



## **AdvaMedDx's Comments on 21<sup>st</sup> Cures-Request for Feedback: A Modernized Framework for Innovative Diagnostic Tests**

AdvaMedDx appreciates the extensive efforts and outreach by Chairman Upton, Representative DeGette, and the Energy and Commerce Committee (or "Committee"). The diagnostics industry is a cornerstone of the modern health care system, providing vital information at every stage from screening to diagnosis to selection of treatment. Rapid advances are being made that are paving the way for more personalized, targeted patient care. At the same time, there have been rapid changes proliferating in the complexity, risk, and marketing of laboratory developed tests (or "LDTs") and the regulatory status quo has been universally recognized as insufficient. The current two-tier regulatory system that differentiates between LDTs and traditional manufacturer developed tests solely on the basis of the type of developer, without regard to patient risk, is fundamentally unsustainable and must be modernized to support the public health and promote innovation of new safe and effective diagnostics.

Our member companies produce advanced, *in vitro* diagnostic tests that facilitate evidence-based medicine, improve quality of patient care, enable early detection of disease and reduce overall health care costs. Functioning as an association within AdvaMed, AdvaMedDx is the only multi-faceted, policy organization that deals exclusively with issues facing *in vitro* diagnostic companies in the United States and abroad. Our membership includes manufacturers engaged in the development of an array of critical technologies supporting the advancement of public health in a variety of health care settings, including laboratories, hospitals, doctor's offices, clinics, and the home.

Maintaining two very different oversight mechanisms for tests that are the same from the perspective of patient safety is bad public policy, provides an opportunity to use tests in clinical settings without sufficient clinical data, and stifles investment in high quality products that can stand up to FDA review. It is imperative that the Food and Drug Administration (FDA or Agency) adopt a risk based regulatory approach for all diagnostics, regardless of where a test is developed. We commend the Committee for its focus on ways to support patient care and robust product development while ensuring that well recognized gaps in oversight are addressed. We believe these considerations should be central to discussion during the current open public stakeholder comment period. Imposition of a regulatory system for tests (i.e., LDTs) can be expected to come with some disruption, but we believe FDA can balance both patient safety and continued and future innovation through appropriate risk based oversight. Patients deserve no less.

AdvaMedDx appreciates the opportunity to provide feedback on this important topic of a modernized diagnostics regulatory framework. We welcome further dialogue on the questions posed in this request for feedback (December 2014) and exploration of ways to support new diagnostic product development. FDA has made great strides in improving the regulatory process for diagnostics, and additional efforts to improve flexibility and support efficient, timely review to aid all IVD innovators, whether LDT or traditional developers, can and should accompany current efforts to implement a risk based framework for LDTs.



### **1) LDTs are a Subset of IVDs, Not Services— Distinct from Practice of Medicine**

A test is a test and presents the same risk for patients regardless of whether it is developed by a manufacturer or a laboratory. Potential harms to patients whose tests return incorrect results include unnecessary treatments with their accompanying costs and side effects and treatment delay or failure to obtain appropriate treatment, all of which lead to worse outcomes for those patients.

FDA has regulatory authority over LDTs as it does with all diagnostic tests (otherwise referred to as “*in vitro* diagnostics” or “IVDs”). Like other IVDs, LDTs are a subset of devices under the Food Drug and Cosmetic Act (“FDCA” or “Act”) and are subject to regulatory oversight by FDA. FDA has the authority to regulate all diagnostics, whether made by manufacturers or clinical laboratories. Tests present the same risk/benefit profile for patients no matter where a test is made.

We note that new terminology for LDTs, e.g., laboratory developed “service” or “procedure,” does not change their status under the FDCA. LDTs are medical devices, not a service. Under the Act, medical devices include any article comprised of “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.” All LDTs meet this definition as collections of “reagents, instruments, and systems” into an article for the same intended use. The only distinction between IVDs and LDTs is this collection of reagents, instruments, and systems occurs at a laboratory rather than a traditional manufacturing facility. This does not affect FDA authority of the article, which is irrespective of where it is made. Furthermore, assembly of 2 or more medical devices creates a new medical device. Developers may not circumvent regulatory oversight when they are manufacturing medical devices for purposes of the Act.

