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OHRP and FDA Issue Guidance on Participation in and Withdrawal from Human Subjects Research

By Rachel Nosowsky*

On December 1, 2008, the U.S. Office for Human Research Protections (OHRP) and U.S. Food and Drug Administration (FDA) issued parallel guidance intended to help clarify how to handle data and specimen retention and destruction following a research participant's decision to withdraw from a study. OHRP is soliciting comments through January 30, 2009; FDA's guidance was published as final.

Both the Common Rule and FDA regulations require that informed consent documents include a "statement that participation is voluntary . . . and that the subject may discontinue participation at any time[;]" and, "when appropriate," information about the "consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject[.]"[1] But the meaning of "participation" and consequences of "withdrawal" have been the subject of substantial controversy for many years.[2] Institutional and ethics committee policies have varied widely. The agency guidance was intended to clarify the meaning of the regulations and, in FDA's case, to assure the retention of documentation relevant to product approvals and safety. In brief, the agencies have clarified that investigators may continue to analyze previously collected data—even individually identifiable data—about a research participant following the individual's withdrawal from a research study. FDA's position is premised on the idea that withdrawal does not justify destruction and, if done in a non-random or informative manner, could undermine data validity and integrity. OHRP's guidance focuses on the definition of a "human subject" and meaning of the word "participation," with a similar result.

Although the OHRP document explicitly references FDA's guidance and characterizes the two as harmonized, they may not be entirely consistent. OHRP's guidance includes case studies suggesting that new data extractions from previously collected specimens are barred following complete withdrawal (but are permitted in partial withdrawal cases where the participant agrees to ongoing data collection). FDA does not explicitly address specimens, but its reasoning seems to suggest that destruction of specimens containing as-yet unextracted data relevant to previously approved and anticipated study analysis might be problematic.

Research institutions and researchers should anticipate updated data retention language in sponsors' clinical trial agreements, and are encouraged to review institutional policies to assure consistency with the agency guidance and, where possible, avoid case-by-case policymaking through IRB discussions on individual studies. For example, many research pathology labs perform batch analyses to more efficiently do their work and do not routinely remove previously collected specimens from those batches, even following complete withdrawal from a study. This approach arguably is consistent with the FDA guidance but clearly would not comply with the Common Rule as now interpreted by OHRP. Research institutions may also wish to consider updating their informed consent templates to address data and specimen disposition following withdrawal and development of standard IRB-approved forms to document a participant's wishes regarding ongoing data collection in those circumstances.

The guidance documents are available on the agencies' respective websites at:

- OHRP
- FDA

The Office for Civil Rights' previously issued guidance on retention of protected health information in connection with a research study following withdrawal is available online.

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[1] 45 C.F.R. §§ 46.116(a)(8) and (b)(4); 21 C.F.R. §§ 50.25(a)(8) and (b)(4).

[2] *See*, e.g., *Wash. Univ. v. Catalona*, 490 F.3d 667 (8th Cir. 2007), *cert. denied*, 128 S. Ct. 1122 (2008).

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Member benefit educational opportunity:
Teleconference on surviving an FDA bioresearch monitoring inspection (January 14, 2009).