February 2, 2015

Submitted electronically via www.regulations.gov

Margaret A. Hamburg, M.D. Commissioner
U.S. Food and Drug Administration
Department of Health and Human Services
10903 New Hampshire Avenue
WO66, Room 5442
Silver Spring, MD 20993-0002

Re: Draft Guidance Documents Titled "Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)" (Docket No. FDA-2011-D-0360) and "FDA Notification and Medical Device Reporting for Laboratory Developed Tests (LDTs)" (Docket No. FDA-2011-D-0357)

Dear Commissioner Hamburg:

The Coalition for 21st Century Medicine (the Coalition) is pleased to submit comments to the Docket on the "Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)" and the "FDA Notification and Medical Device Reporting for Laboratory Developed Tests (LDTs)" draft guidances, as announced on October 3, 2014.[1]

INTRODUCTION

The Coalition for 21st Century Medicine comprises some of the world's most innovative diagnostic technology companies, clinical laboratories, venture capital companies, and patient groups working to support appropriate regulatory oversight and fair reimbursement policies to promote innovation in the development and use of advanced personalized diagnostic testing. Coalition members develop and perform clinical diagnostic testing, so-called laboratory developed tests (LDTs), invest in such companies, and also represent patient groups whose members obtain such tests. Given the Coalition's mission, we have a keen interest in the extent

[1] 79 Fed. Reg. 59776.

to which the U.S. Food and Drug Administration (FDA or the Agency) intends to regulate LDTs as medical devices[2] as well as in the regulation of *in vitro* diagnostics more broadly.

Since its inception, the Coalition has worked closely with FDA to ensure that any new regulatory framework proposed by FDA for LDTs is reasonable, not overly burdensome, and acknowledges the differences between laboratory services and kits that are distributed to laboratories for performance. We appreciate the time and attention the agency has given to considering the Coalition's views over the years, and in particular since releasing these latest draft guidances. The Coalition seeks to continue our efforts to work with the FDA toward the development of an appropriate regulatory model for advanced diagnostic tests that both protects public health and promotes innovation. It is critical that the Agency remains open to stakeholder views and adopts well-reasoned changes to the draft guidance that are both clear and not overly burdensome for laboratories.

Nevertheless, the Coalition strongly believes that the existing medical device framework, under which the FDA intends to regulate LDTs, is ill-suited for the oversight of LDTs and *in vitro* diagnostics generally. The United States is at a crossroads in the ongoing revolution of what President Obama called "precision medicine" in this year's State of the Union address, and could fulfill the promise of "21st Century Cures" --early, rapid and comprehensive diagnosis, and individualized, targeted treatments-- against many serious and life-threatening diseases. However, the medical device framework established nearly 40 years ago, without modernization, poses significant barriers that could greatly impede this critical, beneficial trend in health care.

Our comments to the docket identify and address critical omissions and questions in the draft guidance and propose ways to resolve some of the challenges that are inherent in the Agency's current approach. We offer these comments as part of our continued substantive dialogue with FDA on the policy issues and operational challenges related to the Agency's proposed oversight of LDTs. We note that it is our longstanding position that establishment of a regulatory framework for laboratories under the Federal Food, Drug and Cosmetic Act (FFDCA) is not simply a policy statement under established rules but rather represents the adoption of new rules for laboratories and requires notice and comment rulemaking under the Administrative Procedures Act. Although the Agency itself has recognized the new policies for laboratories as a paradigm shift, the Coalition remains concerned that the Agency's position to the contrary only heightens risks of legal challenge by affected stakeholders, which could delay the regulatory certainty and public confidence that is critical for continued innovation and patient access to new and better test methodologies. Adopting a well reasoned approach consistent with Administrative Procedures Act would certainly make obtaining stakeholder acceptance of this

[2] The Coalition acknowledges that some groups have questioned whether FDA has the authority under the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 301 et seq.) to regulate LDTs as medical devices, including tests that it sought to define for discussion in draft FDA guidance as *In vitro Multivariate Index Assays* ("IVDMIAs"). The Coalition does not address this question in this response. Consistent with the approach that the Coalition has taken throughout the FDA's consideration of this issue, the Coalition's comments supportive of certain approaches to regulation should not be considered an acknowledgement by the Coalition or any of its members that FDA has the authority to regulate laboratory services as medical devices. In addition, these comments do not represent an admission by the Coalition or any of its members that any particular laboratory service is a "device" as that term is defined under Section 201(h) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 321(h)).

new regulatory framework for laboratories substantially less difficult than if the FDA proceeds solely through the issuance of guidance documents and general statements of policy.

