MDMA
MEDICAL DEVICE MANUFACTURERS ASSOCIATION

1333 H Street, NW
Suite 400W
Washington, DC 20005
Phone (202) 354-7171
Fax (202) 354-7176
www.medicaldevices.org

December 4, 2023

**Via Electronic Submission**

Dockets Management Staff (HFA–305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

**RE: Docket No. FDA-2023-N-2177, *Medical Devices; Laboratory Developed Tests***

To Whom it May Concern,

On behalf of the Medical Device Manufacturers Association (MDMA), below please find comments on the proposed rule, *Medical Devices; Laboratory Developed Tests* (the Proposed Rule).[1]

MDMA is a national trade association that provides educational and advocacy assistance to hundreds of innovative companies in the field of medical technology. Our members, the majority of which are small to mid-sized medical device companies, have a strong record of delivering breakthrough therapies to treat chronic diseases and life-threatening conditions while lowering the cost of care. MDMA's mission is to ensure that patients have timely access to the latest advancements of safe and effective medical technologies that improve health outcomes.

We appreciate the opportunity to provide these comments, and we look forward to ongoing collaboration with the U.S. Food and Drug Administration (FDA) to address this important topic. MDMA is committed to facilitating our shared goal of ensuring that patients have access to safe and effective in vitro diagnostics (IVDs), including IVDs currently marketed as laboratory developed tests (LDTs). However, MDMA wishes to express concerns regarding certain aspects of the approach announced in the Proposed Rule.

Specifically, the Proposed Rule departs in several respects from frameworks for the regulation of LDTs proposed by the Agency in 2014[2] and 2017.[3] FDA indicated that those proposals were intended to carefully "balance patient protection with continued access and innovation."[4] MDMA is concerned that the approach articulated in the Proposed Rule may not strike this careful balance by failing to adopt a risk-based approach, resulting in unnecessary strain on both the Agency and other stakeholders, including patients.

---

[1] *See* 88 Fed. Reg. 68,006 (Oct. 3, 2023).
[2] *See* FDA, Draft Guidance for Industry, Food and Drug Administration Staff, and Clinical Laboratories: Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs) (Oct. 3, 2014), https://www.fda.gov/media/89841/download.
[3] *See* FDA, Discussion Paper on Laboratory Developed Tests (LDTs) (Jan. 13, 2017), https://www.fda.gov/media/102367/download.
[4] *Id*. at 1.

The Proposed Rule, if finalized, would end the Agency's policy of enforcement discretion for LDTs[5] using a phased approach.[6] Among other things, under the Proposed Rule, on the later of October 1, 2027 or three and a half years after the "publication of a final phaseout policy," FDA would "[e]nd its general enforcement discretion approach with respect to premarket review for high-risk LDTs," i.e., LDTs "that may be eligible for classification into class III."[7] On the later of April 1, 2028 or four years after "publication of a final phaseout policy," FDA would "[e]nd [its] general enforcement discretion approach with respect to premarket review requirements for moderate risk and low risk IVDs (that require premarket submissions)," defined as those for which a 510(k) premarket notification or de novo classification request may be required.[8] The Proposed Rule further provides that FDA "generally would not enforce" against IVDs for which premarket applications are timely submitted.[9] FDA has further proposed that the effective date of any final rule be sixty (60) days following publication in the Federal Register.[10]

While MDMA recognizes FDA's proposal of a 'phased' approach to lifting enforcement discretion for these tests, MDMA believes that the timelines set forth in the Proposed Rule are insufficient for manufacturers to develop premarket applications. Indeed, it often takes several years for device manufacturers to develop premarket applications for new medical devices.[11] Manufacturers of IVDs not currently subject to FDA oversight, including laboratories, may currently lack the dedicated resources for developing such premarket applications, suggesting these estimates may underestimate the time needed for such entities to prepare premarket submissions. There will likely be a substantial learning curve for such entities in preparing premarket applications, as well as in responding to Agency requests during the course of premarket review. Moreover, test developers newly subject to FDA oversight would simultaneously be required to devote their limited resources not only to developing premarket applications but also to establishing processes for adherence to other aspects of the medical device regulatory framework, including Medical Device Reporting (MDR) and correction and removal reporting requirements[12] and compliance with the Quality System Regulation (QSR).[13]

FDA has acknowledged that it "do[es] not know the exact number of laboratories or IVDs offered as LDTs that would be affected by" the Proposed Rule, if finalized.[14] The Agency

