

Common Rule Overview

Effective Dates

The final rule is effective January 19, 2018 with the exception of cooperative research (mandated single IRB review) for which the compliance date is January 20, 2020. Research approved, waived or determined to be exempt prior to January 19, 2018 will continue to be subject to the pre-2018 rule. Institutions can choose, on a study-by-study basis, whether to subject research to the new or pre-2018 regulations.

Biospecimens and Private Information

The final rule does not expand the definition of “human subject” to include non-identified biospecimens. The preamble to the final rule questions the premise that the majority of the public wishes to be consented for secondary research use of biospecimens based on public comments submitted in response to the NPRM, but notes that Federal departments and agencies have the authority to establish policies with additional requirements related to consent for research with nonidentifiable biospecimens. The definition of “human subject” has been changed, however, (per the preamble, for clarification) to explicitly include identifiable biospecimens. Per the rule:

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

- (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
- (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.”

The final rule provides a definition of “identifiable biospecimens.” The definition of “identifiable biospecimen” and “identifiable private information” will be re-examined within one year of publication of the rule and every four years thereafter. See section 46.103 below for additional information.

The final rule does not adopt the proposal for more stringent waiver criteria that would have made waiver for secondary research use of biospecimens “very rare.” Per the preamble to the rule, the Newborn Screening Saves Lives Reauthorization Act, which does not allow for waiver of consent for federally funded research with newborn dried blood spots will not be effective as of January 19, 2018, the effective date of the final Common Rule.

The final rule allows for the optional use of broad consent for storage and secondary research use of identifiable private information or identifiable biospecimens in lieu of obtaining study-specific informed consent. Investigators can continue to use biospecimens that are coded or to seek waiver of consent for use of biospecimens with identifiers retained consistent with current practices. Where broad consent is obtained, storage and secondary research use is exempt with a requirement for limited IRB review. This exemption does not apply if the investigator includes returning individual research results in the study plan. The preamble indicates that HHS expects to develop guidance on broad consent at a later date which could include a template.

Six additional elements of consent are required for broad consent none of which can be omitted or altered where broad consent is solicited. These include a “general description of the types of research that may be conducted”; a description of the identifiable information or biospecimens that might be used in research, whether sharing might occur, and the types of institutions or researchers that might conduct the research; a description of the period of time identifiable information and biospecimens might be stored and used for research; “a statement that the subject will not be informed of the details of any specific research studies that might be conducted...and that subjects might have chosen not to consent to some of those specific research studies”; unless determined otherwise a statement that research results may not be disclosed to the subject; and contact information for questions and “in the event of a research-related harm.” Detailed language is included in section 46.116 below.

Per the rule, “if an individual was asked to consent to the storage or maintenance for secondary research use of identifiable private information or identifiable biospecimens in accordance with the proposed broad consent provisions and such individual refused to consent, the IRB would be prohibited from waiving informed consent for the storage, maintenance or secondary research use of such biospecimens and information.” A concern is that broad consent sought for one study with one type of form and set of conditions might then apply to other departments and studies using different forms with different information. This would require tracking at the institutional level. Per the preamble, tracking is expected to be managed by investigators or teams of investigators but over time tracked at the institutional level. This would suggest that refusal to consent might be applicable to studies using a particular consent form, particularly as the information provided for the six additional elements of consent will vary by study, but this requires follow-up. Many institutions with biorepositories currently employ broad consent via multiple forms from various departments. Per the preamble, broad consent and institution-wide tracking are expected to be pursued only in situations where it yields net benefits. With respect to waiver, per 46.116(f)(3)(iii) in order for an IRB to waive or alter consent it must find and document that the research could not practicably be carried out without using information or biospecimens in an identifiable format.

Per the final rule, “An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent” if certain conditions are met.

Informed Consent

The final rule indicates that the prospective subject or legally authorized 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. See detailed information in section 46.116 below. Per the preamble, “the final rule does not adopt a requirement that certain information be included only in the appendices.” “In general, our expectation is that this initial presentation of the key pieces of information will be relatively short. This section of the consent could, in appropriate circumstances, include a summary of relevant pieces of information that are explained in greater detail later in the consent form.” The preamble also notes, however, that “information included at the beginning need not be repeated later in the body of the informed consent.” Additional details on expectations are included in the preamble. Further guidance may be provided in the future.