As outlined below, the Coalition has two chief areas of concern:

(1) **Regulatory burden**: the potentially over burdensome requirements could chill current investment in the development of innovative diagnostics for cancer, cardiovascular disease, deadly infectious disease, and countless rare diseases and disorders. The Coalition strongly believes that any effort to modernize the regulatory framework must carefully balance the regulatory burdens on laboratories with the public health risks to patients.

(2) **Regulatory uncertainty**: Finalizing the guidance without substantial changes or, worse, without publishing such changes for additional public comment, would leave stakeholders in the untenable position of hoping that the Agency appropriately resolves those questions through its case-by-case adjudications and decision-making. This presents an unreasonable risk of stifling innovation at a crucial moment in the historic evolution of advanced diagnostics.

EXECUTIVE SUMMARY

The Coalition agrees that appropriate regulation of *in vitro* diagnostic testing is essential to assuring patient safety and public health and to fostering public confidence in diagnostic testing. At the same time, continued innovation is possible only if the FDA provides clear, predictable, and reasonable standards for test developers that permit physicians and patients to rely upon advanced diagnostics to better guide treatment.

The Coalition strongly supports a risk-based framework for the oversight of LDTs based chiefly on the risk of the information derived from the use of the test result in clinical practice, and not the underlying technology or platform used to perform the test. We agree with the Agency's determination that 'IVDMIAs'—even if such term could be defined clearly—are not "high risk" based solely or primarily on the use of multiple variables and an algorithmic analysis to derive the test result. The Coalition opposes FDA oversight of any risk category of LDTs under the proposed draft guidance until the Agency resolves the critical issues outlined in these comments.

Specifically, the Coalition's overarching position is that FDA must address many substantive issues and unresolved questions before it finalizes its framework for regulation of LDTs. Unless such key open issues are resolved appropriately and in a timely fashion in advance of compliance requirements, it is unreasonable to expect that laboratories can comply effectively with the FDA's proposed new requirements.

These key issues include:

- Identifying with specificity **what is the "device" within the LDT service**;
- Providing clear guidance on requirements for obtaining **labeling** that is useful for clinicians and patients;

- Accommodating medical **communications between providers**—laboratories and treating physicians—under an FDA regulatory framework that generally imposes substantial limitations on pro-active communications by medical product manufacturers (subject to risk of extremely serious penalties if violated);

- Establishing a presumption of **sufficient evidence for clinical validity** when there are well-established public data in peer-reviewed studies, or nationally or internationally accepted clinical guidelines or standards;

- **Harmonizing CLIA and QSR** requirements; and

- Clarifying that these new **requirements apply consistently and uniformly** to all clinical laboratories regardless of ownership, and defining more specifically and appropriately proposed carve-outs for important areas such as rare disease testing and testing that support unmet medical needs.

Additionally, a reasonable transition period must be established that recognizes both that LDTs are already on the market lawfully under CLIA and there are inherent challenges for laboratories newly regulated under FDA in understanding, developing, and implementing internal policies to comply with substantial new rules, the specific parameters for compliance which cannot be implemented until the guidance is finalized. It is unreasonable to expect or require that this can be effectively accomplished, along with the preparation of a substantial regulatory submission in the case of LDTs that would require PMAs, and compliance with QSRs, without sufficient transition time after the new rules are established.

Likewise, it is critical that stakeholders have an opportunity to comment on how the Agency intends to resolve the open issues. For example, the Coalition would like to understand more fully the factors the Agency intends to use to make critical benefit-risk determinations in its framework for review of LDTs and how these factors will be reasonably established. Similarly, the lack of clear and appropriate evidentiary standards for evaluating and balancing risk and benefit factors specific to diagnostics will hamper both compliance and the development of both new and improved LDTs.

The Coalition recognizes that the draft framework is an improvement over the 2006 IVDMIA draft guidance, but in its present form leaves too many critical questions unanswered. As a result, it is not sufficiently developed to serve as a clear, effective, and informative basis for implementing new regulatory requirements for LDTs. Consequently, it is imperative that the FDA provide for comment then implement the additional detailed substantive guidance necessary to establish appropriate standards and guidelines that resolve the myriad of questions and outstanding issues *before* its proposed framework is finalized, which starts a clock for compliance among affected laboratories. The risk of threatened enforcement under the final framework as proposed, absent such additional efforts, will severely threaten the investment in innovation and the advancement of personalized medicine that the Agency has committed to supporting.

