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EXAMINING THE REGULATION OF DIAGNOSTIC TESTS

AND LABORATORY OPERATIONS

TUESDAY, NOVEMBER 17, 2015

House of Representatives,

Subcommittee on Health,

Committee on Energy and Commerce,

Washington, D.C.

The subcommittee met, pursuant to call, at 10:00 a.m., in Room 2322, Rayburn House Office Building, Hon. Joe Pitts [chairman of the subcommittee] presiding.

Present: Representatives Pitts, Guthrie, Barton, Shimkus, Murphy, Burgess, Blackburn, Lance, Griffith, Bilirakis, Long, Ellmers, Bucshon, Brooks, Collins, Green, Capps, Butterfield, Castor, Schrader, Kennedy, Cardenas, and Pallone (ex officio).

Staff Present: Rebecca Card, Assistant Press Secretary; Carly McWilliams, Professional Staff Member, Health; Graham

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Pittman, Legislative Clerk; Heidi Stirrup, Health Policy Coordinator; John Stone, Counsel, Health; Christine Brennan, Press Secretary; Jeff Carroll, Staff Director; Tiffany Guarascio, Deputy Staff Director and Chief Health Advisor; Samantha Satchell, Policy Analyst; and Kimberlee Trzeciak, Health Policy Advisor.

Mr. Pitts. The subcommittee will come to order. The chair will recognize himself for an opening statement.

Throughout the 21st Century Cures initiative, biomarkers, precision medicine, and targeted therapies were a few of the most consistently uttered terms and concepts. In order to advance each of them, we must establish a regulatory environment that fosters the development of, and access to, innovative, accurate, and reliable diagnostic testing. Such tests are increasingly important not only in diagnosing the onset of a specific disease or condition, but in determining the right course of treatment or procedure.

It goes without saying that tests providing information to a doctor or consumer are fundamentally different products than traditional medical devices, which actually deliver therapy to, or are implanted in, a patient. Nonetheless, while FDA has used its medical device authorities to review and oversee tests developed by outside entities that are then sold to laboratories, the agency has not actively regulated laboratory-developed tests, or LDTs.

Last year, a week after we held a roundtable downstairs that highlighted the importance of this very topic, FDA announced that it would no longer exercise such enforcement discretion and detailed how the agency proposes to apply its medical device authorities to LDTs.

Today, I am far less interested in litigating the boundaries of current FDA or CMS legal authority, but in hearing from our witnesses how such authority could be clarified or improved, understanding the unique and evolving nature of what is being regulated and each agency's area of expertise.

Response to a white paper the committee circulated at the end of last year asking these very questions, we heard from a number of labs and pathologists that FDA should only have a limited role, if any, in regulating a select set of tests as medical devices. The rest, in their opinion, should be overseen by CMS through an updated Clinical Laboratory Improvement Amendments program. This is despite the fact that CMS has stated that they do not have the resources, the expertise, or the willingness to take on what is being asked of them. I am eager to hear what Dr. Conway has to say on this matter.

We also received comments from a number of manufacturers, as well as over 40 patient groups, that FDA, not CMS, needs to be in the driver's seat, and that tests that have the same impact on a patient should be held to the same standards, regardless of who does the development. This is despite the fact that laboratories are uniquely nimble environments where pathologists continually modify and improve tests in ways that manufacturers cannot.

I am well aware that this has been at times a heated debate

with passionate advocates on both sides. With such a backdrop, I want to particularly commend the manufacturers, the laboratories, and other health care institutions that have been willing to roll up their sleeves and find as much common ground as possible through constructive dialogue, a willingness to compromise, and a pragmatic understanding of what a viable, modern framework entails.

I do not believe that imposing a new regulatory reality on an increasingly important component of our health care system via guidance is the best way to address these issues. These products warrant a regulatory system designed with them in mind. They should not be shoehorned into a system that was drafted in the 1970s.

This committee has clearly shown that we are willing and able to move complicated, comprehensive, bipartisan legislation. The discussion draft the committee circulated, along with the hearing notice, is of course not perfect, but it is a serious document based on significant consensus, and I would ask that all of the stakeholders out there, including our two distinguished witnesses, help us improve it as the process continues.

With that, I would like to think Dr. Shuren, a frequent, always welcome visitor, as well as Dr. Conway, for their willingness to testify today, and I look forward to working with them on these issues going forward.

Mr. Pitts. And I now recognize the ranking member, Mr. Green, 5 minutes for his opening statement.

Mr. Green. Thank you, Mr. Chairman, and thank you for calling this hearing today, and I want to welcome our witnesses from the FDA and the CMS.

The role of diagnostic tests in our health care system has changed dramatically since Congress passed the medical device amendments in 1976 and added in vitro diagnostics to the device definition. It has been almost 4 decades, and the evolution of modern medicine and the advancement of science has surpassed what everyone could imagine at the time. The enthusiasm around precision medicine is high, and the potential of diagnostics to further transform the treatment of disease is limitless.

When the FDA first began regulating medical devices, applicable regulatory requirements for lab-developed tests, or LDTs, were not enforced because they were relatively simple tests, generally combined the local labs, and frequently used for rare conditions.

Today, LDTs have increased in complexity and availability. They are often used to diagnose serious medical conditions, and many have major impact on patient care. Not only have LDTs become sophisticated, the role that these tests play in delivery of health care has expanded.

The Centers for Disease Control and Prevention estimated

that approximately 6.8 billion laboratory tests are administered each year. An analysis found that results from the clinical laboratory tests influence about 70 percent of health care decisions.

The clinical laboratory amendments of 1988 created minimum standards of quality for all clinical labs in the country. The Centers for Medicare and Medicaid Services, CMS, has jurisdiction over the program, and CLIA has successfully improved the quality of the clinical labs in accuracy of testing for nearly 25 years.

However, under CLIA CMS does not confirm the clinical validation of LDTs, meaning that they do not look as to whether it is a particular test accurately that identifies, measures, or predicts the absence or the presence of a clinical condition. These known gaps in oversight have been a source of concern to this committee and to the health care community at large.

Yesterday, the Food and Drug Administration released a report that included 20 case studies of problematic tests from labs that were following the minimum requirements of CLIA but proposed real risk to patients. In an area of so much promise and significance to patient care, the accuracy, reliability, and clinical meaningfulness of all diagnostic tests, regardless of where they are created, must be a top priority for health care providers, test developers, regulators, and lawmakers.

Last year, the FDA issued a draft regulatory framework to

phase in enforcement regulatory requirements, including premarket review, adverse event reporting for LDTs that pose greater risk to patients if their results are not accurate and reliable. And I appreciate FDA's efforts to ensure that tests are supported by rigorous evidence and that patients and health care providers can have confidence in their results.

That said, I share the opinion of my colleagues that legislation is both appropriate and necessary to modernize clinical laboratory diagnostic oversight. The legislative solution is surely the surest way to establish a framework that will be embraced by stakeholders, avoid litigation, extended uncertainty, and foster innovation of new clinical diagnostic tests.

The FDA's approach to this draft guidance let to a number of important questions, but the guidance documents also spurred a larger conversation about the overarching need to modernize oversight of these unique and increasingly important tests.

During the 21st Century Cures initiative, as part of the broad effort to close the gap between science of cures and how we regulate medical products, the committee hosted a roundtable on precision medicine and advances in diagnostic testing. The committee also released a white paper on diagnostic test regulation and received outpouring of feedback from stakeholders.

While all parties did not agree on all the principles, much

less specifics, it was abundantly clear that any regulatory framework for diagnostic tests must prioritize patient benefit and allow for continued innovation and investment through regulatory certainty and appropriate regulatory controls.

There is urgent need to establish clear and logical lines separating the practice of medicine and the actual conduct of the diagnostic tests and the development and manufacturing of diagnostic tests so that the promise of 21st century medicine can be fully realized.

Today, we will hear from FDA and CMS about each agency's respective role in the oversight and regulation of clinical laboratory tests. Members of the committee will have questions about the appropriate role of each agency and any updated framework, and how Congress can best promote robust investment and innovation while protecting patient safety.

Mr. Chairman, I look forward to hearing from our witnesses, and I yield back. Mr. Pitts. The chair thanks the gentleman, now recognizes Dr. Burgess in lieu of Chairman Upton, 5 minutes.

Mr. Burgess. Thank you, Mr. Chairman.

I appreciate the opportunity that we have before us with this hearing, but I do want to say at the outset, with everything else that is going on, this may be one of the most important and at the same time the most frightening concepts that is before the Congress right now. We are talking about a proposal that may not

just stifle but eliminate medical innovation, something which this country has excelled for decades, and we are also opening the door for the first Federal regulation of the practice of medicine, not the needles and IV solutions, the actual diagnostic thought processes that go in to practicing medicine.

Let me just say at the outset I do strongly believe in the potential of genomic medicine. I understand how important it is to really understand illness at a molecular level, quickly diagnose it, and get the treatment that is appropriate for the patient with a minimal amount of side effects.

A year-and-a-half ago when the President talked about precision medicine during his State of the Union address, I thought that was a very positive development. There are not many places where the White House and I agree on anything, but here was some common ground, and I took it to heart.

Laboratory testing produces the informational building blocks that are at the heart of precision medicine. As former Administrator Mark McClellan at CMS said, we have got to get the right treatment at the right time to the right patient.

We are not talking about test kits that are put in a box and shipped across State lines but medical procedures that are carried out by highly trained and qualified health professionals engaged in the practice of medicine.

As we discuss the oversight of laboratory-developed tests,

it is crucial that we do not slow innovation or create unnecessary regulatory hurdles. We have got to ask ourselves first, what is the problem that we are trying to solve, and is our response appropriate, and are there unintended consequences that could result?

Requiring premarket review by the FDA will impose new and arguably unnecessary requirements and costs on clinical laboratories, hospitals, and doctors. Although an additional review of certain tests may be warranted, I actually have a greater confidence in a CLIA-centric approach, but there are others--and certainly people on this committee--who suggested a different track. But it remains unclear to me how we can separate the practice of medicine from these laboratory processes, and if we cannot, are we effectively opening the door to the Federal regulation of the practice of medicine? I reject that notion and believe by segmenting this process out has to be the fundamental first step of any proposal.

Let me just reiterate I do want to be involved in this discussion. There is no question in my mind that CLIA can be improved. I was not a fan when CLIA came to my medical practice in 1988. I was not a fan of having to become a CLIA-certified location. I was not a fan of having to apply for a CLIA waiver. But since that time, I think arguably you can make the case that CLIA has been a useful enterprise.

Look, we want doctors and patients to benefit from clinically valid tests, and the current FDA proposal, as such, creates regulatory uncertainty that will not be a catalyst for innovation.

We talk a lot about the Administrative Procedures Act, we talk a lot about notice of proposed rulemaking. This is not coming through the normal regulatory process. It is coming as a guidance. My understanding is to be issued at the end of this year, and like it or not, there you have it.

But, you know, it is hard. On this committee I still retain that romantic notion that our government exists with the consent of the governed. In my mind that would not include issuing guidances, fiats that are expected to be followed, but rather, you go through the normal administrative procedures, hear people out, and make the best decision based on the information.

Thank you, Mr. Chairman. I yield back the balance of my time.

Mr. Pitts. The chair thanks the gentleman.

I now recognize the ranking member of the full committee, Mr. Pallone, 5 minutes for an opening statement.

Mr. Pallone. Thank you, Mr. Chairman. I want to also thank Dr. Shuren and Dr. Conway for being here today to discuss the regulation of lab-developed tests.

There has been a lot of discussion over how to appropriately oversee lab-developed tests, and it is important that, as the

committee considers this issue, we have a better understanding of the strengths and limitations of both FDA and CMS's authority in this area.

Congress gave FDA authority over lab-developed tests under the Medical Device Amendments in 1976, and at that time, most LDTs were relatively simple tests used more often for rare conditions. Since then, advances in technology and medicine have resulted in LDTs that are increasingly more complex, more readily available to physicians and patients, and used to diagnose and treat a wider range of diseases, including breast cancer and heart disease. LDTs are also increasingly used to provide personalized treatment such as through genetic tests that help physicians to detect the risk of certain diseases earlier or to choose more targeted therapies.

