Background: A Brief History

In 1976, amendments to the Food, Drug, and Cosmetic (FD&C) Act gave the Food and Drug Administration (FDA) the authority to regulate in vitro devices (IVDs, see Inset 1). Following the initial passage of the 1976 Amendments, the Agency concluded that Laboratory-developed Tests (LDTs, see Inset 2) were generally used within the restricted environment of a hospital and for the benefit of institutional clinicians only. Thus, their use and interpretation were limited, and FDA chose to exercise “enforcement discretion” over the commercialization of LDTs.

Beginning in 2010, the Agency signaled a need to regulate LDTs. Pharmaceutical companies complained that FDA needed to provide clear and consistent standards for all IVDs, and Genentech submitted a Citizen Petition to that effect. Other professional societies and industry groups joined the discussion, with some for and some against FDA regulation of LDTs.

In 2014, FDA published two Guidance Documents within which they proposed a framework for regulation of LDTs and notified Congress of their intent to regulate LDTs. In 2016, FDA stated publicly that they would not pursue regulation of LDTs.

FDA subsequently notified several manufacturers who removed references to specific medications in their labeling and test reports. When Inova Genomics declined to do so, FDA issued a Warning Letter dated April 4, 2019. The American Clinical Laboratory Association responded with a strongly worded letter asking FDA to refrain from their recent enforcement actions because they may impact patient care, increase costs, and have a negative impact on the ongoing discussions between industry, FDA and Congress to redesign regulatory oversight of all laboratory tests.

FDA and Industry – when the going gets tense, the tense go to Congress

As the tension between FDA and the laboratory industry has increased, new legislation has been under development in Congress. On the one hand, FDA says “We shouldn’t subject similar tests to different approaches just because they are made by different developers;” on the other hand, the laboratory industry supports new legislation aimed at providing FDA with clear authority to regulate LDTs and streamline the process.

Following the initial draft of DAIA in 2015 (see above), FDA proposed a revised draft, and the proposal later resurfaced as a Discussion Draft titled the “Verifying Accurate Leading-edge
IVDs – are regulated.

provisions that change how laboratory tests – platforms, collection devices, software, certain this will be the case, given that each analyte, in effect, defines its own test group.

In addition, pre-certification excludes test platforms, collection devices, software, certain blood tests, first-of-a-kind tests, home use tests, high risk tests, companion and complementary diagnostics and direct to consumer tests. While well intentioned, this approach is so restrictive as to be of limited value to manufacturers. Other provisions would allow a five-year window to laboratories that utilize research-use only (RUO) platforms to switch to FDA-approved platforms.

Preapproval Requirements – condition kudos...

Some tests would be exempt from preapproval requirements, e.g., “grandfathered tests,” those in use 90 days prior to passage of the Act. Low risk tests, tests for rare diseases (< 8000 individuals tested per year), and pre-certified tests would also be exempt.

The draft ACT includes a good faith effort to minimize the number of tests subject to pre-approval requirements. In fact, Scott Gottlieb stated before he left the Agency that recent FDA proposals would subject only 10% of all IVCTs to preapproval requirements. The current draft of the Act may not achieve that objective, but the effort is to be applauded.

In Vitro Clinical Tests (IVCTs) include devices used to collect specimens from the human body for “identifying, diagnosing, screening, measuring, detecting, predicting, proposing, analyzing, or monitoring a disease or condition” and for “selecting, monitoring, or informing therapy or treatment for a disease or condition.” See in definition in full in Sec. 2 Definitions in the PRELIMINARY DISCUSSION DRAFT, presented to the 115TH CONGRESS 2nd SESSION, Title “To amend the Federal Food, Drug, and Cosmetic Act to provide for the regulation of in vitro clinical tests, and for other purposes,” time stamped: December 6, 2018 (3:09pm), see, e.g., https://www.genomeweb.com/sites/default/files/valid_act_discussion_draft_12.6.18.pdf

What happened to Provisional Approvals?

Notably missing from the discussion draft is reference to provisional approvals. This path has traditionally afforded protection to small biotech start-ups from the time and cost burdens of bringing novel technologies through FDA. Omitting this path may reflect a reality of favoring the needs and interests of larger institutional firms over those of smaller, more agile businesses that respond quickly to customers’ needs.

Parting thoughts

Given the recent course of events, a few points seem more certain:

FDA is intent on pushing to regulate LDTs;

Industry and in Congress are ready to support new (IVCT) legislation;

The VALID Act could create a more comprehensive and harmonized FDA regulatory framework for diagnostic tests.

Note well: There is still time to contribute to the development of this legislation. Industry partners of all stripes should make every effort to participate in the development of the final language. Small business should especially take notice to strengthen the current draft to recognize and represent their needs and interests. 🔮

Jeff Allard, Founder and President, Lakeside Life Science, earned his Ph.D. in Dartmouth College in Biochemistry. Since obtaining his Doctorate, Dr. Allard has brought six “new to the world” diagnostic tests through FDA, with ~30 FDA Clearances and Approvals. He has launched sixteen new products. He has authored over 100 scientific papers and abstracts, and invented, developed, and obtained FDA clearance for the first complexed PSA assay.

Paul Allard, COO, Lakeside Life Science, is a Registered Nurse and Co-founder of Lakeside Life Science. Paul saw the need to bring patients back to the foreground of clinical research. He has a proven history of clinical site management as well as a vision to bring academic centers and community centers together to further medical research. Paul manages all day-to-day operations of the company.

References

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