SPECIFIC COMMENTS AND RECOMMENDATIONS

Given the uncertainty and concerns expressed by stakeholders at the LDT Workshop on January 8-9, 2015, regarding the FDA Draft Guidance, we submit for FDA's consideration the following comments and recommendations. We believe these recommendations will make the proposed framework more suitable to the oversight of LTDs and provide laboratories with necessary transparency and predictability.

a. Definition of Device

The draft guidance does not address how the FDA would distinguish a regulable "medical device" from laboratory services in an LDT. The device component is analogous to a test "kit" currently manufactured then distributed to laboratories to perform, while laboratory services are within the realm of the practice of laboratory medicine and therefore outside of the FDA's statutory authority.

The Coalition supports the establishment of a clear and rational line between what will be the FDA-regulated "test" inside a lab and the practice of laboratory medicine, in particular with regard to iterational changes/modifications and clinical consultations with providers. The Coalition recommends that FDA create a precise definition of the device component or components within an LDT service that is the virtual equivalent of a kit. For example, this definition could comprise the reagents/supplies, directions for use, and intended use/indication for use. FDA should leave the day-to-day performance of the test under CLIA and state law the same as the Agency historically has done with kits.

Unless FDA identifies the "device" in an LDT, laboratories would be unable to comply consistently and effectively with FDA premarket and post market regulatory requirements. Moreover, failure to establish a clear line between the "device" subject to FDA regulation and the performance of laboratory medicine outside FDA regulation will further obscure the regulatory environment and chill continued investment in this critical sector.

b. Test Labeling

FDA should support LDT labeling that is meaningful and consistent with how the test is used in clinical practice. There are historic examples of LDTs subject to premarket review that have resulted in labeling that expressly disclaims how the tests will be used in actual clinical practice-- with limitations against use of the tests (1) to make a diagnosis, (2) to change a diagnosis, or (3) for treatment selection. To promote appropriate clinical use of LDTs and facilitate understanding of their benefits, risks and uses, FDA should encourage the submission of meaningful labeling and avoid it its review and clearance/approval "carving out" clearly foreseeable and likely uses. Labeling appropriately may explain limitations in existing knowledge about the test at the time of the clearance/approval, but a lack of knowledge should not translate into a limitation on how the test may be used in patient management in the absence of evidence of harm.

Consistent with a risk-based approach to regulation, FDA should tailor the requirements to obtain clearance/approval for LDTs with clinically meaningful labeling based upon what experts in the relevant field indicate is the appropriate evidence standard to support such labeling. FDA must consider the feasibility for a single clinical laboratory to obtain outcomes data before the Agency sets unrealistic evidence bars to support labeling.

c. Communications between Laboratories and Providers

Under CLIA, a laboratory director and clinical consultant play a vital role in helping ordering physicians select and understand how to interpret the reported results of diagnostic laboratory tests in specific patient conditions. FDA should make clear in additional substantive draft guidance that these provider-to-provider communications relevant to individual patient care do not constitute "promotion" for purposes of FDA regulation—even if these communications occur in advance of a physician order where the laboratory and physician are discussing the appropriate selection of testing for an individual patient.

d. Clinical Validity

The draft guidances also create considerable uncertainty over the definition and demonstration of clinical validity for LDTs. When a device is regulated, a key issue is what level of evidence the FDA will determine is required to support claims. The draft guidance provides few details of the evidence standards that will be used, mainly noting that laboratories may refer to established literature in lieu of conducting their own studies.

FDA should establish a presumption of sufficient evidence for clinical validity when there is scientific evidence in the form of published peer-reviewed studies, nationally or internationally accepted clinical guidelines, or nationally or internationally accepted standards established by experts in the field. Additionally, the Coalition urges the FDA to clarify that sponsors should not be required to prove clinical validity with new clinical evidence if clinical validity of the analyte is well-established. The final guidance should state that it would be sufficient for the test developer to establish clinical validity of an analyte by reference to peer-reviewed literature, published guidelines, and internationally recognized consensus standards or monographs.

e. Harmonizing QSR and CLIA Requirements

FDA's QSR is a comprehensive complex system of compliance requirements that has been tailored for many types of devices over decades. In the draft framework, FDA proposes to require a vast variety of laboratories to comply with QSR requirements, but provides scarce detail as to how the QSR would apply to LDTs generally and to different kinds of laboratories more specifically. Moreover, LDT laboratories are already subject to the extensive regulatory requirements of CLIA (42 C.F.R. Part 493)—a regulatory reality that is given little to no attention in the draft guidances, except as a topic for future, indeterminate guidance.