Unfortunately, many of these tests have not been reviewed or cleared by FDA prior to coming to the market to confirm that these tests are accurate, reliable, or provide clinically accurate results. This can result in patients going undiagnosed with certain medical conditions or undergoing treatment that is not medically necessary.

For example, tests have been developed to identify certain gene sequences that can help determine appropriate treatment for ovarian cancer. I am sure many members here are familiar with the example of OvaSure, which claimed to detect early-stage

ovarian cancer in high-risk women. This test, though, was not properly validated and was found to provide high numbers of false positive and false negative results, and this means many women who received a false positive result may have undergone unnecessary surgery to remove healthy ovaries, or some women may have gone undiagnosed after receiving a false-negative result.

Patients deserve to know that the test results they are relying on to diagnose or treat a condition is accurate, a comfort that they do not always have today. And as we have heard from many organizations, patients and their physicians should be able to trust the results of their tests, regardless of how or where a test is developed or performed. It does not make sense to regulate tests differently based on who develops them.

I also believe that we can provide patients and providers with this certainty without endangering or inhibiting the medical innovation that is occurring today. Scientific progress has been made to help facilitate the development and use of personalized medicine, which you all agree is the future of medicine, but this development can only be successful if we know that these complex, sophisticated tests are clinically valid.

So I am glad that today we will have the opportunity to better understand FDA and CMS's authority in this area and hear their perspective on what regulatory changes, if any, are needed to address the future development of lab-developed tests. And I

hope moving forward that both agencies will work with the committee on the discussion draft circulated today to ensure that any legislation that moves forward will ensure that LDTs are accurate, reliable, and safe for patients.

I yield back.

Mr. Pitts. The chair thanks the gentleman.

As usual, all the written opening statements of the members will be made part of the record.

That concludes the opening statements.

I would like to submit under U.C. request the following documents for the record: a November 16 letter from a number of organizations and laboratory directors, and a November 11 letter from organizations representing patients, advocates, caregivers, and health care professionals.

Without objection, so ordered.

[The information follows:]

********** COMMITTEE INSERT **********

Mr. Pitts. On our panel today we have two witnesses, and I welcome them, thank them for coming. First, Dr. Jeffrey Shuren, Director, Centers for Devices and Radiological Health, Food and Drug Administration, Department of Health and Human Services; and Dr. Patrick Conway, Deputy Administrator for Innovation and Quality, and Chief Medical Officer, Office of the Administrator, Centers for Medicare and Medicaid Services, Department of Health and Human Services.

Thank you for coming. Your written testimony will be made part of the record. You will each be given 5 minutes to summarize.

Dr. Shuren, you are recognized for 5 minutes for a summary.

STATEMENTS OF JEFFREY SHUREN, DIRECTOR, CENTERS FOR DEVICES AND RADIOLOGICAL HEALTH, FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES; AND PATRICK CONWAY, DEPUTY ADMINISTRATOR FOR INNOVATION AND QUALITY, AND CHIEF MEDICAL OFFICER, OFFICE OF THE ADMINISTRATOR, CENTERS FOR MEDICARE AND MEDICAID SERVICES, DEPARTMENT OF HEALTH AND HUMAN SERVICES

STATEMENT OF JEFFREY SHUREN

Dr. Shuren. Well, thank you, Chairman Pitts, Ranking Member Green, members of the subcommittee. Thank you for the opportunity to testify today.

We are excited about scientific developments in genomics and molecular biology that are leading to advances in health care, particularly in precision medicine. Getting the right treatment to the right patient at the right time, though, depends upon having accurate, reliable, and clinically valid tests. If not, we give the wrong treatment or we give no treatment, and patients get hurt.

FDA has been regulating in vitro diagnostics for almost 4 decades, and when such a test is made by a laboratory, we call it a laboratory-developed test, or LDT. And the law doesn't distinguish on who makes it. We regulate the test regardless of who makes that test. And we ensure that those tests are analytically and clinically valid.

Now, when we first started regulating IVDs, as a matter of

policy, we decided not to actively enforce existing requirements on LDTs because at the time they were generally simple, low-risk tests used on uncommon conditions in often a local setting, typically in a hospital for patients in that hospital. But over time they have come increasingly more complex, higher risk, they are used on common conditions like heart disease, and they may be offered on a national basis. In addition, we have been coming across increasing examples of problematic LDTs. We put out examples of 20 of them just yesterday, and there are others.

As a result of this, the problems we have seen and the increasing complexity, there have been calls on the FDA to actively enforce existing requirements that started in the 1990s, NIH and the Department of Energy. In the 2000s two advisory committees to the Secretary of Health and Human Services called on us to regulate. The Institute of Medicine has asked us to regulate.

So in 2007 we put out draft policy to begin to actively regulate a subset of LDTs, and what the lab community said is don't pick off tests one by one. Please put in place an overarching framework. So in 2010 we had a public meeting to get input, and we were told put in place a risk-based phased-in approach.

And then in response in October of last year we did just that. We put out draft policy to now put in place that framework. And what we heard from the lab community then, oh, no, there are no

problems with LDTs. We don't need FDA oversight of anything, maybe a little beefing up on CLIA but that is it.

And now, just a few months ago, we started to see several proposals come out from the lab community that now, for the first time, acknowledge that LDTs must demonstrate that they are analytically valid and clinically valid, that they should be subject to premarket review, at least moderate- and high-risk tests, the some modifications need to be subject to premarket review, that certain problems need to be reported to the government, and they need to be under a risk-based approach with a three-tier risk classification system. None of those are currently enforced on them today. They all exist under an FDA framework.

But what most of these proposals except one would do is it would create a duplicative program under CMS and a bifurcated system, leading to more inefficiencies, higher costs, and still putting patients unnecessarily at risk. For example, you can have a conventional manufacturer who makes an IVD we regulated. Now, a laboratory makes a big enough change to it, which laboratories do, and it is regulated by CLIA. Then the original manufacturer makes a change to that test and it bounces back to the FDA. So we will be stuck in a game of regulatory ping-pong, and the real loser here is patients.

Doctors and patients don't care about who makes a test. They

do care that their tests are accurate, reliable, and clinically valid.

Now, some labs have already been working with us, and we congratulate them for crossing that picket line. But our message in our invitation to the rest of the lab community is to put down the swords, that for the sake of our patients it is time to end the saber-rattling and instead partner with us moving forward.

Thank you.

[The prepared statement of Dr. Shuren follows:]

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Mr. Pitts. The chair thanks the gentleman, now recognizes Dr. Conway, 5 minutes for his summary.

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STATEMENT OF PATRICK CONWAY

Dr. Conway. Thank you, Chairman Pitts, Ranking Member Green, and members of the committee. Thank you for the opportunity to talk about our work at the Centers for Medicare and Medicaid Services related to ensuring accurate and reliable laboratory testing.

The Clinical Laboratory Improvement Amendments of 1988, commonly referred to as CLIA, of which CMS has primary jurisdiction, created minimum standards of quality for all clinical laboratories in the United States. CLIA successfully worked for approximately 25 years and has contributed to major improvements in the quality of clinical laboratories, promoted accurate testing, and improved patient safety.

As of July of 2015 there were roughly 250,000 laboratories that have registered with CMS and held CLIA certificates. CLIA responsibilities are divided between three agencies: CMS; the Centers for Disease Control, or CDC; and the Food and Drug Administration. CMS conducts laboratory inspections to make sure that laboratories have appropriate controls, expertise, training, and procedures to ensure that tests are accurate and reliable. CMS also approves accreditation organizations and manages the laboratory certification process. CDC conducts laboratory quality improvement studies that guide policy

determination and development of laboratory practice guidelines.

FDA's primary responsibility under CLIA is to classify clinical tests into one of three categories--waived, moderate complexity, and high complexity--based on their level of complexity and risk to patients. FDA also has a critical role in determining clinical validity of tests and premarket evaluation. Standards that laboratories must meet under CLIA are based on the complexity of the tests they perform. Laboratories that perform more complex must meet higher standards.

Laboratories that perform moderate- and high-complexity tests must meet requirements on quality assessment, quality control, personnel qualifications and education, general laboratory systems, and proficiency testing, among others. Laboratories that only perform waived tests, simpler tests that pose a low risk to patients, are exempt from most CLIA requirements. In addition, laboratories performing the same tests must meet the same standards, whether located in a hospital, doctor's office, or other site.

This framework is designed to reduce the risk of potential harm and ensure patients receive the same high-quality clinical laboratory testing no matter where the test is performed.

CLIA's provisions apply to all laboratories in the U.S., not just those that receive Medicare payment in order to ensure uniform quality across all laboratories.

CMS enforces CLIA standards by requiring laboratories to obtain certificates in order to operate. CMS conducts onsite surveys prior to issuing a certificate to a lab that performs high- or moderately-complex tests. Labs are resurveyed every 2 years, and the surveys also assist laboratories in improving patient care through education.

Laboratories may also receive CLIA certification by obtaining accreditation from one of the seven private nonprofit accreditation organizations approved by CMS. To receive CMS approval, the accreditation organization requirements must meet or exceed CLIA's requirements.

Moving forward, we believe CLIA and our implementing regulations create the necessary framework to effectively oversee laboratories day-to-day operations and into the future, including those operations that pertain to the use of laboratory-developed tests and other high-complexity tests. We have several principles that have helped guide our work in CLIA, which may also be useful when informing future efforts of this committee.

First, we aim to prevent duplicative oversight efforts across agencies. CLIA requires coordination across CMS, FDA, and CDC. We have worked to ensure our oversight efforts are consistent and complementary and not duplicative. In doing so, we have ensured that we take advantage of the unique expertise of each agency and its staff.

Second, we focus on our agency's oversight strengths. When CLIA was implemented in the early 1990s, the responsibility to conduct certifications of laboratories was a natural fit for CMS because of our survey and certification experience. On the other hand, CMS does not have scientific staff capable of reviewing complex medical and scientific literature in determining clinical validity. This expertise resides within the FDA, which assesses clinical validity in the context of premarket reviews and other activities aligned with their regulatory efforts under the Food, Drug, and Cosmetic Act.

Third, we value our relationship with our private accreditor organizations and State-based partners. These organizations play an important role in evaluating and certifying laboratories.

Fourth, we take targeted, risk-based approaches to oversight to improve patient safety without creating burdensome administrative requirements. We believe the current approach in which laboratories must meet higher standards if they are to perform more complex tests has paid dividends in improving the quality of the testing process.

Finally, as a practicing physician who works clinically on weekends, I know the importance of tests being assessed for clinical validity, as well as the need for assessment for laboratory standards. FDA and CMS can work together utilizing their respective authorities and strengths to assess premarket

clinical validity and laboratory standards respectively.

Thank you again for the opportunity to discuss CMS's work related to ensuring accurate and reliable laboratory testing. I look forward to your questions. Thank you.

[The prepared statement of Dr. Conway follows:]

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Mr. Pitts. The chair thanks the gentleman, both witnesses for your opening statements. I will begin the questioning. I will recognize myself 5 minutes for that purpose.

The discussion draft, which the committee circulated before the hearing, divides FDA and CMS responsibilities based upon the type of activity being conducted by the regulated entity. FDA would regulate test development activities in a risk-based manner, and CMS would regulate lab operations.

Unlike the discussion draft, some alternative proposals being floated would divide regulatory oversight between CMS and FDA depending on the type of test.

I would like each of you to respond. Dr. Shuren, would you comment on the implications of an approach that would divide oversight between CMS and FDA based on the type of test, as opposed to the type of activity?

Dr. Shuren. So such a system is going to lead to inefficiencies. It is going to lead to inconsistent standards, treating the same kind of test differently depending upon who makes the test. And as a result, you can go to one institution, get a test, and it is regulated by FDA. You can get the same kind of test across the street and it is regulated by CMS. And the people who are put at risk, it is patients.

If we are going to assure that tests work, we need one unified system that we are applying consistent standards and we are

assuring that those tests are accurate, reliable, and clinically valid.

Mr. Pitts. Dr. Conway, would you comment on that, the implications of an approach that divides oversight between CMS and FDA based on the type of test, as opposed to the type of activity?

