

April 3, 2024

The Honorable Bill Cassidy, MD
Ranking Member
Senate HELP Committee
Washington, DC 20510

RE: Request for Information (RFI) – Diagnostic Reform

Dear Ranking Member Cassidy,

The Infectious Diseases Society of America (IDSA) appreciates the opportunity to provide feedback to you and the Health, Education, Labor and Pensions (HELP) Committee regarding diagnostics reform. IDSA represents more than 13,000 infectious diseases (ID) physicians, scientists and other health care and public health professionals who specialize in infectious diseases. Our members work across a variety of settings, including hospitals, academic medical centers, clinical microbiology laboratories, public health departments and laboratories, publicly funded clinics and private practice.

We appreciate the Committee’s leadership in developing policies to improve diagnostics reform and regulatory frameworks. IDSA wants to ensure effective and safe usage of laboratory developed tests (LDTs) in clinical practice, while also ensuring that patients continue to be able to access LDTs and receive the highest standard of diagnostic care. We are deeply concerned that the proposed rule from the FDA will dramatically curtail patient access to testing, with devastating outcomes for patients with serious infections. We outline our recommendations to for effective regulation of diagnostics, including LDTs, below.

FDA Regulatory Framework for Diagnostics

1. How well is FDA’s medical device framework working for the regulation of diagnostic products? Are there improvements that should be made?

IDSA is generally supportive of the current medical device framework regulating diagnostic products. LDTs are reliable for use in patient care under the Clinical Laboratory Improvement Amends of 1988 (CLIA), and in many cases, are the diagnostic standard. It’s important to note that LDTs used under CLIA, specifically in infectious diseases (ID) practice, are utilized in conjunction with a broader range of verification tests and assays to accurately determine clinical treatment.

While we support strong regulation of LDTs to ensure patient safety and clinical validity, there are trade offs to this increased regulation that would detrimentally impact LDTs utilized in ID. Improvements in regulating LDTs need to take into account the financial impact increased regulation would have on academic medical centers, nonprofit laboratories, and public health laboratories. Many of these labs do not have the financial and personnel capacity to manage the proposed FDA regulations outlined in the rule.

- a. **Of these specific changes, which would require Congressional action, and which can be effectuated by FDA alone?**
- 2. Does the current device regulatory framework support the review of diagnostics that are developed using AI or that incorporate AI?**
- 3. What, if anything, makes diagnostics distinct among FDA-regulated medical products to warrant specific attention to how AI may be used in the review of product submissions?**
- 4. Are the regulatory pathways intended to evaluate diagnostics for special populations (i.e. rare diseases or genetic disorders) working?**
 - a. **How could they be enhanced to accelerate and authorize products for special populations, for example, certain companion diagnostics for rare biomarkers?**
- 5. Are there regulatory hurdles to expanding the settings in which diagnostics are performed, i.e. point-of-care (POC) tests performed in patients' homes?**
 - a. **In what ways could/should FDA leverage regulatory flexibilities to reduce testing barriers?**
- 6. What are your views on [FDA's implementation of predetermined change control plans](#); is FDA's approach in its recent guidance readily applicable to IVDs and other diagnostic products?**
- 7. Does FDA's current risk classification framework properly measure risk versus regulatory controls for diagnostics products?**
 - a. **If not, how can FDA's risk-based regulatory approach to diagnostics be improved to better align the degree of regulatory oversight with patient risk and benefit?**
- 8. In considering reforms to FDA's risk classification framework for diagnostics, what types of IVDs should be exempt from premarket review?**

LDTs are procedures intrinsic to ID medical practice, and have been used for decades to diagnose and manage a variety of infectious diseases. In many instances, ID LDTs have become the diagnostic standard of care and are included in many clinical guidelines. Importantly, these LDTs are utilized in conjunction with a variety of diagnostic tests and clinical decision making before making final recommendations on patient care. Because of the ubiquity of LDTs in ID practice, and the significant analytical and clinical validity studies supporting their use, they should not be subject to premarket review.

Current CLIA and College of American Pathologists (CAP) accreditation requirements provide sufficient oversight for the vast majority of ID LDTs. These tests are developed, validated and implemented by individual laboratories that are CLIA-certified for high complexity testing; testing is performed only at the originating laboratory. Contrary to FDA assertions, clinical validity is assessed for each LDT by laboratories, and is a requirement of CAP accreditation. Often LDTs are clinically validated in the same way IVDs are, in the same laboratories that perform testing for clinical trials aimed at data generation for FDA. Additionally, many of these

tests are developed because there is a void in the market for tests for conditions that are of low prevalence, complicating development of a profitable diagnostic product.

Additionally, the proposed rule offers no exemptions for antimicrobial susceptibility testing. Most susceptibility panels for fungal, viral, and bacterial infections are LDTs. Without this testing, patients will not receive the correct treatment, damaging patient care and accelerating the already rapid onset of antimicrobial resistance. We support exemptions for premarket review for these tests to ensure patients receive the susceptibility testing they need to receive treatment.

