Diagnostic Test FDA Reform Pathway Updated

VALID Act Amendments Likely June 14 Mark-Up

Senate HELP Committee leadership released their FDA User Fee Bill today, including the VALID Act test regulation details the premarket, abbreviated premarket, and supplemental application review and approval process, provides certain exemptions, and describes a technology certification pathway for moderate-risk IVCTs to be certified to offer multiple tests, using the same technology. VALID Act changes / updates are below

- **Inclusion of the role of professionals as a "mitigating measure" is good for lab developed tests (LDTs) and test makers.** This expands the criteria of mitigating measures significantly and may help move LDTs from the high-risk category to moderate-risk or low-risk category. Further changes to VALID during markup may only require a fraction of so-called LDTs to require regulatory review.

- **We do not see any new FDA regulatory exclusions for (1) academic medical labs, (2) hospital-based labs, (3) public labs, or (4) other providers but we could see some tweaks in the Senate markup this week (June 14).** We previously noted that academic medical center labs may be excluded from VALID (good for John Hopkins, Mayo Clinic and all AMCs that use their own tests). New exclusions are still possible during Committee markup and VALID Act may be further neutralized with any of these exemptions.

- **Inclusion of FDA guidance for Dx tests that detect rare diseases and unmet needs.** FDA must provide guidance for these developers that face significant issues in data collection and timely evidence generation. Congress has historically been sympathetic to the research barriers faced by manufacturers for rare disease products.

- **Grandfathered test reporting requirement is clarified for less patient confusion.** The new template moves away from requiring grandfathered tests to bear on each test report "this test has not been FDA reviewed" to a more neutral "this test…is exempt from FDA premarketing review". This is a change in tone that is positive for currently available tests that are expected to be grandfathered and will reduce confusion among test users and patients.

- **The effective date of the VALID Act is still October 1, 2027**, **as the new rules will require user fees**, we expect to see FDA start establishing regulations and guidance within 3 years of enactment as required by the bill. FDA will also be required to report its recommendations to Congress on the authorization of the In Vitro Clinical Test User Fee program in 2025. We may see public meetings related to IVCTs as early as Spring 2023, as well.

- **Additional bill changes provide clarity provided on definitions, timing, and requirements.** The definition of "develop" now includes importing. The definition of "laboratory operations" is further clarified, and lab operations are excluded from the quality requirements of VALID. Incomplete premarket or abbreviated premarket applications will receive an FDA response within 45 days, less than the original 60 days.

- **NEXT STEPS**: VALID Act is scheduled to be marked up this Tuesday, June 14th. We do expect additional amendments and changes to the framework based on the minimal changes seen here. Following passage from Senate HELP committee, the entire FDA User Fee bill, including the VALID

Contact Ipsita Smolinski - 202.250.3741 - Ipsita@capitol-street.com

Act, bill will head to the Senate floor for passage. The Senate is taking the lead on VALID Act and the framework that passes the Senate is likely to be the final version to passed in 2022.

Background

- **VALID framework mirrors prior legislations introduced, but is more complex, with the following provisions.** We previewed the legislation, and the framework does not appear onerous but there are more specific needed.

  - **Definition of (1) High-risk, (2) Moderate-risk, and (3) low-risk tests are related to the health risks of an inaccurate test.** A moderate-risk test would cause only non-life-threatening injury, injury that is medically reversible, or significant delay in necessary treatment with an inaccurate rest, or may meet the criteria for a high-risk, but one or more mitigating measures can sufficiently prevent or detect an inaccurate result or otherwise mitigate such risk. A high-risk test is a test with substantial likelihood to result in serious or irreversible harm or death (or cause serious harm to the public health), and sufficient mitigating measures are unable to be established to prevent, mitigate, or detect the inaccurate result.
  - **Premarket, abbreviated premarket, and supplemental application review and approval process are outlined.** IVCTs are expected to submit premarket applications that include information on risk-benefit profile, mitigation measures, supporting validation studies and clinical data, potential modifications, and proposed labeling. There is also a voluntary process to provide clarity on risk designation. FDA may redesignate certain IVCTs in response to new information.
  - **Premarket review exemptions include low-risk IVCTs, humanitarian use IVCTs, custom and low volume IVCTs, modified IVCTs, and manual IVCTs.** We noted previously that a Humanitarian exemption may be provided, but exemptions appear to be fairly generous, including low volume IVCTs and modified IVCTs. We note that IVCTs used for research purposes (investigational use) are also exempt, but it is on the developers to maintain records on the use of investigational IVCTs and provide to FDA research plans for the development of such IVCTs.
  - **Technology certifications do <u>not</u> expire for multiple tests using the same underlying technology.** The technology certification pathway allows moderate-risk IVCTs to be certified to offer multiple tests, using the same technology, and does not require FDA to review each test individually. However, a representative IVCT must be submitted for FDA to review to help determine the scope of the technology certification order.
  - **High-complexity grandfathered tests will be unaffected by premarket review.** Tests that were developed by a laboratory with an existing high complexity certificate under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and available for clinical use before the date of enactment are exempt from premarket review, labeling, test design, and quality requirements. However, the FDA may still request information on testing accuracy and safety.
  - **Breakthrough (BT) process is established.** FDA is expected to expedite the development and priority review of a breakthrough IVCT, a technology that does not have an alternative on the market or the availability of which is in the best interest of patients or public health.
  - **Post-market surveillance and remedies may be mandated**. FDA will be allowed to order developers to conduct post-market surveillance of a high-risk or moderate-risk IVCT. Developer will be required to submit a plan within 30 days of receiving a surveillance order and required to start surveillance not later than 15 months. FDA will be able to direct the developer to immediately cease distribution and if a premarket-approved IVCT is found to cause serious adverse health consequences or death. Judicial review is also available to any person adversely affected by a premarket review or technology certification if filed within 30 days.

Contact Ipsita Smolinski - 202.250.3741 - Ipsita@capitol-street.com

- **Who is impacted?** No one for now given start date is 2027, indicating a possible need for new funding, via user fees. However, as envisioned we see impacts to.

  - **Larger diagnostic companies – like Abbott and Roche among others -- are well-resourced and therefore likely unaffected by the VALID Act, as currently written**. It's a risk-based system, so requirements would depend on the risk of the test. Those companies and stakeholders already familiar with the FDA process (and with the resources to seek FDA authorization) will fare just fine.

  - **The new rules could affect almost every single clinical laboratory in the US + IVD (in vitro diagnostics) makers, including tools manufacturers, however the delayed rollout indicates changes to this initial framework are very likely.** Essentially the entire diagnostics industry could be impacted. We would expect that the reforms will most likely negatively affect hospitals and academic medical centers the most. We would anticipate that onerous requirements may partially shut down their clinical labs or narrow test offerings.

  - **What specific tests are impacted – oncology? others?** It is extremely difficult to define, given the omission of test examples in the framework. The lack of clarity around risk classification has been an ongoing concern among all stakeholders, even those who support VALID, so the devil still remains in the details.

Contact Ipsita Smolinski - 202.250.3741 - Ipsita@capitol-street.com