FDA Clarifies Consent Requirements for Certain Minimal Risk Clinical Investigations

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FDA’s guidance, which permits institutional review boards to waive informed consent for certain clinical investigations, may facilitate valuable personalized medicine research.

On July 25, the US Food and Drug Administration (FDA or the Agency) issued a clarifying guidance document, titled “IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects” (Guidance), for immediate implementation. Through the clarifying Guidance, the Agency announced that it does not intend to object to an institutional review board’s (IRB’s) waiving or altering the informed consent requirements for certain FDA regulated minimal risk clinical investigations. Such research may include certain prospective and retrospective bio-sample trials, including studies evaluating genetic and other biomarkers that may predispose patients to certain diseases or conditions, or that may make certain patients more likely to respond to treatment. In accordance with the clarifying Guidance, with an IRB waiver, sponsors and investigators may not be required to obtain specific consent from subjects in order to reanalyze biological samples that they may have collected during prior studies. The clarifying Guidance, however, does not give sponsors and investigators complete freedom to reanalyze biological samples without subject informed consent, as there may be other reasons why subject informed consent may be required.

Background on Informed Consent Requirements for Minimal Risk Clinical Trials

Under the US regulatory system, depending on the clinical study, multiple regulatory authorities may govern whether informed consent is required. For FDA regulated clinical trials before the clarifying Guidance, sponsors and investigators were generally required to obtain subject informed consent for most forms of clinical research.\[1\]

Studies that do not concern FDA regulated products, however, are generally governed by the Department of Health and Human Services (HHS) informed consent requirements, known as the Common Rule.\[2\] While FDA’s regulations are generally consistent with the Common Rule, the Common Rule includes a provision that explicitly permits IRBs to waive informed consent for minimal risk clinical studies.\[3\]

This inconsistency caused a research disruption that Congress attempted to remedy in the recently passed 21st Century Cures Act (Cures Act). The Cures Act explicitly granted FDA the authority to permit an exception to informed consent requirements when clinical testing poses no more than minimal risk to human subjects and includes appropriate safeguards to protect subject rights, safety, and welfare.\[4\] Under this authority, FDA intends to enact a direct final rule to clearly permit IRBs to waive informed consent under certain conditions for minimal risk clinical investigations.\[5\]

FDA Informed Consent Clarifying Guidance

In order to bridge the gap between the Cures Act and a final FDA rule concerning informed consent, on July 25, FDA issued the clarifying Guidance, which states that the Agency does not plan to object to minimal risk clinical research where an IRB waives informed consent requirements.
To waive informed consent for minimal risk clinical studies, the IRB must find and document that:

- the clinical investigation involves no more than minimal risk to the subjects;[6]
- the waiver or alteration will not adversely affect the rights and welfare of the subjects;
- the clinical investigations could not practicably be carried out without the waiver or alteration; and
- whenever appropriate, the subjects will be provided with additional pertinent information after participation.

These informed consent requirements for minimal risk clinical studies are consistent with the Common Rule that has already been adopted by HHS and other federal departments. FDA intends to withdraw the clarifying Guidance once new regulations are finalized.

**Discussion and Key Takeaways**

FDA’s clarifying Guidance may simplify and encourage more minimal risk clinical investigations for the development of new products to diagnose and treat disease. For example, in the area of precision medicine that targets treatments based on individual biomarkers, researchers may have access to stored biological specimens from prior research. Under the text of FDA’s existing regulation, researchers would generally not be permitted to analyze such specimens for new studies, unless study subjects had consented to the specific research. Under the clarifying Guidance, with the agreement of an IRB to waive the informed consent requirements, FDA now clearly may permit researchers to use existing specimens without having to obtain broad consents or go back and specifically obtain consent from subjects for the new study.

While FDA will now explicitly permit minimal risk clinical trials to be conducted without informed consent, if a waiver is granted by an IRB, there may be other restrictions that sponsors, investigators, and IRBs should consider.

- First, the clarifying Guidance is not permission to conduct all minimal risk clinical investigations without subject informed consent. Rather, sponsors and investigators must first obtain an IRB waiver from FDA’s informed consent requirements. To obtain an IRB waiver, among other requirements, researchers must show not only that the investigation involves no more than minimal risk, but that the waiver will not adversely affect the rights and welfare of subjects. The clarifying Guidance, however, does not describe how the Agency will interpret this prerequisite.

- Second, individual states may have informed consent requirements that place additional requirements on investigations involving human subjects or the handling of biological material containing genetic information.

- Third, for existing biological samples, language in the informed consent forms used in the original research may restrict the use of the specimens. Accordingly, sponsors and investigators should review the informed consents provided by subjects to determine if there are any restraints on the reuse of samples.

- Finally, researchers must continue to obey research protocols in coordination with their IRBs, as well as other applicable laws, including the Genetic Information Nondiscrimination Act and the Health Insurance Portability and Accountability Act, and basic principles of medical and scientific ethics. Thus, for example, even if informed consent is not required, study subjects still must receive all information that is required by law regarding the use of their medical information. Additionally, for biological material collected from patients through medical procedures, patients must still provide their consent for such materials to be used for research purposes.

Thus, while FDA’s clarifying Guidance potentially may enable industry to efficiently conduct research with existing biological specimens, it is not without limits. Before reanalyzing existing biological samples, sponsors and investigators should carefully consider whether there are other constraints on the conduct of the research.

Although the clarifying Guidance is for immediate FDA implementation, the Agency is open to receiving public comments. Accordingly, if regulated industry has any questions or comments on any aspect of the clarifying Guidance, they may be submitted for FDA’s consideration.

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[1] 21 C.F.R. Part 50. Informed consent has not been required by FDA for certain categories of research. For instance, the Agency issued guidance on its intent to exercise enforcement discretion concerning informed consent for in vitro diagnostic (IVD) device investigations using leftover human specimens under certain circumstances (see Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens That Are Not Individually Identifiable).


[6] Minimal risk is defined as “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.” 21 C.F.R §§ 50.3(k), 56.102(i).

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