Physicians utilize IVDs in the care of their patients, but the IVDs themselves are not the practice of medicine. The results of the tests are used in the practice of medicine. For example, an x-ray machine is a device regulated by FDA. Reading and interpretation of an x-ray is the practice of medicine. Physicians are free to use their expertise and judgment in the use of the test results for the care of their patients. The argument that laboratory developed tests are services or the practice of medicine has been presented at different times and has been considered and rejected by both FDA and the Centers for Medicare and Medicaid Services (CMS).

### **2) LDTs, Like other Diagnostics Tests, are Medical Devices Regulated by FDA**

Per our discussion in response 1, a test is a test and presents the same risk for patients regardless of whether it is developed by a manufacturer or a laboratory. Potential harms to patients whose tests return incorrect results include unnecessary treatments with their accompanying costs and side effects and treatment delay or failure to obtain appropriate treatment, all of which lead to worse outcomes for those patients.

FDA has regulatory authority over all diagnostic tests (or IVDs). IVDs are devices that are used in laboratory analysis of human samples and include commercial test products and instruments used in testing, among other things. Medical devices include any article comprised of “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.” Diagnostics



tests are produced by manufacturers for distribution to laboratories and other users, by laboratories for distribution to additional laboratories, or produced and used in a single laboratory for use only within that laboratory (the latter two are treated as LDTs for purposes of FDA's proposed framework). IVDs may be used in a variety of settings, including a clinical laboratory, a physician's office, or in the home. It is important to note that the test is separate and distinct from the laboratory personnel's following of good laboratory practices governing testing, which must be implemented by all laboratories that use LDTs and/or FDA approved or cleared tests.

The 1976 Medical Device Amendments require FDA to review the safety and effectiveness of all medical devices, specifically including diagnostic tests. As a category of diagnostics, LDTs are subject to the provisions of the FDCA and FDA regulation that require assurance of safety and effectiveness for diagnostics.

To date, however, FDA has exercised enforcement discretion for LDTs, meaning that FDA has not enforced applicable regulations with respect to these tests and has not been reviewing LDTs to assure safety and effectiveness. LDTs also have not been subject to numerous other aspects of FDA regulation that are designed to protect patients. When FDA began regulating medical devices, LDTs generally were relatively simple, low-risk tests and FDA exercised enforcement discretion by not regulating them. Now, LDTs encompass even the most advanced molecular diagnostics, such as higher risk tests that are essential for safe and effective use of cancer therapeutics or a critical determinant in the treatment of serious, life-threatening diseases. In order to assure access to safe and effective LDTs, the FDA has announced its plans to exercise its existing enforcement discretion authority over LDTs through implementation of a risk based regulatory framework.

### **3) *Implementing FDA Risk Based Approach for All Diagnostics***

AdvaMedDx has long called for FDA to modernize its regulation by ensuring risk based regulation of all diagnostics, regardless of where they are made. As it does for all medical devices, FDA regulates diagnostic tests according to risk. Risk posed to a patient is irrespective of where a test is developed. The classification process is well described in the FDCA and its codified regulations. For diagnostics, risk assessment considers harm that could occur if test results are incorrect. The majority of diagnostics are low- and/or moderate-risk devices based on the nature of the claims made for them (i.e., intended use), and therefore, respectively Class I and II devices. Therefore, the majority of diagnostics does not require premarket approval (PMA) and are subject to the premarket notification (or 510(k)) process. We also note that newer regulatory tools such as the *de novo* 510(k) process have allowed for improved, appropriate risk based review of tests in addition to the traditional 510(k) process.

