective human subjects of research, provided that the research proposal includes an assurance that the investigator will implement standards for protecting the information obtained, in accordance with and to the extent required by __.105. |
| ▪ **46.116(h) -** Not applicable. This is a new sub-section. | ▪ **__.116(h) –**<br>(1) This new provision requires that a copy of the final version of the informed consent form for each clinical trial conducted or supported by a Federal department or agency be posted on a publicly available federal Web site that will be established as a repository for such informed consent forms. The informed consent form must be posted in a prescribed manner, which will include at a minimum posting, in addition to the informed consent form, the name of the clinical trial and information about whom to contact for additional details about the clinical trial.<br>(2) This new provision requires that form be posted on the federal Web site within 60 days after the trial is closed to recruitment. |
| **__.117 Documentation of informed consent.** | |
| ▪ **47.117(a) -** Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form. | ▪ **__.117(a) –** This provision has been modified to include a note indicating that this does not apply to research for which consent is obtained in accordance with __.116(c). |

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| ▪ **47.117(b) -** Except as provided in paragraph (c) of this section, the consent form may be either of the following:<br>(1) A written consent document that embodies the elements of informed consent required by §46.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or<br>(2) A short form written consent document stating that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject's legally authorized representative. This method requires the use of a witness or the oral presentation. The IRB is also required to approve a written summary of what is to be said to the subject or the representative. Only the short form must be be signed by the subject or the representative. However, the witness must sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form. | ▪ **__.117(b) –** This section details the form that the consent form should take. Modifications have been made to this section in relation to the new requirements at __.116.<br>(1) Provision modified to indicate that the written informed consent form should include only the information required by § __.116, and appendices should include any other information. The rest of the requirements remain the same.<br>(2) Provision modified to indicate that the information required by __.116 should be presented first, followed by any additional information. The rest of the requirements remain the same. |
| ▪ **47.117(c) -** An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:<br>(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. In such cases, subjects will be asked whether they want documentation; or<br>(2) That the research presents no more than minimal risk of harm and involves no procedures for which written consent is normally required outside of the research context.<br>(3) Not applicable. This is a new provision in the NPRM.<br>When the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research. | ▪ **__.117(c) –**. A new category of waiver of documentation of informed consent has been added to this section:<br>(1) No substantive changes.<br>(2) No substantive changes.<br>(3) If subjects are members of a distinct cultural group or community in which signing forms is not the norm, that the research is minimal risk, and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained. Documentation must include a description as to why signing forms is not the norm for the distinct cultural group or community. |
| **__.118 Applications and proposals lacking definite plans for involvement of human subjects.** | |
| ▪ **46.118 -** Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period | ▪ **__.118 -** No substantive changes except for elimination of the sentence that these projects need not be review before an award is made and the addition of excluded research in the list of |

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| of support, but definite plans would not normally be set forth in the application or proposal. These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived, no human subjects may be involved in any project until the project has been reviewed and approved by the IRB and certification submitted, by the institution, to the department or agency. | exceptions. |
| **__.119 Research undertaken without the intention of involving human subjects.** | |
| ▪ **46.119 -** Research undertaken without the intention of involving human subjects, that is later proposed to involve human subjects must first be reviewed and approved by an IRB, a certification submitted, by the institution to the department or agency, and final approval given to the proposed change by the department or agency. | ▪ **__.119 -** No substantive changes except for the addition of language that notes that this does not apply to excluded, waived, or exempted research. |
| **__.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal department or agency.** | |
| ▪ **46.120(a) -** The department or agency head will evaluate all applications and proposals involving human subjects submitted to the department or agency as the department or agency head determines to be appropriate. Evaluation will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained. | ▪ **__.120(a) –** No substantive changes. |
| ▪ **46.120(b) -** On the basis of this evaluation, the department or agency head may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable one. | ▪ **__.120(b) –** No changes. |
| **__.122 Use of Federal funds.** | |
| ▪ **46.122 –** Federal funds administered by a department or agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied. | ▪ **__.122 –** No substantive changes. |

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| **__.123 Early termination of research support: Evaluation of applications and proposals.** | |
| ▪ **46.123(a) –** The department or agency head may require that department or agency support for any project be terminated or suspended, when the department or agency head finds an institution has materially failed to comply with the terms of this policy. | ▪ **__.123(a) –** No substantive changes. |
| ▪ **46.123(b) –** In making decisions about supporting or approving applications or proposals covered by this policy the department or agency head may take into account, whether the applicant has been subject to a termination or suspension under paragraph (a) of this section and whether the applicant or the person or persons who would direct or has/have directed the scientific and technical aspects of an activity has/have materially failed to discharge responsibility for the protection of the rights and welfare of human subjects. | ▪ **__.123(b) –** No substantive changes. |
| **__.124 Conditions.** | |
| ▪ **46.124 –** With respect to any research project or any class of research projects the department or agency head may impose additional conditions prior to or at the time of approval when in the judgment of the department or agency head additional conditions are necessary for the protection of human subjects. | ▪ **__.124 –** No substantive changes except for the addition of language noting that additional conditions can be imposed by department or agency heads of either the conducting or supporting department or agency. |

If you have any questions about this chart or PRIM&R's public policy activities more broadly, please feel free to contact us at publicpolicy@primr.org. 