

## New Final Common Rule Published Many Changes Are Required by Gary L Chadwick

The Final Common Rule (HHS 45CFR46, subpart A) was published in the January 19<sup>th</sup> Federal Register (the last day of the Obama Administration). Assuming that the Rule is not rescinded or ordered to be revised or not enforced, listed below are the most significant changes that will affect research institutions, IRBs and investigators. Note that not every change is listed here and regulated institutions and organizations are advised to analyze the changes and their effect on internal operational procedures and policies (SOPs). Given the current uncertainty about the fate of the rule, HRP's advice at this point is to begin to draft or otherwise prepare for changes to your SOPs and materials, but delay implementation until more is known.

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Compliance dates and transition provisions are listed in section .101. Generally, the new regulations will go into effect in one (1) year, i.e., January 2018. January 2020 is the effective date for the requirements related to cooperative research (i.e., the single IRB requirements).

The Common Rule numbering scheme and section titles remain largely intact, but with some movement of subtext and sub-section numbering revisions. (Some SOPs and checklists will need to be revised to reflect the new numbering).

Regulatory references that cite state or local law now include “tribal law passed by the official governing body of an American Indian or Alaska Native tribe.”

Section .101 adds that institutions that are engaged in research and institutional review boards (IRBs) reviewing research must comply with this policy. This new statement supports the use of external IRBs and facilitates “single IRB” use. The old footnote has been eliminated to facilitate “unchecked the box” in a Federalwide Assurance (FWA).

Section .102, Definitions, has been alphabetically reordered and new terms are defined (*clinical trial, public health authority, and written, or in writing*). *Intervention, interaction, private information* and *identifiable private information* are elevated to get their own sub-numbers. Of note, the definition of *minimal risk* has not changed. Three definitions have been changed in significant ways. Sub-section .102.e, Human Subject now references biospecimens and adds obtaining, storing, using, studying, analyzing, or generating identifiable private information or identifiable biospecimens as trigger events. The definition of *legally authorized representative* now adds specific authorization to use institutional policy when there is no applicable law

addressing this issue. The definition of *research* has been expanded to list activities that are specifically deemed not to be research (e.g., oral history, journalism, public health surveillance, criminal justice or criminal investigative activities, and activities in support of intelligence, homeland security, defense, or other national security missions). Of interest is a regulatory federal agency commitment to reexamine the meaning of “identifiable private information” and “identifiable biospecimen.” Organizational SOPs will have to be updated to add the new/revised definitions.

Section .103 drops the list of written procedures needed for FWAs, but these now appear in the [IRB Operation section .108](#), which conforms to FDA’s regulations (21 CFR 56.108). Added to this section is a requirement that the institution and the organization operating the IRB document 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 the final rule (e.g., in a written agreement between the institution and the IRB, by implementation of an institution-wide policy directive providing the allocation of responsibilities between the institution and an IRB that is not affiliated with the institution, or as set forth in a research protocol).

Section .104, previously “Reserved” has now been assigned as “Exempt Research”. The old .101(b)(1-6) exemptions have been moved here and new restrictions have been added to each of them but the taste and food quality study exemption (i.e., that exemption still maintains congruence with FDA). Sub-section .101(b) is now “Reserved,” which should help avoiding confusion when implementing the new Common Rule. This section specifically states the applicability of the exemption categories to 45 CFR 46, subparts B, C, and D, and changes the current policy, which was in a [footnote \(1\)](#) in the old regulations, to allow the exemptions at this section to apply to research subject to subpart C aimed at involving a broader subject population that only incidentally includes prisoners.

New “conditional” exemptions have been added that were originally proposed as “excused.” The new exemptions include research involving benign behavioral interventions in conjunction with the collection of information from adults. Three new exemptions include conditions for *Secondary Research*; research uses of private information or identifiable biospecimens; storage or maintenance for secondary research use of private information or identifiable biospecimens; and research involving the use of private information or identifiable biospecimens that have been stored or maintained for research use. Organizational SOPs will have to be updated to add the new/revised categories and the new numbering structure.

