November 29, 2018

Another Step Toward Harmonization: FDA Issues Proposed Rule to Waive Informed Consent Requirements in Minimal-Risk Studies

On November 15, 2018, the U.S. Food and Drug Administration ("FDA") published a proposed rule[1] that would allow institutional review boards ("IRBs") to waive or alter informed consent when a clinical investigation poses no more than minimal risk to, and includes appropriate safeguards for, human subjects (the "Proposed Rule"). If finalized in its current form, the Proposed Rule would harmonize FDA consent requirements with those of the "Federal Policy for the Protection of Human Subjects," known as the "Common Rule."[2]

Background

Both FDA regulations and the Common Rule have provisions to protect human research subjects, including requirements pertaining to IRB review and informed consent. FDA regulations govern clinical investigations (1) that are subject to FDA's investigational product application requirements (either an investigational device exemption under 21 U.S.C. § 360j(g) or an investigational new drug application under 21 U.S.C. § 355(i)) or (2) the results of which will be submitted to FDA in support of a product application or held for inspection by FDA.[3] Currently, FDA's regulations require investigators to obtain informed consent of clinical investigation participants, except (1) in certain life-threatening situations[4] or (2) for emergency research.[5]

In contrast, the Common Rule applies to research conducted or supported by certain federal government departments or agencies that have adopted the Common Rule (*e.g.*, the Environmental Protection Agency, Department of Health and Human Services, and National Science Foundation). The Common Rule allows IRBs to grant a waiver of informed consent for certain minimal-risk research (*e.g.*, observational research).

This discrepancy in approach to informed consent has frustrated the research community for years, particularly when research is subject both to the Common Rule and to FDA regulations, in which case informed consent, even in low-risk studies such as registry studies, has been required.

In an effort to promote scientific research and harmonize the Common Rule and FDA regulations, Congress passed the 21st Century Cures Act (the "Cures Act") in December 2016. The Cures Act included a provision amending the Federal Food, Drug, and Cosmetic Act ("FDCA") to permit waiver of informed consent for research involving no more than minimal risk to human subjects, if appropriate safeguards are in place to protect the rights, safety, and welfare of subjects.[6] The Cures Act provision requires FDA, through regulation, to define and describe the conditions under which an IRB may waive informed consent for FDA-regulated minimal-risk research activities.

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[1] *See* Institutional Review Board Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations, 83 Fed. Reg. 57378 (Nov. 15, 2018), available at https://www.federalregister.gov/documents/2018/11/15/2018-24822/institutional-review-board-waiver-or-alteration-of-informed-consent-for-minimal-risk-clinical.

[2] *See* 45 C.F.R. Part 46, subpart A.

[3] *See* 21 C.F.R. §§ 50.1 and 56.101.

[4] *See* 21 C.F.R. § 50.23.

[5] *See id*. at § 50.24. FDA enforcement discretion policy announced in 2006 also allows for FDA-regulated clinical research on "leftover" de-identified specimens to be conducted without informed consent. *See* Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable (April 25, 2006), *available at* https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071265.pdf.

[6] *See* Section 3024 of Pub. L. 114-255.

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In advance of issuing such regulations, on July 25, 2017, FDA issued a guidance document ("Consent Waiver Guidance")—described in this Ropes & Gray alert—announcing its intention not to object to an IRB's waiving or altering of the informed consent requirements for an FDA-regulated clinical investigation that presents no more than minimal risk and involves adequate human subjects protections.[7] FDA stated that it planned to withdraw this guidance upon its promulgation of relevant regulations.

The Proposed Rule

The Proposed Rule would allow an IRB to approve an informed consent process that omits or alters certain elements of informed consent[8] or that waives the informed consent requirement altogether, if the IRB finds (and documents) the following four criteria, all of which are required under the Common Rule[9]:

1. The clinical investigation involves no more than minimal risk to the subjects;

2. The waiver or alteration of informed consent will not adversely affect the rights and welfare of the subjects;

3. The clinical investigation could not practicably be carried out without the waiver or alteration of informed consent; and

4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation in the clinical investigation.

On January 19, 2017, the U.S. Department of Health and Human Services, together with 15 other federal departments and agencies, issued a final rule to revise and modernize the Common Rule (the "Revised Common Rule").[10] The Revised Common Rule retains the four criteria listed above, but also includes a *fifth* criterion for waiver of informed consent: "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."[11] The Proposed Rule adopts the four criteria above from the Common Rule, but does not adopt this new fifth criterion from the Revised Common Rule—although FDA does not explain in the Proposed Rule its decision to omit this new criterion, it has invited comments on this point.

Under the Proposed Rule, if the four criteria are satisfied, an IRB may waive or alter certain required elements of informed consent, including certain statements regarding reasonably foreseeable risks or appropriate alternative procedures. However, the regulations as proposed would not permit an IRB to allow the omission or alteration of the required statement regarding posting of study information at https://www.ClinicalTrials.gov.[12] In addition to requiring

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[7] *See* FDA guidance, IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects (July 2017), *available at* https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM566948.pdf. *See also*Mark Barnes et al., *What to Know About New FDA Informed Consent Guidance* (August 14, 2017), https://www.ropesgray.com/en/newsroom/alerts/2017/08/What-To-Know-About-New-FDA-Informed-Consent-Guidance.

[8] These informed consent elements are found at 21 C.F.R. § 50.25(a) and (b).

[9] *See* 45 C.F.R. § 46.116(d).

[10] *See* 82 Fed. Reg. 7,149 (Jan. 19, 2017). The changes announced in the Final Rule were originally scheduled to take effect in January 2018, but the effective date was delayed in January 2018 until July 19, 2018. More recently, the Common Rule departments and agencies issued a notice of proposed rulemaking proposing to delay further the general compliance date of the 2017 Final Rule until January 21, 2019. *See* 83 Fed. Reg. 17,595 (Apr. 20, 2018).

[11] 45 C.F.R. § 46.116(f)(3)(iii).

[12] Informed consent for clinical trials requires the following statement to be provided to each study subject: "A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information

certain substantive elements of informed consent, FDA regulations also set forth documentation requirements for informed consent (*i.e.*, that *written* consent be obtained), and provide scenarios where an IRB may waive the written consent requirement.[13] The Proposed Rule states that it does not affect these provisions relating to waiver of *documentation* of informed consent.

Takeaways for Companies and Institutions Conducting FDA-Regulated Research

Comments to the Proposed Rule must be submitted by January 14, 2019. The Proposed Rule, once finalized, would allow investigators to engage in low-risk research without having to obtain informed consent. The Proposed Rule would also reduce or remove certain administrative burdens associated with IRB review of minimal-risk studies, as IRBs would no longer need to review informed consent forms. This could result in cost and time savings to IRBs, research institutions and industry, particularly when the research at issue must comply with both FDA regulations and the Common Rule, as IRBs and researchers will no longer need to determine compliance with different requirements.

that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time." 21 C.F.R. § 50.25(c).

[13] *See* 21 C.F.R. § 56.109(c).

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