Medical Devices; Laboratory Developed Tests (RIN: 0910-A185)

April 12, 2024

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Agenda

- Introductions
- About C21
- C21 position
- Key points/concerns
- Closing

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About C21

The Coalition (C21) represents the world's most innovative diagnostic technology companies, clinical laboratories, researchers, physicians, and venture capitalists—all linked by a common mission: to develop and commercialize state-of-the-art diagnostics that improve patient health.

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Disclaimer

C21 acknowledges that some groups have questioned whether FDA currently has authority under the Federal Food, Drug and Cosmetic Act (FDCA) (21 U.S.C. § 301 *et seq*.) to regulate LDTs as medical devices, including the subset of LDTs that FDA sought to define for discussion in draft FDA guidance as *In Vitro Multivariate Index Assays* (IVDMIAs). C21 does not address this question in this presentation.

Consistent with the approach that C21 has taken throughout consideration of this issue, C21's comments supportive of certain approaches to regulation should not be considered an acknowledgement by C21 or any of its members that FDA currently has authority to regulate laboratory services as medical devices.

In addition, these comments do not represent an admission by C21 or any of its members that any particular laboratory service is a "device" as that term is currently defined under Section 201(h) of the FDCA.

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Longstanding Involvement

- C21 has worked closely with FDA and Congress for nearly 18 years on the agency's proposed regulation of LDTs
  - Primary goals: to ensure that any new regulatory framework is reasonable, not overly burdensome, and acknowledges critical differences between laboratory procedures and distributed kits
- Engaged in mutually educational, productive dialogue with CDRH leadership, including:
  - Coordination of FDA "tours" of C21 member laboratories
  - Participation in public meetings/public forums
- C21 appreciates FDA's willingness to engage and consider stakeholder input
  - Best evidenced by publication of substantially revised position in 2017 White Paper (and decision not to finalize 2014 Draft Guidance)
- Submitted detailed comments in response to September 2023 proposed rule

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Overall Position on Proposed Rule

- **C21 opposes finalization of the Proposed Rule as written**
  - C21 believes a diagnostics-wide, comprehensive approach to regulation of all testing (including LDTs) – such as those under consideration by Congress – would be preferable to treating all diagnostics as medical devices under the FDCA
- **If FDA insists on proceeding, however, the agency should significantly modify and extend implementation of the Proposed Rule**
  - **FDA should proceed only with registration/listing and adverse event reporting, and rescind the quality systems and premarket submission components of the Proposed Rule until it has actual data to inform critical assumptions regarding the agency's expected workload**
    - After FDA has collected and reviewed this information, FDA should propose an updated timeline for compliance with these requirements
  - **FDA should continue enforcement discretion for "high-quality" LDTs**
    - Consistent with written comments on proposed rule – i.e., tests approved by NYS Dept. of Health, tests covered by MolDX, tests performed in CAP-accredited labs
  - Modification/extension would allow agency to strike a more appropriate balance between:
    - Perceived need for regulatory oversight; and
    - Patient access to novel, innovative tests

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Key Concerns/Points

- FDA lacks information necessary to propose definitive compliance timeline
- FDA strategies are unlikely to adequately manage expected application volume
- FDA should exercise continued enforcement discretion for “high quality” tests
- FDA should more carefully consider the costs incurred by laboratories in complying with additional requirements

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FDA Lacks Information Necessary to Propose Definitive Compliance Timeline

- FDA proposes to end longstanding LDT enforcement discretion in five stages over a four-year period (post-finalization)
- However, FDA proposes this timeline without the benefit of critical, definitive information needed to evaluate the feasibility of the agency's plans:
  - How many labs currently offer LDTs?
  - How many LDTs are currently on the market?
  - How frequently are LDTs modified? What is the nature of those modifications?
  - What are the intended uses of those LDTs?
- Without clear and transparent answers to these questions, it is impossible to evaluate:
  - The feasibility of FDA's proposed timeline; OR
  - Whether FDA's proposal appropriately focuses the agency's limited resources on problematic tests

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FDA Lacks Information Necessary to Propose Definitive Compliance Timeline (cont'd)

