UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

+ + +

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES ADVISORY COMMITTEE

+ + +

MEDICAL DEVICE USER FEE AMENDMENTS FOR FISCAL YEARS 2023 THROUGH 2027

+ + +

October 27, 2020
9:00 a.m.

Via webcast videoconference

FDA REPRESENTATIVES:

LAUREN ROTH, J.D.
Associate Commissioner for Policy

FDA PRESENTERS:

STEPHEN HAHN, M.D.

JEFFREY SHUREN, M.D., J.D.
CDRH

PETER MARKS, M.D., Ph.D.
CBER

Free State Reporting, Inc.
1378 Cape Saint Claire Road
Annapolis, MD 21409
(410) 974-0947

PERSPECTIVES ON THE NATIONAL EVALUATION SYSTEM FOR HEALTH TECHNOLOGY (NEST)

PAMELA GOLDBERG, M.B.A.
President and CEO, Medical Device Innovation Consortium

FLORA SANDRA SIAMI, M.P.H.
Senior Vice President, NESTcc

INDUSTRY PANELISTS:

JANET TRUNZO, M.S.
Advanced Medical Technology Association (AdvaMed)

MARK LEAHEY, J.D., M.B.A.
Medical Device Manufacturers Association (MDMA)

PETER WEEMS
Medical Imaging and Technology Alliance (MITA)

THOMAS SPARKMAN, R.Ph., J.D., M.P.P.
American Clinical Laboratory Association (ACLA)

SCIENTIFIC, ACADEMIC & HEALTH CARE PANELISTS:

KATHLEEN BLAKE, M.D.
American Medical Association

PATIENT & CONSUMER PANELISTS:

JEFF ALLEN, Ph.D.
Friends of Cancer Research

BRENDA HUNEYCUTT, Ph.D., J.D., M.P.H.
FasterCures

MICHAEL ABRAMS, Ph.D., M.P.H.
Public Citizen

MICHAEL WARD, M.S.
Alliance for Aging Research

DIANA ZUCKERMAN, Ph.D.
National Center for Health Research

PAUL CONWAY
American Association of Kidney Patients

LEANNE WEST
International Children's Advisory Network

OPEN PUBLIC HEARING SPEAKERS:

LAURA KOONTZ
Flatiron Health

MARIA GMITRO
TrackMySolutions

MADRIS KINARD-TOMES
DeviceEvents

DYLAN SIMON
EveryLife Foundation

LINDA RADACH
USA Patient Network

LISA McGIFFERT
Patient Safety Action Network

JOHN OWEN
CDISC

INDEX

	PAGE
WELCOME & INTRODUCTION - Lauren Roth, J.D.	6
OPENING REMARKS - Stephen Hahn, M.D.	7
CDRH UPDATE - Jeff Shuren, M.D., J.D.	14
CBER UPDATE - Peter Marks, M.D., Ph.D.	18
PERSPECTIVES ON NEST:	
Pamela Goldberg, M.B.A.	20
Flora Sandra Siami, M.P.H.	25
INDUSTRY PERSPECTIVES:	
Janet Trunzo, M.S.	30
Mark Leahey, J.D., M.B.A.	33
Peter Weems	39
Thomas Sparkman, R.Ph., J.D., M.P.P.	42
SCIENTIFIC, ACADEMIC & HEALTH CARE PERSPECTIVES:	
Kathleen Blake, M.D.	46
PATIENT & CONSUMER PERSPECTIVES:	
Jeff Allen, Ph.D.	55
Brenda Huneycutt, Ph.D., J.D., M.P.H.	60
Michael Abrams, M.P.H., Ph.D.	65
Michael Ward, M.S.	71
Diana Zuckerman, Ph.D.	76
Paul Conway	81
Leanne West	90

INDEX

	PAGE
OPEN PUBLIC HEARING	
Laura Koontz	97
Maria Gmitro	99
Madris Kinard-Tomes	102
Dylan Simon	104
Linda Radach	108
Lisa McGiffert	110
John Owen	113
CLOSING REMARKS - Lauren Roth, J.D.	116

M E E T I N G

(9:00 a.m.)

MS. ROTH: Good morning. I think we're ready to begin. Welcome to our public meeting to discuss the 5th Medical Device User Fee Reauthorization, MDUFA-5 for short.

My name is Lauren Roth. I'm FDA's Associate Commissioner for Policy and I'll be leading FDA's negotiations for this 5th MDUFA cycle.

As you may know, today's public meeting was originally scheduled to take place in March, but it was delayed while FDA, industry, and the broader health care community focused our attention on response to the COVID-19 pandemic.

Although FDA remains focused on that response, we also continue to address other mission critical priorities, including preparation for MDUFA. That begins with this kickoff meeting today.

The Medical Device User Fee program began in 2002 and the MDUFA agreements have been reauthorized every five years since then. The agreements provide critical support that sustains and improves FDA's ability to conduct timely and efficient review of medical device pre-market submissions.

As a result, the MDUFA agreements have helped make the United States a more attractive place for innovators, and they've helped to enable timely patient access to important technologies, while also assuring the devices in the U.S. market are safe, effective and of high quality.

As we begin the process of negotiating our 5th MDUFA agreement, I want to thank all of the speakers whose perspectives we'll hear today and to welcome all the participants who joined the webcast.

We look forward to this dialog. And we also invite you to submit any additional feedback to us in the public docket of the meeting. So I'm delighted to introduce Dr.

Stephen Hahn, who was sworn in as the 24th Commissioner of Food and Drugs in December of 2019.

Dr. Hahn is a dedicated clinician who trained in both medical oncology and radiation oncology. Prior to joining FDA, Dr. Hahn's distinguished career involved, serving as the chief medical executive at the University of Texas, MD Anderson Cancer Center and before that, as the radiation -- in the radiation oncology department at the University of Pennsylvania's Perelman School of Medicine.

Dr. Hahn previously earned the rank of commander in the U.S. Public Health Service Commission Corps while at the NIH's National Cancer Institute. He's joining us today through a video telecast, which we will turn to now. Thank you, Dr. Hahn.

DR. HAHN: Good morning. It is a pleasure to be with all of you, albeit virtually, for this public meeting on the Reauthorization of the Medical Device User Fee Amendments, MDUFA.

MDUFA plays an important role in helping the FDA meet the demands of our increasingly complex and diverse mission at home and abroad. The breadth of those demands grows more expansive all the time, both as a result of new responsibilities placed on the FDA and by advances in science and technology. This year, those demands have risen to unprecedented levels, not because of any new authorities given to us, but because the FDA has a vital role in responding to the COVID-19 public health emergency.

So, before I turn to the specifics of this important reauthorization, I want to say a few words about the more than 17,000 FDA employees who every day bring extraordinary professionalism, knowledge and commitment to their jobs and the agency's mission.

Like so many Americans across the country, eight months ago, the FDA staff had their world turned upside down by COVID-19. Since then, they have faced significant challenges both in the workplace, including working in a virtual environment, and in the

personal arena, whether juggling at home child or elder care responsibilities or simply managing the fear and anxiety that the pandemic is imposing on our families, friends and communities.

Remarkably, the pandemic did not stop or even slow FDA's pace of work. It actually accelerated it with our workload essentially doubling and our workforce immersed in an around the clock response to COVID-19.

Incredibly, this remarkable effort has taken place as our centers and offices have continued to fulfill the agency's regular mission critical responsibilities from the approval and clearance of medical devices to the approval of safe and effective new drugs and biological products, to maintaining our high standards of food safety and ensuring our continuing oversight of tobacco products, including e-cigarettes, to name just a few areas.

Of course, COVID-19 continues to be a primary focus. I'm so proud of the employees in all of our medical product centers who have addressed and solved problems involving some of the most challenging public health issues we faced in over a century, including supporting the development of therapeutics and vaccines.

Our teams in the Centers for Devices and Radiologic Health and Biological Evaluation and Research have done an extraordinary job helping to ensure the availability of essential medical devices to respond to the pandemic.

Starting back in January, they facilitated alternative testing strategies to address supply shortages; worked to augment increases in personal protective equipment, ventilators and other essential medical devices; ensured continued access to necessary medical products and address the sale of fraudulent products.

And at an incredibly fast pace, they reviewed and issued emergency use authorization for medical devices for COVID-19. Since the beginning of February, CDRH has received more than 5,000 requests for EUAs and pre-EUAs.

We have authorized the emergency use of over 550 medical devices, including more than 280 tests, at a rate of review that amounts to authorizing, on average, one test every single day.

One way that we've accomplished that is by working closely with developers. For example, in January, the agency had begun engaging with commercial manufacturers of diagnostic test kits and laboratories to streamline submissions and help foster accurate test development and validation. The agency developed EUA template with recommendations on validating a molecular diagnostic test for SARS-CoV-2 and outlined the required information.

By July 31, the FDA had authorized 163 COVID-19 diagnostic tests. We also continue to rapidly adapt our policies to meet evolving circumstances. The FDA has issued more than 60 guidances so far, including more than 20 specific-to-medical devices that provide targeted regulatory flexibilities to respond to the pandemic.

In developing these policies, we considered what was needed to address COVID-19 specifically -- for instance, policies designed to expand the supply of diagnostic tests, ventilators, infusion pumps and personal protective equipment.

But we also thought about what was needed to respond to the collateral effects of the pandemic, such as the need for technologies to help protect patients and providers from exposure to COVID-19 by better enabling social distancing measures and to facilitate the ability of patients to receive their health care remotely.

We issued policies for medical imaging equipment, remote monitoring devices and ophthalmic and other devices. We provided regulatory flexibility for certain changes designed to enhance the functionality of these devices under the circumstances caused by the pandemic and made adjunctive digital health therapeutics for psychiatric conditions more readily available.

It has been an extraordinary response by the entire FDA workforce, demonstrating professionalism, knowledge and dedication to public health.

I want to underscore two important points in this regard. First, in all the work done in response to the pandemic, we at the FDA have maintained our focus on applying rigorous science and the best available data to any policies being developed and any decisions made, no matter how quickly.

And second, which I already mentioned briefly, is that we have continued to fulfill our regular responsibilities even as we have worked to respond to the pandemic.

Those two points are important as we consider the subject of today's meeting, how the FDA has continued to work hard to meet our performance goals and other commitments under the current MDUFA agreement.

The FDA's user fee programs help us fulfill our mission to protect public health while also helping to accelerate innovation and bring new treatment options to the American public. Despite the pandemic, non-COVID submissions have not decreased.

Remarkably, in the first eight months of 2020, which included the height of the COVID pandemic response, the numbers of original premarket applications, De Novos and 510(k)s under review all exceeded the numbers from a year ago.

We continue to perform our user fee review activities for these non-COVID therapies and diagnostics. And this year we approved or authorized several novel devices, including three aimed at improving the health and well-being of children.

