**A Summary of**

**The Verifying Accurate Leading-edge IVCT Development (VALID) Act of 2018**

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 A discussion draft of the VALID Act was circulated in early December 2018. This proposal has many problems that should be addressed.

The draft defines *in vitro* clinical tests (IVCTs) very broadly to include any test that is intended for “identifying, diagnosing, screening, measuring, detecting, predicting, prognosing, analyzing, or monitoring a disease or condition, including by making a determination of an individual’s state of health; or selecting, monitoring, or informing therapy or treatment for a disease or condition.” IVCTs also include all parts and components of such tests, with certain limited exclusions (e.g., general laboratory equipment). The regulated components and parts will include test protocols, test platforms, collection devices, sample preparation devices, and software. Thus, the IVCT definition encompasses both traditional *in vitro* diagnostic devices (IVDs) regulated by FDA and laboratory developed tests.

Overall, under the discussion draft IVCTs will be subject to the new FDA regulatory framework with regard to design, development, manufacturing, etc. This framework will apply, in many cases, to laboratories because they will have designed or developed the IVCT. These labs will also, however, still be required to comply with the Clinical Laboratory Improvement Amendments (CLIA) with regard to its lab operations. Thus, for labs, the draft bill will result in some duplicative regulation.

Below we discuss several key provisions/concepts in the discussion draft. In our view, this proposal is bad for all involved – labs, IVD manufacturers, and patients. The regulatory burdens will be increased substantially, and the gaps and ambiguities will give rise to rampant confusion.

 **Classification**

 Unlike the current 3-tier approach for devices, the discussion draft proposes having only two classes of IVCTs: (1) low risk, and (2) high risk. Low-risk IVCTs are those that would likely cause minimal or no harm from inaccurate results. High-risk IVCTs are those that would likely cause serious harm or death from an inaccurate result. There is a subset of high-risk IVCTs for which FDA will create mitigating measures (e.g., special controls requirements for test development, labeling, validation) to mitigate risk. This subset sounds like a moderate level, but its not entirely clear.

**Premarket review**

 IVCTs would require premarket review by FDA, unless an exemption applies. Notable exemptions include: “grandfathered tests,” IVCTs that are currently 510(k)-exempt (both pre-VALID IVCTs and those introduced post-enactment, with certain limitations), low-risk IVCTs, tests for rare diseases (note: this is for tests for fewer than 8,000 individuals tested per year, among other limitations), pre-certified tests, and modifications to tests so long as the modifications do not make it a new IVCT. Such changes include changes to the elements that define a “test group” (see below), changes to performance claims, changes that make a test no longer comply with mitigating measures, and changes affecting the safety of a sample collection.

Even if there is an exemption, FDA can require premarket review of specific tests, if certain criteria are met.

The premarket review process will be onerous. It appears to be modeled on FDA’s premarket approval (PMA) process required for high-risk, Class III medical devices. Among other things, applicants will need to demonstrate clinical and analytical validity of a proposed IVCT through “valid scientific evidence” – a demanding standard.

Congress is seeking input on the timing for premarket review. There is currently no proposed timeline. It is also unclear how certain of the premarket review requirements will apply to components of a tests system (e.g., a platform, collection device), even though they will be subject to premarket review.

 Certain persons may be accredited to perform premarket reviews on FDA’s behalf.

**Precertification**

 Most IVCTs are eligible for precertification, meaning that a “test developer” can apply to have a test group precertified by FDA (note: the term test developer and the types of activities included in that phrase appears not to be defined). This would require an application and possible facility inspection. The timing is not yet defined. Congress proposes that precertification would last for only two (2) years, and sponsors would need to reapply before its precertification expires.

Precertification will apply to a “test group,” which the draft defines as a group of IVCTs that have the same analyte of interest, specimen, method, purpose, disease/condition, intended patient population, and context of use. This is an incredibly narrow definition, which will sharply limit the utility of precertification. In addition, precertification would be unavailable for many products: test platforms, collection devices, software, certain blood tests, first-of-a-kind tests, tests for home use, high-risk tests, cross-referenced tests (e.g., companion and complementary diagnostics), and direct-to-consumer tests.

**Grandfathered tests**

Grandfathered tests are exempt from premarket review as well as the quality system regulation (QSR), and labeling requirements. An IVCT is grandfathered if it, (1) was in the market 90 days prior to enactment of the law; (2) was developed by a laboratory with a high complexity CLIA certificate; (3) the IVCT is performed in the same lab in which it was developed or by another lab “within the same corporate organization and having common ownership” so long as the other lab has a valid CLIA certificate; (4) has not received FDA clearance or approval; and (5) there have been no modifications to the IVCT such that it would be a new IVCT. This is a narrow definition, which will limit its scope and create definitional questions.

 **Transitional devices**

 The narrow definition of a grandfathered test means there will be tests on the market, if this law is enacted, that will not qualify for grandfather status. The discussion draft calls these “transitional tests.”

 Transitional tests must meet all applicable requirements under the new regulatory framework, including premarket review and approval. However, they would be able to stay on the market while under premarket review, for a currently unspecified period of time.

**Breakthrough IVCTs**

The draft also proposes a Breakthrough IVCT program with nearly identical criteria to FDA’s current Breakthrough device program. This program is for IVCTs that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions compared to existing alternatives, and it meets certain other criteria. Congress is seeking input on this section and the potential for priority review of Breakthrough IVCTs. There is no “provisional approval” process in the bill for promising IVCTs.

**Post-approval requirements/limitations**

 FDA is given the authority to impose other requirements and limitations. For example, FDA could create “mitigating measures” for certain tests. Mitigating measures can include, among other things, labeling, restrictions on advertising/promotion, clinical studies, training, standards, and performance criteria.