- No publicly available definitive answers to these questions
- However, the following objective, verifiable statistics suggest that the agency's proposed regulatory timeline may impose a significant – and potentially unmanageable – administrative burden on the agency
  - **> 32,000 clinical laboratories are currently authorized to perform LDTs** (CLIA Stats (cms.gov))
    - Certificate of Accreditation labs (15,894) PLUS Certificate of Compliance labs (16,643) PLUS Additional labs located in CLIA-exempt states (New York and Washington State)
    - *Compare*: FDA assumes that ~1,200 labs perform LDTs.
      - Unclear why FDA assumes that > 95% of labs that *could* run LDTs do not.
  - **> 10,000 LDTs approved (or conditionally approved) by New York State Dept. of Health)** (Search Approved Laboratory Developed Tests | New York State Department of Health, Wadsworth Center)
    - *Compare*: In 2023, CDRH set a record by giving *de novo* authorization to 124 novel devices (CDRH Annual Report 2023 (fda.gov))

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FDA Strategies are Unlikely to Manage Expected Application Volume

- C21 understands the Agency plans to address bandwidth issues by:
  - Hiring additional staff (with funds from next user fee bill);
  - Leveraging third-party reviewers; and
  - Down-classification of existing Class II/III IVDs
- However, without information on the volume/type of expected submissions, how will FDA know:
  - How many reviewers to evaluate, hire, and train? And with what expertise?
  - How many third-party contractors to evaluate, hire, and train? And with what expertise?
- Utility of (expanded) third-party review program may be limited
  - FDA re-review of third-party reviewer work (The 510(k) Third Party Review Program: Promise and Potential | Journal of Medical Systems (springer.com))
  - Lack of familiarity with application of FDA standards
- Down-classification concept potentially promising, but substantial questions/obstacles
  - *De novo* submissions still require substantial resources
  - Requires notice and comment rulemaking/modification of existing regs – further stretching agency resources for indeterminant number of tests

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FDA Should Exercise Continued Enforcement Discretion for "High-Quality" Tests

- For "high quality" tests on the market prior to the effective date of the Final Rule, FDA should:
  - **Indefinitely extend enforcement discretion** from quality systems and premarket review requirements.
  - Will help ensure FDA initially targets its limited resources towards areas of greatest need
- For "high quality" tests first introduced after the effective date of the Final Rule (or pre-Final Rule tests substantially modified after the effective date of the Final Rule), we recommend that FDA:
  - **Extend enforcement discretion for an additional five years** beyond its scheduled implementation of such requirements for LDTs more generally
- Consistent with the approach taken (with FDA's input) in the VALID Act, the Agency should only end such enforcement discretion for an LDT if credible information establishes that an LDT:
  - Is marketed with insufficient evidence of analytical validity or clinical validity;
  - Is marketed with any false or misleading analytical or clinical claims; or
  - It is probable an LDT will cause serious adverse health consequences.

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FDA Should Exercise Continued Enforcement Discretion for "High-Quality" Tests (cont'd)

- LDTs would be considered "high-quality" if they have been reviewed by or are subject to regulatory requirements that provide assurance of analytically and clinically valid results – i.e., tests that:
  - Receive test-specific approval from the NYS Dept. of Health;
  - Receive coverage from the Palmetto GBA Molecular Diagnostic ("MolDX") Program following successful submission of a test-specific Technical Assessment ("TA"); OR
  - Are performed in a CLIA-certified clinical laboratory that has received accreditation from the College of American Pathologists ("CAP")
- Exempting such tests from review would allow FDA to:
  - Reduce its existing workload to a more manageable level; and
  - Focus enforcement activity on areas of greatest need

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FDA Should More Carefully Consider Total Costs of Compliance

- Assumptions set forth in proposed rule do not reflect actual cost of compliance with FDA regulations
  - Example: FDA estimates that it will cost labs ~$60,000 per lab to implement an FDA-grade quality system
  - However, this does not cover even half of the estimated annual salary for a single employee with FDA QSR skills/experience
    - Mean annual salary = $136,238 (Average Salary for Jobs with FDA Quality Systems Regulations (QSR) Skills | Salary.com)
    - Costs only likely to increase further if proposed rule finalized, as laboratories compete for a limited number individuals with experience applying FDA QS regulations to clinical lab operations

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Conclusion

- C21 opposes finalization of the Proposed Rule
  - Encourages FDA to continue working with stakeholders to develop an updated legislative framework that applies to all diagnostic testing, including LDTs.
- If FDA insists on proceeding under the FDCA, however, it should significantly modify and extend implementation of the Proposed Rule.
  - Should proceed only with registration/listing and adverse event reporting
  - Should delay implementation of quality systems and premarket submission requirements until reliable data obtained regarding administrative burden
  - Should continue enforcement discretion for “high quality” LDTs

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Thank you

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