However, to know all LDTs we should exclude from premarket review, we need a full systematic review of the LDT landscape. Currently, we do not have a full understanding of LDTs used in healthcare practice in the U.S. and the similarities and differences between LDTs used in hospital and health system laboratories (many of which are non-profit entities) and those produced by commercial laboratories. FDA asserts in its proposed rule “Many LDTs are manufactured by laboratory corporations that market the tests nationwide, as they accept specimens from patients across the country and run their LDTs in very large volumes in a single laboratory.” However, many hospitals and health systems produce LDTs for internal use and rely on these tests to inform diagnosis and clinical management of their own patients. A significant number of hospitals and health systems provide diagnostic capacity to smaller, often rural hospitals in their region. Hospital and health system laboratories have key differences from large commercial laboratories. We agree with FDA that “Until FDA systematically collects information on these tests, such as adverse event reports, it will not be able to assess more fully the extent of the risks to patients in the manner it does for other devices.” More extensive study and data collection are necessary to understand the landscape of LDTs and ensure that relevant LDTs are excluded from the premarket review process.

a. What factors related to risk management should be applied to risk classification of IVDs?

9. Is the “safety and effectiveness” standard against which diagnostics are reviewed the most appropriate review standard to assign risk management for clinical tests?

10. Do the proposed reforms to FDA’s device framework warrant the establishment of a new regulatory pathway specific to diagnostics? If yes, what are the principles that should guide such a new framework, as it would be applied to diagnostics currently subject to FDA premarket review?

IDSA asserts that if FDA ends enforcement discretion for LDTs, a risk-based approach to regulation should be developed, ideally prior to the end of enforcement discretion, using comprehensive data (to be gathered by the FDA) on the existing use of LDTs, including any associated adverse-events. Limiting regulation to the highest risk LDTs, such as those that would be categorized as Class III, would help limit undue burden on both laboratories and FDA, target resources appropriately, and protect the ability of laboratories to offer essential, high quality ID testing using LDTs with minimal risk. Most ID LDTs should be considered low or moderate risk, as they are typically used as only one part of a comprehensive patient evaluation and not as a singular factor in clinical decision-making.

CLIA Regulatory Framework for LDTs

- 1. What updates to the clinical laboratory regulatory structure under CLIA should Congress consider to reflect the latest scientific practices and safety standards?**
- 2. What are your views on the effectiveness and use of the Clinical Laboratory Improvement Advisory Committee (CLIAC) in providing scientific and technical guidance to inform potential updates to CLIA standards?**
- 3. Do the proficiency testing programs currently approved by the Department of Health and Human Services (HHS) reflect the latest clinical standards of laboratory medicine? Are there specialties, subspecialties, or analytes that should receive greater consideration for HHS approval?**
- 4. How well does the existing enforcement structure under CLIA work in ensuring compliance with regulatory requirements and taking action against noncompliance? What should be improved if anything at all?**

As previously stated, current CLIA and College of American Pathologists (CAP) accreditation requirements provide sufficient oversight for the vast majority of ID LDTs.

- 5. Should legislative reforms address CLIA's quality system requirements? If yes, which of those changes would require Congressional action, and which could be effectuated by CMS alone?**
- 6. Where does redundancy exist, if at all, within the current CLIA regulatory structure with respect accreditation standards under federal and state licensure programs, as well as through CMS approved accreditation organizations?**
- 7. In considering legislative reforms to CLIA, should LDTs be defined in statute? What aspects of test development would characterize such a definition?**
- 8. How should Congress consider issues relating to the practice of medicine and its relationship with labeling for LDTs? Should there be additional oversight of the information conveyed to patients serviced by LDTs?**

IDSA supports FDA's proposal to phase out its enforcement discretion for registration and listing requirements and medical device reporting (i.e., severe adverse event reporting) for LDTs and urges FDA to ensure registration, listing and reporting requirements are streamlined and do not pose undue burden on laboratories. Registration and listing requirements should not include FDA review of an LDT nor should they impede the use of an LDT.

- 9. Should certain CLIA regulations be updated, would it necessitate a reevaluation of the CLIA fee schedule?**
- 10. What compliance challenges would legislative reforms to CLIA create? How should new regulatory requirements apply to tests currently available to patients?**

Thank you for your consideration of our feedback on diagnostics reform. Should you have any questions, please contact Eli Briggs, IDSA director of public policy, at ebriggs@idsociety.org.

Sincerely,

A handwritten signature in black ink, appearing to read "Steven K. Schmitt". The signature is fluid and cursive, with the first name "Steven" and last name "Schmitt" clearly legible.

Steven K. Schmitt, MD, FIDSA, FACP

President of IDSA