

Summary of Changes to the US Federal Policy for the Protection of Human Subjects

We list here the references first:

- This is the link to the original document we worked with.
<https://www.federalregister.gov/documents/2017/01/19/2017-01058/federal-policy-for-the-protection-of-human-subjects>
- This is the link to a press release summarizing the changes. Summary information is also contained within the document provided above:
https://www.hhs.gov/about/news/2017/01/18/final-rule-enhances-protections-research-participants-modernizes-oversight-system.html?source=govdelivery&utm_medium=email&utm_source=govdelivery

Summary overview:

- When we speak of the “Common Rule”, we are talking about 45 CFR 46 (DHHS) Subpart A. The “Rule” itself only covers trials that are federally funded or supported. While the FDA has not formally adopted the Common Rule, the elements of the Rule are covered in FDA’s 21 CFR Parts 50 and 56.
- Pages 7149-7151 provide a good overall introduction and historical background to clinical research.
- Pages 7150 provide a summary of the revisions made (and not made) to the Common Rule.
- Page 7160 (II H)) is titled “Compliance Dates and Transition Provisions of the Final Rule”. This section is important because it specifies when things go into effect.
- The actual text of the Rule (without comments or explanations) goes from pages 7259 to 7269.
- The following sections within the full document (i.e., with commentary, etc.) are very large and we would suggest a more detailed look: V, XV, and XIV.

The summary of changes included in both the press release and document itself do not adequately capture what are considered to be significant changes.

We have listed here a number of items that were not mentioned in particular, but which might be significant. Therefore, in addition to the items listed in the summaries, please note the following revisions as obtained directly from the full Federal Register document:

- New language has been added that gives Common Rule departments and agencies the authority to enforce compliance directly against IRBs that are not operated by an assured institution.
- Department or agency heads retain final judgement as to whether a particular activity is covered by the Common Rule but with the new limitation that this judgement must be consistent with the ethical principles of the Belmont Report. Therefore, as quoted from the

document ***“the final rule thus formally codifies...the general practice that the ethical standards articulated in the Belmont Report are the ethical standards that Common Rule departments or agencies will use in determining whether an activity is covered under this policy or whether to grant a waiver of the applicability of some or all of the provisions (unless otherwise required by law).”***

- The “old” Common Rule said that for research taking place in non-US countries, those countries can follow their normal procedures for protecting human subjects. In this case, the “Rule” recognized the Declaration of Helsinki as an example of an acceptable ethical standard. The reference to the Declaration of Helsinki has been removed in the revised “Common Rule”. As per a direct quote: ***“Although the pre-2018 requirements cited the Declaration of Helsinki as an example of internationally recognized ethical standards that a foreign country might use as it’s ethical base, we note that providing a specific example of an internationally recognized ethical document is concerning because such a document is subject to change independent of Common Rule department or agency policies, and therefore might be modified in ways that create standards that are inconsistent with U.S. laws and regulations.”***
- Evidently, the “old” Rule did not include a definition of “clinical trial”. As per a direct quote: ***“The final rule...adopts the NPRM definition of ‘clinical trial’, which is 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.”*** The commentary goes on to say: ***“In response to public concerns about an overly expansive definition of ‘clinical trial’ given the importance of that definition to the proposed extension of the rule to clinical trials previously not covered by the rule, we have eliminated that proposed expansion of coverage in this final rule. As such, the definition that appears in the final rule will only be relevant to the requirement for posting of consent forms for clinical trials conducted or supported by Federal departments or agencies (§ __.116(h)). It should be appropriate for that relatively narrow regulatory purpose.”***
- The previous Rule did not include a definition of “public health authority”. As per a direct quote: ***“In the final rule, as in the NPRM, the term ‘public health authority’ 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, 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.”***
- Please read section IV, starting on page 7180 in its entirety: “Assuring Compliance with This Policy” which relates to IRBs. But in particular (direct quote), ***“...the final rule eliminates the requirement that appeared in the pre-2018 rule that an up-to-date list of the IRB members and their qualifications be included in an institution’s assurance. Instead, §§ __.108 (a) (2) and __.115 (a) (5) in the final rule require that an IRB or the***

institution prepare and maintain a current list of IRB members. This eliminates the previous requirement that changes in IRB membership be reported to the department or agency head or to OHRP when the existence of an assurance approved by HHS for federal-wide use is accepted. Of note, SACHRP recommended in March, 2008 that OHRP pursue harmonizing the Common Rule with FDA's human subject's protection regulations by eliminating the requirement to submit IRB membership lists."

- With regard to the section on "References to Vulnerability": the revised Rule ***"no longer includes pregnant women or 'handicapped' or physically disabled individuals as examples of populations that are potentially vulnerable to coercion or undue influence."***
- Another direct quote: ***"The final rule does not require investigators to provide annual confirmation to the IRB that such research is ongoing and that no changes have been made that would require the IRB to conduct continuing review. Institutions that choose to require some accounting of ongoing research not subject to continuing review have significant flexibility in how they implement their own requirements. Note that under the final rule, investigators would still have the current obligations to report various developments (such as unanticipated problems or proposed changes to the study) to the IRB."***
- Consent forms would need to be posted. Here is a direct quote: ***"As a means of increasing transparency and facilitating the development of more informative consent forms, the final rule accordingly requires at § __.116(h)(1) that for clinical trials conducted or supported by a Common Rule department or agency, a copy of an IRB-approved version of a consent form that was used to enroll subjects would need to be posted by the awardee or the federal department or agency conducting the trial on a publicly available federal Web site that will be established as a repository for such forms. Unlike the NPRM, which required that the 'final version' of the consent form be posted, the final rule adds flexibility in merely requiring that it be an IRB-approved consent form that was used for enrollment purposes."***
- A review of section XIV (General Requirements of Informed Consent) will give more insight.