Life Sciences & FDA Alert

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New Guidance on RUOs and IUOs May Affect LDTs

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On June 1, 2011, the Office of In Vitro Diagnostics (OIVD) in the Food and Drug Administration's (FDA) Center for Devices and Radiological Health and the Center for Biologics Evaluation and Research issued the first of several anticipated guidance documents intended to clarify the regulation of clinical diagnostic tests and related items. The draft guidance, which is entitled "Commercially Distributed In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only: Frequently Asked Questions" (the Guidance), clarifies FDA's regulations for labeling and marketing "research use only" (RUO) and "investigational use only" (IUO) tests. The Guidance will apply to reagents, instruments and systems intended for use in the collection, preparation and examination of human specimens in order to diagnose disease or other conditions, including a determination of the state of health. Although it is directed toward manufacturers and distributors of RUOs and IUOs and anyone else who labels in vitro diagnostic (IVD) products, the Guidance may indirectly affect laboratory developed tests (LDTs) and other IVDs that incorporate RUOs or IUOs.

The FDA describes a RUO IVD in 21 CFR 809.10(c)(2)(i) as a product in the laboratory research phase of development and not represented as an effective IVD product. RUOs must be labeled "For Research Use Only. Not for use in diagnostic procedures." Examples of RUOs provided in the Guidance include tests in development to identify test kit methodology, necessary components and analytes to be measured, instrumentation or other electrical/mechanical components under development to determine basic operational characteristics and possible use methods, and products for use in research attempting to isolate a gene linked to a particular disease.

The FDA describes an IUO IVD in 21 CFR 809.10(c)(2)(ii) as a product being tested prior to full commercial marketing that is labeled "For Investigational Use Only. The performance characteristics of this product have not been established." For example, the FDA would consider a product being used on human specimens to compare the usefulness of that product with other products or procedures in current use as an IUO IVD. An IUO IVD is not a product that is being studied under an investigational device exemption (IDE), to which other regulations apply. A manufacturer may market its IUO-labeled product only for clinical investigations that are exempt from the IDE requirements.

The most significant and unusual part of the Guidance relates to a manufacturer's marketing responsibilities. The FDA reiterated a previously expressed position that its determination of whether a regulated product is being improperly promoted and marketed will be based on the totality of the circumstances surrounding the promotion and sale of a product, including overt expressions such as those in labeling, advertising and verbal statements. What is new here is that the FDA may also consider the manufacturer's knowledge that its product is used for a purpose for which it is neither labeled nor advertised, i.e., clinical diagnostic purposes, or the manufacturer's provision of technical support for those activities to be evidence that the IVD product is intended to be used for such

purposes. In such a case, the FDA would impose a responsibility on the manufacturer to stop selling its RUO and IUO IVDs to customers who use them for clinical diagnostic purposes. Alternatively, a manufacturer could obtain clearance or approval for the test.

Although the FDA has long viewed LDTs as regulated products for which it has mostly exercised enforcement discretion, the FDA specifically exempted LDTs from the definition of an IVD for the purposes of the Guidance. Nevertheless, the Guidance could have a significant effect on an LDT if it uses an RUO- or IUO-labeled reagent and/or instrument and the manufacturer or distributor is aware of that use. In addition, it's not clear how the Guidance would affect the efforts of a laboratory offering an LDT to obtain information from the IUO or RUO manufacturer that might be needed if the laboratory decided to submit a 510(k) or premarket approval application for its test.

This Guidance is a draft and it begins with FDA's usual notice that guidance documents describe its current thinking on a topic and do not establish legally enforceable responsibilities. There is an opportunity to comment on the Guidance, which can be accessed by the link below, by August 30, 2011. If you have any questions about this alert or would like to submit a comment, please contact the author or your Mintz Levin attorney.

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Click Here to View Draft IUO and RUO Guidance on the FDA Website

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