



AMERICAN SOCIETY OF HEMATOLOGY

2021 L Street, NW, Suite 900, Washington, DC 20036-4929 **ph** 202.776.0544 **fax** 202.776.0545 **e-mail** ASH@hematology.org

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President

Robert Brodsky, MD
Johns Hopkins University
Ross Building, Room 1025
720 Rutland Avenue
Baltimore, MD 21205
Phone 410-502-2546

President-Elect

Mohandas Narla, DSc
New York Blood Center
310 E 67th Street
New York, NY 10065
Phone 212-570-3056

Vice President

Belinda Avalos, MD
Atrium Health
215 N. Pine Street, Unit 4703
Charlotte, NC 28202
Phone 980-442-2000

Secretary

Cynthia Dunbar, MD
NHLBI/NIH
Translational Stem Cell Biology Branch
Building 10-CRC, Room 5E-3332
10 Center Drive
Bethesda, MD 20892
Phone 301-402-1363

Treasurer

Joseph Mikhael, MD, FRCPC, MEd
Translational Genomics Research Institute,
City of Hope Cancer Center
445 N. Fifth Street
Phoenix, AZ 85004
Phone 602-343-8445

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Executive Director

Martha Liggett, Esq.

Robert M. Califf, MD
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Medical Devices; Laboratory Developed Tests Proposed Rule (FDA-2023-N-217)

Dear Dr. Califf:

On behalf of the American Society of Hematology (ASH), thank you for the opportunity to provide comments on the U.S. Food & Drug Administration's (FDA) Medical Devices; Laboratory Developed Tests proposed rule.

ASH represents more than 18,000 clinicians and scientists worldwide committed to studying and treating blood and blood-related diseases. These disorders encompass malignant hematologic disorders such as leukemia, lymphoma, and multiple myeloma, as well as classical (or non-malignant) conditions such as sickle cell disease, thalassemia, bone marrow failure, venous thromboembolism, and hemophilia. In addition, hematologists are pioneers in demonstrating the potential of treating various hematologic diseases and continue to be innovators in the fields of stem cell biology, regenerative medicine, transfusion medicine, and gene therapy. ASH membership is comprised of basic, translational, and clinical scientists, as well as physicians providing care to patients.

ASH appreciates the FDA's interest in addressing safety concerns related to laboratory developed tests (LDTs). LDTs are critical to providing diagnostic, and prognostic information, as well as insights that could inform counseling and potential therapeutic options for the patient. LDTs allow healthcare professionals and clinicians to provide personalized treatments and are used to support the practice of medicine based on a patient's needs. For example, diagnosis of (and therapeutic options for treating) myeloid neoplasms or acute leukemia cannot be made without genetic characterization of the disease. Therefore, diagnosis and therapy for these diseases, among many others, cannot be performed without an LDT.

However, the proposed modifications to current oversight mechanisms in this rule have the potential to significantly affect many academic medical centers, clinical testing laboratories, public health laboratories, healthcare providers, and patients throughout the United States. At a time when laboratories are experiencing workforce shortages, the administrative responsibilities outlined in the FDA proposal would increase the workload pressure on an already overburdened workforce. The burden of effort required to submit sufficient documentation for each LDT to obtain approval would take significant lab personnel, even with the FDA's proposed phases. ASH members are

concerned that delays from the administrative requirements may have the potential to delay and/or interrupt patient access to necessary treatments. ASH urges the FDA to consider the impact of the proposed rule to avoid unintended consequences that may ultimately restrict innovation and harm patient access to valuable and lifesaving clinical testing.

Classifying LDTs as medical devices and requiring FDA approval has the potential to stifle innovation. Additional regulatory oversight poses an entry barrier for the development of new and innovative LDT assays for in-house testing. The increased burden of the proposed changes in regulations may put substantial pressure on academic medical centers, community hospitals, and small clinical laboratories to maintain their current diagnostic capacity rather than pursue the development of new and innovative LDTs. The regulatory and administrative burden of applying for 510(k) market approval for small independent laboratory tests may be a factor that could eventually push smaller laboratories out of the market due to the weight of non-reimbursement for the activities associated with the regulatory processes. It is likely that only large corporate laboratories would be able to afford an entire regulatory department, limiting competition in the market of LDTs and the agility achieved through in-house testing. This would disincentivize smaller laboratories from developing personalized or innovative diagnostics that fill current gaps, thus stifling innovation.

Limitations to in-house LDT testing within community hospitals, independent clinics, and academic medical centers may result in incomplete diagnoses for local populations, delays in diagnosis as the testing is processed, or, worse yet, no diagnosis at all. In-house testing is notably better for personalized patient care than sending specimens to commercial laboratories. ASH members, specifically hematopathologists and molecular pathologists, cited the importance of using LDTs when examining the results of patients from their own institution. A pathologist noted their ability to provide a much more personalized care approach than could be achieved when using a reference laboratory. For example, the agility that can be achieved through in-house testing supports the molecular analysis of chimerism for allogeneic hematopoietic stem cell transplants. In-house testing also allows clinicians to meet the needs of target patient groups when appropriate commercial tests are not available. The Penn Medicine Coagulation Laboratory developed an LDT radioimmunoassay to diagnose heparin-induced thrombocytopenia (HIT) – a severe prothrombotic disease with an associated 30-40 percent bleeding risk – before the FDA approved ELISAs diagnostics. Meanwhile, concentrating diagnostic testing in only a handful of large commercial laboratories may have a detrimental effect on test pricing and availability, leading to access to care issues.

Lastly, ASH members have raised concerns about how the FDA's proposal to move LDT oversight to the FDA's medical device classification and approval process may take years to implement. The sheer volume of LDTs that currently exist and the potential quantity of future LDTs must be fully appreciated to understand the administrative burden that may also impact the FDA. The FDA would need significant personnel and resources dedicated to this effort, and the Society is concerned that the current volume and limited guidance for implementation will create a considerable backlog in approval of LDTs. If this proposed rule is implemented, we suggest that the FDA release regulatory guidance as to how the process will be implemented to clarify any ambiguities that may exist.

For the reasons mentioned above, ASH urges the FDA to consider the potential unintended consequences of this proposed rule on innovation and patient access to care. More time and diverse stakeholder agreement is ultimately needed to undertake the proposed change of regulatory oversight for LDTs. ASH therefore recommends the FDA take an interim step to first understand the full scope of LDTs currently in use before making any further policy changes. A market scan, including registration, listing, and reporting requirements of LDTs would support the FDA's understanding of LDTs and their importance for patient access to care and public health.

ASH appreciates the opportunity to provide these comments. Please use ASH Manager for Health Care Access Policy, Carina Smith (casmith@hematology.org or 202-292-0264), as your point of contact if you have any questions or if we can provide additional information.

Sincerely,

A handwritten signature in black ink, appearing to read "R. Brodsky", with a stylized flourish at the end.

Robert A. Brodsky, MD
President