FDA RELEASES GUIDANCE ON HOW RECENT CHANGES TO THE COMMON RULE MAY AFFECT FDA-REGULATED CLINICAL TRIALS

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Health Care / FDA Alert

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On October 12, 2018, the U.S. Food and Drug Administration ("FDA") released a guidance document titled "Impact of Certain Provisions of the Revised Common Rule on FDA-Regulated Clinical Investigations," (the "Guidance Document") which offers interim guidance to Institutional Review Boards ("IRBs"), sponsors, and investigators on how FDA-regulated clinical trials might be impacted when changes to the regulations governing federally-sponsored human subjects research take effect this coming January.

Multiple U.S. federal agencies have an interest in protecting the welfare and safety of individuals participating in clinical research. In addition to being subject to FDA regulations, FDA-regulated clinical investigations often must also comply with the human subject research protections set forth in the Federal Policy for Protection of Human Research Subjects (45 C.F.R. Part 46, "the Common Rule"). The Common Rule applies to human subject research that is conducted or supported by one of 17 federal departments and agencies, including the U.S. Department of Health and Human Services ("HHS").

On January 19, 2017, HHS, in conjunction with sixteen other federal agencies, issued a final rule (the "2018 Requirements") containing multiple revisions to the Common Rule that (after several delays) is set to become effective on January 21, 2019. [1] These revisions touch on several areas that directly affect the approval, performance, and oversight of FDA-regulated clinical trials. Notably, the 2018 Requirements include changes to informed consent requirements for study subjects, IRB-expedited review procedures, and certain IRB continuing review requirements.

In light of the 2018 Requirements, FDA is planning to undertake notice and comment rulemaking to update FDA regulations, consistent with language in the 21st Century Cures Act that directs the Secretary of HHS to harmonize differences in HHS and FDA regulations regarding human subject research. [2] However, this FDA rulemaking has yet to occur, and with implementation of the Common Rule changes imminent, FDA has recognized that there is some stakeholder confusion about how current FDA requirements are affected by the 2018 Requirements. The Guidance Document clarifies FDA's position on the following matters:

- **Informed Consent.** The 2018 Requirements introduced several new requirements for study participant informed consent, including requirements related to what information must be included in informed consent forms, how that information must be presented, and how investigators may interact with potential study subjects to facilitate their decisions about whether to participate in a study. [3] For example, the 2018 Requirements added a requirement that informed consent forms contain a statement specifying either that identifiable biospecimens collected from study subjects will not be used for future research

studies, or that identifiable biospecimens will be distributed to other investigators for use in future research studies, in which case the biospecimens must be stripped of identifiers. [4]

> In the Guidance Document, the FDA states that it has received a number of questions from stakeholders inquiring whether the new informed consent requirements will make necessary the use of two separate informed consent forms for study subjects involved in FDA-regulated clinical trials: one to satisfy FDA informed consent requirements and another to satisfy the new informed consent requirements under the Common Rule. In response, the FDA clarifies that the new informed consent requirements imposed by the 2018 Requirements are not inconsistent with the FDA's current informed consent requirements, and investigators will not be required to use separate forms to satisfy FDA and Common Rule informed consent requirements when the Common Rule revisions are implemented.

- **IRB Expedited Review.** Under FDA regulations and the Common Rule, before a research study involving human subjects may commence, it must be reviewed and approved by an IRB. Generally, when reviewing a research study an IRB evaluates the study for compliance with a number of different factors and may either approve the study, require modifications to the study, or disapprove the study altogether. [5] However, for certain types of research, both FDA regulations and the Common Rule provide that the study may undergo expedited IRB review. [6] Under FDA regulations, a study can qualify for expedited review if it involves a category of research found on a list of categories last promulgated by the FDA in 1998 and if an IRB determines **and** documents that the study involves no more than minimal risk. [7]

> While current Common Rule requirements for expedited research are quite similar, the 2018 Requirements modify this process slightly, particularly in terms of the IRB's burden. Under the new requirements, if the research fits a category found on HHS's list of eligible categories, the presumption is that the research will involve no more than minimal risk, unless an IRB reviewer determines that it does involve more than minimal risk. [8] In the Guidance Document, the FDA acknowledges this revision, but states that because the FDA has not yet modified its own regulations, IRBs are still required to abide by the requirements of 21 C.F.R. §56.110(b). Thus, the IRB must continue to use the FDA's 1998 list of categories for determining whether FDA-regulated clinical investigations qualify for expedited review, and the IRB reviewer must determine, and document, that a study involves no more than minimal risk (without the presumption provided for in the 2018 Requirements).

- **IRB Continuing Review.** After an IRB approves a research study, the IRB must engage in continuing review of the study as it progresses. [9] Pursuant to the 2018 Requirements, IRBs are not required to engage in continuing review of a research study if it:

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> (a) is eligible for expedited review; or (b) has progressed to the point that the only remaining research activities involve data analysis or accessing follow-up data from procedures subjects would undergo as a

> part of clinical care. [10]

As with the revisions to the IRB expedited review procedures, the FDA points out in the Guidance Document that the FDA has not yet revised its regulations, and consequently, IRBs are still required to engage in continuing review of all approved research studies at intervals appropriate to the degree of risk involved in the study.

In addition to offering the guidance summarized above, the FDA acknowledges in the Guidance Document that there will be continuing questions regarding the implementation of the 2018 Requirements to FDA-regulated clinical trials, and encourages stakeholders to contact the FDA with questions and comments requesting further clarification. K&L Gates will continue to monitor and provide updates on further developments related to the implementation of the Common Rule changes enacted by the 2018 Requirements as the effective date approaches, as well as any resulting changes to FDA regulations, policies, and procedures.

For additional background on the Common Rule, please see our previous alerts. (Federal Agencies Delay Implementation of Common Rule Revisions and Federal Agencies Propose to Further Delay Implementation of Sweeping Revisions to the "Common Rule" - but Offer Incentives for Institutions Willing to Transition Existing Research Projects)

NOTES:

[1] 82 Fed. Reg. 7149 (January 19, 2017).
[2] Public Law 114-255, enacted Dec. 13, 2016, §3023.
[3] *See, e.g.*, 45 C.F.R. §§ 46.116(a)-(c).
[4] 45 C.F.R. § 46.116(b)(9) (Jan. 21, 2019).
[5] *See* 45 C.F.R. § 46.109.
[6] 45 C.F.R. § 46.110; 21 C.F.R. § 56.110.
[7] 21 C.F.R. § 56.110(b); *see also* 63 Fed. Reg. 60353 (Nov. 9, 1998).
[8] 45 C.F.R. § 46.110(b)(1).
[9] 45 C.F.R. § 46.109(e).
[10] 45 C.F.R. § 46.109(f)(1)(i) (Jan. 21, 2019).