Dr. Conway. Yes, I agree with Dr. Shuren. The concern here is we want to reduce and avoid duplication and ensure coordination across agencies. You know, from a CLIA construct we really are focused on post-market review, laboratory by laboratory, and we are really focused on the things such as the protocols in place in the laboratory, the equipment and equipment maintenance, the training of staff and personnel. So CLIA's focus really is on that laboratory-by-laboratory assessment of quality standards.

Mr. Pitts. And expand a little bit more on whether such an approach would create administrative duplication or any inconsistencies, Dr. Shuren?

Dr. Shuren. That is correct. It will create inefficiencies and higher costs because essentially we have duplicative systems in FDA and CMS, and the real distinction is just simply who makes the test, which doesn't make sense. And we will have inconsistent standards. We can try to coordinate between ourselves, but quite frankly, that becomes much more challenging as tests also begin to bounce between FDA oversight

and CMS oversight.

Mr. Pitts. Okay. Dr. Conway, you stated in your testimony that "CMS does not have a scientific staff capable of determining whether a test is difficult to successfully carry out or likely to prove detrimental to a patient if carried out improperly. This expertise resides within the FDA.@ From your perspective at CMS, what would be the impact on patients if FDA were precluded from reviewing the clinical validity of most LDTs?

Dr. Conway. Yes. So as Dr. Shuren mentioned, I think the challenge is if FDA is not reviewing the test in a premarket manner for clinical validity, then our surveyors in CLIA are not assessing clinical validity. They are assessing laboratory practices and the protocols and standards in those laboratories. So as a practicing physician, it is critical, as Dr. Shuren said, that we know that a test is clinically valid, meaning it is truly detecting the presence or absence of disease. Therefore, the premarket review by FDA is important.

Mr. Pitts. Now, some stakeholders have said that CMS should be tasked with reviewing tests for clinical validity. What are your thoughts on that approach?

Dr. Conway. So our survey staff are not trained to assess clinical validity, and then let me build on that. Our survey staff are trained in laboratory protocols, equipment, standards around those protocols, whereas--and Dr. Shuren can certainly

speak directly to FDA's staff--is, you know, physicians, Ph.D.'s, biostatisticians who are trained in assessing the scientific literature in its entirety and assessing clinical validity.

Mr. Pitts. Now, some stakeholders have suggested that CMS should regulate tests developed by labs. FDA should regulate tests developed by manufacturers. Some have proposed carving out a role for FDA only when a test developer chooses not to publicize their methodologies. Shouldn't the test's impact on the patient, regardless of who developed it, be the primary factor in developing a regulatory framework? Dr. Shuren and then Dr. Conway.

Dr. Shuren. Well, we agree that this should be a risk-based framework. We also think that you should have one agency that is reviewing those tests to assure that they are accurate, reliable, and clinically valid. That assures consistency.

But also, one of the things we have found is when someone makes a test, another lab or another entity makes a similar test, we learn from that, and we sometimes identify problems or common problems and we are able to feed that back to test developers. If you split it between two agencies, we are going to lose all that learning that ultimately benefits innovation and benefits patients.

Mr. Pitts. Dr. Conway, do you want to comment?

Dr. Conway. So I agree with Dr. Shuren. I believe one

agency doing the premarket review, as Dr. Shuren said, and that agency being FDA, makes sense given the training and expertise. We also, as you have heard, have a principle of coordination and using each agency's expertise. CMS's focus and expertise is in the area of laboratory assessment, laboratory by laboratory, on protocols, equipment, et cetera.

Mr. Pitts. My time is expired. The chair recognizes the ranking member, Mr. Green, 5 minutes for questions.

Mr. Green. Thank you, Mr. Chairman.

I would like to ask unanimous consent to submit a letter from the American Cancer Society Cancer Action Network for the record.

Mr. Pitts. Without objection, so ordered.

[The information follows:]

********** COMMITTEE INSERT **********

Mr. Green. Dr. Shuren, with other medical devices, FDA has proposed regulating lab-developed tests based on the risk of the test to the patient and the public. Under proposed FDA would classify LDTs into three risk classes: low, moderate, and high. Can you explain how FDA proposes to finding the low, moderate, and high risk in the agency's framework describing how premarket or post-market requirements would vary among these risk classes?

Dr. Shuren. So we look at risk based upon what the risk is to patients if that test provides a false result, an incorrect result. And we estimate that for low-risk tests we do not conduct premarket review because they are so low risk. We think about 50 percent of the tests out there--that has been our experience--are low risk. And then we conduct premarket review for high-risk and moderate-risk tests. High-risk tests are only about 1 to 2 percent of the tests out there, moderate risk about 48 percent.

And the data needed to demonstrate analytical and clinical validity differs depending upon the risk of the disease. There is less burden involved when it is a less-riskier test rather that we are reviewing, and that is the risk-based approach that we apply.

Mr. Green. FDA's approval standard for drugs and medical devices safe and effective, can you just please discuss the approval standard FDA has proposed using for the regulation of

lab-developed tests?

Dr. Shuren. So we would apply the same standard we would apply to in vitro diagnostic tests that are not made by a lab, that they are analytically valid, they are clinically valid, and they are safe to use under their conditions to use. That means they are accurate on what they measure, they are reliable, and they will identify they in fact do identify a disease.

Mr. Green. Companion diagnostics is an area of great interest and enthusiasm. Can you talk about how the FDA views this category of tests, in particular the level of risk posed to patients and how they would be treated under the proposed guidance?

Dr. Shuren. So companion diagnostics are increasingly playing a bigger role in health care. Essentially, companion diagnostic is a test where the safety and effectiveness of the therapeutic depends upon the diagnostic because the diagnostic informs whether or not that patient should receive a particular treatment. And that is why it is critically important that those tests truly work, because if not, then patients are not getting the right treatment or they may be getting no treatment at all.

For example, we had a test for providing treatment for women with breast cancer and found that LDTs in the past were producing as much as 20 percent of them incorrect or inaccurate results. That means that women who should have gotten treated with the right

treatment were not. And that is preventable.

Mr. Green. Okay. Thank you. Dr. Conway, I want to thank you also for participating. As you are aware, following the release of the FDA's guidance on enforcing requirements for lab-developed tests, a number of stakeholders called for enhancement of CLIA as a more appropriate way to regulate the tests. And I appreciate your testimony on outlining the difference between FDA and CMS authority over the tests.

One of the key differences is the fact that under CLIA CMS does not review a test for the clinical validity, that is, accuracy on which the test identifies measures or predicts the presence and absence of a clinical condition or predisposition to a patient. Rather, CMS reviews look at analytical validity. You noted that the experience and expertise in assessed clinical validity resides instead with the FDA.

Despite CMS stating on more than one occasion that the agency does not have the experience or the scientific expertise to assess clinical validity in premarket review, many stakeholders continue to advocate for additional authority in that area for CMS. Can you please discuss further CMS capabilities in implementing regulations for overseeing LDTs, and can you also please comment on whether CMS would have the capability of conducting any type of premarket review or regulatory review of LDTs?

Dr. Conway. Yes. So our framework that we believe is

working well now is CLIA is focused on assessment of the protocols, the standards, the equipment, the training, and the personnel. Even in analytic validity, we are simply looking at, you know, does the lab test detect the analyte described? That is very different than clinical validity, which is assessing whether, you know, the test reliably and accurately detects the presence or absence of disease, as Dr. Shuren said.

You know, the majority of our staff are--you know, we have got approximately 25 people in the central office running CLIA, a little over 100 surveyors across the States, all of the States. They are generally medical technologists, former laboratory personnel trained to assess laboratory by laboratory. They are not trained to assess premarket scientific literature and determine clinical validity.

Mr. Green. Okay. Thank you, Mr. Chairman.

Mr. Pitts. The chair thanks the gentleman and now recognizes the vice chair of the full committee, Mrs. Blackburn, 5 minutes for an opening statement.

Mrs. Blackburn. Thank you, Mr. Chairman.

Dr. Shuren, looking at the LDT guidance, do you plan to finalize that guidance that you issued last year? Do you plan to finalize that this year?

Dr. Shuren. Yes, we do plan to finalize that.

Mrs. Blackburn. Okay. When?

Dr. Shuren. In 2016.

Mrs. Blackburn. Okay. So basically you are going to put it off another year?

Dr. Shuren. I don't get to determine when, but the plan is to put it out in 2016.

Mrs. Blackburn. In 2016. Early or late?

Dr. Shuren. Hopefully earlier than later.

Mrs. Blackburn. Okay.

Dr. Shuren. I wish I could give you an answer. Again, it is so far above my pay grade. I don't even know the people who make the decisions.

Mrs. Blackburn. Well, my goodness, we need to have a meet-and-greet over at the FDA and see if we can't get some wheels turning over there. We should help with that.

Let me ask you this. As you finalize that guidance, do you intend to use what I think is the outdated 1970s definition of a medical device in order to regulate the LDTs? Dr. Shuren. Well, so that definition also includes a distinct definition for in vitro diagnostics, which then incorporates laboratory-developed tests. It does not distinguish who makes the tests.

Mrs. Blackburn. Okay. Let me ask you this. Each improvement in an LDT technology or an upgrade or an update, will that need to go back through the medical device approval process?

Dr. Shuren. No. Most modifications to tests are not reviewed by FDA. We only focus on those that have the really big impact, yes.

Mrs. Blackburn. Okay. Do you intend to add to the rapid growth of health care costs by taxing LDTs as medical devices in addition to charging the innovators the user fee?

Dr. Shuren. So we are not responsible for administrating the device tax. That is IRS. We have nothing to do with it.

That said, one of the reasons we put in place that laboratories could notify us about their tests as opposed to registering and listing was that it would not trigger the device tax.

Mrs. Blackburn. I think your guidance informs the IRS, though, is that not correct?

Dr. Shuren. No, the IRS would look separately to if that device has listed.

Mrs. Blackburn. Okay. I want to thank you for the report that you sent to the Congress last night. It was an interesting read. And what I found most interesting about it was what was left out and that you didn't discuss the FDA front-end process, which deserves some attention and some discussion, specifically the PREDICT program. Twenty-eleven this was put in place. It is a compliance program. It is an artificial intelligence program that is supposed to identify high-risk shipments at our

ports of entry. And the problem with PREDICT is that it is significantly delaying the shipment of needed medicine and medical supplies. Medical shipments are often sent by express service to get them to patients in time for critical usage. And once a shipment is held up by PREDICT, almost all of them are subsequently released without any physical inspection.

So when you look at it from the outside, Dr. Shuren, what it appears to be and the impression is that the bureaucracy of the FDA is keeping medicines and medical supplies from patients because of concerns that there may have been contamination in some cilantro that was in the very same shipment. And I would really like to see the FDA spend the effort to fix this before they try to regulate another area of commerce.

I noticed in that report also that it is based on 20 case studies. And how often does the FDA use case studies as sufficient evidence to approve or deny a medical therapy?

Dr. Shuren. So in terms of approval, we don't tend to rely on an example. We have used a series of case studies as part of support for valid scientific evidence as we have approved certain tests or other products.

I will note one thing about the cases, too, we put out yesterday. One of the challenges is that we don't have post-market surveillance in place for laboratory-developed tests as we do for tests made by other manufacturers. And as a result,

it is very hard to identify when problems arise. And yet we know on the IVD side, when made by conventional manufacturers, we do detect problems, the manufacturers detect problems, and they fix them because that is in place.

One of the other features in the FDA system is the post-market surveillance to identify problems and to fix problems, and that is just as important as premarket review to prevent faulty tests from getting on the market in the first place.

Mrs. Blackburn. Well, as I yield back my time, I hope that you will fix PREDICT. I yield back.

Mr. Pitts. The chair thanks the gentlelady and now recognizes the gentlelady from California, Mrs. Capps, 5 minutes for questions.

Mrs. Capps. Thank you both, each of you, for your testimony, and thank you, Mr. Chairman, for putting together this hearing. I appreciate the opportunity to further discuss the strengths and challenges, have a real conversation about laboratory-developed tests as they guide medical decision-making by patients and providers. There are a lot of question marks and a lot of concern about where do we go from here, how do we dovetail these two agencies and giving the best outcome the patients.