Consistent with AdvaMedDx's approach, FDA proposes a risk based, phased-in approach aimed to support both innovation and the public health. In its proposed framework, FDA has indicated that it will take a risk based, phased-in approach that appropriately focuses the Agency's resources on tests that pose the highest risk to patients. Further, FDA plans to phase in this oversight over a minimum of nine years following finalization of the LDT guidance. In addition to focus on tests that pose higher risk to patients, we note that FDA should strive to expedite patient access to lower risk tests—regardless of where made—by more efficient use of premarket review process, including additional exemptions for well-established tests.



We note that FDA includes helpful examples of risk classification factors in its proposed LDT framework guidance (e.g., Is the device intended for use in high-risk disease/conditions or patient populations? Is the device used for screening or diagnosis? What is the nature of the clinical decision that will be made based on the test result? Does the physician/pathologist have other information about the patient to assist in making a clinical decision? Are there alternative diagnostic and treatment options available to the patient?).

Higher risk tests generally comprise tests where a false result could lead to incorrect and harmful clinical management, an unnecessary invasive procedure, or failure to follow up a serious condition. Examples include tests for cancer diagnosis, tests that directly or very strongly influence management of serious disease, tests for serious or fatal communicable diseases and most companion diagnostics. The underlying factor for determining higher risk tests is the nature of the claims made for them (i.e., intended use). These tests are distinguished from tests where there are multiple findings used to direct clinical management and where each finding has a specific weight in disease management. They are also distinguished from most tests used to monitor already detected and diagnosed disease and genetic tests where the phenotype is already known and is now being confirmed genetically. These tests are also distinct from low-risk, well-established tests such as cholesterol, iron, and nicotine as well as urine and blood collection kits.

Apart from considerations of risk classification, AdvaMedDx has long reiterated that efforts must be undertaken to assure that tests should be cleared or approved through an approach where the data submission requirements are commensurate with the level of risk of the test. With respect to specific application of risk based oversight for all diagnostics, FDA can and should consider:

- 1) Clinical use of a test (risk associated with how the test is used in the treatment of patients)—e.g., seriousness or prevalence of the condition, prevalence of condition, reversibility of intervention, or standalone use (not supplementary to other clinical information);
- 2) Novelty of analyte (the substance that is undergoing analysis or is being measured);
- 3) Novelty of technology (or test platform);
- 4) Experience or training of the person performing the test; and
- 5) Factors that reduce or mitigate risk—e.g., scientific information, literature, general and/or special controls.

The first four considerations are risk elements. Data that mitigates risk should be considered as available for all four categories and may be different (e.g., literature for 1 and 2, experience of FDA for 3, human factors studies/design elements for 4).

The last consideration is of particular note as FDA specifically recognized in its draft guidance that literature may be considered to support clinical validity. We strongly support FDA embracing this acceptable source of valid scientific information to promote investment and innovation for diagnostics as part of an overall efficient, risk based approach to regulation. Any and all factors that reduce or mitigate risk, including already existing sources of information (e.g., studies in peer-reviewed journals, outside of U.S. data), should be considered in the regulatory review process. Also, FDA must ensure its statutory duty is met to apply the “least burdensome concept” by appropriate reviewer training to require only the evidence necessary to evaluate submissions.



#### **4) *Ensuring Safe and Effective Diagnostics Under Flexible, Risk Based Approach***

FDA should oversee the safety and effectiveness of all diagnostics, including LDTs. The degree of regulation needed to ensure the safety or effectiveness should be determined by the risk devices present to patients. Tests present the same risk/benefit profile for patients no matter where a test is made.

With respect to demonstrating safety and effectiveness, the main elements in FDA's review of diagnostics are analytical and clinical validity. This is specific to diagnostic tests with regard to analytical and clinical performance under the FDA review process. Analytical validity refers to the accuracy of a test in detecting the specific characteristics that it was designed to detect – for example, the presence or absence of a particular gene or genetic change. This is often measured by sensitivity, specificity, detection, precision, and repeatability. Sensitivity refers to how often the test is positive when the target is present, and specificity refers to how often the test is negative when a target is not present. Clinical validity refers to how well the target being analyzed is related to the presence, absence or risk of a specific disease or disorder. This is often measured by sensitivity and specificity. Sensitivity refers to how often the test is positive when the disorder is present, and specificity is how often the test is negative when the disorder is not present. Assurance of both analytical and clinical validity is essential to patient safety. By way of illustration, a test can be very accurate but not clinically valid and present significant potential of harm to patients.