Additional elements of informed consent have been added. The final rule adds a requirement for language indicating that identifiers might be removed from identifiable private information or biospecimens and whether such information or biospecimens could or will not be used for

future research studies without additional informed consent. In addition, “when appropriate,” one or more of the following elements of information are to be provided: information on whether biospecimens will be used for commercial profit; whether results will be disclosed to the subject; and whether the research might include whole genome sequencing. See detailed language in section 46.116 below. Per the preamble, the final rule does not include an element providing subjects or their representatives “the option to consent or refuse to consent to being re-contacted to obtain additional information or biospecimens, or for future research” as proposed in the NPRM.

The final rule allows waiver of consent if subjects are members of “a distinct cultural group or community for whom signing documents is not the norm” where there is no more than minimal risk of harm and there is an appropriate alternative method for documenting informed consent.

With respect to posting clinical trial consent forms, the final rule includes a requirement that a copy of an IRB approved consent form for clinical trials conducted or supported by a Common Rule department or agency be posted by the awardee or agency in a publicly available federal repository. There are no restrictions on which version must be posted. Posting can take place any time after recruitment closes but not later than 60 days after the last study visit by any subject. See information on specific changes in section 46.116 below. The final rule allows for redaction. “If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal website (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.” Per the preamble, “in rare instances, it could be the case that the federal department or agency would determine that the very existence of a particular clinical trial should not be publicly disclosed, in which case no posting related to such a trial would be required.” The preamble suggests that HHS is considering whether to use ClinicalTrials.gov as the repository.

Exclusions and Exemptions

The final rule does not include the proposed concept of “excluded” activities. The rule modifies the definition of research, “what constitutes research.” Under the definition of research, the rule identifies activities that do not meet the definition of research (are excluded; per the preamble, “explicitly removes four categories of activities that would meet that definition”), including: “Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research and historical scholarship)...that focus directly on the specific individuals about whom the information is collected.”; public health surveillance activities authorized by a public health authority to assess onsets of disease outbreaks or conditions of public health importance.; and certain criminal justice and intelligence activities. See changes to the definition of research in 46.103. Per the preamble, the proposed exclusion in the NPRM for QA/QI activities was dropped “because it could create more confusion than it resolved” and “might have inadvertently created inappropriate obstacles” to those activities that should not fall under the rule. The proposed exclusion of program improvement activities was not included for similar reasons.

The rule adds to and modifies existing exemptions. Eight categories of research are considered exempt (previously six). Some “exempt” activities now require limited IRB review. See information on specific changes in section 46.104 below. This includes modifying previous exemptions to allow use of identifiable information with limited IRB review; inclusion of benign behavioral interventions; and storage, maintenance and secondary use of identifiable private information and identifiable biospecimens where broad consent is obtained consistent with the

final rule, including six additional consent elements. Secondary research using identifiable private information or identifiable biospecimens without consent is exempted if the research only involves collection and analysis of identifiable information regulated under HIPAA or non-research government information in compliance with applicable federal requirements. A decision tool for exemptions was not included. Per the preamble, such a tool may be developed at a future date. Use would be voluntary and it would be publicly vetted.

Continuing Review

Per the preamble, “continuing review is eliminated for all studies that undergo expedited review, unless the reviewer explicitly justifies why continuing review would enhance protection of research subjects.” Continuing review has also been eliminated for research that has progressed to the point that it involves only data analysis or “accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.” See information on specific changes to section 46.109 below. Per 46.115, the reviewer must “provide a rationale for conducting continuing review of research that otherwise would not require continuing review as described in 46.109(f)(1).” As noted in the preamble, the final rule does not require investigators to provide annual confirmation to the IRB that research is ongoing and that no changes have been made.

Extending the Common Rule to All Clinical Trials

The final rule does not extend coverage to non-federally funded clinical trials.

