FDA recently published a draft guidance document titled “Principles for Codevelopment of an In Vitro Companion Diagnostic Device with a Therapeutic Product.” A companion diagnostic is an in vitro diagnostic device that provides “information that is essential for the safe and effective use of a corresponding therapeutic product.” The new draft guidance is intended by FDA as a “practical guide” to assist sponsors of therapeutic products and IVD companion diagnostics in the codevelopment process.

Companion diagnostics are a critical element of the advancement of precision medicine, a focus of FDA under the President Obama’s Precision Medicine Initiative, launched earlier this year. There is increasing interest in identifying biomarkers that may be targets for therapeutic product development, prognostic indicators, or predictors of patient response to a particular therapy. An estimated quarter of new drugs approved over the last two years were approved with a
corresponding IVD companion diagnostic. But codevelopment of IVD companion diagnostics and therapeutic products is often complicated by the fact that the products may be developed on different schedules, are subject to different regulatory requirements, and have different points of interaction with the appropriate review centers at FDA. The draft guidance is intended to help sponsors and FDA reviewers navigate these challenges.

In the draft guidance, FDA reiterates its policy stated in the 2014 guidance document that IVD companion diagnostic devices should receive marketing authorization contemporaneously with the approval of the corresponding therapeutic product. Ideally, the need for an IVD companion diagnostic would be identified early in the development of the therapeutic product “so that an analytically validated test can be prospectively incorporated into the design of the therapeutic product trials.” The agency notes that while simultaneous development of the IVD companion diagnostic and the therapeutic product from beginning to end is not required, “the availability of an IVD with ‘market-ready’ analytical performance characteristics . . . is highly recommended at the time of initiation of clinical trials intended to support approval of the therapeutic product.” FDA also states: “Using an analytically validated test is important to protect clinical trial subjects, to be able to interpret trial results when a prototype test is used, and to help to define acceptable performance characteristics for the development of the candidate IVD companion diagnostic.”

In addition to general principles—most of which had been previously articulated by FDA in prior guidance documents—the new draft guidance provides significantly more information about the technical and scientific aspects of the development process. Among other topics, the guidance addresses:

- the need for an investigational device exemption (IDE) for clinical trials involving the IVD companion diagnostic to enroll, assign, or manage subjects;
- the use of IVD prototype tests solely for the purpose of testing the therapeutic product early in development, often referred to as a clinical trial assay (CTA);
- the use of research use only (RUO) components as part of a CTA;
- considerations for planning and executing a therapeutic product clinical trial that also includes the investigation of an IVD companion diagnostic;
- use of a prospective-retrospective study approach, which includes a pre-specified plan to prospectively collect specimens and retrospectively analyze outcomes in subgroups based on the IVD result;
- the use of training and validation sample sets;
- modifications to the IVD companion diagnostic during the development process and the need for and design of bridging studies;
- evidence to support predictive claims, patient selection claims, and monitoring claims for companion diagnostics in labeling for the therapeutic product and companion diagnostic;
- considerations for the submission and review process for the therapeutic product and
companion diagnostic to facilitate contemporaneous marketing authorizations;

- use of a master file for the therapeutic product to provide data in support of the IVD companion diagnostic marketing application; and

- shipment to labs for setup and verification of an IVD companion diagnostic prior to obtaining a marketing authorization.

While the draft guidance is focused on IVD companion diagnostics, FDA stated that many of the principles discussed in the draft guidance “may also be relevant to the codevelopment of therapeutic products with IVDs that do not meet the definition of an IVD companion diagnostic but that are nonetheless beneficial for therapeutic product development or clinical decision making.” As we previously discussed, last year FDA indicated that it was considering recognizing a category of “complementary diagnostics,” which are tests that provide additional information about how a drug might be used but are not “essential” for the safe and effective use of the drug. FDA has approved several complementary diagnostic tests for use with therapeutic products.

FDA is hosting a webinar to answer questions about the draft guidance document on August 18. Stakeholders may submit comments electronically by October 13.

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National Law Review, Volume VI, Number 215

Source URL: https://www.natlawreview.com/article/fda-publishes-draft-guidance-codevelopment-companion-diagnostics