[5] The Proposed Rule would also apply to IVDs which "do not fall within FDA's traditional understanding of an LDT because they are not designed, manufactured, and used within a single laboratory." 88 Fed. Reg. at 68,021.
[6] *See id*. at 68,007.
[7] *Id*. at 68,024, 68,026.
[8] *Id*. at 68,024.
[9] *Id*. at 68,026-27.
[10] *See id*. at 68,027.
[11] *See* Van Norman GA. Drugs, Devices, and the FDA: Part 2: An Overview of Approval Processes: FDA Approval of Medical Devices. JACC Basic Transl Sci. 2016 Jun 27;1(4):277-287. doi: 10.1016/j.jacbts.2016.03.009. PMID: 30167516; PMCID: PMC6113340.
[12] *See id*. at 68,024.
[13] *See id*. at 68,024, 68,026.
[14] *See*, FDA, Laboratory Developed Tests Proposed Rule: Preliminary Regulatory Impact Analysis; Initial Regulatory Flexibility Analysis; Unfunded Mandates Reform Act Analysis, FDA Docket No. FDA-2023-N-2177, at 21, https://www.regulations.gov/document/FDA-2023-N-2177-0077.

estimates that there may be as many as 160,800 IVDs currently on the market that would be affected by the Proposed Rule, with up to 14,400 such new IVDs offered each year.[15]

Assuming that FDA's estimates are accurate, the Agency would likely be inundated with tens of thousands of premarket applications by the compliance deadlines set forth in the Proposed Rule. Specifically, FDA estimates that there are currently as many as 8,040 IVDs which would require Premarket Approval (PMA) applications; 64,320 IVDs which would require 510(k) premarket notifications; and 8,040 IVDs which would require de novo classification requests.[16] However, MDMA believes that this likely substantially underestimates the share of IVDs which will require a PMA or de novo classification request, as most assays offered as LDTs are developed due to the lack of a commercially available assay, generally precluding use of a 510(k) premarket notification. Further, this estimate assumes that the number of new IVDs offered as LDTs each year will be consistent with prior years; however, these numbers may be greater if test developers seek to offer new IVDs ahead of the compliance deadlines in order to avail themselves of the general enforcement discretion policy for timely-submitted premarket applications. Moreover, changes to the enforcement discretion policy for LDTs may necessitate changes for sample collection devices, such as blood collection tubes, potentially triggering the need for premarket review for these devices as well.

This volume of applications would place a significant strain on the Agency's limited reviewer resources, along with stakeholders responsible for developing such premarket applications, and would likely implicate the Agency's ability to meet its Medical Device User Fee Act (MDUFA) performance goals.[17] Indeed, the COVID-19 pandemic provides an illustration of the potential strain that the Office of Health Technology 7 (OHT7) could experience when faced with premarket applications for LDTs newly subject to FDA oversight. As a result, the market for LDTs is likely to remain in a state of enforcement discretion for several years, if not longer. Indeed, in implementing similar requirements in other product category contexts, FDA has determined it was necessary to operate under *de facto* policies of enforcement discretion in light of the volume of applications and the Agency's limited resources.[18] On the other hand, while

---

[15] *Id*. at 24.

[16] *See id*. at 75-76. The Agency further estimates that there will be up to 7,776 new IVDs requiring premarket applications each year. *See id*. at 76.

[17] MDMA believes that the Agency is unlikely to be able to identify and recruit sufficient resources to alleviate this anticipated strain, and further believes that the 510(k) Third Party Review Program in its current form is not positioned to ameliorate such strain due to its current limitations, such as inability of third parties to access relevant information regarding predicate devices to facilitate a substantial equivalence assessment.

[18] In 1962, Congress amended the Federal Food, Drug, and Cosmetic Act to require FDA to evaluate the effectiveness of drugs approved only for safety between 1938 and 1962. To date, the administrative process for such evaluation, the drug efficacy study implementation (DESI), remains ongoing. Further, in implementing a similar program in which tobacco products already on the market were required to submit premarket applications, FDA elected to "remove from review approximately 1,500" applications determined "less likely" to raise public health questions in light of the volume of applications in its review queue. FDA, Final Regulatory Impact Analysis: Content and Format of Substantial Equivalence Reports; Food and Drug Administration Actions on Substantial Equivalence Reports; Final Rule, FDA Docket No. FDA-2016-N-3818, at 49, https://www.fda.gov/media/152854/download. Similarly, FDA has operated under a policy of *de facto* enforcement discretion with respect to another set of tobacco product applications required under a rulemaking similar to the Proposed Rule, citing the "unprecedented" strain on its review staff due to the influx of a "large number of applications" received by the relevant compliance deadline. FDA, Perspective: FDA's Progress on Tobacco Product

FDA is likely to be inundated with premarket applications for certain high-volume tests, the Proposed Rule also has the potential to stifle innovation and to discourage the continued marketing of certain tests, including for rare diseases. Indeed, FDA has acknowledged that, if the proposed rule is finalized, "some IVDs may need to come off the be market because . . . the laboratory chooses not to invest resources to meet these requirements."[19] Currently, FDA will approve a therapeutic product without an approved or cleared companion diagnostic under circumstances in which the benefits of the therapeutic product outweigh the risks associated with the lack of an approved or cleared companion diagnostic.[20] In such circumstances, providers and patients rely on the availability of LDTs to help ensure that therapeutic products are available to patients most likely to benefit. The Proposed Rule fails to address the potential impact to patients and the availability of suitable treatment options in light of the proposed phaseout policy. MDMA is deeply concerned about the potential impact to patients, particularly in the rare disease community, if such tests are no longer available.