These include a first of its kind, automated insulin delivery and monitoring system for use in pediatric patients aged two to six years old. It is the first legally marketed device that can automatically adjust insulin delivery based on continuous glucose monitoring values for this patient population.

We also granted marketing authorization through the De Novo pathway to the first

game-based digital therapeutic device to improve attention function in children ages eight to 12 years old with attention deficit hyperactivity disorder.

This was the first digital therapeutic intended to improve symptoms associated with ADHD, as well as the first game-based therapeutic granted marketing authorization by the FDA for any type of condition.

And we granted marketing authorization to a new device indicated to provide continuous hemodialysis or hemo-filtration therapy to certain critically ill pediatric patients.

It was the first continuous renal replacement therapy device intended for a lower weight specific pediatric patient population who have a sudden or temporary loss of kidney function or too much water in their bodies because their kidneys are not functioning properly.

We have also continued to advance other important initiatives, such as launching the Digital Health Center of Excellence, which will focus on aligning digital health efforts and act as a hub for regulatory innovation. And we continue to take strong measures to address device safety concerns working to deliver on our vision of being consistently first among the world's regulatory agencies to identify and act upon device safety signals.

To that end, our efforts to build a robust device (ph.), a patient safety net (ph.) in the United States are continuing. Through the National Evaluation System for Health Technology Coordinating Center, or NEST, we've embarked on a potentially transformative public/private partnership to perform active surveillance; perform timely, efficient post market safety studies and develop tests and apply new methods to detect and evaluate. For enhanced safety signals.

We have also continued to act in specific cases when new information emerges about the potential risks of any device. I encourage you all to review the video series prepared by CDRH that highlights the significant progress the Center has made to date with

implementing and going beyond the MDUFA-4 commitments.

As we enter the next cycle of MDUFA negotiations, it is imperative that we continue to build on the successes of the past few years and to look for opportunities that enable us to work smarter.

As a starting point, we must acknowledge the significant strain that the response to COVID-19 pandemic is having on our ability to continue to meet user fee goals, as well as the toll it is taking on FDA staff.

It is no exaggeration to say that the work I've witnessed from my colleagues over the past eight months has been nothing short of heroic. But it is also a level of effort that cannot be sustained in perpetuity.

Even absent the COVID-19 pandemic, the FDA's medical device team was already operating at a breakneck pace. The MDUFA-4 agreement set ambitious review performance goals and included a host of infrastructure and process improvement commitments that the center has worked tirelessly to meet.

Yet the size of the Device User Fee Program and the resources that come with it are only a fraction of the size of the programs for prescription and generic drug user fees. This makes the program's success all the more remarkable.

However, it also causes me concern for the long-term health of the program and its ability to both protect and promote public health, particularly in light of the ever-accelerating pace of device innovation. It should also cause us to pause and reflect on what we can achieve through MDUFA reauthorization.

Today's public meeting is an opportunity to begin a dialogue about how FDA and industry can collaborate to work both hard and smart to achieve our mutual goal of supporting timely patient access to safe and effective medical devices.

It also provides the occasion to hear from other stakeholders on what the medical

device user fee program should accomplish during MDUFA-5 and how we can achieve it. This is a chance, for instance, to see what investments we can make in human resources and programs that enhance opportunities for meaningful, early and ongoing communication between FDA and device sponsors.

As demonstrated by the Breakthrough Devices program, as structured well (ph.), such interactive programs help bring safe and effective devices to patients more quickly than standard premarket reviews.

It's also an opportunity to consider, for instance, what further investments can be made in the development and evaluation of real-world data from patient registries, electronic health records and other sources.

Evaluation of real-world data has the potential to provide a wealth of rapid, actionable information to better understand device performance and safety under a variety of use conditions.

And the enhanced understanding from real-world data can, in turn, spur advances in product development and help to inform clinical and public health decision making that pays dividends for patients, industry, FDA and our society as a whole. Finally, it's an opportunity to consider how we can provide technological, programmatic and other resources to the device team -- resources that enable the FDA to build a program that can continue to sustain its success by investing in our most important resource, our people, throughout the next MDUFA cycle and for years to come.

In conclusion, today's meeting offers the opportunity to examine the best ways to accomplish these goals. I can assure you that whatever changes are put in place, the FDA's decisions will always be driven by facts and data and made by FDA experts, scientists with scientific rigor, integrity and the public interest at the center. Thank you.

MS. ROTH: Thank you, Dr. Hahn. And next, I would like to turn to Dr. Jeff Shuren,

the Director of FDA's Center for Devices and Radiological Health. Dr. Shuren, if you can go ahead and unmute while we're -- I'm introducing you.

Dr. Shuren received his medical degree from Northwestern, his law degree from the University of Michigan. He completed his medical internship at Beth Israel Hospital in Boston and his neurology residency at Tufts New England Medical Center.

Since 1998, Dr. Shuren has held various policy and planning positions within the FDA, and he assumed his current role as the center director in September of 2009. While at FDA, Dr. Shuren has been involved in each of the MDUFA reauthorizations. So, to say he brings a reservoir of experience to this undertaking is an understatement. Welcome, Dr. Shuren.

DR. SHUREN: Well, thank you and good morning. It's a pleasure to be here today to kick off the first leg of the process for reauthorizing the Medical Device User Fee Amendments. I want to thank Dr. Hahn for his remarks and to welcome and thank all the speakers for today.

The medical device user fee program is critical for our community's ability to assure that medical devices are safe and effective and that patients have timely access to them.

We look forward to hearing your feedback on how the program is performing and to get your ideas for how best to improve it as we move forward in our discussions about the next user fee agreement.

FDA will not spend much of its time talking about its performance under the current agreement so that we can give as much time as possible to hear from you. And that's why we've already posted on our Web page for this meeting a series of videos that describe our current performance under the agreement, as well as several of the many actions we have taken to go beyond those baseline activities that we committed to meet.

The past eight months have been particularly challenging for our team and for our society as a whole. Want to echo Dr. Hahn's gratitude to my FDA colleagues for their

exceptional work, working round the clock to address the pandemic.

And as I've reflected back on our experience and our accomplishments over these months, I think one of the greatest tragedies would be if we did not learn from it, not just how to be better prepared for the next outbreak, but how to take those lessons learned to best serve patients at all times. So, let me offer three lessons learned from CDRH's perspective. And they really build on some of the themes that you heard from Dr. Hahn.

First is the importance of regulatory flexibility to rapidly adapt as the circumstances warrant. Much like in health care, particularly early on in the pandemic, when health care professionals had to make decisions on how best to treat their COVID-19 patients with limited data available to them because they didn't have the luxury of time, so did the FDA have to take actions based on the limited information available to us at that time but then adapt as new information and circumstances changed.

So starting in January, we proactively used our Emergency Use authorities to develop recommendations for how developers test and validate their products with the goal of streamlining the development, validation/authorization of tests down to weeks rather than the typical months to a year or longer.

And we put that out in what we call Emergency Use Authorization templates. And now we have ten of those that provide recommendations for a variety of tests. And we use those authorities, as you've heard, to now authorize over 550 medical devices.

And we've provided additional regulatory flexibility through the issuance of over 20 devices that pertain to guidances that pertain to medical devices, including flexibility for those products already approved or cleared on the market to be able to make changes to increase the capability to provide remote care.

And this level of regulatory flexibility not to mention the pace of guidance development can serve as a model for us in the future. But we do face a challenge moving

forward.

The regulatory paradigm that we operate under is over 40 years old and not well suited for many of today's modern technologies to both advance device innovation and optimally assure patient safety.

So, as we look to the future, we should consider how these approaches that arose out of our response to the crisis can be adopted and adapted for our routine operations. In particular, we should consider how we can tailor the regulatory paradigm and the evidence needed to best meet the technology and its tentative use.

And we should consider how we more routinely develop and issue guidances and adjust policies in near real-time as circumstances warrant. And we should also continue to invest in the development of templates and guidances, such like we did with the EUA templates and now with the e-STAR submissions that provide a level of greater transparency, predictability, consistency and efficiency in how the device industry prepares and how FDA reviews their submissions.

A second lesson learned is on engagement. Now, we took the level of collaboration that we provide in our Breakthrough Devices program. We essentially put it on steroids through a number of innovations.

We created something called the pre-EUA process where we provide advice or feedback in real or near real-time through informal emails and phone calls and the opportunity to review data on a rolling basis. We established a 24/7 1-800 hotline.

We also responded to over three hundred forty thousand email and telephone inquiries. And this level of engagement has been instrumental in accelerating the development, validation, authorization and availability of essential medical devices throughout the pandemic.

In the future, we should consider finding ways in which this level of engagement,

where it could be most beneficial and apply it such that we can significantly impact medical device innovation and patient care in the U.S.

And third, we've witnessed the value of our total product lifecycle or TPLC approach. And luckily, we had reorganized within CDRH to optimize the use of this approach before the pandemic, and we already see dividends paying off through our restructuring of our pre-marketing, post-market surveillance and compliance and quality activities from siloed offices to integrated teams.

In fact, now we're even seeing some companies reorganize in a similar fashion. In the future, we should all consider how we might better apply this approach to all that we do.

And as we look to the future CDRH's North Star will continue to be our vision, that patients in the U.S. have access to high quality, safe and effective medical devices of public health importance first in the world.

And patients are at the core of our mission to protect and promote public health. And when we think of patients, we include all consumers because all of us have been or will be patients and all of us are at risk for illness or injury.

And our vision recognizes that for patients to benefit from high quality, safe and effective technologies, they must have timely access to them. And as we've seen with the current MDUFA agreement, sound strategic investments in the FDA to modernize our regulatory program, to keep pace with the speed of device innovation, and to build out our infrastructure in ways that sustain the success of our program for years to come is absolutely critical. But is it good enough, in particular, in supporting our ultimate goal of improving the health and the quality of life of patients? That's what we need to figure out together. And as we do so, we should consider the use of the program not within a vacuum.

Instead, we should engage in a dialogue about where we want the medical device ecosystem to be at the end of MDUFA-5 and then consider how the user fee program can best be used to support achieving that future state, as well as additional actions that we should take.

I look forward to hearing feedback from today's sessions and from the patient provider communities, from industry and from others on how the MDUFA program is and is not at serving patients.

And I hope the discussion will help illuminate the ways that we can build on the foundation laid by MDUFA-4, incorporate the lessons learned from COVID-19 and to take into consideration where we collectively want to be the end of 2027 and beyond.

Thank you very much for joining us today. I look forward to our conversation.

MS. ROTH: Thank you, Dr. Shuren. Next, I'd like to turn to Dr. Peter Marks, the director of the FDA Center for Biologic Evaluation and Research.

