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# FDA PUBLISHES PROPOSED RULE ASSERTING MEDICAL-DEVICE JURISDICTION OVER LABORATORY-DEVELOPED TESTS

To Our Clients and Friends:

On September 29, 2023, the U.S. Food and Drug Administration (FDA) released its highly anticipated proposed rule on laboratory-developed tests (LDTs) ("LDT Proposed Rule"), which was officially published in the *Federal Register* on Tuesday, October 3, 2023.[1] In the LDT Proposed Rule, FDA announced plans to formally classify LDTs as medical devices under its regulations, subjecting these tests to extensive premarket review and postmarket compliance requirements. If finalized, the LDT Proposed Rule would result in a significant impact to the growing laboratory testing industry. In addition, even if the Proposed Rule is not finalized, federal healthcare programs and private payors may use issuance of the Proposed Rule and its assertion of FDA authority over LDTs to refuse payment for tests on the basis that those test lack necessary premarket clearances or otherwise are not reasonable and necessary. FDA has invited interested stakeholders to submit comments to Docket No. FDA-2023-N-2177 by December 4, 2023.[2]

***Historical Background***

LDTs are diagnostic tests that are designed, manufactured, and used within a single laboratory.[3] FDA has historically asserted that LDTs are *in vitro* diagnostics,[4] which it regulates as medical devices under the Federal Food, Drug, and Cosmetic Act (FDCA).[5] In relevant part, the FDCA defines "device" as " an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article . . . which is . . . intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals."[6] Industry has pushed back on these characterizations, including in several citizen petitions,[7] claiming that LDTs are not "articles" that meet the definition of "device" under the FDCA, but are rather laboratory "services" that are instead regulated by the Centers for Medicare & Medicaid Services (CMS) and state agencies under the Clinical Laboratory Improvement Amendments (CLIA).[8] They have also asserted that tests that are manufactured and conducted solely in a single laboratory fall outside of FDA's regulatory authority because they are not placed in commercial distribution or into interstate commerce.[9] Seemingly acknowledging the uncertain nature of FDA's jurisdiction, Congress has considered, but not yet enacted, legislation to expressly provide FDA authority over LDTs, referred to as the Verifying Accurate Leading-edge IVCT Development (VALID) Act.[10]

Nonetheless, prior to Proposed Rule, FDA exercised enforcement discretion for LDTs it considered "low-risk," as well as LDTs for certain specific uses.[11] It did, however, indicate its intention to enforce medical-device requirements for "medium" and "high-risk" devices.[12] Indeed, in 2019, FDA issued a warning letter to Inova Genomics Laboratory for marketing genetic tests for "predicting medication

response," "reducing negative side effects from certain medications," and aiding in drug and dose selection without premarket clearance or approval.[13] FDA also issued a 2017 discussion paper, in which the agency proposed to phase in medical device requirements for all LDTs over a four year schedule, but has not yet taken action to implement this plan.[14]

In the LDT Proposed Rule, the Agency asserted that it had made clear that LDTs were medical devices at many points dating back to at least 1997, but had taken an enforcement discretion policy with these products.[15] FDA cited various concerns with the safety, validation, quality, and increasing complexity and ubiquity of LDTs, and their use in making critical medical decisions – including whether or not patients should seek, or healthcare providers should prescribe, treatments – as the basis for its decision to update its regulations to explicitly subject LDTs to its medical device authorities.[16]

As described in greater detail below, if finalized, the LDT Proposed Rule would subject LDT manufacturers to extensive medical device regulatory requirements. In addition, even if the Proposed Rule is not finalized, federal healthcare programs and private payors may use issuance of the Proposed Rule and its assertion of FDA authority over LDTs to refuse payment for tests on the basis that those test lack necessary premarket clearances or otherwise are not reasonable and necessary. Accordingly, it is crucial for interested stakeholders to participate actively in the notice-and-comment process to help shape a final rule on LDT regulation and to prepare for eventual litigation.

***Proposed Changes to Assert Medical-Device Jurisdiction over LDTs***

The actual changes FDA proposes to make to its regulations are minimal as its redline reflects:

- FDA plans to amend the authority to 21 C.F.R. Part 809, which governs IVDs as follows: "21 U.S.C. 321(h)(1), 331, 351, 352, ~~355, 360b,~~ 360, 360c, 360d, 360e, 360h, 360i, 360j, 371, 372, 374, 381." The added authorities include the definition of "device" under the FDCA; provisions for medical device establishment registration, product listing, and premarket notification (510(k)); and, the statutory provision for premarket approval (PMA).[18] The deleted authorities address applications for the approval of new drugs for humans and animals.[19]