In recognition of these factors, FDA has previously described a potential prospective LDT oversight framework "focuse[d] on new and significantly modified high and moderate risk LDTs" that "would best serve the public health and advance regulatory medicine."[21] Under the 2017 prospective framework, new "[l]ow risk LDTs" would have been exempt from premarket review (as well as Quality System Regulation and registration and listing requirements) unless FDA determined regulation of such a test was "necessary to protect the public health,"[22] while LDTs already on the market would have been exempt from premarket review (i.e., "grandfathered").[23] Further, the 2017 proposal would have exempted from medical device requirements certain "LDTs for rare diseases."[24]

Any final rule concerning LDTs should adopt an approach that is better tailored to focus the Agency's limited resources on tests most likely to raise public health concerns, and to be consistent with FDA's longstanding, Congressionally-mandated, risk-based approach to the regulation of medical devices.[25] Such an approach could be accomplished by one or more of the grandfathering approach articulated in 2017, exemptions from premarket review for certain low-risk IVDs or IVDs intended for rare diseases, and/or further staggering of the compliance deadlines based on the anticipated benefit-risk profile of such tests. The Proposed Rule, if finalized, should adopt one or more of these approaches, and should further expressly clarify that modifications to such IVDs when not significant (i.e., are not major changes to the IVD's intended use or changes which could significantly affect the safety or effectiveness of the device)

---

Application Review and Related Enforcement (Sep. 9, 2021), https://www.fda.gov/tobacco-products/ctp-newsroom/perspective-fdas-progress-tobacco-product-application-review-and-related-enforcement.

[19] 88 Fed. Reg. at 68,014.

[20] *See* FDA, Guidance for Industry and Food and Drug Administration Staff: In Vitro Companion Diagnostic Devices (Aug. 6, 2014), at 8, https://www.fda.gov/media/81309/download.

[21] *See* FDA, Discussion Paper on Laboratory Developed Tests (LDTs) (Jan. 13, 2017), at 4, https://www.fda.gov/media/102367/download.

[22] *Id*.

[23] *See id*. at 3.

[24] *Id*. at 4.

[25] 21 U.S.C. § 360cc.

will remain exempt from premarket review, consistent with the Agency's longstanding approach to premarket review.[26]

Finally, MDMA welcomes FDA's proposal to continue to apply its general enforcement discretion approach to certain Human Leukocyte Antigen tests,[27] tests exclusively for public health surveillance,[28] and tests intended solely for forensic purposes.[29] Consistent with the approach first outlined by the Agency in 2017, any final rule should expressly exempt the following categories from the phased-in enforcement approach set forth in the proposed rule: tests intended solely for public health surveillance; tests intended solely for forensic use; and tests used in CLIA-certified, high-complexity histocompatibility laboratories to perform allele typing, antibody screening and monitoring, or crossmatching in connection with organ, stem cell, and tissue transplantation.[30] The Proposed Rule, if finalized, should also make clear that IVDs intended solely for employment and insurance testing are not subject to the enforcement phaseout policy.[31]

MDMA appreciates the opportunity to provide these comments concerning the Proposed Rule, and wishes to reiterate its concern regarding the potential impact of the Proposed Rule if finalized without a risk-based approach with feasible timelines to ensure that these important tests remain available to patients, and which is best-tailored to promote access to high-quality tests while efficiently stewarding Agency and other stakeholder resources.

* * * * *

We appreciate the opportunity to comment on this important topic. If we can provide any additional information, please contact me at mleahey@medicaldevices.org or (202) 354-7171.

Sincerely,

Mark Leahey
President & CEO
Medical Device Manufacturers Association

---

[26] *See generally* 21 C.F.R. § 807.81(a)(3); FDA, Guidance for Industry and Food and Drug Administration Staff: Deciding When to Submit a 510(k) for a Change to an Existing Device (Oct. 25, 2017), https://www.fda.gov/media/99812/download.
[27] *See* 88 Fed. Reg. at 68,022.
[28] *See id*. at 68,023.
[29] *See id*. at 68,022.
[30] *See* FDA, Discussion Paper on Laboratory Developed Tests (LDTs) (Jan. 13, 2017), at 4, https://www.fda.gov/media/102367/download. *See also* 21 C.F.R. § 801.125.
[31] *See* FDA, Drugs of Abuse Tests, https://www.fda.gov/medical-devices/in-vitro-diagnostics/drugs-abuse-tests ("FDA does not review drugs of abuse tests intended for employment and insurance testing provided they include a statement in their labeling that the device is intended solely for use in employment and insurance testing, and does not include test systems intended for Federal drug testing programs").