While the Coalition appreciates and understands the need to enable flexibility in how a lab might choose to comply with quality regulations, FDA should provide a roadmap for doing so, since labs are already subject to existing quality regulations and often seek additional quality certifications. The Coalition believes it is imperative for stakeholder comprehension and the

development of a flexible, efficient regulatory system that the FDA should conduct and publish an extensive side-by-side comparison of CLIA requirements and FDA QSRs. FDA should defer to CLIA requirements wherever there is overlap, and FDA should limit the requirements for QSR compliance to the "device" consistent with the recommendations for the definition of device above. FDA should harmonize the QSR requirements with the CLIA requirements to prevent duplicative efforts and ease the regulatory burdens.

At a minimum, FDA should release a separate guidance outlining the application of QSR to laboratories that develop LDTs. The guidance can propose a straightforward crosswalk outlining the additional steps for CLIA-compliant laboratories to satisfy the QSR requirements. For any areas where there is conflict between QSR and CLIA regulations, FDA should provide specific guidance regarding the conflict. For areas where FDA believes that other regulatory requirements are insufficient to comply with QSR, specific guidance should be developed that both identifies those areas and provides a new checklist for laboratory compliance.

As a first step, the Agency should work with willing laboratories to identify and propose best practices and models for the effective and least burdensome implementation of dual regulatory systems. Through this process the Agency should seek to develop specific and meaningful tools for laboratory compliance with the various new regulatory requirements, such as model formats for submissions and checklists clarifying which existing laboratory procedures and certifications are sufficient for FDA. These potential models could be published first as part of an interactive informational Agency dialogue with stakeholders, rather than draft "guidance," so the focus first can be on establishing the best policies that enable the continued success of laboratories while still supporting public health policy objectives.

In its implementation and enforcement practices, the FDA must maximize the use of third-party certification and rely upon College of American Pathologists (CAP), state regulatory agencies, and other established certifying entities to the maximum extent possible. However, it is essential that FDA develop appropriate and consistent programs to ensure that inspectors, including third-party inspectors, are trained to cover the new hybrid type of inspections in which they would inspect for compliance with both CLIA and QSR requirements. These inspections would optimally make it more efficient for CMS and FDA to monitor compliance without creating overlapping regulatory requirements for laboratories.

f. Timeline for Implementation and Supplemental Guidance

The numerous, complex regulatory requirements that the FDA proposes to implement under the framework guidance necessitate the additional provision of clear milestones and expectations from the FDA for all affected stakeholders. The Coalition strongly urges the FDA to hold additional public meetings on specific subject areas, such as quality systems, defining the device, and labeling issues, as well as publish additional draft guidance for comment so that stakeholders will be able to understand, anticipate and develop compliance strategies with the new regulatory requirements and the resources necessary to support such strategies well in advance of publication of any final guidance. Additional and supplemental guidance documents should incorporate all of the comments to the first draft guidance as well as propose the additional necessary guidance developed with substantial stakeholder input that would better enabling reasonable and timely compliance and the further development of LDTs that are

clinically meaningful, in particular specific guidance on QSR, labeling, and adverse event reporting.

g. Public Process for Classification and Prioritization of LDTs

In the draft guidance, FDA indicated that it would commission an advisory panel to classify LDTs by risk based on the existing risk classification framework for medical devices and the Agency provided examples of different levels of risk associated with various diagnostic tests. FDA has indicated in public discussion that it believes that the majority of tests subject to FDA premarket review under the draft guidance would be moderate risk, but test classification remains unclear, creating substantial regulatory uncertainty, which has a chilling effect on investment in innovative tests.

The Coalition requests that FDA provide more details regarding the risk classification "public process," and the criteria and selection process for the "expert advisory panels." FDA should convene the advisory panels and issue a supplemental guidance for comment with more information regarding the risk classification categories and process, prior to the issuance of the final guidance. This supplemental guidance would reduce the unpredictability of future investment in innovative LDTs.

h. Test Modifications

Laboratories regularly modify test processes and improve test systems. Under the draft guidance, modifications that affect an LDT's performance or intended use would be subject to premarket review. The framework guidance explains that modifications to FDA cleared/approved tests would render the modified test subject to the requirements of the regulatory framework (if the modification affects device performance or intended use).