As previously referenced, all efforts must be undertaken to assure that tests are cleared or approved through an approach where the data submission requirements are commensurate with the level of risk of the test to support reasonable assurance of safety and effectiveness. What is sufficient for purposes of a diagnostics submission, for example, should consider risk associated with diagnostics (e.g., clinical use of the test), novelty of analyte, novelty of technology, experience or training of the person performing the test, and any and all factors that reduce or mitigate risk, including already existing sources of information (e.g., studies in peer-reviewed journals, outside of U.S. data). A least burdensome approach must be ensured for diagnostics review to appropriately align evidence requirements with risk associated with the diagnostic test. FDA must ensure reviewer training and apply its "least burdensome concept" to require only the evidence necessary to evaluate all IVD submissions and avoid inflexible, excessive or redundant requirements.

#### **5) *Striking Improved Premarket and Postmarket Balance To Support Diagnostics***

Implementation of a transitional approach for emerging diagnostics is specified in the current user fee agreement. Presently, discussion has been productive and industry looks forward to implementation of a transitional approach as part of the FDA's arsenal of innovative programs to support new diagnostics innovation in the U.S. Diagnostics, including molecular diagnostics, represent in many ways the future of healthcare. They are key to personalized care. They assist in rapid and precise diagnosis, in targeting existing treatments, and in pointing the way to the development of new treatments. Improved premarket/postmarket balance will go far to support timely access to emerging diagnostics and the transitional approach described in the user fee agreement is an important step toward spurring development and availability of these new diagnostic technologies. While such a program is currently intended for traditional IVD developers, this could provide a helpful pathway for interested and qualified LDT developers. The intent of this initiative is to optimize the delivery of new and innovative IVDs for



patients, better harness the latest science, and encourage the development of emerging technologies by sponsors who commit to conduct agreed upon postmarket data collection for their tests.

**6) *Assessing Modifications as Critical Part of the Regulatory Process***

Regulatory requirements should not depend on where a test is developed. Tests present the same risks to patients, irrespective of developer. Changes to tests could significantly affect safety or effectiveness and therefore require a new submission. FDA has provided guidance (K-97) on the decision making process to determine when a change to a Class II medical device requires a new 510(k) submission. Guidance is also provided for when a PMA supplement is required for a Class III device. When submissions for a change are required, these changes must be cleared or approved by FDA prior to product access. Quality systems processes play an important role in deciding whether a new submission is required. This importantly underscores that innovators must develop and implement a quality system that addresses appropriate practices through the lifecycle of a device from development through the postmarket phase, including how to verify, document, and implement change. FDA seeks to address this quality systems gap in LDT oversight through its risk based framework to equally assure the ongoing safety and effectiveness of LDTs and other IVD tests. The FDA Quality System Regulation's (QSR) requirements provide a solid basis for assuring that device modifications are appropriately evaluated via risk management prior to marketing and that the methods and results of evaluation are well documented. In this way, ongoing timely innovation and public health are supported throughout the product lifecycle.

**7) *Providing Appropriate Information in Diagnostics Labeling***

As previously referenced, a two-tiered regulatory system is bad public policy, fails to promote innovation in safe and effective diagnostics, and is not in the best interests of the public health. However, a risk based regulatory framework can accommodate differing labeling needs for LDT developers and traditional developers. In the case of an LDT, FDA requirements related to labeling remain important. All the detailed labeling requirements outlined in 21 CFR § 809.10 may not be necessary, however, for tests that are manufactured for use solely in-house, where the developer and testing site are the same. More tailored specific protocol language for that site could provide sufficiently understandable instructions to the laboratory employee as the test would only be available at that laboratory while assuring that performance and other relevant information about LDTs is still made available to the public. This flexibility would likely be appropriate while ensuring robust premarket/postmarket oversight that addresses key recognized public health gaps for LDTs and ensures availability of accurate, truthful information about available tests.

