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Client Alert

Government Matters

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FDA Issues Final Rule Permitting IRB Waiver or Alteration of Informed Consent for Certain Minimal Risk Clinical Investigations

The Food and Drug Administration (FDA) has issued a final rule, *Institutional Review Board Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations*,[1] which allows an exception from the requirement to obtain informed consent if the reviewing Institutional Review Board (IRB) determines that an FDA-regulated clinical investigation (i) poses no more than minimal risk to the human subjects and (ii) includes appropriate safeguards to protect the rights, safety, and welfare of the human subjects. The rule, which implements a 2016 amendment to the Federal Food, Drug, and Cosmetic Act (FD&C Act) authorizing FDA to permit an exception from informed consent for certain minimal risk clinical investigations,[2] modifies 21 C.F.R. Parts 50, 312, and 812. It affects sponsors, investigators, IRBs, and healthcare institutions that sponsor or conduct clinical research.

The rule is effective January 22, 2024.

In part, the rule harmonizes FDA regulations with the criteria for IRB waiver or alteration of informed consent for minimal risk clinical investigations outlined in the Common Rule (i.e., the "Federal Policy for the Protection of Human Subjects") that became effective January 19, 2017. Prior to this new rule, FDA regulations permitted an exception from the requirements for informed consent only in a life-threatening situation or under Presidential waiver related to a military operation (21 C.F.R. § 50.23), or in accordance with the requirements for emergency research (21 C.F.R. § 50.24). On July 15, 2017, FDA released guidance informing sponsors, investigators, and IRBs that FDA "did not object" to IRB waiver or alteration of informed consent for certain minimal risk clinical

investigations,[3] and the agency issued a proposed rule on November 15, 2018.[4]

FIVE CRITERIA FOR EXCEPTION FROM OR MODIFICATION OF INFORMED CONSENT

To waive or alter informed consent, IRBs must identify and document that each of the following five criteria are met:

1. The clinical investigation involves no more than minimal risk to human subjects. It is important to appreciate that the meaning of "minimal risk" is very different from the term "significant risk"[5] that is applicable to investigational devices. In the preamble, FDA clarifies that it relies on the definition of "minimal risk" in 21 C.F.R. § 50.3 that states: "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." In the preamble, FDA states: "This rule permits a waiver or alteration of consent only in limited circumstances where the risks posed to subjects by the research are very low." FDA also opines: "In general, we do not believe that a study involving an invasive procedure being used for research purposes would qualify as presenting no more than minimal risk to subjects." We anticipate that, in the context of potential treatment utilizing novel investigational drugs and devices, IRBs may struggle to determine (i) whether the harm or discomfort anticipated is greater than that encountered in daily life and (ii) what constitutes "routine physical or psychological examinations or tests" in a very sick adult or child.
2. The clinical investigation could not practicably be carried out without the requested waiver or alteration. In the preamble to the rule, FDA explicitly clarifies that, if the research can be "practicably" conducted without a waiver of informed consent, then an exception from informed consent is not warranted. The preamble provides little insight into the criteria or procedures an IRB should use to determine if a proposed clinical study cannot be practicably carried out without the waiver of consent. FDA emphasizes that IRB consideration of the "practicably" criterion should be carried out on a "case-by-case" basis.
3. If the clinical investigation involves using identifiable private information or identifiable biospecimens, then the clinical investigation cannot practicably be carried out without using such information or biospecimens in an identifiable format. Although these terms are defined in the revised Common Rule, this is the first time that FDA regulations introduce the concepts of "private information" and "identifiable" private information or biospecimens. These concepts were not included in the 2018 proposed rule; however, in the final rule, FDA explicitly declines to add a definition of "identifiable." Instead, FDA refers to the definitions of "identifiable private information" and "identifiable biospecimens" in the Common Rule and in the 2022 proposed rule[6] that would broadly amend Part 50, Protection of Human Subjects, and Part 56, Institutional Review Boards. Importantly, this final rule that is specific to informed consent clarifies it is permissible for an IRB to consider the waiver or alteration of informed consent in FDA-regulated clinical investigations that involve identifiable private information or identifiable biospecimens.
4. The waiver or alteration will not adversely affect the rights and welfare of the subjects. In the preamble, FDA explicitly declines to provide a definition of the "rights" or "welfare" of subjects and places reliance on the familiarity of IRBs with these concepts.
5. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation. FDA does not provide clear examples of what such pertinent information might entail.

