Tel: 347.862.9321
info@thehrpconsultinggroup.com
thehrpconsultinggroup.com

Summary of Proposed Changes – FDA Regulations 21 CFR 50, 21 CFR 56, and 21 CFR 812: Protection of Human Subjects and Institutional Review Boards

A proposed rule titled "Protection of Human Subjects and Institutional Review Boards" was issued by the FDA on 09/28/2022. *At this time these are proposed revisions, so it is possible that the FDA final rule may look different. This is an opportunity to help organizations prepare for the final rule.*

- ***This proposed rule**, if finalized, would harmonize **certain sections** of FDA's regulations on human subject protection (21 CFR 50), institutional review boards (21 CFR 56), and IDEs (21 CFR 812) with the revised Common Rule.*
- ***FDA final rule** Institutional Review Board Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations (effective 1/22/24) added new section 21 CFR 50.22 to harmonize FDA's requirements for waiver or alteration of informed consent for minimal risk clinical investigations with the revised Common Rule.*
- ***FDA proposed rule** Institutional Review Boards; Cooperative Research (proposed 9/28/22) seeks to harmonize FDA's cooperative research requirements by requiring use of a single IRB for multisite research conducted in the U.S. (with some exceptions) and IRB recordkeeping requirements for research overseen by an IRB that is not operated by the institution where the study is conducted. HRP Consulting Group has summarized these proposed changes in a separate document.*
- ***FDA is continuing to analyze changes that would be relevant to FDA-regulated research**, including applicability of other revised Common Rule provisions such as posting of informed consent forms, broad consent, limited IRB review, exempt research, and public health surveillance activities.*

Section	Summary of Proposed Changes to Harmonize with the Revised Common Rule	Impact	Organizational Notes
Elements of informed consent 50.25(d) 50.25(e) **Cooperative research** 56.114 **Circumstances in which IRB review is required** 56.103(c)	All 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."	Documents such as standard operating procedures (SOPs) may need to be updated if they directly cite the current regulatory language.	Click or tap here to enter text.

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Membership 56.107(a) **Criteria for IRB approval of research** 56.111(a)(3) and 56.111(b)	Revised description of "vulnerable" • Removed "pregnant women". • Replaced "handicapped or mentally disabled persons" with "individuals with impaired decision-making capacity".	Documents such as SOPs, submission forms, and reviewer worksheets may need to be updated. Consider updating IRB member records and roster to capture expertise for modified vulnerable populations.	Click or tap here to enter text.
Definitions as used in this part 56.102 50.3	New definitions • Private Information 50.3(u), Identifiable Private Information 50.3(v), Identifiable biospecimen 50.3(w), and Written, or in writing 56.102(n), 50.3(t). Revised definitions • Legally authorized representative 50.3(l) adds specific authorization to use institutional policy when there is no applicable law addressing this issue.	Documents such as SOPs, submission forms, and reviewer worksheets may need to be updated.	Click or tap here to enter text.
Membership 56.107	In 56.107(a) make minor changes to characteristics of IRB members and the description of categories of subjects who are considered vulnerable. Delete 56.107(b) because the requirement for IRB membership diversity would be included in 56.107(a); redesignate remaining sections.	Citations in documents such as SOPs may need to be updated.	Click or tap here to enter text.

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IRB functions and operations 56.108	• The IRB roster detail requirements formerly in old section 56.115(a)(5) have been included at 56.108(a)(2). • Editorial changes were made to harmonize the language with the revised Common Rule.	Citations in documents such as SOPs may need to be updated.	Click or tap here to enter text.
IRB review of research 56.109	Addition of "or legally authorized representative, when appropriate" 56.109(b) • To clarify that subjects or LARs must be given informed consent information in accordance with 50.25. In 56.109(c)(3) add a new exception to the requirement for documentation of informed consent in specific circumstances. • The IRB is allowed to waive documentation of consent if the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm. This is restricted to minimal risk research and requires an appropriate alternative method for documenting that informed consent was obtained. **Note:** FDA is **not** proposing to add the revised Common Rule exception to the requirement for documentation of informed consent at 45 CFR 46.117(c)(1)(i) for situations in which the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. See the proposed rule for more information.	Documents such as SOPs, submission forms, and reviewer worksheets may need to be updated. Procedures that may currently be tied to continuing review (e.g., training verification, conflicts review) may need to be modified. IRB electronic systems may require modification. Consider whether organization would benefit from an annual report in lieu of IRB continuing review.	Click or tap here to enter text.