We request that FDA clarify whether the Agency expects that within 6 months of final guidance, all laboratories would be required to notify FDA and begin to report MDRs for all modifications of FDA-cleared/approved tests where the modification may affect performance or intended use. If so, this requirement would create an unreasonable and unfeasible burden on clinical laboratories in the U.S.

The draft guidances note that modifications would fall within the framework based upon the risk category under which the modified device falls. We believe that this standard is unreasonable. Whether a modification to an LDT should require pre-market review should depend upon the risk created by the modification—not the risk of the underlying diagnostic test itself. Otherwise, any modification to a high-risk diagnostic test would require pre-market review even if the modification does not change the intended use or impact the clinical performance of the test.

A more appropriate approach would be to reserve the premarket review process to major modifications such as a change in the intended use of the LDT in order to ensure least burdensome regulatory requirements. The Coalition recommends that FDA specifically limit additional premarket oversight to modifications that change the intended use of the test or have a clinically meaningful impact on the performance of the test. If a modification does not change the intended use and is not one that has a clinically meaningful impact on the performance of the

test, the laboratory should be required only to document the modification and the basis for determining that premarket review in the sponsor's internal records, which are subject to inspection.

i. Third Party Review

The Coalition is also concerned that the Agency underestimates the number and substantive burdens of any new oversight of the innovative tests, active clinical laboratories and potential sponsors that will be subject to its newly proposed requirements. The Coalition strongly supports the establishment of clear policies and appropriate training programs to enable the use of third-party certification to the maximum extent possible. In the draft guidance, FDA proposes a third-party premarket review process for Class II LDTs, but does not elaborate further.

FDA should provide additional details regarding the third-party review process, including the types of entities that could conduct the review, the criteria for such third party reviewer certification, the timelines under which the review would be conducted, how such reviewers will be trained to ensure consistent application of FDA requirements, and any fee requirements. In doing so, it is critical that the Agency clearly define these essential elements, which these certifying entities will be expected to implement under their new role as accreditors for inspections or as third party reviewers of pre-market submissions for FDA, in advance of the new laboratory compliance requirements. This is important in order to minimize or prevent redundant regulatory burdens stemming from compliance with QSR in addition to ongoing compliance with CLIA and state quality system requirements as well as pre-market review requirements under applicable state law. FDA should also identify which interested parties will the agency work with.

j. LDTs for Rare Diseases: Definition of Rare Disease

Under the draft guidance, FDA would continue to exercise enforcement discretion toward "LDTs used for rare diseases," defined as those tests for which the number of persons that *may be tested* is fewer than 4,000 per year. This draft definition is clearly insufficient, since it captures *rarely performed* tests rather than tests *for rare diseases*. Therefore, the Coalition proposes that FDA correct its approach, and use a definition that would exempt LDTs used for rare diseases, by adopting a definition that is tied to disease prevalence rather than the number of tests performed. The appropriate prevalence for the definition of a rare disease is already provided by the Orphan Drug Act as 200,000 or fewer in the United States, and is used for the designation of drugs and biologicals as orphan drugs.

The HDE (Humanitarian Device Exemption) definition is not appropriate because it was developed considering application to devices such as those implanted in the body. *In vitro* diagnostics are not implanted in the body and are commonly used to identify candidates for drug therapy, so the orphan drug definition seems a more appropriate standard for a rare disease population than the HDE definition. The FDA should work with stakeholders to develop the appropriate definition for rare disease, particularly in oncology where genomics is leading to new refinement of disease categories.

k. LDTs for Unmet Needs: Healthcare System Requirement

Under the draft guidance, FDA would continue to exercise enforcement discretion toward "LDTs for unmet needs." To fit within this category, LDTs must be developed and used in a health care facility laboratory. The draft guidance document explains that "healthcare system" refers to a collection of hospitals that are owned and operated by the same entity and that share access to patient care information for their patients.

FDA has stated in public discussions that it predicated this exemption on the testing being performed as part of a hospital organization with the view that the affiliation, increased coordination of care, and joint responsibility for the diagnostic test performance and the therapeutic care of the patient mitigates risk. However, there is no evidence that laboratories in health care facilities are any different from other laboratories, and no evidence that risk related to the diagnostic is mitigated simply because responsibility for the diagnostic test performance and the therapeutic care of the patient is shared based on ownership arrangements or shared health records.