SECONDARY RESEARCH INVOLVING LEFTOVER BIOSPECIMENS

The amended text to current regulations does not explicitly cite secondary research involving leftover biospecimens. The preamble to the final rule, however, suggests that the rule may facilitate and provide a platform for the use of leftover biospecimens for secondary research without affirmative subject consent or denial of consent if an IRB determines that such research use meets the five criteria described above.

ADDITIONAL CONSIDERATIONS

The final rule provides limited guidance on important interpretive issues that may arise. For example, FDA-regulated clinical investigations of drugs and medical devices are commonly conducted at multiple clinical sites that rely on local IRBs, rather than a single central IRB. The preamble and final rule do not address how to handle conflicting IRB opinions as to whether an exception from consent is appropriate. The use of the concept of "identifiable private information" is novel for FDA regulations concerning the protection of human subjects, and it is not synonymous with "protected health information" (PHI) under the Health Insurance Portability and Accountability Act (HIPAA). The application of a potential exception from consent for use of "identifiable private information" in the context of subject authorization of access to PHI for conduct of a clinical study may cause confusion for all parties—IRB, investigators, and patient subjects—at some institutions.

SUMMARY

In this new rule, all parties involved in the sponsorship or conduct of FDA-regulated clinical investigations will be affected by the new option for IRBs to allow an exception to informed consent or a modification of informed consent requirements if five criteria are identified and met. Because the new rule is effective on January 22, 2024, sponsors will need to rapidly understand the new rule and initiate effective processes for the development of new internal policies, as well as procedures for training personnel, clinical sites, and investigators.

If you have questions regarding the new rule or would like assistance in preparing revised policies and procedures, we are glad to help. Please contact Beverly Lorell, Chris Markus, Kyle Sampson, Jeff Shapiro, or Elaine Tseng for more information.

[1] *See* FDA, Final Rule, Institutional Review Board Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations, 88 Fed. Reg. 88,228 (Dec. 21, 2023), https://www.federalregister.gov/documents/2023/12/21/2023-27935/institutional-review-board-waiver-or-alteration-of-informed-consent-for-minimal-risk-clinical.
[2] *See* FD&C Act §§ 505(i)(4) & 520(g)(3) (amended by 21st Century Cures Act, § 3024, Pub. L. 114–255, Dec. 13, 2016).
[3] *See* FDA, Notice of Availability, *Institutional Review Board Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects; Guidance for Sponsors, Investigators, and Institutional Review Boards*, 82 Fed. Reg. 34,535 (July 15, 2017), https://www.federalregister.gov/documents/2017/07/25/2017-15539/institutional-review-board-waiver-or-alteration-of-informed-consent-for-clinical-investigations.
[4] *See* FDA, Proposed Rule, *Institutional Review Board Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations*, 83 Fed. Reg. 57,378 (Nov. 15, 2018), https://www.federalregister.gov/documents/2018/11/15/2018-24822/institutional-review-board-waiver-or-alteration-of-informed-consent-for-minimal-risk-clinical.
[5] See 21 C.F.R. § 812.3(m).
[6] See FDA, Proposed Rule, *Protection of Human Subjects and Institutional Review Boards*, 87 Fed. Reg. 58,733 (Sept. 28, 2022), https://www.federalregister.gov/documents/2022/09/28/2022-21088/protection-of-human-subjects-and-institutional-review-boards.