Dr. Marks received his graduate degree in cell and molecular biology and his medical degree at New York University. He completed an internal medicine residency and a hematology/medical oncology training at Brigham and Women's Hospital in Boston. He's worked in academic settings, teaching and caring for patients and in industry and drug development.

He joined up FDA in 2012 as Deputy Center Director at CBER, and he became center director in January of 2016. We're glad to have him here today. Thank you, and welcome, Dr. Marks.

DR. MARKS: Thanks very much. And thanks for everyone for joining today. I'm going to keep my remarks relatively brief. We at the Center for Biologics Evaluation and Research appreciate the opportunity to take part in this meeting today.

Although CBER oversees only a relatively small fraction of devices relative the Center

for Devices and Radiologic Health, devices that we regulate across the spectrum, from tests to screen the blood supply to systems to ensure the safe administration of blood to devices for the selection of specific cells for use in stem cell transplants.

Additionally, our center regulates a number of highly innovative combination products consisting of devices and biologics, such as cells on scaffolds. We recognize the device work that we do in our center needs to be well harmonized with that done by the rest of the agency. And we very much look forward to contributing to the process here, moving forward.

And so, with that, I'll yield back some time here, because, really, we look forward to hearing what people have to say. Thank you.

MS. ROTH: Thank you, Dr. Marks. For the remainder of the day, this meeting will be devoted to hearing perspectives from outside stakeholders.

We look forward to hearing your assessment of the current MDUFA agreement thus far, what programs and commitments are working well, what could be added or improved under the next MDUFA agreement to further enhance the efficiency and effectiveness of the medical device review process.

In particular, we hope this meeting will begin a dialogue about what the medical device ecosystem and our medical device program and FDA, in particular, should look like in the future and how the next MDUFA agreement can help support our ability to achieve that future state.

We're running a little bit ahead of schedule, but I think our next two presenters are here. They are Pamela Goldberg and Sandy Siami. I want to thank you both for joining us.

They're from the Medical Device Innovation Consortium. And they're going to be discussing the National Evaluation System for Health Technology, or NEST.

If I can invite both of you to please unmute your phones, at this point, I will just say

that we appreciate you joining us today to discuss the progress of the NEST Coordinating Center to advance real-world evidence generation to support regulatory and clinical decision making.

And with that, I will hand it over to you.

MS. GOLDBERG: Thank you. I believe we have some slides. There they are. Thank you. So, I'm Pamela Goldberg and I'm the CEO of the Medical Device Innovation Consortium.

It's a pleasure to be part of today's forum with you. We appreciate the opportunity to share the progress of NEST, the National Evaluation System for Health Technology Coordinating Center. Next slide. I'd like to share a brief agenda for a glimpse of what we will cover today. I will be providing an introduction to NEST and the progress we've made to date toward our MDUFA-4 commitments.

I'm joined today by Sandy Siami, the senior vice president at MDIC and the leader of NEST, who will outline where NEST is today and its initiatives moving forward. Next slide.

One of the primary reasons our community needs NEST is that the medical device ecosystem faces a key challenge: how to ensure timely access to technology while also providing evidence to guide safe and effective use. There is a significant role for NEST to play in addressing that challenge. Next slide.

NEST is a national evaluation system developed to efficiently generate better evidence for medical device evaluation and regulatory decision making. NEST is operated by the Medical Device Innovation Consortium, a public/private partnership.

MDIC was initially created as a partnership between the FDA and industry to improve the medical technology environment. Since then, the organization has expanded to partnering with CMS, NIH and additional stakeholders to improve product safety and patient access to cutting edge medical technology while reducing cost and time to market.

In 2016, MDIC was awarded a grant from the FDA to establish the NEST Coordinating Center as an operational business unit within MDIC that provides governance for the NEST ecosystem, development and maintenance of the research infrastructure, standards for methodology and data quality, and finally, insight into the strengths and limitations of real world data sources. Next slide.

NEST is an independent coordinating center established by the FDA to drive quality and efficiency in the use of real-world data and real world evidence to inform medical device development and evaluation.

The mission of the initiative is to catalyze timely, reliable and cost-effective development of real world evidence to enhance regulatory and clinical decision making. And our vision is to be the leading organization within the health, technology and medical device ecosystem for conducting efficient and timely, high quality, real world evidence studies throughout the total product lifecycle. Next slide.

So, I'm going to spend a little time talking through some of the milestones that have brought NEST from its inception to where we are today.

As I mentioned, MDIC received grant funding for NEST in 2016. Since that time, we've been focused on developing the team, the infrastructure and the processes to establish the foundation of NEST and drive real world evidence forward.

We started by bringing together representatives from diverse stakeholder groups into the NEST governing committee to reflect the perspectives of industry, regulators, patients, payers, health systems and clinicians.

We formed partnerships with nationally recognized health organizations and research institutions, which we call our network collaborators, to build out the NEST research network.

This was a vital step to ensuring that the initial data sources, such as electronic

health records, claims and patients generated data and research expertise would be in place for NEST to break new ground in conducting real-world evidence studies.

Beyond access to real-world data, it was also important to work with leaders across the ecosystem to establish rules of the road for the generation of high-quality evidence. NEST again, engaged multiple stakeholders and experts to develop rigorous guidelines for real-world evidence research.

With these key pieces in place, NEST issued to public calls for concepts, for pilot real-world evidence studies from all stakeholder groups. The aim was to undertake projects that would explore the feasibility for stakeholders to work with real world data sources and NEST initial set of network collaborators, as well as to identify areas where NEST could create efficiencies.

We'll touch on those 21 pilots or test cases later in the presentation this morning. This year has been an important one for NEST milestones as we have accelerated our trajectory. We've published a research methods framework and a data quality framework.

We also announced the launch of NEST 1.0, opening the doors of NEST to broader ecosystem or ecosystem engagement and taking a key step forward on the path to sustainability. We are adding to the research network to expand the depth and breadth of NEST research expertise, including adding our first network collaborator outside the United States.

The path that we have taken has primarily been informed by and aligned with the commitments set forth in MDUFA-4, for which I will address next. Next slide.

NEST is advancing toward completion of the four key commitments in the MDUFA-4 commitment letter. These include implementing real-world evidence pilots, the NEST test cases; conducting an independent third party assessment of the test cases; posting a public meeting to review the progress and outcomes of the test cases, and seeking ways to make

NEST self-sustaining in the long term.

I will talk through each one of these commitments with an update on our progress to date. Next slide.

All of the NEST test case projects are in progress. So, as I mentioned, we had two public calls for concepts which yielded 21 test case projects. All of them have been launched.

The test cases cover a range of therapeutic areas, product codes, stages of the total product lifecycle and regulatory pathways as outlined in our MDUFA commitment.

Of the 21, eight are pre-market and five of them have been completed. Of those same 21, we have prioritized 12 of the test cases, six of which are pre-market and three of which have been completed. Next slide.

NEST is also committed to completing a third-party assessment to evaluate the strengths, limitations and appropriate use of real world evidence. We've contracted with the RAND Corporation to complete this analysis of the test cases, and that work is in progress.

Surveys and interview questions for the test cases have been finalized. Rand has initiated the assessment of the completed NEST test cases and will be conducting initial interviews for those projects over the next few months. The assessment will continue on an ongoing basis through the conclusion of all 21 test cases. Next slide.

We hosted the NEST forum on September 22nd to share learnings and findings of the test case projects to date. More than 300 attendees joined the virtual event with representation from industry regulators, health systems, patient groups, payers and physician groups.

In addition to discussing NEST initiatives and progress, the program included individual sessions with findings from the five completed test cases, collaborative

presentations with study sponsors, network collaborators, representatives from FDA and NEST staff. Recordings of the sessions from the NEST forum are available online. Next slide.

In June, we launched what we call NEST 1.0, a key milestone for us as we move toward a sustainability model. This is an exciting opportunity to further deliver on the vision and value of NEST using the infrastructure we've developed with our research network, using the learnings from our test cases to provide high quality, real-world evidence for the broader medical device ecosystem.

We have begun developing an early sales pipeline, are in active discussions with multiple organizations to conduct externally funded real-world evidence studies as customers of NEST. Next slide. We've learned a lot over the past couple of years in standing up a national evaluation system for health technology. In particular, the test case projects have yielded key findings which continue to inform NEST focus and efforts.

The test cases have already generated promising results. A few of our test cases started as feasibility studies to determine whether the results generated would be appropriate for regulatory submission. We are pleased to report that because of those promising results, a few have moved into Phase 2.

Prior to NEST, there was no playbook for connecting siloed data for research across different institutions, geographies and rock, real-world data sources. We continue to define and refine those processes.

Test case projects demonstrated our ability to facilitate collaboration among interdisciplinary team members across multiple network collaborator organizations. As we prepared to launch the test cases NEST needed to lay the groundwork for contracts and agreements around data use and data sharing due to our novel consortium structure.

Now that we have those templates in place, we expect those challenges will not

recur. Those challenges included data sharing and use agreements, as well as sub-award contracting. This early learning was important for NEST, and we have taken steps to expand resources and create efficiencies to address this challenge over the past year.

The NEST Research Methods Framework and the data quality framework have been critical in creating quality and defining principles for study design and data about validation.

As we continue to identify efficiencies, the creation of a centralized research infrastructure where participating network collaborators may contribute data, will help alleviate contract and data sharing issues. Next slide.

So, to recap, we have made exciting progress over the last few years, building NEST from concept to reality. Our test cases are all underway, with five completed to date demonstrating promising results for real world evidence.

The independent assessment of the test cases has kicked off and is ongoing. We completed our commitment to host a public meeting with the NEST forum last month. And we have launched NEST 1.0 to continue building towards self-sustainability.

So many people have helped to create all this progress. I want to take a moment to recognize the NEST and MDIC teams, the NEST governing committee and subcommittees and the many colleagues who have contributed to a great start for NEST, and we look forward to continuing this important work.

I will now hand it over to Sandy Siami to share more on the bright future for NEST. Sandy?

MS. SIAMI: Thank you, Pamela. Next slide.

As we look to the future, NEST will continue to work towards completing our remaining MDUFA-4 commitments, which include the completion assessment and dissemination of the test cases that we will use in our learning health system to continually assess outcomes, refine processes, and create a feedback cycle for learning and

improvement, for the use of real world data, for regulatory coverage and clinical decision making.

In addition, we're working on releasing our next iterations of the research methods framework and data quality framework that will constitute the playbook for using different types of real world data, depending on the type of clinical study and ensuing quality.

And finally, our efforts in building our infrastructure, our frameworks and pilot cases have allowed us to seek ways to make NEST financially self-sustaining as we continue through our current grant.

However, NEST will still require next round of funds as we will not yet be fully sustainable as we pivot towards a viable business model. Next slide.

