THE DIAGNOSTIC ACCURACY AND INNOVATION ACT
Advancing innovation and safety for patients in diagnostics

In an effort to better protect patients and provide access to innovative diagnostics, the Diagnostic Accuracy and Innovation Act (DAIA) provides a predictable and timely path to market for these increasingly important clinical tests. This legislation has benefited from extensive collaboration with patient groups, researchers, laboratories, diagnostic test developers, innovators, FDA, and others.

The DAIA addresses longstanding concerns with the regulation of diagnostic tests and will bring much needed certainty to the diagnostic industry and its critical role in patient care. This legislation ensures reasonable risk-based regulation, avoids duplicative regulation, advances precision medicine, and applies the same regulatory principles to the same activity regardless of where the test is developed. The DAIA also modernizes the Clinical Laboratory Improvement Amendments (CLIA) program at the Centers for Medicare & Medicaid Services (CMS) to maintain quality laboratory operations. The legislation assigns certain responsibilities to FDA (test development and manufacturing generally) and assigns exclusive jurisdiction over laboratory operations to CMS under CLIA.

SCOPE

The DAIA applies to any *in vitro* clinical test (IVCT), which includes both finished products (*e.g.*, test kits and platforms) and laboratory test protocols (often referred to in the past as "laboratory develop tests" or LDTs). IVCTs will be a new category and regulatory structure under the Food, Drug, and Cosmetic Act, and will not be regulated as devices, drugs, or biologics. Laboratory operations will be regulated exclusively by CMS/CLIA.

JURISDICTION

The DAIA establishes three distinct, non-overlapping categories of activity and jurisdiction.

- *Test development and manufacturing*, which includes the design, development, and validation of an IVCT as well as the production of an IVCT for distribution to another facility or third-party. FDA will have exclusive jurisdiction over these activities under a new FDA Center devoted to IVCTs.
- *Laboratory operations*, which are all the activities necessary to perform or "run" a developed IVCT, including the preparation of reagents for use in a single CLIA facility, sample preparation, and other pre-analytical processes. CMS/CLIA will have exclusive jurisdiction over laboratory operations.
- *Medical use and interpretation,* by a health care professional and the related medical consultation. Jurisdiction over the practice of medicine will continue to be reserved to the states.

FDA REGULATION OF TEST DEVELOPMENT

The DAIA establishes a new regulatory structure for IVCTs. Hallmarks of the new structure include:

- *Risk Classification:* Each test will be classified as high-risk, moderate-risk, or low-risk.
- *Pre-Market Requirements:* To market an IVCT, the developer must establish a reasonable assurance of analytical validity and clinical validity for the intended use. Premarket submission/listing requirements will be based on risk classification with no premarket submission required for low-risk IVCTs. The 510(k)/predicate system, used for therapeutic devices, is not part of the new submission process.
- *Modifications:* Modifications to moderate- or high-risk IVCTs must be submitted for approval only if the modifications change intended use of the IVCT, or have a meaningful clinical impact. A

submission is not required if the modification complies with a recognized standard (e.g., CLSI) or FDA guidance, or if validated pursuant to protocols reviewed and approved by FDA. Additionally, specimen-related changes are not required to be submitted if made solely for the purpose of extending specimen stability.

- *Quality requirements*: For test development activities, finished products and laboratory test protocols will be subject to design controls. Production of finished products for distribution to other facilities and third parties will be subject to relevant FDA quality requirements. Laboratory operations will be subject to modernized CLIA quality requirements.
- *Post-market systems*: Obligations for test developers will largely resemble current FDA requirements for *in vitro* diagnostics, except adverse event reporting will be updated to: (1) limit individual submissions to those events that involve death or imminent threat to public health, and (2) use quarterly summary and trend reporting for all other adverse events, including malfunctions. There will be no overlap of CLIA and FDA requirements.
- *Innovation:* The Act advances innovation by providing certainty and risk-based pathways for innovative new products. Special pathways will accelerate access to diagnostic tests for rare diseases and unmet clinical needs.

CMS/CLIA REGULATION OF LABORATORY OPERATIONS

CLIA, exclusively, will regulate laboratory operations. CLIA is revised by the ___ Act to:

- Modernize applicable quality requirements.
- Harmonize FDA and CLIA quality terminology and requirements where appropriate (*e.g.*, purchasing controls).
- Eliminate requirements related to test development, which will now be regulated by FDA.

TRANSITION

The DAIA includes a detailed transition phase to allow industry and the regulatory authorities adequate time to implement the new construct:

- IVCTs introduced by laboratories prior to three months before enactment will be grandfathered. No submission obligations will apply to such IVCTs prior to the effective date of the regulations (i.e., five years after enactment).
- New regulations would be required to be promulgated within 3 years of enactment.
- Compliance would be required no later than 2 years after that (with some opportunity to take advantage of the new system one year post promulgation.

The DAIA provides for the development of user fees, but user fees will not be the primary funding source for the new regulatory structure (i.e., user fees will be capped at 30%).

OTHER KEY PROVISIONS

- FDA will have the authority to withdraw IVCTs from the market that present an unreasonable and substantial risk of illness or injury when used as intended.
- FDA and CMS will retain the right to conduct inspections and oversee recalls.
- Third party review processes are encouraged; CMS may delegate inspection and certification.