- FDA also plans to amend the definition of IVD in 21 C.F.R. § 809.3(a) to expressly note that IVDs are medical devices regardless of whether they are manufactured by a laboratory: "***In vitro diagnostic products*** are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. These products are devices as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the act), and may also be biological products subject to section 351 of the Public Health Service Act, including when the manufacturer of these products is a laboratory."[20]

The impact of these changes, however, is significant. Indeed, as described throughout the LDT Proposed Rule, FDA intends to subject LDTs to the same extensive regulatory requirements applicable to other IVDs, including those pertaining to premarket review, as applicable, (e.g., 510(k)s, PMAs, or de novo classifications, for both current LDTs and for future changes made), the quality system regulation (QSR),

medical device reporting (MDR), reports of corrections or removals, establishment registration and product listing, product labeling, and investigational use.

***Compliance Policy for LDTs***

Acknowledging the significance of the impacts of the proposed rule, FDA stated its intention to follow a four-year "phaseout" of its current enforcement discretion policy.[21] FDA specifically plans to extend this policy to "IVDs that are manufactured and offered as LDTs," recognizing that some manufacturers have marketed IVDs as LDTs even where those tests do not fit what FDA generally considers an LDT. *Id.* FDA proposes that the phaseout policy proceed as follows:

- Stage 1 (1 year after FDA publishes a final phaseout policy, planned for the preamble of the final rule): end of general enforcement discretion with respect to MDR and correction and removal reporting requirements.

- Stage 2 (2 years after FDA publishes a final phaseout policy): end of general enforcement discretion for medical device requirements other than MDR, correction and removal reporting, QSR, and premarket review.

- Stage 3 (3 years after FDA publishes a final phaseout policy):end of general enforcement discretion with respect to QSR requirements.

- Stage 4 (3.5 years after FDA publishes a final phaseout policy, but not before October 1, 2027): end of general enforcement discretion with respect to premarket review for high-risk LDTs. *Id.* at 58, 64-66. FDA notes that it does not intend to take enforcement against high-risk devices with timely submitted PMAs until the agency completes review of its application.

- Stage 5 (4 years after FDA publishes a final phaseout policy, but not before April 1, 2028): end of general enforcement discretion with respect to premarket review for medium and low-risk LDTs.[22]

The phaseout policy is, however, subject to a number of carveouts:

- The phaseout policy does not extend to certain classes of tests that FDA considers not to have been subject to its prior enforcement discretion policy. These include tests intended for screening of donors for blood, or for human cells, tissues, and cellular and tissue-based products (HCT/Ps) required for infectious disease testing; tests intended for emergencies, potential emergencies, or material threats declared under FDCA section 564; and, direct-to-consumer (DTC) tests.[23]

- Nor does FDA consider test components manufactured outside of a laboratory to be subject to the phaseout policy. FDA states that such components have always been outside the definition of LDT, and therefore of any FDA enforcement discretion policy.[24]

- FDA is also "proposing to continue to apply the current general enforcement discretion approach going forward" to certain classes of tests.[25] These include "1976-Type LDTs," which are generally less-complex tests with characteristics common at the time of the 1976 Medical Device Amendments (MDA) to the FDCA; human leukocyte antigen (HLA) tests within a single CLIA-certified laboratory which meets requirements to perform high-complexity histocompatibility testing; tests intended solely for forensic or law enforcement purposes; and, tests used exclusively for public health surveillance.[26] Although it is not abundantly clear, FDA appears to intend to exercise enforcement discretion for these classes of tests indefinitely – even beyond the end of the four-year phaseout period.

- FDA expressly indicates that it does not intend to exercise general enforcement discretion to certain categories of tests for which it had previously done so: low-risk tests that are class I devices; tests currently on the market; and, tests for rare diseases. The agency observed that these tests are among those that have prompted its safety and validation concerns. These tests would therefore appear to be subject to the four-year phaseout policy, rather than a general enforcement discretion policy.[27]

FDA also noted that it may also adopt other enforcement discretion policies as appropriate, and sought input on particular types of enforcement discretion policies that would be appropriate for the agency to adopt. Specific types of LDTs for which FDA has solicited input on enforcement discretion include class I devices, tests in academic medical centers (AMCs), and tests regulated under existing programs, such as the New York State Department of Health Clinical Laboratory Evaluation Program (NYSDOH CLEP) and the Veterans Health Administration (VHA).[28]

Stakeholders should consider submitting comments on the LDT Proposed Rule to help shape FDA's rulemaking, including whether FDA should regulate LDTs as medical devices at all. In particular, sponsors should seek to identify costs and complications not identified as considerations by FDA, such as the impact of increased compliance costs on affordability of LDTs, the possibility that LDTs may no longer be reimbursable under federal healthcare programs, and whether LDTs, even if regulated as medical devices, should be exempt from particular medical-device requirements; reliance interests that have been built up around the FDA's longstanding enforcement policy but would be upset by adoption of the LDT Proposed Rule; and potential alternatives or modifications to FDA's approach that the agency should consider, including any enforcement discretion policies.