A key for our current pilot research experience was to make sure that we covered a wide range of therapeutic areas and product codes, from cardiology to orthopedics to urology, as well as the total product lifecycle, pre-market, post-market label expansion, surveillance and the regulatory pathways whether it's a 510(k) or PMA.

You'll see, we partnered with large midsize and smaller device manufacturers, as well as FDA and patient advocacy organizations on the different test cases. We are aiming, with these pilots, to explore the feasibility of working with various types of real world data sources to determine fit for purpose, identify areas of deficiencies and help position us for self-sustainability.

It's important to note these test cases could not have been conducted without our amazing research network that represent health systems, academic medical centers, payers, registries and registry networks providing the real world data from electronic health records to public or private claims data like Medicare, patient registries and patient-generated data such as questionnaires, patient reported outcomes, wearables like Fitbit or other digital technologies.

Through our network, we have access to over 141 million lives in the U.S. and are expanding both in the U.S. and internationally. Next slide.

We continue towards our MDUFA-4 research objectives. First, with regards to our test cases that have not yet been completed, we'll continue to implement quality improvement initiatives to standardized reporting progress towards completion, as well as actively participate in study design development and results review in order to better track timelines and deliverables, as well as facilitating potential discussions with regulators.

Our test cases are currently being socialized across the applicable review groups. And this collaboration not only helps us to better understand reviewer thresholds, but also, I hope, it helps make reviewers comfortable with the type of evidence that is generated using real world data compared to traditional trial sources.

While we've met our commitment to hold a public meeting, it's important for NEST to continue to hold many forums as test cases are being completed to continue the discussions of progress and outcome as a part of our learning health system.

And finally, our independent assessment of test cases has kicked off since we started -- we've started to see our pilot projects being completed. We are soliciting interviews from the proposal submitters which, in most cases, are the device manufacturers, the research collaborators who generated the evidence and, as appropriate, FDA reviewers and our NEST research team.

By conducting assessments as test cases are being completed, we're able to make continuous quality improvements. But the comprehensive assessment itself will be generated after all the test cases are completed. Next slide.

In order for NEST to continue to mature, to achieve a 100 percent self-sustainability, we need to accomplish a few more things to advance the use of real world data that generates real world evidence that is fit for purpose, for medical devices, radiological

imaging laboratory, in vitro diagnostics, as well as digital health technologies.

A solid quality management system is the backbone for systematic processes and procedures that will allow for standardization, consistency, continuous quality improvement and improved client satisfaction.

This includes designing standard operating procedures, processes and templates for operational excellence, training our staff, scientists, researchers to applicable regulations and guidance and implementing a new culture of client satisfaction. Next slide.

To truly provide quality evidence by design, we're changing the traditional research paradigm. In order to provide high quality evidence to ensure the availability of safe, effective and innovative technologies for patients, we need to first curate the right data sources and research expertise, dig deep into our research network and data characterization and research expertise.

The unique feature of NEST is that we are not only able to provide retrospective data, but also link the data across various networks to collect prospective data. Part of this curation could be a certification process that will benefit multiple stakeholders, from regulators and industry to payers, providers and patients.

And of course, we need to continue to expand our research network. The next pillar is catalyzing transparent and traceable real-world data provenance that leads to actionable evidence for regulatory decision making.

This means refining our research methods framework and data quality framework that will define the various types of real world data, characterize their applicability or fit for purpose of the various types of studies that may include first in man or early feasibility as well as pivotal label expansions, post-market surveillance and post-approval studies.

The frameworks will also better define the data maturity model of our networks and the quality thresholds that are based on the total product lifecycle.

And our third pillar is to create a neutral space or a safe harbor to share data for effective research by engaging with multiple stakeholders in all aspects of NEST. In order for us to move forward with full sustainability, NEST will have to offer a depth and breadth of expertise in research and data to ensure the research is being conducted within the NEST ecosystem that is expected to provide the data quality that is fit for purpose.

In addition to these three pillars, as a part of self-sustainability efforts, we're looking to provide more services outside of just the regulatory decision making. This includes pair driven research for coverage, reimbursement and even technology evaluation and clinically driven research for proof of principle, class effects and health care quality improvement activities. Next slide.

NEST is asking for consideration in MDUFA-5 discussions to create a true multi-stakeholder learning health system, to be able to provide industry reliable strategies in their regulatory arsenal to help advance safer and more effective devices to the market in order to ultimately benefit the end user, which is the patient.

The innovative technologies and resulting robust data can empower both clinicians and patients for a truly patient-centric experience. We are creating the research paradigm for evidence generation. Thank you.

MS. ROTH: Thank you, Ms. Goldberg and Ms. Siami. We appreciate you joining us here today. And we are indeed running about 20 minutes ahead of schedule.

We'd like to begin with the Industry Perspectives panel at 10:15 on schedule. So, we are going to take a 20-minute break. And we hope that you all will tune back in with us at 10:15. Thank you.

(Off the record at 9:55 a.m.)

(On the record at 10:15 a.m.)

MS. ROTH: Thank you, and welcome back. Next, we will turn to our panel of

leadership from our industry partners. And we're joined today by Janet Trunzo of AdvaMed; Mark Leahey of the Medical Device Manufacturers Association; Peter Weems from the Medical Imaging & Technology Alliance and Thomas Sparkman from the American Clinical Laboratory Association.

If you could please unmute your lines now, that would be great. And while you do, I will just note that the current MDUFA agreement we did before was transformational in many ways. But one particular innovation was the establishment of shared outcome goals between FDA and the industry.

MDUFA-4 recognized that ensuring timely patient access to safe and effective devices involves effort both by FDA and by our partners in regulated industry. And we appreciate your contributions to this effort. And we thank you for sharing your perspectives today. And with that, I will turn it over to you.

MS. TRUNZO: Great. Thank you very much for the opportunity to speak today. Good morning. This is Janet Trunzo. I am with AdvaMed, the Advanced Medical Technology Association.

Before I begin the AdvaMed comments, I'd first like to acknowledge the accomplishment of FDA's review of emergency use authorizations for the current COVID-19 pandemic.

FDA met the challenge by establishing flexible regulatory policies to ensure that needed medical technologies such as COVID diagnostics, ventilators, personal protective equipment was available to address the pandemic. FDA's work has been critical to our country's emergency response.

Now I'd like to begin the AdvaMed comments. We're very pleased to be able to provide comments today as we continue to work with FDA to prepare for the next user fee agreement.

The medical device user fee program represents a commitment among three parties: FDA, Congress and the medical device industry. Additional resources support the review process to ensure greater predictability, consistency and efficiency.

FDA commits to a set of performance goals worked out with the industry. It is important to note that review metrics established by MDUFA are defined by time to an FDA decision, not an approval. Whether that decision is positive or negative is entirely up to FDA.

FDA's primary objective is to protect and to promote public health. User fee agreements do not change that objective. In fact, they help make that objective more achievable by providing additional resources to ensure timely access to safe and effective medical technology.

I quote from Page 1 of the current MDUFA-4 commitment letter. "Nothing in this letter precludes the agency from protecting the public health by exercising its authority to provide a reasonable assurance of safety and effectiveness of medical devices." It is clear in no way is safety and effectiveness compromised by the user fee agreements.

The proof is all around us. Consider the hundreds of millions of medical devices successfully implanted or interacted with on an annual basis as a measure of a strong safety record. We are here today to continue the process we began back in 2002 with the first user fee program to provide safe and medical -- effective medical technology to patients who need them.

Now that we are well into the fourth year of the current MDUFA-4 program, the investment of resources into the device program has yielded positive results. We have come a long way since that first user fee program in 2002.

Because of the financial stability that user fee revenues have brought to the device center, hundreds of scientists, status petitions, engineers and medical officers have been

added to the FDA staff.

FDA has improved the pre-submission process, which is such a critical component for an efficient review process so the submitter has a better understanding of FDA's expectations and can deliver on those expectations.

Additionally, once the submission review is under way, the use of interactive review has increased, allowing the FDA and the submitter to resolve minor review issues more quickly and efficiently.

For more significant issues, FDA can use the substantive interaction midway in the review process to formally identify and communicate any deficiencies in the submission.

One MDUFA-4 commitment requires FDA to provide a statement of the scientific basis for the cited deficiency. FDA's own quality audit of this process identified a need for improvement in the frequency of stating the justification for the deficiency.

We look forward to FDA's advancing improvements in this priority commitment. MDUFA-4 user fee funding supported the establishment of the center's Digital Health Program, the Patient Engagement and Science of Patient Input Program and Enhanced IT to support the submission tracker.

AdvaMed commends the agency for significant progress in these key program areas. In MDUFA-4 FDA committed for the first time to a decision goal for De Novo submissions. With resources to support the De Novo submission reviews, we commend FDA for meeting those goals.

As MDUFA-4 continues for the next two years, and in order to support the commitments in the final two years of the program, we urge FDA to complete hiring of all MDUFA-funded FTEs as soon as possible. We encourage FDA to focus on the basics of the review process to advance the principles of consistency, predictability and efficiency.

We have the tools we need with the current infrastructure and now we just need to

focus on sharpening those tools and maximizing their use. As we begin the MDUFA-4 discussions, we recommend continued improvement in MDUFA-4 successes achieved thus far and focusing on review process basics from the -- submission process to interactive review to the final decision.

We look forward to the results of the Phase 2 report of the independent assessment as we enter the discussions. We also look forward to the results of the CDRH Quality Management Systems Program and other programs, such as the improved third-party review program and the use of real-world evidence to support pre-market regulatory decisions.

In closing, I would like to reemphasize under the user fee program, we share a common goal with FDA and Congress to ensure that patients have timely access to safe and effective medical technology. Furthering that shared goal should be the foundation for the next MDUFA-5 negotiation. Thank you very much.

MR. LEAHEY: Okay, thanks, Janet. Again, thank you, FDA, for the opportunity to present at today's public meeting to kick off the MDUFA-5 process.

My name is Mark Leahey. I'm the president and CEO of Medical Device Manufacturers Association. And I'd like to begin also in just thanking Dr. Shuren's extraordinary team at FDA, within CDRH and across the agency for the extraordinary work, the dedication, the commitment, the effort that they've put in over the course of this year to battle the COVID health pandemic.

I think in these times, the value of public health officials and innovative collaborating and working together has never been greater on behalf of public and on behalf of patient care.

And it's also important to note that beyond the COVID-related products, that the EUAs were able to help drive and increase capacity for, there are a number of non-COVID

related products that the reviewers continue to bring to the market to improve patient care.

So again, I think FDA and the team has done extraordinary work. We know that many folks have been working both on the FDA and the innovators seven days a week, 18 hours a day. And again, the impact that they're having to improve public health and to fight this public health emergency is clear to all.