Sections .105 and .106 remain Reserved; no investigator responsibilities were added to the Common Rule.

Section .107, *Membership* now includes a revised definition of “vulnerable” (drops “pregnant women” and replaces “handicapped or mentally disabled persons” with “individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons”).

Section .108(a) is significantly changed, but no new requirements added. As indicated above the FWA requirements for written procedures described in the old section 46.103(b)(4) and 46.103(b)(5) have been included at 108(a)(3) and (4) as requirements for IRB operation. The IRB roster detail requirements formerly in old section 46.103(b)(3) is now found at .108(a)(2). These three subsections agree with FDA regulatory wording. The requirement for meeting space and sufficient staff to support the IRB in old section 46.103(b)(2), which is not in FDA regulations, is now found at .108(a)(1).

Section .109 has been revised to address the new “limited IRB review.” This section also includes a new subsection (.109(f)(1)) eliminating the continuing review of research (annual and ongoing) in some circumstances. Organizational SOPs will have to be updated and IRB members trained for the new “limited IRB review” procedures and procedures for continuing review will need to be changed.

Section .110 has been revised to permit “limited IRB review” to be conducted through expedited review. Also, there is a regulatory federal agency commitment to evaluate the expedited review category list at least every 8 years and amend it as appropriate.

Section .111 survives largely intact with the updated wording for vulnerable populations added to .111(a)(3) and 111(b). A new subsection has been added to essentially eliminate the “111 criteria” when conducting “limited IRB review,” but adds new consent determinations. Organizational SOPs will have to be updated to add the new “limited IRB review” criteria.

Section .112 and .113 are unchanged.

Section .114 has been changed to add a requirement for institutions located in the United States that are engaged in cooperative research to rely upon approval by a single IRB for that portion of the research that is conducted in the U.S. The reviewing IRB will be specified by the federal department or agency supporting or conducting the research; the lead institution may propose the reviewing IRB, but final federal approval will be required. This part of the regulations will go into effect in three (3) years, i.e., January 2020. Organizational SOPs will have to be updated to add new procedures and agreement templates for multi-site studies. Research sites will have to develop ceding processes and organizations that have lead investigators (grant recipients) will need to develop processes for becoming single IRBs that review for other sites.

Section .115 is largely intact with an addition for documentation specifying the responsibilities of each entity when research takes place at an institution in which IRB oversight is outsourced. More burdensome are two additions requiring documentation of the rationale for conducting continuing review of research that otherwise would not require continuing review and for an expedited reviewer’s determination that research appearing on the expedited review list is more than minimal risk. Organizational SOPs and checklists will have to be updated and IRB members trained for the new documentation requirements.

Section .116 is one of more extensively modified sections, primarily due to added regulations for the use of biospecimens in research. The unnumbered list of conditions appearing in the old “preamble” before .116(a) has been separated and the conditions numbered as .116(a) (1-3) and (6). Subsection .116(b) now contains the basic elements of consent and .116(c) the additional elements. A new subsection .116(a) has been added that is essentially a table of contents, which states that broad consent may be obtained in lieu of informed consent only with respect to the storage, maintenance, and secondary research uses of private information and identifiable biospecimens. Organizational SOPs, consent templates and checklists will have to be updated and investigators and IRB members trained for the new biospecimen and general consent requirements. This will be a major change.

Subsection .116(a)(4) is new and states that subjects must be provided with the information that a “reasonable person” would want to have in order to make an informed decision and subjects must be provided an opportunity to discuss that information.

Subsection .116(a)(5)(i) is new and states that the informed consent process must begin with a concise and focused presentation of the “key information” that is most likely to assist a prospective subject in understanding the reasons why one might or might not want to participate in the research. This subsection also requires that this part of the informed consent be “organized and presented in a way that facilitates comprehension.” Presumably further guidance will explain what that means and how to achieve the goal along with what qualifies as a concise and focused presentation.

Subsection .116(a)(5)(ii) is also new. It takes the form of an admonition to present informed consent information in sufficient detail and organize and present the information in a way that does not “merely provide lists of isolated facts, but rather facilitates the prospective subject’s ... understanding of the reasons why one might or might not want to participate.”