**8) *CMS Oversight of Laboratories is Distinct and Not a Substitute for FDA Oversight of Diagnostic Tests***

Laboratories are regulated by CMS under CLIA – the Clinical Laboratory Improvement Amendments of 1988. CMS itself has acknowledged the clear differences between CLIA oversight of laboratories and FDA oversight of diagnostic tests, noting FDA's unique role, scope, and qualification to assure the safety and effectiveness of tests. CLIA regulations focus on laboratory practices, including testing procedures, certification, and personnel. As CMS has explicitly stated, CLIA does not regulate the safety and effectiveness of tests and is not a substitute for FDA oversight. Critical features of FDA oversight are not



covered under the CLIA program, which regulates good laboratory practices and is required for all laboratories performing tests, including both FDA approved/cleared tests and LDTs. Furthermore, CMS does not have the expertise or resources to oversee LDTs in the same manner as FDA. Unlike FDA oversight of diagnostics, CLIA:

- Does not regulate the safety and effectiveness of diagnostic tests;
- Does not require premarket review of tests;
- Does not require demonstration of clinical validity (whether the test is meaningful for clinical decision making);
- Does not require systematic adverse event reporting;
- Does not have a process for corrections or recalls.

Under FDA's proposed framework to address gaps and ensure transparency on the scope and use of LDTs, LDT developers will also need to provide information to the public on available LDTs and associated facilities. This is an important and critical step. Up to this point, this information has only been available for diagnostic tests that have listed their facilities or received clearance or approval from FDA.

Beyond critical oversight of the safety and effectiveness of tests, FDA's LDTs framework would require that, among other things, all LDT developers comply with medical device adverse event reporting requirements. Adverse event reporting enables necessary corrective action and helps to prevent injury and death by alerting the public when potentially hazardous devices are discovered. Analyzing adverse event reporting also enables detection of unanticipated events and user errors, monitoring and classifying of recalls, updating labeling information, and developing educational outreach. Using adverse event report data, FDA can detect problems previously unknown as well as problems with similar devices or device categories.

For years, stakeholders have recognized the inadequacy of current oversight of LDTs and called for FDA to enforce existing regulations that apply equally to LDTs as they do to all diagnostics. FDA and CMS are not alone in their recognition of gaps in the regulation of LDTs. In a landmark report by the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) *U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services*, FDA is called upon to "address all laboratory tests, regardless of how they are produced (i.e., as a commercial test kit or laboratory developed test)" in order to help close the gaps in oversight related to clinical validity and assure the appropriate use of laboratory tests. SACGHS cited various gaps related to oversight of laboratory testing that can lead to harms. Writing to the White House in 2012, 24 patient advocacy organizations called for FDA to publish draft guidance on LDT regulation. As one letter from numerous organizations stated, "[t]he promise that advanced diagnostics hold for patients is tremendous, but, at the same time, the increasingly pivotal role of these diagnostics in patient care makes it imperative that their safety and effectiveness is assured by the FDA prior to use." Various stakeholders from patient and consumer groups to healthcare professional societies support FDA action on LDTs and implementation of a risk based framework.

Despite these widely recognized gaps, we do expect specific discussion on how to best implement quality system requirements in clinical laboratories and who and how quality system inspections might be conducted for clinical laboratories developing LDTs. FDA and CMS via CLIA have different roles and



regulatory goals. FDA regulation addresses the safety and effectiveness of the diagnostic tests themselves and the quality of the design and manufacture of tests. CLIA regulates the quality of the clinical laboratory. We note there may be opportunities, however, to implement a quality system for LDTs that leverages CMS current oversight of laboratories. We understand that FDA plans to implement QSR in an incremental, phased approach and there will be further discussion on how to best move forward. In a positive development, we note that new and helpful resources are now available from the Clinical and Laboratory Standards Institute, in addition to FDA existing resources, to help laboratories working to implement a quality system for LDTs that best leverages existing laboratory practices and complies with FDA quality systems regulation. However, we note that implementation of a quality system for LDTs to support safety and effectiveness through the continuous product lifecycle from test development through the postmarket phase is essential and not currently in place for LDTs under CLIA.