I recognize there are many perspectives in this space. I appreciate this conversation to try to illuminate some of the issues. Over the years, it goes without saying these tests have

come more tailored and more elaborate, and this conversation is important to ensure that these tests do produce meaningful and reliable results for those who trust them.

Dr. Conway, I will turn to you first. In your testimony you note that there are six key performance specification assessments for lab-developed tests: accuracy, precision, reference range, reportable range, analytic sensitivity, analytic specificity. This committee has heard a lot about how different research institutions are driving the future of medicine toward more personalized medicine. This has been particularly true in the field of cancer where the development of multi-gene panels is being used to identify important molecular characteristics of a tumor.

And my question to you is whether the current CLIA regulations ensure these gene panels developed by different institutions or manufacturers will produce the same results? For example, if I am a patient and I am tested with hospital A's gene panel, how do I know I would get the same result if I am tested with hospital B's gene panel? Would each hospital reach the same treatment decision, and where does this lead us?

Dr. Conway. Yes, you have highlighted--thank you for the question, and you have highlighted one of the challenges. And Dr. Shuren could certainly speak more.

You know, our assessment of analytic validity is laboratory

by laboratory where we are looking at the areas you described and the laboratory director's documentation, that they are following a protocol to detect the appropriate analyte.

And you highlighted a great example, genetic testing. It is not assessing whether different genetic testing kits or combination of tests are detecting the disease with the same clinical validity and rigor. So you could in fact in the current framework, without premarket assessment of clinical validity, have different tests giving different answers to clinicians that could drive treatment that is inappropriate, which is why we think the assessment of premarket clinical validity in this area is critical and important.

Mrs. Capps. So that leads me to focus now with you, Dr. Shuren. Many have argued that there is no need for greater FDA oversight of lab-developed tests, as we have not had the same types of problems with LDTs as we have had with drugs such as the outbreak of adverse events associated with use of contaminated heparin, for example, or adverse events associated with contaminated compounded drugs. They assert that if there are greater health risks associated with LDTs, we would have heard about them.

I am not sure you agree, but it is clear to me from the report that FDA released yesterday that lab-developed tests do present real risks to patients. Can you please explain whether or not you agree with this criticism that came out? Would health care

providers and patients necessarily know if tests were not giving good advice for clinical decisions?

Dr. Shuren. I don't agree with that criticism. And doctors and patients would not know who made the device and whether it is one that was approved by FDA or it was one that was not approved by FDA. Quite frankly, the reason you don't see as many problems, you don't have the systems in place to identify them. So, for example, for IVDs we regulate, in 2014 we had over 300 recalls. It is not unusual.

Things change, problems arise, but you need the systems to identify the problems and to fix them. And we have some labs who have submitted their tests to us, and we have approved or cleared some LDTs. And when they put the systems in place, these started to identify problems. One of them has already had eight recalls, but they only found the problems because they put in the systems that they should have in place.

Mrs. Capps. Well, now, how can patients--I am just about out of time, but how can patients, providers, and payers be assured that the tests they are paying for are providing real value and enhancing the care of patients?

Dr. Shuren. Well, that is why we would like to have a uniform, consistent approach to diagnostic tests, regardless of who makes them. That information will be made available to the public so they know what tests have been approved. There is

information about what those tests are for. The makers have to put out information that explains its performance characteristics, its intended use, how to use it properly, and all that will provide necessary information to doctors and patients so they can use those tests appropriately.

Mrs. Capps. Thank you.

Dr. Shuren. Right now, they can't.

Mrs. Capps. Okay. It sounds like we need a follow-up. I yield back.

Mr. Pitts. The chair thanks the gentlelady and now recognizes the chair emeritus of the full committee, Mr. Barton, 5 minutes for questions.

Mr. Barton. Thank you, Mr. Chairman. I want to thank both our witnesses for attending today. I appreciate the subcommittee chairman, the full committee chairman issuing the proposal as a discussion draft, which to me means that their minds are still open and that we can make some changes and things of this sort.

I am one of those skeptics that Mrs. Capps just talked about. I am not sure that we need to get more Federal regulation. I don't necessarily think more Federal regulation is going to give us a safer, more efficacious result.

So I guess my first question to either of you gentlemen would be what is the real problem? I mean why in the world would a laboratory develop a test that wasn't safe and accurate? My

office is not being overrun with phone calls or emails from doctors, patients, hospitals, advocacy groups that there is some terrible laboratory diagnostic test out in the marketplace.

Dr. Shuren. But those tests are out on the marketplace. So, for example, a test was developed for something called KIV 6. It was supposed to predict the risk of heart disease and response to statin treatment. And the lab came out with it, promoted it, said they had studies, but then subsequently good studies were performed and in fact found that there was no association between KIV 6 and those conditions. And by the time it came out, though, over 150,000 people had the tests performed. We estimated the cost to our health care system was over $2 billion. That is not money we can afford to waste on bad testing.

Mr. Barton. And what happened--

Dr. Shuren. So what happened--

Mr. Barton. I assume that test was taken off the market and without FDA having to do anything.

Dr. Shuren. It remained on the market and there was continued use for a while and then use started to dip down. But is that really the system we want, that we have bad tests, people can get hurt by it, and then afterwards if you find the problem and you get on top of it, then something happens to the test? The whole point of premarket review is and why we do that for the other tests--

Mr. Barton. You are going to guarantee if we would let your agency review all these diagnostic tests, the laboratory tests, that something like that will never happen again, that you all are perfect and all-knowing and you are going to do it in a cost-effective way and it will be peace and light from now until Judgment Day?

Dr. Shuren. I will not promise you perfection, and I will leave it to God to decide if there will be peace on Earth, but--

Mr. Barton. Well, I am glad to hear somebody use--

Dr. Shuren. But that said, we have--

Mr. Barton. --the Divinity's name in a positive way. That is--

Dr. Shuren. Yes, well, they can fire me.

Mr. Barton. That is a good thing.

Dr. Shuren. But we have almost 40 years of experience of regulating in vitro diagnostic tests and assuring that those tests are accurate, reliable, and clinically--

Mr. Barton. I mean, granting your point at least partially, wouldn't it be better to give FDA or some State regulatory agency--it doesn't necessarily have to be Federal--some sort of a penalty assessment that we can immediately put a stop if there is a bad test? Wouldn't that be a better use of your agency's resources? So to use your example, if that were to happen again, boom, we catch it, we stop it, we hit them with a big penalty and

get that test off the market. I am not being a horse's rear on this, but, you know, if it is not broken, don't fix it, and it looks to me like we are just looking for ways to give the CMS and the FDA more authority. And it is obvious that Chairman Pitts and Chairman Upton and I assume Mr. Pallone and Mr. Green are concerned, too. But more regulation is not always the best answer.

I guess my last question would be under the current system what role if any do the States play in looking at these tests?

Dr. Shuren. So there are States--I can let Dr. Conway talk about it in terms of States that are involved in accreditation of laboratories, but they are not involved in premarket review for those tests with certain exceptions. New York State does do a review of tests. And quite frankly, under the proposal we have, we have the opportunity to leverage third parties. If New York State is meeting appropriate standards, we could leverage some of the work that they are doing.

But I will tell you the problems are more prevalent than people want to recognize. You know, one of the medical centers at the University of Texas was concerned about this--

Mr. Barton. I went to A&M so that doesn't scare me.

Dr. Shuren. No, no, no--well--but I will tell you what they were finding is--

Mr. Barton. I am going to hear it whether I want to or not.

Dr. Shuren. That is right. Thank you for that. But there were inconsistencies in what they were seeing reported by labs for the same kind of tests, so what they did is they took results from 105 of their cancer patients and they had results from one laboratory, they sent it to a second laboratory, and of the 32 gene variants, they found 50 percent disagreement, 50 percent. And so they even concluded that this suggests physician care would differ based on different interpretations of different companies. And this is not the only report out there, other ones reporting 27 percent finding of incorrect or inaccurate results. This is not uncommon. This goes on.

It is fixable, and it shouldn't be fixed after the fact. Why should our people get hurt, and only when that happens--and if we can find it because we don't have the systems to do that--do we take action. Is that really the kind of health care we want to provide? Do we want to spend money on unnecessary care or do we want to spend it on innovation and assuring those tests work.

Mr. Barton. Well, I am with you on the innovation part.

Mr. Chairman, you know, the other subcommittees got the FCC commissioners downstairs so I am not going to be able to stay, but I appreciate you holding this hearing, and thank you for the courtesy of the time.

Mr. Pitts. The chair thanks the gentleman and now recognizes the ranking member of the full committee, Mr. Pallone,

5 minutes for questions.

Mr. Pallone. Thank you, Mr. Chairman.

I wanted to ask Dr. Shuren. As you know, various stakeholders have been circulating legislative proposals regarding the regulation of lab-developed tests. Among these various legislative proposals, there seems to be a great deal of variance around moderate-risk tests. Some proposals have suggested that no premarket review is necessary for moderate-risk tests, and one proposal would require premarket review of moderate-risk tests but would allow such tests to be deemed approved if FDA did not act in a specified time frame.

So I wanted to ask you a couple questions about this. In your testimony you noted an example of a test that is moderate risk would blood glucose strips used by people with diabetes and tests to help doctors diagnose heart failure. Could you discuss what FDA considers to be moderate risk and provide some examples of tests that would be considered moderate risk?

Dr. Shuren. So other moderate-risk tests would be for diagnosing cystic fibrosis, herpes, heart failure are all moderate-risk tests--

Mr. Pallone. Okay.

Dr. Shuren. --that we currently regulate.

Mr. Pallone. Does the FDA believe that premarket review of moderate-risk tests that there should be, and if so, can you

describe when you believe that premarket review of a moderate-risk test would be necessary?

Dr. Shuren. So we do believe that most moderate-risk tests would be subject to premarket review. That is what we do now, but we do find that there are certain circumstances where we can put other mitigations in place that are good enough and you don't need premarket review. We just did that a little while back for next-generation sequencing platforms, when they are just making tool claims. We just did that for autosomal recessive carrier screening tests. And that is a natural course of action. As the science develops, technology evolves, we can actually change risk classification or what a test will have to do to come on the market. That is hallmarks of a risk-based approach.

We are also very concerned about this deemed-approved approach. It essentially says if we don't make it decision in time, it is approved. So a test goes on the market that may be inaccurate simply because we didn't have enough time to finish up the review or, alternatively, we will not approve it to not let it go on the market. And yet if we had the time to work with the lab, we might get a good test on the market. Either way, bad tests on the market, good tests not going on a market, the loser is patients.

Mr. Pallone. Okay. I think you answered my next question, which would be, you know, the deemed approval if FDA does not act.

But let me say, can you comment on whether or not--yes, I think you already talked about the deemed approved. So let me go to another question, Dr. Shuren.

I understand that once the test is approved or cleared by FDA and enters the market, laboratories frequently modify the kits either to expand uses or to make improvements to the way the test is performed. And some stakeholders in the lab community have even suggested that manufacturers rely on laboratories to modify tests in order to expand the uses because it is too costly or burdensome to have a test approved for every use. So do you believe that modifications to LDTs should be subject to premarket requirements, and if so, what types of modifications would FDA want to look at before they are put in place?

Dr. Shuren. So we think most changes that are made would not be subject to FDA review, and that is actually what occurs now for other IVDs. We would review those changes when there is a new intended use because it truly is a new test. Even CLIA have used that as a new test. Or if there is a big enough change that when a test is approved would determine what its performance specifications are, if now you make a change and it goes outside the performance specifications, we would review that as well.

Mr. Pallone. Okay.

Dr. Shuren. But it is those kinds of changes.

Mr. Pallone. Let me go back. There was other thing that

I could have asked you about, these tests are deemed approved if FDA didn't act in a certain time frame. Can you explain whether or not you believe patients, physicians, or payers would know which tests were affirmatively cleared or approved by FDA versus tests that were deemed to be approved? Is there any way that they would know that?

Dr. Shuren. No. I mean if the test is approved, the test is approved.