Privacy and Security Safeguards

Per the preamble, “the final rule does not adopt the privacy and security provisions proposed in the NPRM, but rather retains and acknowledges the IRB’s role in ensuring that privacy safeguards are appropriate for the research studies that require IRB review.” The final rule includes a new provision that requires the Secretary of HHS to issue guidance to assist IRBs in assuring appropriate privacy and security safeguards. See section 46.111. Per the preamble, the guidance might address: the extent to which identifiable private information is or has been de-identified and the risk that it can be re-identified; the use of the information; the extent to which it will be shared, transferred to a third party or otherwise disclosed; the likely retention period; the security controls that are in place to protect confidentiality; and, the potential risk of harm should the information be lost, stolen, compromised or “otherwise used in a way contrary to the contours of the research under the exemption.”

Cooperative Research

Mandates the use of a single IRB for multisite studies covered by the policy. OHRP is suggesting that agencies have significant flexibility in implementing this policy. From the HHS press release: “The proposal from the NPRM has been modified, however, to add substantial increased flexibility in now allowing broad groups of studies (instead of just specific studies) to be removed from this requirement.”

Senior OHRP officials have suggested that agencies could determine that all of their research should be removed from this requirement but the rule does not make this explicit. The following is the new language: “The following research is not subject to this provision: (ii) Research for which any 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

context.” The final language allows the lead institution to propose the reviewing IRB, “subject to the acceptance of the federal department or agency supporting the research.” The effective date for this provision is 01/20/20. See information on specific changes to section 46.114 below.

Regulatory Impact

The final rule suggests net cost savings of over \$1 billion over a ten year period. For cooperative research the analysis suggests \$538 million in benefits over 10 years and \$157 million in costs, or \$381 million in net benefits. The analysis assumes a reduction in burden associated with site-specific review but an increase in burden in the form of coordination with other sites. Estimated quantified benefits were “revised downward by 27%.” The rule estimates that investigators will spend half as much time engaging in the review process. The preamble to the final rule suggests that “RIA comments did not provide the evidence necessary to improve our estimates, and thus, limited changes have been made.” Per the impact analysis, “some cost shifting may occur as certain IRBs assume the role of reviewing IRB. However, these will be offset by savings at other IRBs that are no longer required to conduct additional reviews of the same research study.” “It is expected that, over time, reliance agreements and other methods of documenting external reliance will become standardized, which will result in reduced costs associated with multiple reviews and time savings for investigators who no longer must wait for multiple reviews.” As part of the impact analysis it is estimated that 40,523 multisite studies are reviewed each year and that 40% are funded by NIH. The analysis also suggests \$798 million in benefits for the expansion of exempt categories of research and \$326 million for eliminating the requirement that the grant application undergo IRB review and approval.

Other Changes of Interest

The final rule notes the intent to “eventually” amend subparts B, C, D and E and to consider updates to FDA and other relevant federal regulations.

HHS plans to “implement the proposed nonregulatory change to the assurance mechanism to eliminate the voluntary extension of the FWA to nonfederally funded research.” The preamble notes that institutional policy can require IRB review of research not funded by Common Rule departments and agencies. Per the preamble, this change is expected to encourage institutions to explore flexible approaches to overseeing low-risk research not covered by the Common Rule.

The final rule eliminates the requirement that “grant applications undergo IRB review and approval for the purpose of certification.” See section 46.102.

The Secretary’s list of categories of research that may be reviewed through expedited review will be evaluated at least every 8 years. Proposed changes to the list will be published in the Federal Register to allow for public comment. If a reviewer determines that a study on the list involves more than minimal risk and is not eligible for expedited review this must be documented.

The final rule removes pregnant women as an example of populations that are potentially vulnerable to coercion or undue influence.

46.101 To what does this policy apply?

The following language is omitted:

“Research that is conducted or supported by a federal department or agency, whether or not it is regulated as defined in §46.102, must comply with all sections of this policy.”

“Research that is neither conducted nor supported by a federal department or agency but is subject to regulation as defined in §46.102(e) must be reviewed and approved, in compliance with §46.101, §46.102, and §46.107 through §46.117 of this policy, by an institutional review board (IRB) that operates in accordance with the pertinent requirements of this policy.”

Agency waiver of applicability now requires identification of conditions to which it will be applied, justification and how it is consistent with the principles of the Belmont Report.

The final rule clarifies that the Common Rule does not affect AI/AN tribal law that may provide additional protections for human subjects.

As proposed in the NPRM, for the purposes of harmonization, federal guidance “shall be issued only after consultation” with other federal agencies, unless it is not feasible.

