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More FDA regulation of diagnostic tests and services ahead?

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Recent regulatory developments continue to signal that, barring congressional or judicial intervention, the U.S. Food and Drug Administration (FDA) intends to bring many more diagnostic test products and systems under regulation as "medical devices" under the Federal Food, Drug, and Cosmetic Act (FDCA). This move may have broad implications for companies in Florida and elsewhere that develop or manufacture diagnostic test products and systems that fall within FDA's revised definition of In Vitro Diagnostic Multivariate Index Assays (IVDMIAs). IVDMIAs include many genetic-based tests as well as many diagnostic test systems/services developed and marketed by clinical laboratories. While many such products are on the market or currently under development, as a matter of traditional FDA enforcement policy very few have been regulated as medical devices to date.

However, FDA's current — and still evolving — policy signals a strong possibility that previously unregulated diagnostics could require FDA approval or clearance prior to marketing as well as being subject to other medical device requirements under the FDCA including compliance with FDA's Quality Systems Regulations (QSRs), product listing and facility registration, and adverse event reporting.

Florida companies selling or developing such diagnostic test products and systems would be well-advised to keep track of developments in this field, and the test products and systems growth sector in Florida would be affected by changes in regulations. The specific class of products to be regulated as IVDMIAs was recently redefined by FDA as part of a revised draft guidance document, Draft Guidance for Industry, Clinical Laboratories, and FDA Staff – In Vitro Diagnostic Multivariate Index Arrays (July 26, 2007) (Revised Guidance). The Revised Guidance replaces an earlier version issued in September 2006. Both versions of the guidance represent a significant shift from traditional FDA enforcement policy, under which FDA did not consider it necessary as a matter of public health and safety to regulate various diagnostic tests and test components, including those now defined as IVDMIAs.

As newly redefined, an IVDMIA is a medical device that (1) combines the values of multiple variables using an interpretation function (algorithm) to yield a single, patient-specific result (e.g., a "classification," "score," "index," and so forth) that is intended for use in the diagnosis of disease or other conditions; and (2) provides a result whose derivation is non-transparent and cannot be independently derived or verified by the end user.

Examples of IVDMIAs identified in the guidance include:

- Gene expression profiling assays for breast cancer prognosis
- Products/systems that predict disease risk by integrating results from multiple immunoassays
- Those that predict risk or diagnose disease by integrating age, sex, and genotype of multiple genes

The Revised Guidance also provides multiple examples of devices that are not considered to be IDVMIAS. While it provides a general overview of medical device requirements and their potential application to IVDMIAs, it anticipates a transition period of 12 months following the issuance of additional and more detailed guidance on the application of particular device requirements such as QSRs.

The draft IVDMIA policy was widely opposed by diagnostic test manufacturers and clinical laboratories as unnecessarily burdensome, confusing, and detrimental to the development and commercialization of needed diagnostic technologies. Preliminary comments indicate that the Revised Guidance will be equally controversial, and that many details remain to be resolved before it can effectively be implemented.

For example, the newly added provision that IVDMIA results are "non-transparent" and "cannot be independently derived and verified by the end user" appear potentially subject to debate, as does the application of various examples newly added to the Revised Guidance. As the guidance itself recognizes, still further details will need to be developed in order to apply the medical device QSR regulations to laboratory-developed IVDMIAs, and to resolve potential overlap or conflict with separate regulations applicable under the Clinical Laboratories Improvements Act of 1988 (CLIA).

Finally, there may grounds for potential legal challenges to FDA's interpretation of its "medical device " jurisdiction as well as its use of non-binding guidance documents rather than notice-and-comment rulemaking to impose the requirements at issue.

In addition to FDA's ongoing guidance process, a separate but related development has been unfolding at CMS, which is responsible for the regulation of clinical laboratories under CLIA. Many comments on FDA's regulatory policies involving IVDMIAs and other diagnostics not historically regulated as medical devices have argued that such products are already adequately regulated under CLIA. Additionally, parties across the spectrum of public debate about genetic-based testing have proposed that such products and services should primarily be regulated by CMS under a new CLIA "specialty" for genetic testing, and in 2002 CMS announced plans to do so. In August 2007, however, CMS formally declined to proceed with such rulemaking at this time.

In summary, as matters now stand, it is clear that many questions about the appropriate role of federal agencies in regulating genetic testing and other innovative diagnostic products and technologies remain to be fully identified, much less resolved. Based upon recent events, however, it appears that FDA is poised to take a far more active role than it has in the past. Companies in Florida that may be affected by the changed approach would be well-advised to take steps to understand the issues and implications on their business.

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