Mr. Pallone. So that is one of the dangers if you will. In other words, you said before that you would be concerned that you might approve something that shouldn't be or not approve something that could be. But the secondary problem is that the user is not going to know.

Dr. Shuren. That is exactly right.

Mr. Pallone. All right. Thanks a lot.

Mr. Guthrie. [Presiding] Thank you. And the gentleman yields back. I now recognize myself for 5 minutes for questions.

Dr. Shuren and Conway, what does premarket review mean in the context of lab-developed tests, or LDTs? And how important is it and who should be responsible for such reviews?

Dr. Shuren. So our premarket review is to determine if the tests are analytically valid, clinically valid, and they are safe for use under their conditions for use. And it is important to conduct those reviews for moderate- and high-risk tests to make

sure they work because doctors and patients rely on those tests to make well-informed health care decisions. If they get inaccurate results, they could make the wrong decisions and people get hurt as a result.

Mr. Guthrie. Thank you. Dr. Conway?

Dr. Conway. I agree with Dr. Shuren. And from the CLIA/CMS perspective, you know, we are really focused on laboratory-by-laboratory post-market review of those laboratory protocols, equipment, training of personnel, et cetera.

Mr. Guthrie. Okay. Thank you. And I have heard that the same type of diagnostic test that is commonly available as both an LDT and a manufacturer kit that can be purchased by a lab, and tests for melanoma are one example. In other words, I could go to hospital A where they have a lab that developed their own test or, by chance, I could go to hospital B, whose lab purchased a test from a manufacturer. Can either of you walk me through this scenario from a regulatory perspective? In the case of hospital A, is it true that neither FDA nor CMS will have reviewed that test for clinical validity?

Dr. Shuren. That is true. The test across the street would have been reviewed, and therefore, doctors and patients have the confidence to be able to rely on it, and you don't know in the case of the other one that has been offered.

Mr. Guthrie. Okay. Same--

Dr. Conway. Yes, same. And CMS, once again, would not review clinical validity as part of the CLIA process.

Mr. Guthrie. Okay. Doing the premarket review of these types of tests, could each of you describe the general education and professional background and expertise of your reviewers?

Dr. Shuren. So our review, particularly for more complex tests, tends to be performed by a team of experts. They may include physicians, Ph.D. scientists, and statisticians that do a deep dive into the scientific data. We review the science to see if in fact and not only that test works but what it is claiming to do matches up with the science.

Mr. Guthrie. Thank you. Dr. Conway?

Dr. Conway. Our CLIA team does not include any medical officers or other personnel trained in detailed biostatistics or Ph.D.-level training. Our CLIA team is really focused on, as I mentioned, laboratory assessment on an accreditation and quality and survey and certification framework in a post-market manner laboratory by laboratory.

Mr. Guthrie. Thanks. And, Dr. Shuren, you previously testified about challenges you face in hiring and retaining sufficient medical expertise. How would your ability to do so be impacted if CMS were required to have the same types of expertise regarding test design and development?

Dr. Shuren. Well, first off, I want to thank the committee

for trying to take actions in 21st Century Cures to help us to better be able to attract and retain high quality talent. And that is where the answer lies.

Mr. Guthrie. So the competition if CMS is doing the same would be--

Dr. Shuren. Well, it makes no sense for competition, so all we are going to do is create a duplicative system in another agency. I mean it is interesting that people have raised concern about do not have duplicative regulatory frameworks in place, and yet some of the proposals we have seen now to put this under CLIA would do exactly that. It would create all this duplication the right now, as you have heard from both of us, doesn't exist.

Mr. Guthrie. All right. Thank you. And I yield back the balance of my time.

And I now recognize Ms. Castor from Florida.

Ms. Castor. Thank you, Mr. Chairman. And thank you both for being here today.

As we continue to develop a greater understanding of the genetics of individuals who have a wide variety of diseases and conditions, we are moving away from one-size-fits-all medicine to more targeted and effective prevention strategies and treatments and even cures. This is known as personalized medicine, and I believe it is fundamental to the vision of 21st Century Cures and holds great promise.

This vision, though, will in large part be dependent upon accurate genetic tests, so it is imperative that these tests are scientifically credible. Dr. Shuren, can you provide some examples of the types of genetic tests that are being developed to help deliver personalized treatment? And describe in greater detail the role that these tests play in precision medicine.

Dr. Shuren. So increasingly, we are seeing genetic tests being developed to help identify what the appropriate treatment may be for patients who have various conditions, including cancer. And it is critically important that those tests work, because if not, people are not getting the right treatment or they are not getting treatment when in fact they should get treatment.

I will say that as we approach this, though, government can be innovative. Increasingly, we are seeing next-generation sequencing tests being used, and last December, we put out a proposal for a new approach on next-generation sequencing that, rather than your standard model of maybe doing a clinical study is to leverage data in existing curated databases, which can allow for the clinical community to crowd-source the evidence, and as the science ultimately evolves to where it needs to be to be able to make claims about the use of that test. That way, the regulatory framework can stay step-in-step with the evolution of the science.

In fact, we just held a two-day public meeting last week on

this. There is a lot of support for moving forward with this approach. We have even relied on those curated databases to approve a test for cystic fibrosis.

So that is where we need to focus our attention, and that is why we want the lab community at the table with us. Let's focus on the science. That is what we need to do. We have the regulatory tools. It is the science we have got to work together on. And we can do it if people are willing to work with us.

Ms. Castor. Yes. And during our 21st Century Cures hearings and briefings, there was a lot of talk about data-sharing. What is going on--because we can't wait for Congress to act, frankly. What is going on with FDA and NIH and a lot of those research institutions across the country in being able to look at that data, share it, so we can develop the cures and treatments of the future?

Dr. Shuren. Yes. So NIH has its own database of genetic variants. They do an assessment. We have other databases out there. We are now trying to work with these various groups on what the appropriate standards should be for the quality check for the curation and what should be the standards for clinical validity when you are evaluating that science.

Also, we at the FDA have been developing a platform called precision FDA that would allow these test developers to essentially either share their genetic data to compare or

providing analytical tools so they can test-drive some of these next-generation sequencing technologies to see if they are accurately sequencing the genome. We think this is a great role, if you will, to provide these common goods to all developers.

Ms. Castor. Great. I do, too. Thank you. And I yield back my time.

Mr. Guthrie. Thank you very much. The gentleman from Illinois, Mr. Shimkus, is recognized for 5 minutes.

Mr. Shimkus. Thank you, Mr. Chairman. And welcome.

Actually, I appreciate the comments from my colleague from Florida. That is kind of where I was just heading to a little bit, too, with the personalized medicine and the genetic testing and really being accurate on that test so then you can, as we talked about in the other piece of legislation, target based upon the genetic code or the individual patient. That is very exciting.

And the other thing I think we have followed through the hearings and the 21st Century Cures is that then you just don't go down the route of prescribing remedial health action to someone without really full information, so the high cost of health care because you try this, didn't work, try this, didn't work, now you are trying this, and you can get more specific information. So it is very exciting times. And I think people were going around the same issues.

But I wanted to ask this, and it is probably something I

should know if I would have more thoroughly read my briefings, but when we talk about risk--basic, moderate, or high--so we are really focusing on moderate and high risk of the tests. What is the risk component? Is the risk component the risk of conducting it, the risk of not having accurate information, or the risk to the patient who hopes to get good information from a test because of the health care environment they presently find themselves in? So can you both talk on how do we define risk?

Dr. Shuren. Yes. So the key consideration is the risk to the patient if they are getting an inaccurate result, they are getting a wrong result, and that is within the context of what would otherwise happen to that patient in clinical care. That is the way we look at it.

Mr. Shimkus. So when you use the example of heart, you put that in a moderate--when you were giving the examples of--and I was kind of surprised. I mean, heart disease or heart issues, I think people would find it pretty risky if you have got heart disease, a higher risk than just in the moderate category. So there is some subjectivity to this or--

Dr. Shuren. Well, so when we look at it, you put it within the clinical context. So in the case of heart failure, when you are making, you know, a diagnosis, there are other things that the clinician takes into account in making that determination. That is a little bit different, though, when I am dealing with

something, let's say, like HIV where not only am I dealing with a high-risk condition, right, the risk to the patient is huge, secondly, I don't have another great means of truly determining is that HIV. And then there is also the risk of if I am wrong about this and that person goes out and doesn't know they have HIV, they may engage in activities that they will spread the disease. So we are really looking at it in the practical context of what in fact happens to the patient, not just simply the condition itself.

Mr. Shimkus. Right. And I think this is a tough area for conservative Republicans who think government is too big, costs too much, but there is obviously a position of we want to make sure that people are advertising and using tests, that they are given some stamp of approval, that they meet the requirements and the desires of what they are.

So, Dr. Conway, real quick, you admit that the volume and complexity of these tests have kind of grown, I don't know, I would say exponentially almost. Would you agree with that?

Dr. Conway. Yes. We don't have exact numbers for some of the reasons described, but it seems exponential.

Mr. Shimkus. But you haven't asked for new authorities because of this growth, have you?

Dr. Conway. So CMS has not put forward additional requests for statutory authority. As I mentioned, we think FDA can play

a critical role in the premarket review, and we can play a critical role laboratory by laboratory, post-market.

Mr. Shimkus. Yes, in your area do you require an individual review of the area that you have been involved with? Is there an independent review process of decisions that you are making, you know, in the CLIA process?

Dr. Conway. Let me try to answer that. So I think we have a central office that has oversight of State surveyors, and therefore, oversight of the processes of those State surveyors. We also oversee accrediting organizations, of which there are seven. They have to meet or exceed CLIA standards, and we review that, including if any--

Mr. Shimkus. But you are almost evaluating the organizations. The organizations aren't evaluating the independent decisions?

Dr. Conway. We have bidirectional communication both with the States and their accrediting organizations like in any of our accrediting organizations, including at times in various programs accrediting organizations identify regulations or standards that need updating.

Mr. Shimkus. Great. Thank you very much. I yield back my time.

Mr. Guthrie. I thank the gentleman. The time is expired.

And I recognize Dr. Schrader from Oregon for 5 minutes for

questions.

Mr. Schrader. Thank you, Mr. Chairman. And I would like to thank Dr. Shuren and Dr. Conway for being here. Interesting topic. I would hope that the chair or vice chair and ranking member would hopefully have us have an opportunity to talk to the stakeholders, including the physician groups, just to get a balanced perspective here. This is pretty darn important if we are going to go down this road, and I think the tender of the questions so far indicate that.

And I appreciate the fact both of you testified in total agreement in pretty clear terms about how you guys have two different jobs in the different agencies. It is tough from a practitioner's standpoint, being part of the medical community, to really understand why that has to be. I understand it is right now, but I am not sure why it has to be. It seems odd to me that the Center for Medicare Services--medical services would not have some sort of health regulatory role or clinical analyzation capability.

And it seems to me both of you are going to have to staff up, well, particularly FDA if you take on this new role of premarket approval. There is going to be a huge staffing increase. Why would that not also be possible for the folks in CLIA or somewhere in CMS to do the same thing? I ask both of you that question.

Dr. Shuren. So we already have existing staff who do exactly these kinds of reviews, and we have years of experience on it. We have training programs for our people. And in terms of additional resources, one of the reasons that we put in place a phased-in approach would be also for tests that are out there, one, not disrupt the market; two, that we could try to accommodate what resources we have. But in addition, if we need additional resources, we have a user-fee program under which we work with the regulated community about appropriate funding for services that we then provide back like performance and premarket review. And that program, as you know, has been in place for a number of years.

Mr. Schrader. So minimal staffing increase is what you are suggesting?

Dr. Shuren. It depends on the ultimate framework that goes into place as to what that workload would look like.

Mr. Schrader. All right. Mr. Conway, if you can.

Dr. Conway. On the CMS side, as I mentioned in the central office we have approximately 25 people in total overseeing CLIA. They are trained for their job, which they do well, which is oversight of laboratories, laboratory by laboratory. There are no medical officers, there are no Ph.D.'s, biostatisticians because we do not do premarket review.

