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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of In Vitro Diagnostics and Radiological Health
Division of Dockets Management (HFA-305)


To Whom It May Concern:

We are writing on behalf of the International Clinical Cytometry Society (ICCS) to comment on the above-referenced draft guidance. As the world’s largest organization of practicing physicians, scientists, medical technologists, and laboratory personnel involved in clinical flow cytometry testing, ICCS is proactively engaged in assuring the highest possible standards for these informative but technically demanding assays, almost all of which are LDTs. By attempting to impose unnecessary and misguided regulatory burden, this guidance puts at risk current patient access to timely and accurate assessments of life-threatening conditions such as leukemia, lymphoma, and immune deficiencies. Furthermore, were it to be implemented, this guidance would effectively stifle any further development of assays in the promising areas of microparticles, infectious diseases, and minimal residual disease, among others. We would like to emphasize the following points and urge you to consider the ramifications of this guidance in the larger context of patient care.

- Clinical laboratory testing, whether performed using FDA-approved in vitro diagnostic kits or LDTs, is regulated under the Centers for Medicare and Medicaid Services as mandated by the Clinical Laboratory Improvement Amendments of 1988 (CLIA).\(^1\) All licensed clinical laboratories are subject to oversight by accrediting bodies such as the College of American Pathologists (CAP) and the Joint Commission, and/or state departments of health. This system has been an effective means of ensuring
compliance with best laboratory practices of quality assurance and assay validation while permitting ongoing test development and advancements in laboratory medicine.²

- According to CMS, of the 36,432 laboratories regulated under CLIA, 11,633 perform at least one LDT; the majority of them are moderate to high complexity. With no prior experience in oversight of LDTs and a record of very slow approvals of typically high complexity assays submitted for pre-market approval (PMAs), the FDA currently has neither the expertise nor the staffing levels to implement the guidance.

- The high complexity assays performed by flow cytometry are interpreted in the context of other clinically relevant information, including patient history, physical and radiologic findings, and other laboratory tests, and clearly fall within the practice of medicine. Only the most basic of these assays (typically those for which commercial IVD kits have already been developed) meet the description of “medical devices” and fall under the purview of the FDA. The FD&CA does not regulate medical practice.³

- ICCS has proactively drafted and promoted guidelines⁴ for clinical flow cytometry and has participated in public workshops with the FDA that address cell-based assays. To date the FDA has failed to demonstrate an understanding of the nuances of validation for cell-based assays.⁵,⁶ The recently released “Flow Cytometric Devices Draft Guidance for Industry and Food and Drug Administration Staff” illustrates the challenges faced by the FDA.⁷

- Any further consideration of this issue must address the enormous costs that would result from implementation of this guidance or similar oversight. In addition to the financial burden that would be imposed on clinical laboratories and eventually passed on to third party payers and patients, long-term damage to the clinical laboratory infrastructure and loss of expertise that currently support widespread application and development of high complexity testing like flow cytometry would result.
We look forward to working with the FDA, other federal agencies, and stakeholders to ensure that changes to current policy regulating LDTs do not jeopardize the delivery of healthcare in the country or the practice of medicine, and that patients continue to have access to medically necessary clinical care.

Sincerely,

The ICCS Advocacy Committee

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References

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3. 21 U.S.C.396