 Certain tests (e.g., high-risk tests, home-use tests, direct-to-consumer tests, and over-the-counter tests) will be deemed “restricted tests.” This means that FDA would be able to issue regulations to impose restrictions on their sale, distribution, use, and advertising.

 If FDA concludes that an IVCT presents an unacceptable risk to patients, FDA could take additional actions, including issuing safety notices or requiring test developers to recall a test. FDA can also ban certain IVCTs if certain criteria are met.

 **Registration and notification**

 Much like medical device establishments are required to register and list their devices with FDA, the draft proposes that test developers (along with other entities, including contract manufacturers) will need to register with FDA and notify FDA of their tests. The registration process appears administrative. The IVCT registration process, though, will be much more burdensome than the current device listing process. The IVCT notification process appears exceedingly substantive requiring test developers to submit to FDA, among other things, a description of the test, analytes, specimen type, test method, intended patient population, summary of analytical and clinical performance data, and labeling. All of this information would be public.

 **QSR**

 Test developers will be required to comply with the device QSR. The QSR includes, among other things, requirements for design controls, production controls, supplier controls, records, and corrective and preventive actions. The requirements appear to be essentially the same as those for medical devices, but they omit complaint handling.

The QSR will not govern laboratory operations; CLIA will still apply. For laboratories that hold a high-complexity CLIA certificate, only a subset of the QSR requirements would apply.

 **Labeling**

 The discussion draft includes proposed labeling requirements for IVCTs. The proposed labeling requirements essentially mirror FDA’s current IVD labeling requirements in 21 C.F.R. Part 809. The discussion draft clarifies that test labeling can take the form of a report or report template and provides requirements for such reports. For certain tests, the labeling requirements could be met by posting the required information on the lab’s website. The labeling exemptions for research and investigational use (RUO and IUO) are preserved in this discussion draft.

 **Adverse events (*i.e.*, MDR reporting)**

 While the IVCT QSR requirements do not necessitate complaint handling, test developers must develop a process for identifying and reporting certain adverse events. The adverse event standard mirrors FDA’s medical device report (MDR) definition in 21 C.F.R. Part 803, requiring reporting of test-related deaths, serious injuries, and certain malfunctions.

The reporting times are more favorable than the MDR program with only deaths and imminent threats to public health requiring reporting within 5 days. All other events would be submitted in quarterly reports to FDA.

 **Corrections and removals**

 Test developers will also be required have processes to evaluate, perform, and report corrections and removals (i.e., recalls) to FDA. These requirements are essentially the same as the requirements for medical devices in 21 C.F.R. Part 806.

 **Investigational use**

 Test developers intending to study the safety and effectiveness of an IVCT will need to obtain approval to do so from FDA. This approval and the process for obtaining it will track the Investigational Device Exemption (IDE) requirements for medical devices (21 C.F.R. Part 812). Under the IDE regulations, most IVD studies are exempt from the requirement to obtain IDE approval. This appears to still be the case under the proposed regulations, and the types of tests that will require approval appear to mirror those that currently require approval. Under the proposed draft, however, even if FDA approval is not required for a study, the study sponsor must still submit certain information to FDA regarding the informed consent process.

 **Appeals**

 The discussion draft includes an appeal process for sponsors to dispute decisions regarding applications for premarket review, precertification, investigational use, and/or emergency use. Appeals would be required to be submitted within 30 days of FDA issuing its decision. Unlike the current device appeals process, there is no required timeline for FDA to respond to IVCT appeals.

 **Violative acts**

 Failure to comply with the requirements set forth in the discussion draft would result in an IVCT being adulterated and/or misbranded under the FDCA. Placing an adulterated and/or misbranded IVCT into commerce would violate the FDCA. The discussion draft also states that failure to maintain complete and accurate documentation of an exemption under the law would violate the FDCA. This is a very technical violation and could mean that minor nonconformances in documentation could result in a violation. There is no similar requirement under the FDCA for IVDs currently, and there are many exemptions under the current regulatory framework. Another violative act, under the proposal, is vague: “the making of a false, fraudulent, or materially deceptive analytical or clinical claim” for an IVCT.

 **Test platforms**

 Test platforms are defined in the discussion draft to include hardware and associated software intended to be used to perform a clinical test(s). Most general‑purpose test platforms intended for clinical use are currently regulated by FDA as devices and are classified as Class I, 510(k)-exempt. Under the discussion draft, test platforms on the market prior to enactment of the new law that are currently classified as 510(k)-exempt can remain on the market and will be exempt from the premarket review process. It appears that the other requirements (e.g., QSR, adverse event reporting) would apply.

 New test platforms and those that are not currently classified as 510(k)-exempt will require premarket review. The premarket review requirements are somewhat more limited for test platforms, but it is unclear if a test platform alone could satisfy some of the premarket requirements. It is possible that test platform developers will need to partner with test developers to bring full tests through the premarket review process.

It appears that labs would be allowed to use test platforms purchased prior to enactment of the law for only a certain period of time. The discussion draft proposes a 5‑year time period after enactment, although Congress is seeking input on this time period. After this period, new IVCTs developed and introduced into interstate commerce must utilize a platform that complies with the requirements of the new law. It would appear that 510(k)-exempt platforms would comply with the new law, so long as the manufacturer has complied with other applicable requirements (e.g., QSR, adverse event reporting). It is possible that Congress is contemplating RUO test platforms that are in use at clinical laboratories. We would recommend seeking clarification on the 5-year platform limitation.

 **Conclusion**

 The draft document would have far-reaching consequences for IVDs. Many of those consequences would be adverse, because of complexity, ambiguity, and increased burdens without offsetting benefits.