CLIENT ALERT

ROPES & GRAY

HEALTH CARE/LIFE SCIENCES May 9, 2006

Food and Drug Administration Releases Guidance on Informed Consent for *In Vitro* Diagnostic Device Studies Using Leftover Human Specimens

Food and Drug Administration (FDA) regulations requiring the informed consent of all human subjects encompass research using human tissue specimens. The lack of regulatory exceptions concerning this type of research and the fact that an institutional review board (IRB) cannot waive the informed consent requirement under FDA regulations have caused industry sponsors and clinical investigators to question whether leftover specimens from routine clinical care or other research studies can be used in research to support FDA submissions or applications.

On April 25, 2006, in response to these concerns, the FDA issued a guidance document on *in vitro* diagnostic (IVD) device studies with leftover human specimens. The document not only offers a clear set of conditions under which the FDA will not seek to enforce the informed consent requirement, but also demonstrates flexibility on the part of the FDA with respect to human subject protection regulations when the specimen acquisition process and related study design adequately protect the privacy of the individual source of the specimen.

Background of Informed Consent Requirements for *In Vitro* Diagnostic Device Studies

Under FDA regulations, all clinical investigations must be in compliance with the agency's human subject protection regulations (21 CFR Part 50), which require informed consent of research subjects. The definition of "subject" in the regulations for Investigational Device Exemptions (IDE) includes "a human … on whose specimen an investigational device is used," leading some to conclude that in device studies, investigators using specimens for which the identity of the source is known must obtain informed consent from the individuals whose specimens are used. The definitions of "subject" in regulations for parallel drug studies and in the regulations regarding the informed consent requirement make no similar reference to "specimens." Therefore, tissue studies in support of Investigational New Drug applications arguably do not require investigators to obtain informed consent from specimen sources.

IVD device studies often use leftover tissue specimens to asses feasibility and characterize device performance. It is important to note that IVD device studies that are exempt from most of the FDA regulations regarding Investigational Device Exemptions are still subject to the regulations protecting human subjects. There are no specific

exceptions in the IDE regulations for research using leftover specimens that would otherwise be discarded or specimens from individuals who cannot be identified from the specimens and accompanying information. Until this new FDA guidance was released, clinical investigators and study sponsors were forced to obtain informed consent before using these readily-available specimens in any device studies. This guidance effectively creates a new exception for certain IVD studies

Food and Drug Administration Guidance Document

The new guidance on informed consent in IVD device studies does not change existing FDA regulations and is not binding on the agency. Instead, it sets forth conditions under which the FDA will not enforce the informed consent requirements. According to this guidance document, if an IVD device study meets all of the following requirements, the FDA will exercise discretion in its enforcement function and will *not* consider a clinical investigator, sponsor, or IRB in violation of FDA's human subjects protection regulations.

1. The study meets the IDE exemption criteria at 21 CFR 812.2(c)(3)
2. The study uses leftover specimens that are collected in routine clinical care and that would otherwise be discarded, specimens from tissue repositories, or specimens that were previously collected for other research purposes. The specimens *must not* have been collected specifically for the proposed study
3. The identity of the subject is not known to the investigator and may not be readily ascertained. Coded specimens, meaning those specimens for which identifying information has been replaced with a code that still exists and may be used to link the individual to a specimen, may be used as long as the study investigator, individuals associated with the study, and the study sponsor do not have the key to the code and are unable to link the specimen with an individual
4. The specimens may be accompanied by clinical information as long as no individual associated with the study is able to use this information to identify the individual source of the specimen
5. The individuals providing clinical care for individuals from whom specimens were obtained must be different from (and not share information with) those conducing the study
6. The specimens are provided to the investigator without individually identifying information and the supplier of the specimens has established policies and procedures to prevent release of personal information
7. The study is reviewed by an IRB

The full text of the guidance document is available online at: http://www.fda.gov/cdrh/oivd/guidance/1588.pdf

Implications for Research with Leftover Human Specimens

In its structure and content, this FDA guidance closely parallels guidance from the Office for Human Research Protections (OHRP) regarding human subject research involving coded private information or biological specimens (issued August 10, 2004, available at http://www.hhs.gov/ohrp/policy/index.html#coded). Unlike the OHRP regulations though, FDA regulations contain neither exemptions for certain types of research nor the possibility of IRB waiver of the informed consent requirement. This FDA guidance provides criteria under which IVD device research does not need to meet the informed consent requirements, but this document explicitly states that a study that fails to meet any of the listed criteria does not "fall within the intended enforcement discretion." By implication then, this guidance document indicates that all other device-based research with individually identifiable tissue specimens requires investigators to obtain informed consent from all identified persons who are sources of those specimens.

The requirement that specimens in studies covered by this FDA guidance must not be individually identifiable by the investigators or sponsors highlights the differences between the FDA and OHRP regulations regarding human subjects research. The FDA device regulations protect all subjects, identified and unidentified, in that their definitions of "subject" and of "clinical investigation" for purposes of the informed consent requirements do not depend on whether the individual from whom the specimen was obtained can be identified. The OHRP regulations, however, explicitly define "human subject" as a living individual with whom an investigator interacts or about whom an investigator collects data or identifiable private information. If the source of a tissue specimen is not identified, under OHRP regulations an investigator is not conducting research with human subjects, and no informed consent is required. The criteria listed in the new FDA guidance therefore create an exemption for device-related research that would not be considered human subjects research at all under OHRP regulations.

Contact Information

Ropes & Gray has considerable expertise in these issues and in many areas of research compliance and FDA law and regulations. Ropes & Gray attorneys have substantial experience in developing research compliance policies and helping study sponsors, clinical investigators, research institutions, and IRBs to interpret and comply with clinical research requirements. If you have any questions about these matters, please contact your Ropes & Gray attorney or any of the attorneys listed below.

Mark Barnes
212-497-3635
mark.barnes@ropesgray.com

Albert F. Cacozza, Jr.
202-508-4611
albert.cacozza@ropesgray.com

Glenn L. Krinsky
415-315-6316
glenn.krinsky@ropesgray.com

Clinton D. Hermes
212-841-0694
clinton.hermes@ropesgray.com

ROPES & GRAY