#### **9) *Spurring Access to Specialized Diagnostic Test Categories, Particularly Rare Disease***

We strongly concur with clinical laboratories that all efforts should be made to assure patient access to specialized test categories (i.e., rare diseases and/or rare usage). As with all diagnostics, FDA should continue to leverage existing accelerated pathways and seek to continuously improve the regulatory process for diagnostics. While we will provide more detailed comments to the FDA draft LDT guidance docket, we note that FDA has proposed several categories of LDTs for exemption from premarket review, including low-risk tests, rare disease testing, traditional LDTs, and unmet needs LDTs. These categories are explicitly outlined by FDA in its draft guidance proposal and cover a wide scope of products that would be exempt from premarket review while assuring key premarket and postmarket controls are in place for these products. AdvaMedDx supports FDA's intent in continuing to exercise enforcement discretion in specific circumstances in which LDTs play a meaningful and needed role in patient care, and risks to patients are minimized or appropriately balanced against patient needs even in the absence of FDA premarket review. Similarly, we support discussion of other mechanisms to support all diagnostic innovation, regardless of where the test is made.

We draw attention by the Committee to a significant policy problem in need of attention. FDA's application of the rare disease pathway, Humanitarian Use Device (HDE), has been a significant obstacle for the development of diagnostic devices for rare diseases and must be improved to serve as a meaningful pathway for diagnostic developers for rare disease. Under the FDCA, an HDE is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 4,000 individuals in the U.S. per year. To obtain approval for an HDE, companies submit an HDE application to FDA, which has special requirements. This hard cap at 4,000 individuals is excessively restrictive. Provisions related to the statutory cap continue to be interpreted very narrowly by FDA and block the development of diagnostic devices for rare diseases and conditions. There is no scientific evidence behind the original statutory 4,000 person cap. In particular, it is a significant hurdle for the development of diagnostic devices for rare diseases to demonstrate the number of patients that would be subject to diagnosis by the device, rather than the number of individuals affected or manifesting the rare disease. If a diagnostic test were developed to diagnose patients with a condition that manifests in 4,000 people or less per year, it is quite likely that physicians would prescribe the test more than 4,000 times a year to diagnose those with the rare disease.

To address this limitation, we recommend flexibility to FDA to allow HDEs that benefit patient populations that exceed the 4,000 limit. Applicants would be required to demonstrate that the severity



of the disease or condition is such that the public health requires a greater availability of the device to treat or diagnose that population. This provision clarifies that in the case of IVDs, the 4,000 person limit does not apply to the number of tests needed to treat or diagnose a specific patient population.

With respect to the current emergency use authorization process, we note it has yielded a number of new tests (e.g., Ebola most recently) to meet public health needs and was greatly improved when, on March 13, 2013, President Obama signed into law the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA). PAHPRA built on the availability and use of an unapproved medical product (such as a diagnostic test) and the unapproved use of an approved medical product during or before an emergency to diagnose, treat, or prevent a serious life-threatening disease. Other available FDA pathways to meet unmet needs and promote development of emerging diagnostics should be explored when appropriate and vigorously placed in use in the review process to support diagnostics innovation and the public health. Improving the HDE process for diagnostics tests should be first in order if we are to support development of rare disease diagnostics for patients.

#### ***10) Transition Process for Diagnostics Under a Modernized Regulatory System***

As articulated in earlier responses, we believe FDA should oversee the safety and effectiveness of all diagnostics, including LDTs. A test is a test and presents the same risk for patients regardless of whether it is developed by a manufacturer or a laboratory. Potential harms to patients whose tests return incorrect results include unnecessary treatments with their accompanying costs and side effects and treatment delay or failure to obtain appropriate treatment, all of which lead to worse outcomes for those patients.