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	In 56.109(d) provide that LARs may also receive written statements, if required by the IRB, when documentation of informed consent is waived. In 56.109(f) add reference to new subsection 56.109(g). New subsection 56.109(g) eliminates continuing review in the following circumstances (unless an IRB determines otherwise) • 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. **Note:** FDA is **not** proposing to adopt the revised Common Rule provision at 45 CFR 46.109(f)(1)(i), which eliminates the requirement for an IRB to conduct continuing review of research that is eligible for expedited review unless the IRB determines otherwise. See the proposed rule for more information. FDA is **not** proposing to adopt provisions from the revised Common Rule related to limited IRB review at this time, including 45 CFR 46.109(f)(1)(ii) which eliminates the requirement for an IRB to conduct continuing review of exempt research reviewed in		

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	accordance with the limited IRB review described in 45 CFR 46.104. See the proposed rule for more information.		
Expedited review procedures 56.110	Remove the parenthetical phrase "(of 1 year or less)" from (b)(2) because continuing review would not be required in certain circumstances. **Note:** FDA proposes to **maintain** the requirement that the reviewer determine that the research involves no more than minimal risk. This differs from the revised Common Rule. Once the 1998 HHS Expedited Review List is finalized, the revised Common Rule will allow an IRB to use the expedited review procedure to review studies that involve activities appearing on the expedited review list, unless the IRB reviewer determines that the studies involve more than minimal risk (see 45 CFR 46.110(b)(1)(i)). See the proposed rule for more information.	Documents such as SOPs, submission forms, and reviewer worksheets may need to be updated. IRB electronic systems may require modification	Click or tap here to enter text.
Criteria for IRB approval of research 56.111(a)	Delete the phrase "and to the extent required" from 56.111(a)(5) so that the requirement would read "Informed consent will be appropriately documented or appropriately waived, in accordance with § 50.27 of this	Documents such as SOPs, submission forms, and reviewer worksheets may need to be updated.	Click or tap here to enter text.

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	chapter."		
IRB records 56.115(a)(3)	Revised to add language that would require the IRB to maintain a record of the rationale for conducting continuing review, if the IRB determines that continuing review of research is necessary (when research otherwise would not require continuing review under 56.109(g)).	Documents such as SOPs, submission forms, and reviewer worksheets may need to be updated. IRB electronic systems may require modification.	Click or tap here to enter text.
General requirements for informed consent 50.20	Proposal to redesignate existing requirements as 50.20(a), (b), (c), and (f) and add new paragraphs (d) and (e). • New paragraph (d) states that subjects or subjects LAR 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. • New paragraph (e)(1) requires that informed consent begin with a concise and focused presentation of the "key information" that is most likely to assist a prospective subject or LAR in understanding the reasons why the subject might or might not want to participate in the research. This part of the informed consent be "organized and presented in a way that facilitates the subject's or LAR's comprehension." • New paragraph (e)(2) requires that informed consent as a whole must present information in sufficient detail and organized in such a way that does not	Documents such as SOPs, guidelines, submission forms, reviewer worksheets, and consent templates may need to be developed or updated.	Click or tap here to enter text.

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	"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."		
Elements of informed consent 50.25	50.25(a) and (b) adds the phrase "or legally authorized representative" to clarify to whom informed consent information must be provided. 50.25(a)(9) adds a new basic element of consent that would require a description of how information or biospecimens may be used for future research or distributed to another investigator for future research. **Note:** While FDA is not proposing to use language verbatim from the revised Common Rule for this new basic element of informed consent at 50.25(a)(9), FDA's proposal similarly requires the provision of additional information to potential subjects about the possible future use of their information or biospecimens. 50.25(b) adds "or the legally authorized representative" to the end of the sentence to clarify to whom informed consent information must be provided. 50.25(b)(2) adds "or legally authorized representative's" to clarify that the investigator may terminate the research without the consent of the subject or LAR. 50.25(b)(7)-(9) – Summary of new requirements: • (b)(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.	Documents such as SOPs, guidelines, submission forms, reviewer worksheets, and consent templates may need to be developed or updated.	Click or tap here to enter text.

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	• (b)(8) requires a statement about whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.(b)(9) requires a statement about whether a research project involving biospecimens will (if known) or might include whole genome sequencing.		
Documentation of informed consent 50.27	Revisions to 50.27 documentation requirements (see section IRB Review of Research 56.109 for other changes related to documentation of informed consent). • 50.27(a) clarifies that consent forms in an electronic format are acceptable and added the term "informed consent" before the term "form". • 50.27(b)(1) add "or the subject's legally authorized representative" to clarify that the subject or LAR shall have the opportunity to read the informed consent form.50.27(b)(2) requires that, when using the short form to document consent, that key information be presented first before other information, if any, and addition of "legally authorized representative". **Note:** FDA is **not** proposing to add the new provision found in the revised Common Rule at 45 CFR 46.116(g) - *Screening, recruiting, or determining eligibility* at this time. The FDA already allows for such activities because they do not consider them to be part of the clinical investigation. For more information, see the proposed rule and FDA Guidance on Informed Consent (Section V, #15).	Documents such as SOPs, guidelines, submission forms, reviewer worksheets, and consent templates may need to be developed or updated.	Click or tap here to enter text.
Reports 812.150	Revise 812.150(a)(3) and 812.150(b)(5) to say that IDE progress reports must be submitted to the reviewing IRB to the extent that continuing review is required by part 56.	Documents such as SOPs, guidelines, submission forms, and reviewer	Click or tap here to enter text.