MDMA's mission is to ensure that patients have timely access to safe and effective products. And the FDA has always been a global gold standard when it comes to ensuring patient safety. It also continues to make enhancements to accelerate patient access here in the U.S. Ten years ago, there were a number of novel medical technologies that were based here in the U.S. and in some instances, the U.S. was the 40th or 70th country to provide regulatory approval for those U.S. based technologies.

But based upon the investments that industry and FDA has made, the greater collaboration and coordination, we're moving much more quickly. And now there's been tremendous progress where U.S. based novel technologies are now, many of them, coming to the market first in the world in the U.S. and maintaining that strong safety profile.

So again, I think there's been extraordinary progress that FDA has made, working with innovators, working with patients to ensure that, again, these products are available to them in a timely manner without compromising the strong safety and efficacy thresholds that exists.

And as we look forward to MDUFA-5, I'm sure there'll be ways that we can build upon what we have learned over the course of the previous four MDUFAs. Like Janet, I've been involved in -- this is the fifth user fee negotiation and I've had the privilege of representing MDMA and the industry.

And I think it's worth noting, as we look ahead, where we're at. The first user fee

program, MDUFA-1, the total revenue collections were $144 million. In MDUFA-2, the revenue user fee collections went to $312 million dollars.

In MDUFA-3, they jumped to $658 million. And in MDUFA-4, the industry to be providing over a billion dollars -- over a billion dollars -- in industry funds to help support pre-market reprocess so that again patients have timely access to safe and effective products.

To put things in perspective, just in FY-19 alone, the total collections were $208 million. That exceeds the entire user fee collections of the -- in the entire MDUFA-1 program. So, there have been significant investments that we've made.

And throughout the negotiations, too, we've been told multiple times that, well, PDUFA's a more mature program. You're 10 years behind. So, you know, the first four legs of PDUFA, they really had to make significant investments, but then it was really more of a maintenance pathway.

And I'm pleased, and I know that that was a key selling feature to get industry to agree to the billion-dollar threshold of MDUFA-4.

As Janet said and as others have indicated, there has been great progress that has been made and we've created a solid foundation. Now it's making sure that tools are utilized wisely, that if there are lessons learned from COVID or others, we can enhance the process, make it more efficient -- again, without compromising patient safety.

And that really is going to be, I think, the focus of MDMA and our members as we enter into the MDUFA-5 negotiations.

When we surveyed our members at the beginning of the last user fee program, 95 percent prioritized the quality of the journey over the time of the journey, meaning the more consistent, transparent, predictable it was, that was far more important than a day or two on decision goal with the understanding that if you have a more well-defined,

consistent process that the net output here should be a more efficient review at the end of the day.

And so, again, these are the things and kind of the mindset as we go into MDUFA-5 that I think are important for folks to understand. And the other critical piece is not just the total dollars in the significant ramp up that we've made in an investment, but fundamentally, our members believe that the primary source of funding for the agency should be congressional appropriations.

It's Congress's duty to fund federal agencies. It was always intended the user fees were supplemental in nature, not to be the primary source of funding. We think that's a critical tenet to maintain as we enter the MDUFA-5 discussions as well.

And again, given the extraordinary work that FDA and the professional team, the public health officials have done during COVID, we recognize certain things have fallen on the backburner, so to speak, you know, software as a medical device draft guidance.

There was [sic] other issues on -- or commitments, but we recognize that no one could have predicted the circumstance and that people were working very diligently. So, our hope is that, again, as we look ahead here, given some of the uncertainty, we can focus in on areas that may have fallen behind a little bit.

And let's make sure that, in those commitments, that we dedicate resources to execute on those. One that's important that Janet mentioned also to our members is the key commitment in MDUFA-4 that in the deficiency letters that reviewers send to sponsors, that they indicate with specificity, setting a statute guidance or reg, a reason for the request or the deficiency justifying that.

As was stated earlier there was this -- and this is really a fundamental foundation, a priority commitment to help with that quality of the journey. And based upon FDA's audit in 2019, only 27 seven percent of the deficiency letters that came out actually had that

citation of specificity.

There was additional training, education and an audit was done this year, and we're up to 50 percent. So again, progress is being made, but clearly, if 50 percent of deficiency letters that companies are receiving, don't cite with specificity the rationale, there's an opportunity for enhancement.

So, again, I think that's just one example. Before we go and work to create new initiatives or priorities, there's some foundational MDUFA-4 commitments that I think we should focus on that were important, that were negotiated. We need to make sure those are realized before we look too far ahead to try to create a number of new initiatives.

I also think that when you look at the capacity issues, and we're sensitive to the dramatic amount of time and energy that FDA has is taking to review the -- not only the traditional submissions, but also the COVID-related and EUA, understanding that the number of EUAs and pre-EUAs has significantly increased.

And that's -- and I don't think that most of those so probably require the same amount of energy as a traditional submission, but they require time and effort and resources that need to be allocated elsewhere.

And I think, as was said by Janet as well, we would certainly hope that in order to provide additional capacity at last count, based upon the 2nd quarterly meeting, I think there were still about 50 MDUFA-4 FTEs that industry has currently funded that have not been hired yet.

So that's a great opportunity, I think, to make sure that those folks are brought on. We understand there maybe additional challenges during a public health emergency. But again, we're providing the funding for those FTEs and we're doing so prior to the public health emergency.

Hopefully, steps can be taken to bring those folks on board. That should provide for

additional capacity, additional throughput, which, as Dr. Shuren said earlier in his remarks, will provide for more collaboration, interaction between the sponsor and FDA, hopefully, to enhance the outcome for patients.

I would like to note too that when we look at funding the FTEs, you know, MDMA and our members feel very strongly that as we begin the MDUFA-5 negotiations, there is a better methodology to calculate the cost per FTE.

Current methodology takes the total device review budget, divides by the number of FTEs, and that's the cost per FTE. I don't think anyone would agree that that's a very scientific or precise methodology.

Most would say that you start with the average salary, add benefits and a portion of overhead and that -- you kind of build that piece up to a cost per FTE. So that is something we are hoping to have a conversation with the FDA to have a better assessment and more accurate cost per FTE as we look to see if there are additional resources and investments we make in MDUFA-5.

At this point, again, I don't want to get into too many particulars because I think we're waiting for some data responses from FDA.

But again, I want to close where I opened, with the extraordinary work that the -- Dr. Shuren and all the professionals at CDRH have demonstrated over the past, not just seven months during the public health emergency, but really over many, many years.

This has -- there's certainly been some challenges in the regulatory process along the way. But I think now, what FDA has done both in the pre-market side and the post-market side, again, has maintained that global leadership position, that gold standard when it comes to safety and efficacy, but also making progress so the patients have timely access to innovative products.

I think one thing that is often not appreciated is that if you have a patient who needs

a critical medical technology that's based here in the U.S., there are stories 10 years ago of patients literally having to fly from California to get to the UK to pay out-of-pocket for a medical device that was developed 30 miles from their house. That is unacceptable.

And the patient harm that resulted, the opportunity costs of patients not getting access to these medical technologies in a timely manner, killed countless Americans.

But again, I give FDA tremendous credit for advancing the process, making it more transparent, effective, efficient, and that has resulted in saving countless lives for the timely products coming to the market. Patients have access again without compromising that full standard with safety and effectiveness.

So MDMA looks forward to working with FDA, patient groups, Congress and other stakeholders to reauthorize a user fee program to assess what has worked, what hasn't, where we need to refocus previous commitments so that we have a strong and robust user fee program, MDUFA-5, that enhances patient care, that promotes innovation, and that continues to make sure that U.S. patients have access to the best health care in the world. Thank you.

MR. WEEMS: Thanks, Mark. Good morning. My name is Peter Weems. I'm the senior director of policy and strategy with the Medical Imaging and Technology Alliance, also known as MITA.

MITA is the Primary Trade Association and Standards Development Organization for Manufacturers of Medical Imaging Devices, software solutions contrast agents and radiopharmaceuticals. We appreciate the opportunity to share some thoughts this morning.

First, though, I would like to start by commending the agency for the work it has done over the last nine months, especially helping to ensure that patients and health care providers have been able to receive the safe and effective medical products they need to

combat the COVID-19 pandemic, doing this while still meeting user fee commitments.

During the pandemic of medical imaging technologies such as mobile X-ray, chest CT and Point-of-Care ultrasound have been able to get to health care facilities serving COVID-19 patients in an expedited manner and with greater regulatory flexibility thanks to actions taken by the FDA.

Beyond COVID-related products, MITA member companies have in recent years brought to market innovative technologies including low dose CT scanners, high Tesla MRIs, ultrasound elastography and advanced AI algorithms.

Our technologies play an essential role in health care infrastructure in the care pathways of screening, staging, evaluating, managing and effectively treating patients with cancer, heart disease, neurological degeneration and numerous other medical conditions.

Our member companies' ability to bring these innovative technologies to market in a safe and effective way has been supported by the efficient, predictable and transparent pre-market review pathway created by the medical device user fee program.

Under the user fee program, medical imaging technology manufacturers have been able to deliver and iterate on safe and effective innovations for patients and health care providers in a timely manner. And by timely, I mean timelines measured in a few short months or a matter of weeks.

Under the current iteration of the user fee program, MDUFA-4, FDA has produced very satisfying and highly satisfactory premarket review performance results, which we hope to carry into MDUFA-5.

The ground that has been gained for pre-market review performance under MDUFA-4 needs to serve as the foundation for ongoing success during MDUFA-5.

Under MDUFA-4, the agency has launched new initiatives, pilot programs and special projects to investigate new sources of data, the use of standard novel digital technologies

and other emerging regulatory considerations.

These initiatives are in various stages of maturity, some having only very recently been launched. The value proposition of these ancillary programs remains to be seen. But we look forward to continuing to work with the agency over the remainder of the current user fee iteration to determine the value for pre-market review of these initiatives.

As these programs progress and these discussions concerning MDUFA-5 commence, we will work with FDA to determine whether these programs should continue or not into MDUFA-5 and whether these programs should be funded by user fees or if they should be funded by appropriations or become self-sufficient via other revenue streams.

Given the satisfactory performance the agency has achieved under MDUFA-4, at this time we do not anticipate any need for major new programmatic initiatives or major new commitments in MDUFA-5. We hope to carry forward what has been working and leave behind what has not.

And what has been working under MDUFA-5 before is the efficient, predictable and transparent pre-market review process supported by these user fees. MDUFA-4 process changes have allowed for increased communication between industry and regulators throughout pre-market review.

Concrete metrics have been established against which performance is measured as reviewers evaluate medical device submissions. The 510(k) review pathway has been modernized to allow for greater reliance on consensus standards. And most importantly, safe and effective innovative technologies have been coming to market on time.