The degree of regulation needed to ensure the safety and effectiveness of diagnostics should be determined by the risk that tests present to patients rather than by arbitrary grandfathering or carve-outs that do not take into account patient risk, particularly of potential harms resulting from the use of higher risk tests. Tests present the same risk/benefit profile for patients no matter where a test is made.

We commend FDA's commitment to the thoughtful development of a proposed risk based LDT oversight framework that reflects a number of features to ease transition for the laboratory community and support test continuity. Key elements of the proposed framework include a risk based approach, phase in over a 9-year time frame, and continued use of enforcement discretion for many LDTs to minimize disruption and support test continuity. Also, tests undergoing premarket review may notably remain on the market during the review process, which will aid transition of tests under FDA oversight.

We strongly support transitioned requirements to facilitate good faith efforts for laboratories. Furthermore, we would encourage meaningful discussion of ways in which laboratories can be aided in this endeavor and additional measures that might be implemented for diagnostics at large to support robust innovation now and into the future. As previously referenced, opportunity is also ripe as part of FDA regulatory efforts aimed at higher risk tests and implementation of an overall modernized framework to consider appropriate additional exemptions from premarket review of low-risk, well-established diagnostics tests regardless of developer. This would best leverage FDA resources and help pave the way for an overall improved risk based regulatory process for all diagnostics.



Other available FDA pathways to promote development of new cleared and approved diagnostic technologies, such as a transitional approach for emerging diagnostics, should be implemented to aid the regulatory process and support good faith efforts by developers of innovative diagnostic technologies.

### ***11) Overall Incentives to Encourage Development of New or Improved Diagnostics Tests***

In summary, AdvaMedDx has long advocated for a flexible, risk based approach for all diagnostics. Maintaining two very different oversight mechanisms for tests that are the same from the perspective of patient safety is bad public policy, provides an opportunity to use tests in clinical settings without sufficient clinical data, and stifles investment in high quality products that can stand up to FDA review. It is imperative that the FDA adopt a risk based regulatory approach for all diagnostics, regardless of where a test is developed. We believe a proper oversight system that balances both patient safety and continued and future innovation can be accomplished under appropriate risk based oversight by FDA.

While FDA has made tremendous progress in improving the regulatory process for diagnostics and its recent proposed framework for LDTs is a critical step forward, we have noted opportunities to improve the overall diagnostics landscape. In addition to focusing on tests that pose higher risk to patients, FDA should strive to expedite patient access to lower risk tests—regardless of where made—by more efficient use of the premarket review process, including additional exemptions for well-established tests. Efforts must also be undertaken by FDA to ensure that data submission requirements are commensurate with the level of risk of the test. Reviewer training continues to be critical with respect to FDA application of a least burdensome approach to ensure requiring only the evidence necessary to evaluate all IVD submissions. FDA should also continue to leverage available pathways to support bringing new safe and effective products to market and seek to continuously improve the regulatory process for all diagnostics.

In particular, we welcome discussion of how to best assure patient access to rare disease diagnostics. FDA's application of the HDE pathway has been a significant obstacle for the development of diagnostic devices and must be improved to serve as a meaningful pathway for developers of rare disease diagnostics.

AdvaMedDx appreciates the opportunity to work with Chairman Upton, Representative DeGette, and the Energy and Commerce Committee on the 21st Century Cures initiative. We greatly appreciate the Committee's commitment to improving patient care and assuring a modernized diagnostics regulatory framework. We would welcome additional dialogue on any of the concepts presented in response to this request for feedback on the questions posed and are happy to answer any questions on these or other diagnostics issues. U.S. diagnostic innovation is shaping the lives of Americans as well as the greater global community. As innovators, our member companies know well that robust investment in safe and effective diagnostic technologies is critical to the timely development of life-changing diagnostics, treatments, and cures, and sound public policy is essential to sustaining that investment by promoting public health and innovation.