Therefore, we urge FDA to substantially narrow the definition of "health care system." Using the same definition or, worse, a broader definition, would enable and encourage large academic institutions that perform thousands of tests to continue to develop and offer tests that would not be held to the same quality and safety standards as others in the laboratory industry. The Coalition believes that if a test fits the definition of unmet medical need, then it should not be denied to a patient merely because the laboratory offering the tests is housed in an independent facility rather than a health system.

l. FDA Resources to Implement the Proposed Framework

The draft guidance documents do not discuss the cost of the proposed framework and the regulatory burden for laboratories, as would be required by notice and comment rulemaking. The Coalition is concerned that the FDA drastically underestimates the challenges associated with translating the existing medical device regulatory processes to oversee services performed by individual laboratories.

Today, there are thousands of lawfully marketed LDTs performed by clinical laboratories to give providers access to data that enable the development of individualized, patient-specific plans of care. Moreover, the numbers of clinical laboratories across the country offering LDTs for molecular markers alone are easily estimated to number in the hundreds, if not thousands. This would translate into potentially tens of thousands of premarket submissions to the FDA. We believe that the proposed framework creates a high possibility, even with a protracted timeframe for implementation, that the Agency would burden its limited staff (even if the review staff doubled) with a growing backlog of premarket submissions, inhibit insurance coverage and payment, stymie further innovation and investment, and restrict or unreasonably delay patient access to innovative tests.

Without a regulatory impact and regulatory flexibility analysis, the regulatory burden and the appropriateness of the framework are difficult to assess. FDA should conduct a cost analysis as required for every rulemaking to determine the resources that would be required to implement

the LDT regulatory framework. The agency should also conduct a cost-benefit analysis of the proposed framework to ensure that the new regulatory burden to be imposed on an innovative industry is justified by the risk that the industry poses to consumers.

CONCLUSION

The Coalition remains committed to working with the FDA to ensure that patients have access to timely, accurate and reliable testing that can improve patient outcomes and reduce healthcare resource utilization, while at the same time supporting innovation and investment in increasingly targeted diagnostics and related therapeutic products. Our comments are intended to identify areas where the current LDT oversight proposal falls short of establishing a flexible and balanced approach to addressing advanced diagnostics products. Our intent is to support the ongoing dialogue with FDA and to provide specific recommendations that recognize the appropriate role of CLIA and provide regulatory clarity to clinical laboratories who support treating physicians and patients.

The Coalition agrees that appropriate regulation of *in vitro* diagnostic testing is essential to assuring patient safety and public health and to fostering public confidence in diagnostic testing. At the same time, continued innovation is possible only if the FDA provides clear, predictable, and reasonable standards for test developers that permit physicians and patients to rely upon advanced diagnostics to better guide treatment. The Coalition urges the FDA to more specifically define the important differences inherent to *in vitro* diagnostics and identify the most appropriate and least burdensome application of the statutory standards for evidence that would be considered reasonably sufficient to establish the "safety" and "effectiveness" of *in vitro* diagnostics.

The Coalition strongly supports a risk-based framework for the oversight of LDTs based chiefly on the risk of the information derived from the use of the test result in clinical practice, but for such a framework to support public health without doing more harm, FDA must address many substantive issues and unresolved questions before it finalizes its framework for regulation of LDTs. Unless such key open issues are resolved appropriately and in a timely fashion in advance of compliance requirements, it is unreasonable to expect that laboratories can comply effectively with the FDA's proposed new requirements. Likewise, it is critical that stakeholders have an opportunity to comment on how the Agency intends to resolve the open issues.

Finally, we urge the Agency to address the issues raised in this comment letter before issuing a final guidance. This would enable the kind of productive dialog necessary to establish a framework that provides regulatory certainty in a least burdensome manner and supports public health without unreasonably stifling innovation and investment in these technologies that are so critical to advancing clinical care.

We appreciate your consideration of our comments and we look forward to continuing our mutually constructive dialogue with the Agency on these issues specifically, and more generally on issues related to the oversight of laboratory developed tests. If you have any questions about our comments, please contact on behalf of the Coalition for 21st Century Medicine, Sheila Walcoff at 301-355-6226 (Sheila@goldbugstrategies.com) or Mitch Nelles at 415-287-2374 (mnelles@CareDxInc.com).

Sincerely,

The Coalition for 21st Century Medicine

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