So, as we look to MDUFA-5 and the medical device ecosystem it will support, our goal is to maintain safe and effective medical devices delivered in a timely and efficient manner. We look forward to working with the FDA, Congress and others to build on and extend the success of MDUFA-4 into the coming years. Thank you.

MR. SPARKMAN: Good morning. Thank you for the opportunity to speak today. I am Tom Sparkman's Senior Vice President for Government Affairs and Policy for the American Clinical Laboratory Association.

I would like to join in thanking the FDA, my colleagues and their organizations on this panel, numerous attendees and other health care professionals in their continuing incredible work in this amazing response in this current public health emergency with the COVID-19 pandemic.

Moving to my comments, founded in 1971, the American Clinical Laboratory Association has been the leading voice for solutions that expand access to vital clinical laboratory tests that millions of patients depend on for their health.

America's clinical laboratories play a fundamental role in expanding a value-based health care system by advancing the next generation of precision medicine and care delivery; providing accurate and reliable data to inform diagnoses for acute infectious disease and chronic disease; and supporting providers, hospitals, and patients in developing personalized treatment plans and preventing serious, costly complications that burden patients and the health system.

As an advocacy organization, ACLA and its members advocate for reforms that improve patient care by first providing broad access to accurate and reliable clinical laboratory tests.

Second, by supporting a clear and appropriate regulatory framework and market pathway for new innovative laboratory diagnostics, including laboratory developed tests or LDTs and in vitro diagnostics, or IVDs and finally, by improving care coordination among providers, hospitals and clinical laboratories.

ACLA members have been on the front line of the 2020 COVID-19 pandemic response, innovating to rapidly expand laboratory test capacity, increase the types of tests

available for clinicians and patients, and ensure broad patient access to accurate and reliable tests.

Since the beginning of March this year, ACLA member laboratories have performed over 52 million PCR tests for COVID-19 in addition to millions of serology antibody tests, and we are committed to ensuring continued strong patient access to testing through the continuing response and beyond.

Within MDUFA, FDA first invited ACLA to participate in the medical device user fee negotiations in the MDUFA-3 cycle, along with AdvaMed, MDMA and MITA, as representatives of, quote, "regulated industry." ACLA subsequently participated in MDUFA-4 negotiations. As ACLA has stated in these past negotiations, participation in the user fee negotiations by ACLA and ACLA members is not intended to and does not constitute a waiver of any potential argument or legal release to which ACLA and/or its members may be entitled with respect to potential regulatory oversight of LDTs or clinical laboratories by FDA. Participation by ACLA and its members in these negotiations is intended to allow labs to address MDUFA issues that would arise if LDTs are regulated as medical devices and if labs are required to register as device manufacturers.

Before turning to specific issues related to user fees that may apply to laboratories, some background and history regarding FDA regulation of LDTs is needed to provide necessary context. At various points over the years, the FDA has asserted that LDTs are medical devices and that laboratories which performed LDTs are device manufacturers. ACLA has consistently communicated its disagreement with these assertions.

The agency, over time, has articulated a number of LDT regulatory proposals under which FDA proposed regulating LDTs as medical devices through draft guidance documents. FDA has also sought, in certain instances, to bring public and non-public enforcement actions upon certain lab developers, tests, or categories of tests. More recently, the

Department of Health and Human Services announced that FDA cannot require premarket review of LDTs except potentially through notice-and-comment rulemaking. And the FDA has subsequently indicated it will not review LDTs submitted for Emergency Use Authorization within the continuing COVID-19 public health emergency.

Finally, over the past several years, various FDA officials have affirmed the need for a new statutory authority for diagnostic regulation. For example, FDA officials recently published an article in the New England Journal of Medicine citing, quote, "the need for a common legislative framework to ensure that all clinical tests are accurate and reliable," close quote.

In parallel to these administrative activities, ACLA has been actively engaged in discussions with Congress, the current and past administrations, and diverse stakeholders to design and negotiate a modernized statutory framework specific to clinical laboratory tests, whether LDTs or IVD kits. Originally, these discussions focused on the legislative discussion draft of the Diagnostic Accuracy and Innovation Act, or DAIA, and have subsequently evolved to the bipartisan and bicameral Verifying Accurate Leading-edge IVCT Development, or VALID, Act introduced by Senators Richard Burr, Michael Bennett, and Representatives Diana DeGette and Larry Bucshon.

All ACLA members perform laboratory-developed tests, and therefore, ACLA has prioritized both the administrative and legislative discussions. Some ACLA members have voluntarily submitted or may voluntarily submit applications to FDA for medical device clearance or approval for certain LDTs. Within the pandemic response, some ACLA members have also submitted or may submit applications for Emergency Use Authorization of LDTs with the agency.

Against this backdrop, we see a number of scenarios where user fees may be imposed or proposed for clinical laboratories developing and offering LDTs. The various

scenarios, including a potential new statutory framework, make it necessary to outline various uncertainties impacting any proposed user fee allocation. These uncertainties include, first, the number and size of labs that develop and offer LDTs; second, the number of LDTs offered by given laboratories; third, the complexity and burden of any oversight for LDTs and LDT developers; fourth, criteria for and/or exemption from any premarket review or other application type; and finally, the timeframe for any oversight framework.

Previously, in MDUFA-4, ACLA proposed that, one, any FDA user fee data or report metrics should separate and report on voluntarily submitted LDTs distinct from IVDs, and second, that FDA should commit to review and clear or approve voluntarily submitted LDTs no less favorably than other CDRH submissions.

To reiterate, ACLA continues to assert that medical device authority does not apply to clinical labs nor to LDTs. And ACLA and its members do not waive any potential argument or release to which they may be entitled.

ACLA will continue to seek transparency on policies, proposals or activities that may impact clinical laboratories and LDTs and will continue to advocate against policies or activities that would inappropriately impinge upon laboratory innovation and harm patient access to accurate and reliable clinical laboratory services.

Either in the context of MDUFA negotiations or legislative discussions, ACLA and its members are committed to pursue clear and regular -- clear and appropriate regulatory oversight and market pathways for laboratory diagnostics and innovation, thereby ensuring that clinical laboratories remain a strong component of the nation's public health infrastructure and also ensuring broad patient access to accurate and reliable clinical laboratory tests.

Thank you for this opportunity to present today.

MS. ROTH: And thank you again to all of our industry panelists. We look forward to

working with you as we move forward with the negotiations. And because we are running ahead of schedule, again, we will move to taking another short break and resume the meeting at 11:15 with the scientific and academic stakeholder perspectives.

Unfortunately, one of our panelists was unable to join us. And so, we will resume at 11:15 with a presentation from Kathleen Blake, of the American Medical Association. And then after that, we'll break for lunch. So hopefully we will see all of you at 11:15, and thank you very much.

(Off the record at 10:54 a.m.)

(On the record at 11:15 a.m.)

MS. ROTH: Hello. I'd like to welcome everyone back to the MDUFA-5 public meeting. We are set to begin momentarily with Dr. Kathleen Blake of the American Medical Association as we turn to perspectives from our scientific and health care professionals' community.

Unfortunately, our second presenter, wasn't able to join us this morning, so I will ask Dr. Blake to -- she's already unmuted. And after we complete this portion of the agenda, we will go back on break.

We will break for lunch and resume on time this afternoon with a very exciting set of panelists, the patient and consumer perspectives. So, without further ado, if I can please turn it over to you, Dr. Blake, and thank you.

DR. BLAKE: Thank you so much. And if we could bring up my slides, that would be terrific. Perfect.

So first of all, the American Medical Association wants to thank the FDA for the invitation to provide our perspective, and commend them for facilitating this dialogue amongst the many stakeholders to improve the medical device review and approval process, and even more importantly, make sure that devices are available for patients as

their health care needs arise.

I'm Dr. Kathleen Blake. I'm a cardiologist. I'm vice president for Health Care Quality at the American Medical Association. And as I provide my remarks, I want to note that although I am a member of the NEST Coordinating Center Governing Committee, I come today as the American Medical Association's representative and not as a representative of the NEST Governing Committee, about which you've already heard quite a bit today.

I think it might help some in the audience to know a bit more than perhaps they currently know about the American Medical Association. Our mission is to promote the art and science of medicine and the betterment of public health.

AMA was founded a long time ago, back in 1847, to address the use of unproven therapies to treat medical conditions. Notably, it was founded with the same intent, I would say, that many would see as the reason for founding of the U.S. Food and Drug Administration.

We are the largest physician organization in the United States with approximately 256,000 members. What some of you may not know is that AMA policy is set by a House of Delegates and this House of Delegates represents 125 national medical specialty societies and associations, 54 state and territorial medical associations, 5 delegations that represent the uniformed services.

And core to our mission and to our contact is that we are committed to care that is based on the best available science and evidence, is patient centered and collaborative, and that we welcome opportunities such as this one to seek common ground with others working to improve health and health care.

If we could go to the next slide, please. So, I think that, again, from our House of Delegates, we have strong AMA policy to support the funding and the robust work of the FDA. That policy for adequate funding goes back to 1978. So, one can think of that as even

preceding the institution of user fees.

I've already told you about the diversity of our membership and the number of organizations that participate in our house, so it won't surprise you to know that there there's a strong interest among our members and their patients in the regulation of drugs, devices and biologics.

And I would go so far as to say that because of our diverse interests, perspectives and specialties within the house of Medicine, that likely there is no product that is currently regulated by the FDA that does not in some way impact the health of the patients that we care for.

So, we have a strong interest in there being a bright future for MDUFA. And we're pleased to present our views at this meeting. If we could go to the next slide, please.

So first, a few words about the pandemic, and as I've listened to the earlier presentations, I think none of us can avoid talking about the pandemic, nor should we. Although I would also say that we would all hope and expect it to subside by 2022 when the next MDUFA agreement will be reached.

The COVID pandemic has exposed vulnerabilities in global medicine, the device supply chain, medication availability, and it has led to uncertainty. And I think Dr. Shuren's comment earlier about the need for a very agile, adaptive type of professional approach is particularly important at times like these.

We'd also acknowledged the fact, we talk about it frequently at the AMA, that the pandemic is a marathon. It is not a sprint and that we recognize the toll that this has taken on the entire ecosystem, including the 17,000-plus professionals at the FDA.

So, it's really with this perspective in mind that we take note of the significant progress made in meeting the MDUFA performance goals in fiscal years 2018 and 2019, before the pandemic, and that thus far in fiscal year 2020, FDA is continuing to make and

report progress on goals, even in the face of the enormous demands of the pandemic.

Maybe on a sobering note, we would also say that we think the challenges related to product review and the issuance of guidance are likely to continue throughout the rest of the pandemic, associated public health, emergency and beyond. Next slide, please.