Mr. Schrader. I just get concerned still--sorry--because

both your testimonies talk about accuracy, both of you. You both talk about reliability. And that sounds like overlap to me. So I am just concerned that we don't go down that road. Question on peer-review. I mean a lot of treatments and diagnoses are peer-reviewed in the literature and stuff. Has that occurred at all with laboratory tests? Is there any literature reviewing the efficacy of different laboratory tests?

Dr. Shuren. In our review of tests we do look at published literature, and in some cases we have relied completely on published literature for certain tests like hemoglobin A1c for diabetes.

This issue about accuracy, our look at it, though, for analytical validity is complementary but it is different. We truly look at is the test itself and what it measures, is it in fact accurate? CMS will look at is that test performed properly to get a result.

Mr. Schrader. That is correct. So I guess my underlying concern as a medical professional listening to the testimony is that the consumer, as well as the physician or veterinarian, is not misled by having premarket review. There is going to be some certainty that that test is 100 percent appropriate for them in their situation.

The reason I raised the question about the peer review, I mean, generally, the test from my standpoint is a secondary

adjunct to helping establish the diagnosis. You got a lot on clinical sides, you got a lot on knowing your patient, got a lot to, you know, based on the environment they are living in. There are false positives all the time in every single test, false negatives in virtually every single test, whether it is a genetic test or, you know, a simple blood test for goodness sakes. I just don't want the consumer to be misled that by having FDA premarket approval, that that test is going to be 100 percent. I think that is a mistake.

At the end of the day I think it is up to the medical community, the physician to put that one small piece of the puzzle into the, you know, whole diagnostic scheme and come up with whether or not that is actually going to be a valid use of their patient.

I am just very concerned the tone here is that we are going to put certainty into the art of medicine when there is not that much certainty, and the patient will be misled and frankly lead to greater lawsuits and customers frankly not understanding what medicine is really all about.

Dr. Shuren. And so the accuracy of that test will also depend on what the use of the test is for. You know, when you deal with riskier conditions or where there are some tests you truly rely on the result of that test. Companion diagnostics, for example, it is the result of that test that will be telling

you should they get Zelboraf, you know, for melanoma. And in those cases you want to have a higher accuracy.

You are right, it is not 100 percent, but also what we assure you is that that information is made available to the practitioner like you, and you know that when you get that number for how accurate it is, the result, it is correct. It is the--

Mr. Schrader. Well, laboratories have different--laboratory information from one lab to the other is going to be different. I can send the exact same blood sample in to a different laboratory. I can send the genetic code in. You testified a moment ago you are going to get different information back. So the idea that it is going to be dispositive, I would respectfully disagree. And I yield my time.

Mr. Guthrie. Thank you. The gentleman's time is expired.

I now recognize Dr. Burgess of Texas for 5 minutes.

Mr. Burgess. Thank you, Mr. Chairman.

Before I start my time, could I asking for a unanimous consent request?

Mr. Guthrie. The gentleman is recognized.

Mr. Burgess. Ask unanimous consent to enter the statement of the Association for Molecular Pathology into the record. And then a further unanimous consent request for a point of personal privilege, Mr. Chairman.

For the past 7 years I have been joined at these committee

hearings by Mr. Paluskiewicz, whose last name is so difficult to pronounce we all know him by J.P. And if I ever seem adequately prepared for these hearings, it is only because I have had J.P. advising me before we come into the hearing room. And so it is with great sadness that I announce that J.P. will be leaving my employment, but he will be joining the committee staff, so he will be here for all to participate and the wondrous things that he has to offer to any committee hearing.

Thank you, Mr. Chairman. Now recognize for questions.

Dr. Conway, so if Dr. Shuren puts his guidance out in January, are you no longer necessary?

Dr. Conway. No, sir, and let me explain why. I think there will still be a role for CLIA to assess, and this is a critically important role, that laboratories have the proper equipment, training, protocols, and quality assurance procedures in place, and that laboratory-by-laboratory certification, which a few people have talked about, is a critical role for CLIA.

Mr. Burgess. But, you know, we have heard several times the FDA is under-resourced, so why shouldn't the resources that are going to CMS just simply go to the FDA?

Dr. Conway. So I will speak for CMS. You know, I think in the CLIA oversight framework we are efficiently using both central office resources and relying on States, which was a question earlier, and their State surveyors, obviously a user-fee funded

program based on user fees based on moderate, high complexity, et cetera, and volume. And then we also importantly have nonprofit accrediting organizations that are not government organizations, that we--seven of them--approve that they meet or exceed CLIA standards. We are using people outside of the Federal Government as well to perform these important functions.

Mr. Burgess. Dr. Shuren, this question has been posed to you several times in this subcommittee or oversight subcommittees about what is the problem that we are trying to solve? And last night at 7:00 p.m. you put out a report that detailed 20 times where perhaps there were problems with laboratory-developed tests, is that correct?

Dr. Shuren. Yes.

Mr. Burgess. And I am sure you would make the further statement that there are more than that, but we have also seen in testimony that what is the total universe of laboratory-developed tests? It is in excess of 11,000, is that correct?

Dr. Shuren. It is above 11,000.

Mr. Burgess. So the rate at which you have detected problems would be, if my math is correct, .18 percent, which most things in medicine are hardly that reliable. Is that an unfair statement?

Dr. Shuren. Yes. Reporting systems--first of all, there

is no reporting system on LDTs. You are not monitoring for problems. And so you can't say what the rate is, quite frankly.

Mr. Burgess. It took you 3 years to provide us with 20. When I asked you in hearings, when we were doing the FDA reauthorization, what is the problem we are trying to solve? So today, now, I have your report, 20 problems that we are trying to solve, and we have got a universe in excess of 11,000 tests.

So let me just ask you this, since you think the risk is there from laboratory-developed tests, is there an FDA-approved kit that has ever had a failure?

Dr. Shuren. Yes. And the point is the reason we can identify when there are problems and we can deal with it is because we have the systems in place and the maker of the test has implemented systems internally to identify those problems. That is critical. And the work that we are doing doesn't occur right now in CMS. It is not duplicative, and they don't go away.

Remember, if you make a test, if you are a conventional manufacturer, that lab is going to get your test. They still have to perform that test properly, and that is what CMS is overseeing, are the laboratory operations conducted properly. Mr. Burgess. My time is limited. So do you envision any lack of access to testing because of the changes that you are proposing in the guidance or the committee is proposing in their legislation?

Dr. Shuren. So we have tried to--a proposal was put in place so that we would not disrupt the marketplace. Our goal here is to try to assure we do have innovation. We think LDTs are important in health care. There is innovation, but--

Mr. Burgess. I appreciate the recommendation--

Dr. Shuren. --there is no value to patients if the tests in fact don't work. And one of the problems is because we haven't regulated, there has been a disincentive for innovation by conventional manufacturers. And we have heard from them, particularly the smaller companies are saying they are disadvantaged because they make a test and they go through and they have to demonstrate their test works. And then you can have a lab make the same kind of test go out the door--

Mr. Burgess. I am going to have to interrupt you because my time is limited.

Just as far as the labs themselves, who do you expect to be more greatly impacted, large labs and large hospitals or smaller rural labs? Is there likely to be a difference in the impact? It is a yes-or-no question.

Dr. Shuren. The answer is you should regardless be developing the science that your test is validated, whether we review it or not.

Mr. Burgess. If you don't know whether the answer is yes or no, why wouldn't we want to see an economic impact evaluation

such as normally would be required in rulemaking but is not required in guidance?

Dr. Shuren. Well, just to clarify again, whether we were overseeing them or not, a lab shouldn't be putting any test on the market that they haven't gotten the data to validate. What we are saying is you should have the data and we would look at it before the test went on the market to make sure that that test in fact worked.

Mr. Burgess. And to the question--

Dr. Shuren. The tests that wouldn't go on the market are the ones that in fact don't work.

Mr. Burgess. And to the question of an economic impact statement, as would be required under normal rulemaking processes, why shouldn't the committee or the Congress expect that?

Dr. Shuren. We are not under rulemaking because we are not imposing new requirements. These requirements already exist under the law. As a matter of policy, we have not actively enforced them. And in places where we put an enforcement discretion policy, we have withdrawn it. We have done that through guidance. It has been the practice all along.

I would say in terms of economic analysis, too, we now have seen the lab community has come forward to say LDTs need to demonstrate analytical and clinical validity. Moderate- and

high-risk LDTs need to be subject to premarket review. So those pieces, even the lab community has now said, you know what, that kind of a framework needs to be in place.

Mr. Guthrie. The gentleman's time is expired. Would you again, Dr. Burgess, make--you had one unanimous consent request that we did not act on, then you went to a point of personal privilege. Can you make that once again before we move on?

Mr. Burgess. Yes. It was to add to the record the statement from the Association of Molecular Pathology for the record.

Mr. Guthrie. Without objection, so ordered.

[The information follows:]

********** COMMITTEE INSERT **********

Mr. Guthrie. Thank you.

Mr. Burgess. Thank you.

Mr. Guthrie. The chair now recognizes Mr. Sarbanes for Maryland for 5 minutes for questions.

Mr. Sarbanes. Thank you, Mr. Chairman. I thank the two witnesses for being here.

This is obviously a very important discussion, and I always try to look at these conversations through the eyes of sort of my constituents, people out there, and I have got to believe that if some of them are paying attention to this hearing, they would be scratching their head, the typical patient out there, and saying, you mean these kinds of protections and reviews and guidance and so forth are not already in place?

And I understand that, you know, you start out in a different time period, and you are now trying to sort of update the framework that exists to protect patients out there, and I think the average person would think that this is a very reasonable undertaking on your part. So there is going to have to be some heightened degree of oversight and assurance in this arena.

You have probably touched on all this before I came, but could you just take maybe two or three or four of the main categories of kind of constituencies out there and give me a shorthand on their perspective? What are physicians saying about this conversation? What are patient advocate groups saying? I think

I can probably guess. You have alluded to the industry, the lab industry itself, but can you just--and in particular, I guess the physician perspective on it would be helpful to me, but if you can kind of shorthand those different lenses on this discussion.

Dr. Shuren. We have heard mixed perspectives from the physician community. So oncologists have come out to say, yes, you need oversight, you need FDA oversight. Pathologists have felt that, no, we do not. FDA shouldn't be or should have little role in oversight of LDTs. The patient groups have been supportive of FDA. The consumer groups, payers have been--the medical device industry has been, the laboratory community has been split. Some of the labs have been working and promoting a proposal with FDA oversight, and the others have been proposing a system under CLIA.

Mr. Sarbanes. The payers, that is interesting. Can you expand a little bit on that? Is that because they are seeing a lot of costs associated with faulty test results in the use of those?

Dr. Conway. Maybe I will start since I am a large payer. It is a challenge in the payer aspect, so including in Medicare and similar and private payers. If the tests haven't gone through that FDA review, then we have a system of local contract medical directors in our national office also, you know, small numbers of people trying to review thousands of tests that either are

identified to us or we identify that we need to assess reasonable and necessary for coverage. If there were an FDA review, you could potentially take a whole set of those that have been through FDA review and have those be covered and focus on the ones that are leftover. So this is an issue there.

If you don't mind, on the practicing physician point, I am a practicing physician. I train residents and medical students on weekends as well. You know, you want an assurance as a physician that the test is clinically valid and that the report that says the patient has cancer or genetic disease X is correct. And the patient wants that assurance as well.

Mr. Sarbanes. Right.

Mr. Guthrie. Thank you. And the gentleman yields back his time.

Mr. Lance of New Jersey is recognized for 5 minutes for questions.

Mr. Lance. Thank you very much, Mr. Chairman. Good morning to you, gentlemen.

Dr. Conway, it is my understanding that it is the Division of Laboratory Services within the Survey and Certification Group within the Center for Clinical Standards and Quality at CMS that has responsibility for administering the program. How many staff within the division are responsible for inspecting labs and reviewing the tests they performed?

Dr. Conway. We have approximately 25 central office staff, and then we have approximately 110 surveyors across the Nation and all the States, so a small number per State.

Mr. Lance. We have heard that there are tens of thousands of LDTs out there. Do you believe that the division is capable of reviewing all of these LDTs in a timely fashion for clinical validity?