Other consequences from the LDT Proposed Rule that sponsors should consider include:

- Whether FDA's proposed regulatory framework and phaseout policy could impact the ability of laboratories to timely develop tests that are vital to both patients and healthcare professionals;

- Potential enforcement and compliance risks and costs that would stem from implementation of the LDT Proposed Rule, if finalized; and

- Potential impact on reimbursement of diagnostic services by government health care programs and potential related enforcement risks.

Gibson Dunn is prepared to help sponsors and other interested entities consider potential effects of the LDT Proposed Rule, if finalized, and submit comments to FDA regarding the LDT Proposed Rule.

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[1] 88 Fed. Reg. 68006 (Oct. 3, 2023). FDA also published a press release accompanying the proposed rule. FDA News Release, "FDA Proposes Rule Aimed at Helping to Ensure Safety and Effectiveness of Laboratory Developed Tests" (Sept. 29, 2023) ("Press Release").

[2] *See* Docket No. FDA-2023-N-2177.

[3] 88 Fed. Reg. at 68008; *see also* FDA, Draft Guidance for Industry, Food and Drug Administration Staff, and Clinical Laboratories, Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs) (Oct. 2014) ("2014 Draft Guidance"), at 5.

[4] *See* 2014 Draft Guidance at 4 ("This document describes a risk-based framework for addressing the regulatory oversight of a subset of *in vitro* diagnostic devices (IVDs) referred to as laboratory developed tests (LDTs)."") (internal citations omitted).

[5] *Id.* at 4 n.1 ("Per 21 CFR 809.3(a) *in vitro diagnostic devices* are 'those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae.['] Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. These products are devices as defined in section 201(h) of the [FDCA] . . . .").

[6] 21 U.S.C. § 321(h)(2).

[7] *See, e.g.*, Letter to J. N. Gibbs, Hyman, Phelps & McNamara, P.C. re: 92P-0405 (Aug. 12, 1998), Docket No. FDA-1992-P-0047 ("HPM Citizen Petition Response") (denial of 1992 citizen petition requesting that FDA "not regulate as medical device assays developed by clinical reference laboratories strictly for in-house use"); Citizen Petition from Am. Clinical Lab. Ass'n (ACLA) (June 4, 2013), Docket No. FDA-2013-P-0667 ("ACLA Citizen Petition") (citizen petition requesting that FDA confirm that LDTs are not medical devices under the FDCA and refrain from issuing guidance or rulemaking purporting to regulate LDTs as medical devices); Letter to A. Mertz, ACLA re: Docket No. FDA-2013-P-0667 (July 31, 2014) (denial of ACLA Citizen Petition).

[8] *See* 42 U.S.C. § 263a; *see also* 42 C.F.R. Part 493 (CMS implementing regulations for CLIA).

[9] *See* HPM Citizen Petition Response, Enclosure at 7-9 (responding to arguments regarding commercial distribution and the Commerce Clause); ACLA Citizen Petition at 11-22 (asserting that FDA cannot regulate LDTs since they are not placed in commercial distribution).

[10] *See* S. 3404, 116th Cong. (2020); H.R. 6102, 116th Cong. (2020); S. 2209, 117th Cong. (2021); H.R. 4128, 117th Cong. (2021); S. 4348, 117th Cong. (2022); H.R. 2369, 118th Cong. (2023).

[11] 2014 Draft Guidance at 12-13.

[12] *Id.* at 13.

[13] Warning Letter to Inova Genomics Lab. (Apr. 4, 2019).

[14] *See* FDA, Discussion Paper on Laboratory Developed Tests (LDTs) (Jan. 13, 2017), at 4-5.

[15] 88 Fed. Reg. at 68015-20.

[16] *Id.* at 68009-14.

[17] *Id.* at 68031.

[18] *See* 21 U.S.C. §§ 321(h)(1), 360, 360e.

[19] *See id.* §§ 355, 360b

[20] 88 Fed. Reg. at 68031.

[21] *Id.* at 68021.

[22] *Id.* at 68024-27.

[23] *Id.* at 68021-22.

[24] *Id.* at 68022.

[25] *Id.*

[26] *Id.* at 68022-23.

[27] *Id.* at 68023.

[28] *Id.* at 68023-24.

*Gibson Dunn's lawyers are available to assist in addressing any questions you may have regarding the issues discussed in this update. Please contact the Gibson Dunn lawyer with whom you usually work, any leader or member of the firm's FDA and Health Care practice group, or the following authors:*

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