46.102 Assuring compliance

The final rule eliminates the requirement that “grant applications undergo IRB review and approval for the purpose of certification”; the requirement that institutions provide a statement of ethical principles by which they will abide by as part of the assurance; and the requirement to designate one or more IRBs on an institution’s FWA. An updated list of IRB members is no longer required to be submitted with an institution’s assurance; instead the institution must maintain a current list. The rule removes the requirement that a department or agency head’s evaluation of the assurance consider the adequacy of the proposed IRB with respect to the anticipated scope of activities and types of populations anticipated. It requires that for review that takes place by an IRB not operated by an institution, the institution and organization operating the IRB “must document the institution’s reliance on the IRB for its research oversight.”

46.103 Definitions

The final rule includes a definition for “clinical trial” (adopted the NPRM definition); “Federal department or agency”; “public health authority” (per the preamble, to clarify the scope of activities removed from the definition of research); “written or in writing” (per the preamble to clarify that these terms include electronic formats and other media) and “identifiable biospecimen” (previously considered part of “identifiable private information”).

The definition of “identifiable biospecimen” and “identifiable private information” will be re-examined within one year and every four years thereafter (upon consultation with appropriate experts and by collaboration among federal agencies and departments). “If appropriate and permitted by law, such Federal departments and agencies may alter the interpretation of these terms, including through the use of guidance.” A similar process will be followed to “assess whether there are analytic technologies or techniques that should be considered by investigators to generate “identifiable private information,” or “identifiable biospecimens.” “Any such technologies or techniques will be included on a list of technologies or techniques that produce identifiable private information or identifiable biospecimens. This list will be published in the Federal Register after notice and an opportunity for public comment. The Secretary, HHS, shall maintain the list on a publicly accessible website.” Per the preamble, recommendations might then be made with respect to consent and privacy and data security protections. These

technologies might then only be used where consent has been provided or where an IRB has waived consent. Notice and comment would take place before a technology or technique was placed on this list. Per the preamble, “the expectation is that whole genome sequencing will be one of the first technologies to be evaluated to determine whether it should be placed on this list.” Further, “...apart from the consequences of placing technologies and techniques on the new list, the most significant effect of 46.102(e)(7) may be the issuance of guidance from time to time that facilitates understanding of and compliance with existing interpretations.”

The definition of “human subject” has been changed from:

“(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.”

To:

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

- (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
- (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.”

Under the definition of research, the rule identifies activities that do not meet the definition of research (are excluded; per the preamble, “explicitly removes four categories of activities that would meet that definition”), including: “Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research and historical scholarship)...that focus directly on the specific individuals about whom the information is collected.”; public health surveillance activities authorized by a public health authority to assess onsets of disease outbreaks or conditions of public health importance.; and certain criminal justice and intelligence activities.

The term “legally authorized representative” has been modified to address jurisdictions without applicable law and now refers to institutions’ policies.

46.104 Exempt Research

For research that includes only interactions involving educational tests, survey or interview procedures or observation of public behavior, identifiable information can now be used with limited IRB review and appropriate privacy and confidentiality protections.

An exemption is added for research involving benign behavioral interventions (defined in the revised rule) in conjunction with the collection of information from an adult subject if the subject prospectively agrees and one of three criteria are met. The exemption is not applicable for research involving deceit unless the subject authorizes deception through prospective agreement.

Storage or maintenance of identifiable private information or biospecimens for potential secondary research use (for which broad consent is required) is exempt if an IRB conducts a limited review. Secondary research use of identifiable private information or biospecimens is

exempt if broad consent for storage, maintenance and secondary research use was obtained; documentation of informed consent or waiver of consent was obtained; an IRB determines that the research is within the scope of the broad consent; and the study plan does not include return of research results. Secondary research use of identifiable private information and identifiable biospecimens does not require consent if the information is publicly available; is recorded in a way that the identity of the subject cannot readily be ascertained and the investigator does not contact or re-identify subjects; is identifiable health information regulated under HIPAA used for “healthcare operations” or “public health activities”; and research conducted by or on behalf of a federal department or agency using government-generated or government-collected information and maintained in information technology in compliance with applicable laws/privacy protections.

Federal departments or agencies conducting or supporting demonstration projects must publish a list of projects prior to their commencement.

46.105 and 46.106 Reserved

No change.