Dr. Conway. No, they are not, either in a timely fashion or with the current training of the staff that we have.

Mr. Lance. And therefore, do you believe that new innovation would be effective, I presume, negatively because of the potential backlog?

Dr. Conway. Yes, I would be very concerned about a potential backlog and the impact on innovation.

Mr. Lance. Dr. Shuren, how would the FDA handle the workload and how would these submissions be based in line, on what priority if this were to be handled by the FDA?

Dr. Shuren. To handle workload, it is one of the reasons we have put in a phased-in approach over a number of years, and review would occur--be prioritized based upon risk. What we proposed is we would start reviewing higher-risk devices before we would look at--high risk before moving to moderate risk.

Mr. Lance. And to the best of your ability, how long do you believe it would take to review an LDT, your best estimate, Doctor?

Dr. Shuren. So for the moderate risk LDTs now, the review times are--total times are a little over 100 days, thereabouts.

Mr. Lance. Thank you. Thank you, Mr. Chairman. I yield back the balance of my time.

Mr. Burgess. Would the gentleman yield to me?

Mr. Lance. I yield to Dr. Burgess.

Mr. Burgess. Thank you.

Mr. Guthrie. Dr. Burgess is recognized.

Mr. Burgess. On that point, could you state that figure again, the moderate-risk LDTs, 100 days? Is that right?

Dr. Shuren. No, a little over 100 days.

Mr. Burgess. So there are 11,000 and some laboratory-developed tests. You said earlier that 50 percent are low risk, so presumably, that leaves 50 percent that are in the moderate- or high-risk category, is that correct?

Dr. Shuren. Yes, that is correct.

Mr. Burgess. So extrapolating out the number of days, assuming none of them are high risk, they are all low risk, and that is over 100 days of evaluation at the FDA, I mean that is a phenomenal amount of work that is ahead of you, is it not?

Dr. Shuren. That is one of the reasons why we have looked at phased-in approach. We have gotten feedback, too, if we should consider any changes and take a different approach for some of the tests that are currently on the market, which we are doing.

And we are also having those discussions about funding needs as part of user fee discussions, which are going on right now. They get authorized every 5 years. And that has been the natural course of business.

We have those discussions with regulated industry--the laboratory community is that the table--to then talk about if people want to see a certain performance, what does that look like. We know in some of the proposals people have said for moderate-risk tests could that review time be 75 days? We can have a discussion about what it would take for review in 75 days.

Mr. Burgess. I will say some of the performance metrics that were introduced after the last FDA reauthorization in 2012, I don't know that we ever got satisfactory answers back to this subcommittee or the Subcommittee on Oversight as to how the performance was on that, but there is a general unease that the FDA is able to perform its function in a timely fashion. During the time that we were doing the hearings for the FDA reauthorization, there was hardly a week that went by that there was not someone in my office with a tale of woe about a drug or device that just seemed to take forever in development and that the FDA would sometimes change the rules as that drug or device went through the development process. What assurance can we give to the laboratory-developed test community that they won't encounter similar problems with your agency going forward?

Dr. Shuren. Well, our review times have been actually improving under MDUFA III. We are meeting our performance goals, as we committed to do. So we are seeing things move in the right direction. And I don't know what is happening to people coming into your office now. I have heard from other Members that they don't have the parade of people that were coming in several years ago.

And you know when I took over the program several years ago, I was very upfront with this committee and others that there were challenges in the medical device program. We had seen roughly a decade of worsening performance, and we committed to turn that around. We committed to make changes regardless of what happened with MDUFA, and then MDUFA came along to give us additional resources. And we have continued to see improved performance, and we are going to continue to work on it, as we have been doing all along.

Mr. Guthrie. Thank you.

Mr. Burgess. I don't know that I share your enthusiasm. Thank you, Mr. Chairman.

Mr. Guthrie. Thank you. The gentleman from New Jersey's time has expired, and recognizing Mr. Cardenas from California for 5 minutes for questions.

Mr. Cardenas. Thank you very much, Mr. Chairman.

My first question is to FDA and CMS. Today in your

budgeting, are you being asked to do more with less?

Dr. Shuren. Yes.

Mr. Cardenas. I am not talking about prospectively. I am talking about in the cycle that you are currently in.

Dr. Shuren. Yes, and that has been even the cycles before then. We are always asked to do more with less.

Mr. Cardenas. Okay.

Dr. Conway. Yes. So it is also true for CMS, long history of doing more for less. Thank you for the more with less. Thank you for the question. I mean, I have managed in the delivery system. I have managed in CMS. I have never managed somewhere as hard as this. It is ridiculously harder than running a delivery system. And the reason is the amount of resources for the job. We are deploying lien and other operational techniques to increase our efficiency, learning from manufacturing and health systems, and that is working, but this is a major issue.

Mr. Cardenas. Okay. Thank you for clarifying that. I don't think the public understands how taxing it is for our agencies to continue to do more and more and more and try to protect the public and allow the American public to know or feel as though there are protections and the agencies are trying their best to look out for making sure that when they are engaged in something that is a--whether it is FDA-approved or it has gone through review of CMS, et cetera, that they can feel safe.

So thank you for continuing to wade through the struggle of doing more with less and doing your best to keep up with that. I hope that we as the holders of the purse, Congress, will recognize that and realize that we are impeding on the safety of our American citizens when we just say no to a reasonable request of resources and we just say do with what you have and do a better job and just make it happen, easier said than done.

And thank you for clarifying that in the environment that you have been and that this is probably the--I interpret that what you said is this is the most difficult environment for you to do justice to your efforts than any other environment you have been in.

Dr. Conway. Yes. And I--

Mr. Cardenas. And understand you are not coming across to me as complaining.

Dr. Conway. No.

Mr. Cardenas. I think it is important that you just be honest with us the way you have been. Thank you.

Dr. Conway. Yes. No, do you mind if I--

Mr. Cardenas. No, go ahead, please.

Dr. Conway. This is the best job I have ever had and the most impactful, which is why I have stayed, but the challenge of managing in the CMS environment with the resources we have for the duty we have for the American people is by far the hardest

job I have ever had. And I have led in the private sector, large groups, large budgets. It is nowhere close. This is the most challenging job I have ever had in my life.

Mr. Cardenas. And again, I thank you for welcoming the challenge. It is too bad that we don't lessen that challenge by giving you the resources for you to be more effective without worrying about not being effective in your responsibilities.

My family just got the news recently that my wife and I are going to be grandparents for the first time. And just the other day, we were invited to my daughter and my son-in-law's house, and they revealed to us it is going to be a boy. And the reason why they found is because my daughter underwent a test that went to a laboratory and the results came back. And one of the things that they could tell her--it wasn't the purpose of the test, but one of the things they could tell her is the gender of the fetus. And so it was a wonderful moment.

However, what if the purpose of that test had been inadvertent, the results had been inadvertent? I think that is really what the focus of today is about. It is about safety of the public. It is about accuracy of what is going on out there. It is about whether or not they are being effective. And unfortunately, for those people who want less government or no government, there needs to be oversight from somewhere. I personally prefer that government be involved in that oversight

instead of just turning it completely over to private industries, which happens in some cases.

But my question to you is, going forward, how do we as a country make sure that between CMS, between FDA, what your role can be in making sure that these critical tests, these laboratories are being accurate with the information to the patient, to the actual end-user?

Dr. Shuren. Well, we have established a task force between FDA and CMS--NIH and CDC are also participating--to assure that we are not duplicating efforts. In fact, we have had conversations with certified laboratories, accrediting lab organizations under CLIA, two State licensure programs, and confirmed we are not duplicating efforts, but we do want to make sure we have good coordination moving forward. And we provide the education and information out for laboratories as well as we progress, so that work is happening in the task force right now.

Dr. Conway. I agree.

Mr. Cardenas. Thank you.

Mr. Guthrie. They gentleman's time expired. And myself, and I think speaking for the entire subcommittee, we congratulate you on the good news and to your family, the next generation of your family, appreciate that very much.

The chair now recognizes Dr. Bucshon from Indiana for 5 minutes for questions.

Mr. Bucshon. Thank you, Mr. Chairman.

Now, I have heard complaints that the FDA oversight of LDTs would interfere with the practice of medicine. I am a physician, cardiovascular surgeon, so I would like you both to comment as regulators but also as physicians on your view on that.

Dr. Shuren. So we do not--and as a physician, we do not regulate the practice of medicine. Congress actually put in a statutory provision prohibiting us from regulating the practice of medicine in the medical device program. It is a unique provision that pertains to us. What we are regulating, talking about regulating, are the tests, the things that we regulate already today, reagents, the instruments, the protocol, instructions are used that go forward with it.

In fact, a group of laboratories who were working with the device industry, the conventional IVD makers, when they sat down and went through it, they began to realize, too, you know what, there are parts here that is just like what happens in FDA: development, design, validation of tests. Then there are all these other activities that occur that are lab operations or the practice of medicine. They are not under our preview and we have never proposed to ever regulate those.

Dr. Conway. And likewise, CLIA does not regulate the practice of medicine. It does regulate laboratories in terms of equipment, personnel, protocols, et cetera, which its focus is

post-market laboratory by laboratory.

Mr. Bucshon. Okay. Great. And currently, CMS regulates how physicians operates a lab, as you described, and performs tests within it, but I really haven't heard any complaints about interfering with the practice of medicine myself from people that I know. Why is it that physicians feel differently maybe about the FDA oversight of these particular tests, and how can we address those concerns? Does that make sense?

Dr. Shuren. It does. I think what we are dealing with are people who haven't dealt with us necessarily beforehand, and so it is new and they are assuming things that we don't believe to be the case. I hearken back to Dr. Burgess, who I respect very much, when he said when CLIA came in the door you were not a fan, but you began to realize the value of it. I would say the same thing here. As the lab community works with us--well, maybe you will allow it.

Well, hopefully, we will see much the same here with the lab community in working with us. And it is our hope they will work with us to make sure that when we are doing things, it also best fits for their operations. Again, we both are committed and care about that those tests work.

Mr. Bucshon. Yes. I mean I will just make a comment and I will--I mean, as a physician, obviously I want accuracy and patient safety to be at the top of the list, right? And again,

I think Mr. Shimkus said I am not one that is generally for government regulation, but I think in this area that, you know, this is a good discussion to be having on behalf of patients, and that I think the details and how things end up at the end are what are important. So I commend your hard work on trying to find the sweet spot as you go about your job.

Thank you. I yield back.

Mr. Burgess. [Presiding] The chair thanks the gentleman. The gentleman yields back.

The chair recognizes the gentleman from Florida, Mr. Bilirakis, 5 minutes for questions, please.

Mr. Bilirakis. Thank you, Mr. Chairman. I appreciate it. And this question is for the panel.

As we go forward with any new regulation, regulatory scheme, we need to balance the needs between consistency, accuracy, and innovation. In disease areas such as cancer, genetic testing is evolving rapidly, and I am sure you agree with that. Many major institutions today have developed their own gene panels that help diagnose or identify potential treatments for cancer patients.

For example, in Tampa we have the Moffitt Cancer Center, the only NCI-designated comprehensive cancer center in Florida. They have developed a TruSight tumor gene set, which is used to identify lung and colon cancers that will benefit from targeted therapies. In advance of the lab-developed tests is the ability

to rapidly innovate current tests rather than the slower and expensive process of resubmitting to FDA for any changes. Centers such as Moffitt have the ability to innovate and rapidly improve their lab tests as fast as science evolves.

Question, how can we resolve issues regarding consistency and accuracy and not stifle innovation in these labs and important health care institutions?

Dr. Shuren. So one issue for consistency, certainly we don't--we were recommending not to have two duplicative systems out there, one under FDA, one under CMS, or we will have inconsistency. But then we have found that to assure consistency, we work with the community on trying to develop standards or in guidance so that, as we learn and the science evolves, we can have more of a common playing field of what performance should look like for certain kinds of tests. And that can help ensure consistency in terms of approach.

Mr. Bilirakis. Thank you. Anyone else?

Dr. Conway. I agree with Dr. Shuren, and I think, you know, from the CMS perspective, we think our strength is in that post-market review laboratory by laboratory on the qualifications, equipment, and personnel.