As part of this meeting, we did take note that although the usual focus does have to do with the work of the Center for Devices and Radiologic Health, that we appreciate that there has been an opportunity for us to thank and to express our appreciation for the professionalism and dedication of the career scientific staff at CBER throughout the pandemic.

Special thanks also to Dr. Peter Marks, who was our keynote speaker for the first program of AMA's COVID vaccine webinar series. And we strongly support the deliberate, transparent approach that's being taken by CBER to the review of COVID vaccines. We strongly support the additional guidance that FDA has issued to clarify its standards for COVID vaccine licensure and the process by which it intends to review a vaccine or vaccines for emergency use authorization.

And we look forward to working, continuing to work with CBER to inform physicians. And I should extend that and just say also to continuing our longstanding work with the Center for Devices and Radiological Health.

We really do see this as that we are all in this together and it will take that kind of an approach to be able to get the pandemic in our rear-view mirror. Next slide, please.

So, in the considerations for MDUFA-5, we have chosen, instead of focusing on every aspect of the MDUFA-4 agreement to focus on some particular areas, including digital health and artificial intelligence.

First, we are delighted with the recent announcement of the establishment of a digital health Center for Excellence. This is, of course, the fulfillment of a major

commitment made in MDUFA-4 We do hope that this additional focus and allocation of resources that a center will bring will result in additional clarity as to the regulatory requirements in this domain.

A lot of groundwork has already been laid. Much more work remains. In particular, AMA believes there's a pressing need for additional clarity on the appropriate regulatory pathways for artificial intelligence.

And we eagerly await and expect more guidance related to artificial intelligence, because we think that physicians and their patients need assurances of safety and efficacy, particularly when a mode or a product paradigm is new.

Also, that these are products that must be designed with clinical integration in mind and would express our concern that if such information is not available, that it will be difficult for physicians to trust AI-based products.

And that would be the unfortunate outcome because we would then potentially miss out on the potential gains, the significant gains that we could otherwise see in health care.

We do take note of the attention that's been paid to patient concerns and the expression of similar need for trust and transparency by the members of the CDRH Patient Advisory Committee that convened recently to discuss artificial intelligence. Lastly, although it's not directly related to MDUFA but does reflect some of the competing demands within CDRH, the AMA requests that the draft guidance, risk categorization of software as a medical device, FDA interpretation, policies and considerations, the kind of guidance we think would bring great clarity to this space be moved to the highest category, Category A, on the recently published CDRH list for 2021 of priorities for guidance documents. Next slide, please.

Diving a bit further into artificial intelligence. AMA has commented, submitted formal comments, written comments at a variety of stages along the way with respect to

artificial intelligence.

And in particular for this group, I think it's important to note that it's our sense that the International Medical Device Regulators Forum framework did not fully and could not fully at the time it was developed, anticipate some of the additional dimensions of risk that can be associated with particular types of artificial intelligence, especially those that are based on continuously learning systems.

For example, the framework does not clearly specify whether a system and how a system should be regulated if it is autonomous yet preserves the clinician's ability to intervene or override the system or a system is fully autonomous and the clinician does not have the ability to intervene or override and the instances in which the algorithms and the output of the algorithms are assistive, but where human intervention is required for implementation.

So, while we understand the desire, the potential value to achieve a harmonized international regulatory paradigm, we do think that the IMDRF paradigm should be modified to address these issues. The safe years of medical devices depends on well informed users, and it's our belief that the labeling concepts that are used with these new devices need to be modernized from existing labeling concepts and in particular, to provide greater transparency to end users on a safety effectiveness and appropriate use of these products, specifically an explanation of the population from which the training data was derived and any limitations, therefore, in the application of that product to other populations. Next slide place.

One of the major areas of emphasis in the MDUFA-4 agreement is the use and really the further understanding and application of real-world evidence. As I mentioned before, the AMA House of Delegates sets our policy and is available on the AMA website for those that would like to review it.

We have extensive, detailed policy with respect to real world data and evidence. We support the generation and use of it and its application when fit for regulatory purposes for the evaluation of medical products, while at the same time realizing the importance of protecting patient privacy and confidentiality; improving regulatory decision making, reducing, we hope, the cost of medical products and advancing innovative and new models of product development.

We support the work of the FDA and its commitment to expanding the use of real-world data and evidence and to understanding how it can be combined with the data and evidence that comes from what we might call the more traditional, randomized, controlled clinical trials.

We think this is another one of those instances in which it is a team effort. So, we support cooperation and collaboration of all of the stakeholders so that there is broad understanding, commitment and acceptance of its use.

This then takes me next to speaking about the national evaluation system for health technology, because it is on the basis of AMA policy with respect to real-world evidence and data that the AMA has been strongly supportive of NEST from the planning stages to the actual establishment of the center.

We applaud the progress that's been made to date to establish NEST, to engage a wide variety of data partners, including now one partner outside of the United States; to issue methods and guidance or methods and data quality guidance, to support test cases across a wide range of clinical domains and regulatory pathways and to launch NEST 1.0, as you've heard earlier, more about it from the NEST senior management.

As NEST scales up from test cases to evaluation across the medical device ecosystem, we think it's important to remind this group that physicians and patients are the end users and that we will want and expect to be kept in the communications loop so that

the results of the work done by NEST, the analysis, whether they be favorable or unfavorable, that those results be available at the appropriate time to inform physician/patient shared decision making at the point of care. Next slide, please.

So in conclusion, and because of its past and continuing successes, the AMA strongly supports the reauthorization of MDUFA in 2022. We believe that reauthorization is critical to the optimal function of the FDA, expediting patient access to new devices and biologic products; that user fees should continue to be tied to specific performance goals, negotiating with manufacturers, and should not be considered as an offset to any funding cuts for the agency or mixed with general operating funds.

We applaud FDA for its response to the COVID pandemic, particularly the many, many actions taken at great speed and deliberateness by the Center for Devices and Radiologic Health and the commitment of the Center for Biologics Evaluation Research to the rigorous review of vaccines against the SARS-COV-2 virus.

As mentioned, we seek greater clarity for the appropriate regulatory pathways, particularly for digital health and AI products. We strongly support continued investment in NEST so that we can fully realize as a nation the return on the investments made so far.

We look forward to continuing to work collaboratively with FDA. And we thank FDA and its many career professional scientists and others who, with all of us, other stakeholders, are working to improve the health and well-being of our patients and the nation. Thank you so much.

MS. ROTH: Thank you, Dr. Blake. We really appreciate you being here today. And thank you again for all of your support, both the Device Center and the Biologics Center and during the FDA generally.

With that, because we were -- unfortunately, one of our speakers was unable, due to a last minute conflict, to join us today, we now have time for a longer lunch break than we

had previously anticipated.

We're going to go to the lunch break here momentarily and resume promptly at 12:30 with a panel, as I said, of patient and consumer organizations. We're really looking forward to that and so we want to begin promptly at 12:30. Thank you again for joining us. And we'll see you then.

(Off the record at 11:38 a.m.)

(On the record at 12:30 p.m.)

MS. ROTH: Welcome back. Welcome back to this afternoon session of the FDA's public meeting to discuss the MDUFA reauthorization.

This afternoon, I'm very happy to be joined by an esteemed panel of representatives from the patient and consumer advocacy community. We're joined today by Jeff Allen from Friends of Cancer Research; Brenda Huneycutt from FasterCures; Michael Abrams from Public Citizen; Diana Zuckerman from the National Center for Health Research; Paul Conway from the American Association of Kidney Patients and Leanne West from the International Children's Advisory Network.

I would invite all of you to unmute your lines now. And while you are unmuting and turning on your video feeds, I'll take this opportunity to thank you again for joining us today. As Dr. Shuren said, and as we heard from Dr. Hahn, you know, the patients are truly the inspiration for all the work that we do here at FDA.

And this is reflected in CDRH's vision that patients in the United States have access to high quality, safe and effective medical devices of public health importance, first in the world. This vision recognizes that patients are the most important customer and the group most impacted by our decisions, and they are fundamentally the reason why we are all here today.

So, I'm happy to turn over the next portion of the meeting to this group and I'd ask

that we proceed in the order that was listed on the agenda and begin with Mr. Allen. Thank you very much. Dr. Allen?

DR. ALLEN: Thank you. And do I need to pull up slides or we're okay to just proceed?

MS. ROTH: Go ahead.

DR. ALLEN: Great, thanks. So, if we can just move to the next slide?

Well, thank you very much for the opportunity to join such a terrific panel and be part of the meeting today. It's a real honor to be here. In thinking about the user fee program as these discussions get underway, historically, they've provided a great opportunity to move things forward as a greater ecosystem, as well as interactions that sponsors, consumers, patients and end users have with the FDA.

And these come in both terms of expanding access to new products in ways that can be facilitated by alleviating a potential backlog for reviewing new applications, establishing a predictable system in order to review new applications, provide essential personnel in order to review such applications, and ultimately create a process that is predictable, efficient, accessible and participatory for more people.

At the same time, it provides the opportunity to augment and inform the future of science, of developing new products and the processes associated with reviewing them, such things as creating and providing critical support for activities like the development and utilization of real world evidence, as well as providing funding for the exploration of new methodology in order to inform future product development through tools such as patient reported outcomes.

In the next line, I've highlighted just a couple of key programs from the last reauthorization of the Medical Device User Fee Act, which include items such as the expansion of patient engagement in order to create mechanisms to better learn about

patients experiences with underlying diseases as well as the technologies designed to alleviate them.

In addition, the expansion of real-world evidence programs in order to design scientifically based methodologies and standards for which real-world evidence can be used for identifying new uses and monitoring for potential malfunctions of products, and expanding the knowledge about products, evidence-based, over time in a way that wouldn't otherwise be able to be done.

And finally, in areas around digital health, a continuously expanding area which the user fee program has enabled the exploration of these new types of technologies as a part of pre-market review and considers pathways in which new software can be reviewed in itself. Not only has CDRH been at the forefront of developing these programs, it helped inform how they can be applied successfully across other areas of the agency and in the development of other products as well.

Moving into the next slide, Dr. Shuren mentioned this, so given that everyone is affected by what has been happening over the last several months related to COVID-19, that there could be several opportunities that we'll be forced to be part of these discussions and hopefully provide opportunities and thinking about how the collective experience of operating under such strenuous times could inform the future of product development and regulation in itself.

Things like clinical trial design, which will need to be considered into the future, and how patients that have recovered from COVID-19 need to be assessed perhaps in a different way that we never had to think about before.

The expansion of processes that can help launch the development of new studies, expediting things like IRB review or thinking about how modifications to design studies can be done any more predictive and rapid manner so that studies don't get delayed.