46.107 IRB Membership

Removed considerations of gender and profession.

46.108 IRB Functions and Operations

No change.

46.109 IRB Review of Research

*The following language on continuing review has been added as proposed in the NPRM:

“(f)(1) Unless an IRB determines otherwise, continuing review of research is not required in the following circumstances:

(i) Research eligible for expedited review in accordance with §__.110; **[expedited review procedures]**

(ii) Research reviewed by the IRB in accordance with the limited IRB review described in §__.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8); **[exemptions requiring limited IRB review]**

(iii) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

(A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

(B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.”

Per the preamble, “continuing review is eliminated for all studies that undergo expedited review, unless the reviewer explicitly justifies why continuing review would enhance protection of research subjects.”

The following has been added:

“(g) An IRB shall have authority to observe or have a third party observe the consent process and the research.”

The language at 46.109(a) clarifies that IRBs have the authority to conduct limited review with respect to certain categories of exempt research.

46.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

*Changed to indicate that the Secretary’s list of categories of research that may be reviewed through expedited review will be evaluated at least every 8 years [previously “amended as appropriate”]. Per the preamble, the proposed changes to the list will be published in the Federal Register to allow for public comment.

*A third condition for expedited review has been added:

“(iii) Research for which limited IRB review is a condition of exemption under §__.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7) and (8).”

Per the preamble, a study is eligible for expedited review if it involves only activities on the Secretary’s list, unless the reviewer determines that the study involves more than minimal risk and documents the rationale. This documentation requirement is new. It is suggested that this will lead to greater consistency across institutions and could provide a basis for future determinations about the appropriateness of the list.

46.111 Criteria for IRB approval of research.

*Removed pregnant women and “handicapped or physically disabled individuals” as examples of populations that are potentially vulnerable to coercion or undue influence. Replaced “mentally disabled persons” with “individuals with impaired decision-making ability.”

Added that informed consent will be appropriately documented or “appropriately waived” in accordance with the regulations.

*With respect to privacy of subjects and confidentiality of data, the following was added:

“(i) The Secretary of HHS will, after consultation with the Office of Management and Budget’s privacy office and other Federal departments and agencies that have adopted this policy, issue guidance to assist IRBs in assessing what provisions are adequate to protect the privacy of subjects and to maintain the confidentiality of data. Per the preamble, the guidance might address: the extent to which identifiable private information is or has been deidentified and the risk that it can be reidentified; the use of the information; the extent to which it will be shared, transferred to a third party or otherwise disclosed; the likely retention period; the security controls that are in place to protect confidentiality; and, the potential risk of harm should the information be lost, stolen, compromised or “otherwise used in a way contrary to the contours of the research under the exemption.”

*Adds the following:

“(8) For purposes of conducting the limited IRB review required by §__.104(d)(7)), the IRB need not make the determinations at paragraphs (a)(1) through (7) of this section, and shall

make the following determinations:

- (i) Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements of § __.116(a)(1)-(4), (a)(6), and (d);
- (ii) Broad consent is appropriately documented or waiver of documentation is appropriate, in accordance with § __.117; and
- (iii) If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.”

46.112 Review by an institution.

No changes.

46.113 Suspension or termination of IRB approval of research.

No Changes

46.114 Cooperative research.

Changed the language to mandate single IRB approval for studies covered under the policy and involving more than one U.S. institution:

Previous language:

“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 another qualified IRB, or make similar arrangements for avoiding duplication of effort.”

New language:

“(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 identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.”

OHRP is suggesting that agencies have significant flexibility in implementing this policy. From the HHS press release: “The proposal from the NPRM has been modified, however, to add substantial increased flexibility in now allowing broad groups of studies (instead of just specific studies) to be removed from this requirement.” A senior OHRP official suggested that agencies could determine that all of their research should be removed from this requirement but the rule does not make this explicit. The following is the new language:

“(2) The following research is not subject to this provision:

(i) Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or

* (ii) Research for which any 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 context.”

The final language allows the lead institution to propose the reviewing IRB, “subject to the acceptance of the federal department or agency supporting the research.” The effective date for single IRB compliance is delayed until 1/20/2020.

46.115 IRB records.

*To records of continuing review adds: “including the rationale for conducting continuing review of research that otherwise would not require continuing review as described in §__.109(f)(1).”