Mr. Bilirakis. Thank you. Anyone else want to jump in? Okay. Dr. Conway, since both the volume and complexity of lab-developed tests on the market today have drastically

increased in recent years, why hasn't CMS asked for these new authorities?

Dr. Conway. So in terms of authorities we think FDA has a critical role in premarket review of clinical validity. We think CMS's role through CLIA really is and should be focused on laboratory-by-laboratory assessment, survey and certification and oversight of accrediting organizations, ensuring that the protocols, the equipment, and the standards are in place in individual laboratories in a post-market manner.

Mr. Bilirakis. Dr. Conway, does CMS require definitive review of the clinical claims being made about the tests?

Dr. Conway. And Dr. Shuren can certainly comment for FDA. On the CMS perspective, we do basic assessment of analytical validity so the analyte is the actual analyte in the test. We do not do assessments of clinical validity, meaning the test actually identifies the condition, the absence or presence of the condition it is supposed to identify.

In our coverage process, we have occasionally looked at laboratory development tests for reasonable and necessary standard. There, we will look at the effect of the test on patients, but that is a very small number of LDTs we have looked at through that process.

Mr. Bilirakis. Well, thank you very much, and I yield back, Mr. Chairman.

Mr. Burgess. The chair thanks the gentleman. The gentleman yields back.

The chair recognizes the gentleman from New York, Mr. Collins, 5 minutes for your questions, please.

Mr. Collins. Thank you, Mr. Chairman.

Before I start my questions, I would ask unanimous consent to enter into the record a letter from Roswell Park Cancer Institute.

Mr. Burgess. Without objection.

[The information follows:]

********** COMMITTEE INSERT **********

Mr. Collins. Thank you very much.

In that letter they do mention the same we have talked about before, the Association of Molecular Pathology, or AMP, and their proposal, and I would certainly encourage the FDA, as we are in the discussion stage, to again take a look at this.

So I guess one thing I am still trying to get clear on, you know, currently, a commercial test, something sold on the market which does have to go through FDA approval, premarket approval, and I assuming that is currently a 510(k)?

Dr. Shuren. For premarket, most of them are 510(k). A very tiny number are PMA.

Mr. Collins. So as a 510(k) currently, it is a medical device subject to the medical device tax, correct?

Dr. Shuren. Yes.

Mr. Collins. So if I understand what your guidance is now, you are going to move on IVDs out of that world, the medical device world, and have a different classification of class 1, 2, or 3, or low, moderate, whatever. Just a question, does that mean on the good news side that IVDs will no longer be subject to the medical device tax since they are not going to be getting 510(k)s?

Dr. Shuren. So the trigger for the device tax is registering at the listing with the FDA. What we have proposed for LDTs is that--and we use that to know what test is being made, who is making it, and that is a requirement by law. But we have worked through

that instead they can give us a notification and not list with us, and particularly--and that is for starters. And for the tests that don't ultimately come in for premarket review, they also wouldn't end up registering and listing with us. And that would not trigger the device tax.

Mr. Collins. So current tests would be still covered by the medical device tax even though there is not a 510(k) because they would be listed with the FDA?

Dr. Shuren. They are registered and listed with that, and those are--

Mr. Collins. Okay. That clarification is important because I have heard that kind of going all over the board.

Now, another, you know, concern has been, you know, accuracy of testing, and I think it is also important to make clear laboratory-developed tests are not sold to other facilities. They are used inside a facility such as Roswell Park, which is looking at very specific treatments for specific cancers and what we call personalized medicine. They are not then selling those tests to other folks or making claims, which is different than a commercialized test, which currently goes through FDA approvals.

But, you know, Dr. Conway, it is my understanding that over 97 percent of the CLIA laboratory test facilities have subjected themselves to outside third-party proficiency testing of their

tests. Isn't that correct?

Dr. Conway. So proficiency testing occurs in just 13 specialty areas, occurs approximately three times per year. It has improved the accuracy over time. It will not assess for clinical validity of the test, so the premarket clinical validity, which Dr. Shuren spoke to, the proficiency testing does not analyze clinical validity.

Mr. Collins. Well, it certainly analyzes whether you are properly getting--you know, you are identifying the antigen you are supposed to identify.

Dr. Conway. So it will identify--if that laboratory-developed test was within those 13 categories, which they are not all within those 13 areas, but for an LDT that was in one of those 13 areas--and Dr. Shuren may say more--it will detect that the analyte is the analyte, but that is not an assessment of the clinical usefulness or validity of the test.

Dr. Shuren. And it goes to again, if you will, the accuracy of the performance of the test as opposed to the accuracy of the test itself, which is a different look, and that is what we look at for the test.

Mr. Collins. Yes. I guess I would just say it is my belief anyway that the laboratory-developed tests, certainly in institutions like Roswell Park, are being done to get better treatment, quicker treatment to the patients. And a big concern

all of us have, if this goes through, that a test might be used tomorrow to help a patient with cancer now is delayed 6 months as it goes through some kind of premarket review at FDA, which is a life-and-death situation for many of these cancers.

And I think it goes back to--I think I go on to the same bandwagon as Mr. Barton and Dr. Burgess. This has not been a problem that I would identify, and putting any type of delay into this sphere of personalized medicine and treatment especially in the cancer and oncology world runs the risk frankly of causing people to die that don't need to die, treatments that could be given that would be delayed. And in the cancer world, delay is not a good thing.

So personally, I would throw myself into the category I believe it is working now. We do have outside proficiency testing, third-party testing. And we have to remember these are laboratory-developed tests that are not being sold in the marketplace to other facilities, which is very different than what you are doing now.

My time has expired, but if the chair would like to hear a response, I would certainly yield a couple seconds.

Mr. Burgess. Sure. He is recognized for a response.

Dr. Shuren. I truly appreciate those comments because we do not want to stifle innovation in this place. We want to have patients get timely access to tests. And that is why even under

an FDA mechanism if the test is being reviewed, it is being developed, it can still be made available to patients on an investigational basis or for compassionate use. But there at least you are telling the doctor and you are telling the patient we haven't validated this test yet. It is investigational. This may be--

Mr. Collins. You know what, I appreciate that because my worry was they would develop a test, they couldn't use it until they had approval, but if on an investigative basis they know that--they think they have a good test they can use it, then you have actually helped me in a couple of ways there. Thank you for that response.

I yield back.

Mr. Burgess. The chair thanks the gentleman. The gentleman yields back.

The chair recognizes the gentleman from Pennsylvania, Mr. Murphy, 5 questions for questions, please.

Mr. Murphy. Thank you. Doctor, Doctor, it good to have you here, appreciate this.

I want to pivot a little bit here to talk about piecing together post-market and premarket analysis to look at this, and in particular, a couple of devices used in women's health care, one is called a morcellator. Are you familiar with the morcellator, a device that is supposed to shred tumors, et cetera,

but has been associated with complications in women in terms of actually spreading cancer for them?

Now, it has been on the market for 20 plus years, and the FDA admitted for the first time it became aware of the safety issue with power morcellators was after December of 2013, correspondence from a physician citing the case of a family member. This is someone who had just recently had another surgery to remove another recurrence of cancer that was spread it by the morcellator.

The manufacturer was apparently aware of the dangers of this device as early as 2006 based upon a report from Dr. Lamparter, a pathologist from central Pennsylvania, who cited about 1 out of 300 samples of morcellated tissue from his hospital had evidence of a hidden cancer, which is morcellated.

So my question is did the FDA have any evidence of these dangers in 2006 or prior to that? Are you aware of this problem?

Dr. Shuren. So in the past the thought was what risks of cancer there may be for a fibroma--for a fibroid actually to have cancer in there--were significantly less. And one of the things when we looked into it more recently we came to a different conclusion, that the likelihood of cancer is higher. There is still disagreement in the community because, as you know, the health care professional societies disagree. They think we have overestimated the risk of cancer.

We said we have a different perspective, and that is why we went out and we put contraindications and warnings on the use of that device, that it should only be used in a more limited set or offered as an option in a limited set of women and think about primarily women who, in the absence of using the device, would no longer be able to bear children but they want to bear children. And we felt those cases the risk of the cancer is very low. They should have the opportunity to weigh in, but we scaled back dramatically how that should--

Mr. Murphy. So this is a case where the science available, the premarket analysis has changed, and what is being used in the data, you have a mechanism to go forward on this and make some changes. Let me ask another question.

Brigham and Women's Hospital was aware of the dangers in 2012. A patient by the name of Mrs. Erica Katz was seriously injured in 2012 by the device and then died in 2013 according to reports. I wondered, do you know if that hospital reported that to the FDA? Would you know?

Dr. Shuren. I am not aware that--

Mr. Murphy. Is there a mechanism where the hospital is supposed to report that or the manufacturer is supposed to report that so you can do the analysis?

Dr. Shuren. So user facilities have certain requirements for reporting. So do manufacturers if they become aware of

certain events. And what I can tell you is we have been looking into those concerns that have been raised regarding reporting.

Mr. Murphy. Okay. In response to congressional inquiries about this, the FDA admitted that the 1-out-of-350 risk does not address other types of malignancies, which you would add to that risk, you said. They went on to say the FDA also identified studies showing that morcellated patients had worse outcomes than patients who had not undergone morcellation.

So this is more than just the issue with just a fibroid or if it is cancerous. It is also a question of outcomes. Is this something that the FDA is reviewing also with regard to their stamp of approval on these things in terms of the outcome measures?

Dr. Shuren. So in terms of the tests we have looked at, we think where we have constrained it right now is--for use is where the benefits outweigh the risks, but we are continuing to look at new data as it arises, and if so, we will act accordingly.

Mr. Murphy. Thank you. There is another issue in women's health that was brought to my attention. It is a product called Essure. It is a permanent birth control device that went through FDA's rigorous premarket approval process. Yet despite getting the agency's approval, it has been linked to at least four deaths and deaths of five unborn children. Apparently, a total of 24,000 women have come forward claiming that they have been harmed by this device. And so the question is how it remains on the market

with a potential for problems. And because this has the FDA stamp of approval, these women feel at this point they cannot take their cases forward, and they feel they don't have any recourse. Is the FDA also reviewing this issue as well as far as you know?

Dr. Shuren. We are. In fact, we held an advisory committee meeting a few weeks ago at our behest to give an opportunity to put what new evidence is on the table to assure that people who wanted to raise concerns about it had an opportunity to provide those concerns. And we are now currently reviewing the feedback we received from the advisory committee, as well as what we have heard from other people, as well as the state of the evidence, and we will come out with our conclusions on that to the public.

Mr. Murphy. Thank you. And as this goes through, since this hearing has been a lot about premarket analysis, what this comes down to is I just want to make sure that we are aware of what mechanism you have, because I understand the science of 1996 is different from the science of 2015 and our knowledge base, but to have an ongoing mechanism for review and changes, devices and getting information there and looking at those things, I mean, I am glad you had some hearings on this, but I would certainly like to know that that is part of the system.

I am out of time, but I look forward to hearing your comments on that in the future. Thank you.

Mr. Burgess. The gentleman yields back. The chair thanks

the gentleman.

The chair recognizes the gentleman from Texas for a unanimous consent request.

Mr. Green. Mr. Chairman, I ask unanimous consent to place in the record Public Health Evidence for FDA Oversight of Laboratory-Developed Tests, 20 case studies. I ask unanimous to place that in the record.

Mr. Burgess. Without objection, so ordered.

[The information follows:]

********** COMMITTEE INSERT **********

Mr. Burgess. And I recognize myself for an additional unanimous consent request to add the statement of the American Association of Clinical Chemistry to the record. Without objection, so ordered.

[The information follows:]

********** COMMITTEE INSERT **********

Mr. Burgess. Seeing no further members wishing to be recognized for questions, I do want to remind members they have 10 business days to submit questions for the record, and I ask the witnesses to respond to those questions promptly. Members should submit their questions by the close of business on December 2.

With that, the subcommittee stands in adjournment.

Dr. Shuren. Thank you.

[Whereupon, at 12:07 p.m., the subcommittee was adjourned.]