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	Note: • The proposed rule maintains the requirement that sponsors of treatment IDEs submit semi-annual and annual progress reports to all reviewing IRBs and FDA in accordance with 812.36(f) and 812.150(b)(5). • FDA is **not** proposing to amend the requirements for treatment IDEs at 812.36(f), which require semi-annual progress reports to both FDA and the IRB(s) until a marketing application is filed.	worksheets may need to be updated.	

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The below table highlights additional impacts of the proposed rulemaking that are not captured above.

Section	Summary of Other Proposed Changes	Impact	Organizational Notes
Scope 50.1 **Definitions** 50.3 **Exception from informed consent requirements for emergency research** 50.24 **Elements of informed consent** 50.25	**Proposed changes to Part 50 unrelated to harmonization with the revised Common Rule:** • Modify 50.1(a) to remove the list of statutory provisions in the final sentence because the scope of part 50 is already described in the provision. In addition, removing these provisions will delete certain out of date citations and eliminate the need to update statutory references in the future. • Modify 50.3(b)(20) and (j) to remove outdated references to certain provisions of the PHS Act. • Clarify that references in 50.3(b)(16) through (19) and (23) are citations to sections of the FD&C Act. • Add the following sentence, "The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects" to the definition of "institutional review board" at 50.3(i), to be consistent with our current definition of IRB at § 56.102(g). • Revise the citation in 50.24(a)(6) from "§ 50.25" to "this part," to simplify the regulatory text, and to clarify that both the informed consent procedures and documents for studies conducted under 50.24 must be consistent with part 50. • Add a heading to 50.25(c), "Required statement in informed consent documents for applicable clinical trials," to conform to current Federal Register format requirements.	Documents such as standard operating procedures (SOPs) may need to be updated if they directly cite the current regulatory language.	Click or tap here to enter text.

Section	Summary of Other Proposed Changes	Impact	Organizational Notes
Definitions 56.102 **Circumstances in which IRB review is required** 56.103 **IRB review of research** 56.109 **Expedited review procedures** **56.110** **IRB records** 56.115 **Disqualification of an IRB or an institution** 56.121 **Public disclosure of information regarding revocation** 56.122	**Proposed minor changes or deletion of regulatory text in Part 56:** • In 56.102(b)(17) remove outdated reference to the PHS Act, add corresponding FD&C Act reference. • In 56.102(l) replace outdated references to sections of the PHS Act. • In 56.103(a) delete the reference to 21 CFR part 813, which was removed from FDA's regulations in 1997. • In 56.109(h) (now 56.109(j)) delete the second sentence referring to pediatric studies that were ongoing on April 30, 2001, because it is no longer needed. • In 56.110(b) change reference to 56.108(c) to 56.108(b) because of redesignating of sections. • In 56.110(c) change "which" to "that" in two places. • In 56.115(a)(6) revise the citation to written procedure provisions to reflect redesignating. • In 56.121(c) delete "in the Federal Register," because notices may now be posted on the FDA website. • In 56.122 modify section title from "revocation" to "disqualification," and clarify that disqualification of an IRB is also disclosable to the public.	Documents such as standard operating procedures (SOPs) may need to be updated if they directly cite the current regulatory language.	Click or tap here to enter text.
IRB membership 56.107 **IRB functions and operations** 56.108 **IRB review of research**	See the description of the proposed revisions to numbering for regulatory text in Part 56.	Documents such as standard operating procedures (SOPs) may need to be updated if they directly cite the current regulatory language.	Click or tap here to enter text.

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56.109			

Proposed Effective Date: FDA is proposing that the effective date of any final rule that it issues based on this proposal would be 180 days from the date of publication of the final rule to allow the regulated community time to prepare to implement the proposed changes.

For studies initially approved by an IRB before the proposed effective date, FDA would not intend to enforce compliance with the following proposed provisions:

- proposed new § 50.20(d) through (e), which would, among other things, require informed consent to begin with a concise and focused presentation of "key information" and would require informed consent information to be organized and presented in certain ways;
- the proposed new basic and additional elements of informed consent at § 50.25(a)(9) and (b)(7) through (9); and
- the proposed revision to § 50.27(b)(2), which would require the key information required by § 50.20 to be presented first to the subject or the subject's legally authorized representative when informed consent information is provided orally and documented using a short form.

For questions/comments about this table, please feel free to contact us at any time. We will be happy to speak with you!

Karen Christianson, Senior Vice President & Managing Director christiansonk@thehrpconsultinggroup.com