*Adds the following language:

“(8) The rationale for an expedited reviewer’s determination under §__.110(b)(1)(i) that research appearing on the expedited review list described in §__.110(a) is more than minimal risk.”

“(9) Documentation specifying the responsibilities that an institution and an organization operating an IRB each will undertake to ensure compliance with the requirements of this policy, as described in §__.103(e).”

Indicates that records can be maintained electronically or in printed form.

46.116 General requirements for informed consent.

The following language has been added:

“(4) The prospective subject or the legally authorized 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.

(5) Except for broad consent obtained in accordance with paragraph (d) of this section:

(i) Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

(ii) Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject’s or legally authorized representative’s understanding of the reasons why one might participate.”

*The following language has been added to “Basic elements of informed consent” (“the following information shall be provided” except as otherwise provided). Added to increase transparency:

“(9) One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

(i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens 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 legally authorized representative, if this might be a possibility; or

(ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies."

*The following language has been added to "Additional elements of informed consent" (where "one or more of the following elements of information, when appropriate, shall also be provided to each subject or the legally authorized representative"):

"(7) A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;
(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
(9) For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen)."

Per the preamble, the final rule does not include an element providing subjects or their representatives "the option to consent or refuse to consent to being re-contacted to obtain additional information or biospecimens, or for future research."

The following language has been added:

"(d) Elements of broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens. Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or nonresearch purposes) *is permitted as an alternative to the informed consent requirements in paragraphs (b) and (c) of this section. If the subject or the legally authorized representative is asked to provide broad consent, the following shall be provided to each subject or the subject's legally authorized representative:

(1) The information required in paragraphs (b)(2), (b)(3), (b)(5), and (b)(8) [basic elements of informed consent] and, when appropriate, (c)(7) and (9) of this section [use for commercial profit or whole genome sequencing];

* (2) A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted;

(3) A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens;

(4) A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite);

(5) Unless the subject or legally authorized representative will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies;

(6) Unless it is known that clinically relevant research results, including individual research

results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject; and

(7) An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm."

Per the preamble, broad consent may be obtained for the use of identifiable private information or identifiable biospecimens for storage and maintenance for secondary research use and secondary research use in lieu of obtaining study-specific informed consent. Investigators can continue to use biospecimens that are coded or to seek waiver of consent for use of biospecimens with identifiers retained.

"(e) Waiver or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials—(1) Waiver. An IRB may waive the requirement to obtain informed consent for research under paragraphs (a) through (c) of this section, provided the IRB satisfies the requirements of paragraph (e)(3) of this Section [requirements for waiver and alteration]. *If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at paragraph (d) of this section, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens."

"(2) Alteration. An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent set forth in paragraphs (b) and (c) of this section provided the IRB satisfies the requirements of paragraph (e)(3) of this section [requirements for waiver and alteration]. An IRB may not omit or alter any of the requirements described in paragraph (a) of this section. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under paragraph (d) of this section."

Under "Requirements for waiver and alteration" (in order for an IRB to waive or alter consent it must find and document that) adds:

"(iii) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;"

The following language has been added:

"(g) Screening, recruiting, or determining eligibility. An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

- (1) The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or
- (2) The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens."

*"(h) Posting of clinical trial consent form. (1) For each clinical trial conducted or supported by a Federal department or agency, one IRB-approved informed consent form used to enroll subjects

must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal website that will be established as a repository for such informed consent forms.

(2) If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal website, e.g., confidential commercial information, such Federal department or agency may permit or require redactions to the information posted.

(3) The informed consent form must be posted on the Federal website after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.”

46.117 Documentation of informed consent.

Minor variations to the language and adds the following (IRBs may waive the requirement for signed informed consent if): “(iii) If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.”

46.118 Applications and proposals lacking definite plans for involvement of human subjects.

No changes (minor language variation).

46.119 Research undertaken without the intention of involving human subjects.

Adds: “Except for research waived under §__.101(i) or exempted under §__.104,”

46.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a federal department or agency.

No changes.

46.121 Reserved.

No changes.

46.122 Use of Federal Funds

No changes.

46.123 Early termination of research support: evaluation of applications and proposals.

No changes.

46.124 Conditions.

No changes.