Subsection .116(b), the basic elements of consent, has no change to the eight (8) previous elements. Added is a requirement to include one of two statements about the collection of private information or identifiable biospecimens for future research (either that identifiers might be removed and the de-identified information or biospecimens used for future research without additional informed consent from the subject; or, that the subject’s information or biospecimens will not be used or distributed for future research studies even if identifiers are removed).

Subsection .116(c), the additional elements of consent, has no change to the six (6) previous elements, but three new requirements have been added. Subsection .116(c)(7) requires a statement that 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. Subsection .116(c)(8) requires a statement about whether clinically relevant research results, including individual research results, will be disclosed to subjects. Subsection .116(c)(9) requires a statement about whether the research project might include whole genome sequencing.

Subsection .116(d) is new and addresses elements of “broad consent” for the storage, maintenance, and “secondary research use” of private information or identifiable biospecimens. Broad consent for secondary research use is permitted as an “alternative” to the standard informed consent requirements. Subsection .116(d)(1) still requires risks, benefits, confidentiality, voluntary statement, commercial profit, and whole genome sequencing elements be included. Subsection .116(d)(2) requires a general description of the types of research that may be conducted. Subsection .116(d)(3) requires a description of the information or biospecimens that might be used in future research; whether sharing might occur; and, the types of institutions or researchers that might conduct research. Subsection .116(d)(4) requires a description of the length of time that the information or biospecimens may be stored, maintained and used. Subsection .116(d)(5) requires a statement either that subjects will or will not be informed of the details of any specific research studies that might be subsequently conducted. Subsection .116(d)(6) requires a statement that research results either will or will not be disclosed to subjects. Subsection .116(d)(7) requires contact information to be provided in the broad consent. The usefulness and ethics of broad consent remains to be further elucidated in guidance.

Subsection .116(e) is new and addresses waiver or alteration of consent in research involving public benefit and service programs.

Subsection .116(f) addresses “general” waivers or alterations of informed consent. Subsection .116(f)(1) cautions that if an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of information or biospecimens and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use.

Subsection .116(f)(2) addresses alterations (partial waivers) of informed consent. Two new conditions/restrictions are included. An IRB may not omit or alter any of the .116(a) general requirements for informed consent requirements. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required, i.e., alteration is not permitted.

The four existing waiver conditions are included unchanged in subsection .116(f)(3), but added for research that involves accessing or using private information or identifiable biospecimens, is a requirement that the research could not practicably be carried out without accessing or using such information or biospecimens in an identifiable format.

Subsection .116(g) is new. It addresses waivers of informed consent to obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects. One of two conditions must be met: the information will be obtained through oral or written communication with the prospective subject or by accessing records or stored biospecimens.

Subsection .116(h) is new and adds a requirement for posting clinical trial consent forms on a publicly available federal website that will be established (i.e., not yet a reality) as a repository for consent forms. According to subsection .116(h)(3), one consent form for each study 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. The responsibility for posting is the awardee or the federal department or agency component conducting the study.

Section .117 has a few important changes. Subsection .117(a) now specifically allows electronic signatures for consent documentation and specifies that a written copy must be given to the person signing the consent form. Subsection .117(b)(1) specifically allows consent forms to be read to the subject. Subsection .117(b)(2) requires that, when using the short form to document consent, the informed consent must begin with a concise and focused presentation of the key information to assist a prospective subject in understanding the reasons why one might or might not want to participate in the research. This subsection requires that this part of the informed consent must be organized and presented in a way that facilitates comprehension. Subsection .117(c) still addresses waivers for the requirement to obtain a signed consent form and maintains the two pre-existing exceptions. Importantly a third category is added that allows waiver if the subjects are members of a distinct cultural group or community in which signing forms is not the norm. Organizational SOPs, templates and checklists will have to be updated and investigators and IRB members trained for the new waiver and consent requirements.

Sections .118, through .124 are essentially unchanged except for some clarifying wording.