The routine adoption of remote services has been something that has long been advocated for but has been forced upon us as a way of communicating better and perhaps remotely, which will enable data to be collected on more individuals in a more rapid fashion than perhaps has ever been able to be done in the past.

Finally, the expansion of post-market performance data, which will be important in order to provide information about these products over time, particularly when they're approved on the limited evidence base at the beginning.

FDA themselves should be commended for their swift action and putting out over 60 new guidance documents very rapidly to help guide the response to COVID-19. And those types of processes, hopefully, will be able to continue, resource willing.

Moving into the next slide, some specific considerations in thinking about key programs for the medical device user fee and this fifth installment.

The first would be to expand the scope and capabilities for active surveillance and the use of real-world evidence to help balance benefits and risks in order to think about ways that the data safety net can be designed in a way to be more applicable and help strengthen medical product review and allow for additional pre-market safety -- pre-market flexibility by having a safety net in place in order to collect information in the post-market space more readily.

This will enable support for emerging technologies and create a feedback loop which will help provide confidence in these products over time and the ability to collect information to demonstrate their benefit and potential risks associated with them as they emerge.

The second area would be thinking through ways to further enhance and develop and implement digital health strategies across FDA, including aspects related to the digital tool performance, as well as the clinical metrics and standards for including them in clinical

trials in a way that hopefully can be done across the entirety of the agency, as opposed to having one center looking at aspects of these digital technologies without necessarily thinking how they could inform the clinical development of subsequent products such as therapeutics in a different portion of the agency.

And finally, sufficient support processes associated with breakthrough technologies. These technologies have shown to be among some of the most innovative products and represent some opportunities for rapidly addressing unmet medical needs. Researchers should be tied to the specific products, not just in a pool, to support the activities around increased interactions with FDA more generally.

I would also encourage the community to look at the implementation and what happens beyond just a designation of a product as a breakthrough therapy -- or as a breakthrough device in terms of the designation and the requirements to get there, but actually, what happens to that product after it is designated a breakthrough device.

On the next slide, the final area that I think would be very important to add to these discussions is around the oversight of diagnostic testing. As of 2019 in the oncology space, we've seen that 30 -- at least 30 FDA approved products have been developed with a biomarker test.

And these tests can be developed and sold for use, which means they have to be FDA regulated or they can be developed in the lab in which they are intended to be used in which, historically, has not been regulated by the FDA.

We recently published a study looking at non-small cell lung cancer patients and the utilization of molecular testing in that space, which has continued to grow with the advent of available therapies. Based on its test, we saw that over 80 percent of patients that tested positive for an actionable biomarker, the two listed here, that we looked at received the associated targeted therapy with them.

So, while this is very good news in that there's still room for improvement in order to make sure that patients are receiving the most appropriate therapy for them, what we found was that while for both of these tests, there are FDA approved versions is available, as well as versions that are developed in the laboratory, which are also available.

This is not a statement to assess the quality of either one of those tests, but what we found was that 30 percent of patients received a diagnostic test for those biomarkers that I mentioned based on a test that was not approved by the FDA.

And again, while this is not meant to measure the quality of that test, but without the available equivalent data between different tests with the same intended use, it does leave open the possibility of variability between different tests that are being used across similar patient populations.

And with one in three lung cancer patients receiving a test that is not held to the same standards, I think we have a real opportunity to address this here. I encourage the participants and the medical device user fee at the reauthorization process to plan for this and help, as a community, that we should encourage Congress to act in order to establish a framework for the assessment of all tests moving forward.

Finally, to the last question that was posed to us as part of the panel in thinking about what the medical device user fee program could look like by the end of this next reauthorization.

On the next slide, I put up just a simple schematic that goes along to the goal of creating a more lifecycle approach. And I know that CDRH and OPEQ has already adopted this approach and taken steps in order to operate in a more lifecycle management type way in order to begin this process.

And I hope that in the coming years, the larger biomedical ecosystem can also take steps to support this approach.

With the goal being that an innovative and flexible pre-market environment will help to bring novel and beneficial products to patients sooner, a robust post-market environment will allow for long term safety and performance to be assessed, which in turn will identify future innovative therapies and allow that flexibility to continue knowing that the data safety net is in place to be able to learn about these products over time.

So, I thank you for the chance to be part of this discussion today, and I look forward to the discussions in the weeks to come. Thank you.

MS. ROTH: Thank you. I think we can turn to Ms. Huneycutt from FasterCures.

MS. HUNEYCUTT: Great. Thank you, Lauren. Good afternoon, everyone. My name's Brenda Huneycutt and I'm a director at FasterCures, a nonprofit, nonpartisan think tank center of the Milken Institute. Can I have the next slide, please?

With an independent voice, FasterCures is working to build a system that is effective, efficient and driven by a clear vision, working with our partners to build a patient-centric system where science has accelerated, unnecessary barriers are overcome, and lifesaving and life enhancing treatments get to those who need them as rapidly as possible. Next slide, please.

FasterCures appreciate this opportunity to speak on our priorities for the next reauthorization of the Medical Device User Fee Act. I want to add our thanks to the agency for the extraordinary work it has done during the pandemic.

We also applaud the significant progress previous MDUFA commitments have supported, including advances in integrating patient perspectives into device development and review, advancing the use of real-world evidence to enhance device development, and exploring innovative paradigms for regulating new tools for digital health.

I want to speak briefly today on FasterCures' priority areas, as you see here: diversity, patient engagement, digital health, transparency and lessons from COVID-19.

Next slide, please.

FasterCures recognizes the critical need to increase enrollment of underrepresented populations, including racial and ethnic minorities, in clinical trials for high risk medical devices and developing and sharing appropriate approaches for doing so.

With meaningful subgroup analysis for both safety and effectiveness conducted and reported, patients can better understand whether a device is right for them and can make better informed decisions for their care as specific information on relevant outcomes and risks are known.

But meaningful subgroup analyses requires sufficient numbers of trial participants within racial and ethnic minority groups, as well as age and gender groups.

More can be done to increase diversity in device trials, and we recommend FDA build on previous efforts and consider ways to further define agency expectations, share best practices and tools both across the agency and externally, and drive the development of innovative approaches to increased racial and ethnic diversity in clinical trials as appropriate.

This premise of increasing diversity applies equally to patient engagement, where it's essential to have as diverse and also representative voice as possible defined by the aim of the engagement.

In addition to hearing from a diverse set of patients from different ages, racial and ethnic groups, gender, disease, severity or stage of disease, it's important for the agency to solicit and incorporate into its decision making patient input from diverse sources and collection methods.

We applaud FDA's significant work on advancing the development and use of patient preference studies and patient reported outcomes and encourage the agency to also proactively look to sources of patient input beyond these tools.

Patient input comes in many forms, including discussions held in focus groups or public hearings, health data generated by patient use of digital apps and remote tools, patient registries, natural history studies and others.

Patient input from these and other sources and methods can allow a more robust and full rounded understanding of patients' experiences, preferences, desires and needs.

Another issue we encourage FDA to consider is how the agency can ensure patients, industry and the broader public understand the impact of patient engagement and the use of patient input in device development and regulatory decision making. It's important to patients and patient organizations to understand the impact of their efforts so that limited resources can be directed to impactful initiatives and funneled away from work but cannot or does not have to used.

Whether this information makes it into a product label or into a product approval review summary, FDA should consider creating a publicly available set of examples as resources for patients, manufacturers and other stakeholders and other ways to share information on what and how patient input was used in device development and decision making.

Turning to digital health, I wanted to just mention a few areas related to a number of the Digital Health Center of Excellence's current areas of focus. First, with respect to artificial intelligence and machine learning, we encourage the agency to take a proactive approach to understanding and minimizing bias in these tools.

We applaud the agency for bringing this topic to the Patient Engagement Advisory Committee recently and discussing the issue of training and validation data representing a sufficiently diverse set of patients, including demographic considerations, race and ethnicity and age.

We encourage FDA to continue to advance this work and meaningfully engage

patients throughout its development so that all of regulated AI machine learning innovations can perform their best in all populations for which the intervention is intended.

Second, FasterCures believes that clarity and transparency is critical for wearable and patient generated data and arguably for all digital health. Specifically given the newness of these technologies and the overlap or similarities to wellness tools, patients and other stakeholders need to understand exactly what is digital health, which wearables are regulated and which are not, and what is the difference between a wellness tool and a medical device, how is their data protected and what data is actionable and used for what purpose?

Creating specific public facing definitions and explanations to these questions and more can go a long way in building trust and reducing misunderstandings about these tools. Again, meaningful engagement with a diverse group of patients is critical to identifying needs and communicating effectively with patients, other stakeholders and the public at large.

And finally, digital tools hold great promise to build a more nuanced and robust understanding of each patient's experience through their use in clinical studies and as real-world evidence, as well as reduce the clinical trial burden that can allow harder to reach volunteers to participate and complete the trial.

We support FDA's work to advance the understanding and use of fit for purpose real-world evidence in the regulatory context and ensure that clinical studies minimize the burden to participants, allow for greater patient generated data and increase opportunities for a more diverse participant pool to join in complete clinical trials.

In our current landscape, transparency, trust and understanding how medical products are approved is more critical than ever. We appreciate that FDA publicly releases information on how they make their decisions, and we encourage the agency to consider

additional ways to increase transparency. Specifically, we recommend FDA create a position in the commissioner's office that can initiate, lead and oversee the agency's transparency initiatives.

In addition to ensuring that disclosed information is in a usable and understandable format for each audience, including patients and researchers, this group would be responsible for a consistent process of identifying potential transparency initiatives, running pilots and assessing impact or benefit, and ending, modifying or installing pilots as permanent programs and communicating these decisions to the public.

We also encourage FDA to consider additional transparency initiatives, including sharing of information both across the agency and externally on topics I've mentioned today that can benefit the whole device ecosystem through solidifying trust, building, understanding and consistency, and ensuring that lessons learned can be utilized ideally in real-time by not just future sponsors but all stakeholders, including patients.

Finally, FasterCures recognizes that the devastating COVID-19 pandemic offers some lessons that we would like to see continued after the pandemic subsides. We've witnessed unprecedented collaboration between the agency and industry, including nontraditional manufacturers, between diverse industry players and among many stakeholders and across sectors.

The urgency of the pandemic has led to a focus on what is critically important. And we would like to see the agency work to ensure that, as appropriate, these workflows, procedures and forward-thinking flexibilities continue past the pandemic so that patients using future devices can benefit.

Similarly, reducing the time to draft and release guidance documents can lead to these materials. Having more real-time impact and align with the quick iterative development process of many medical devices.

And finally, the increased awareness and use of remote health care and the tools to make that happen, seen during the pandemic, have given us more opportunity to learn about and collect more patient generated data.

We'd like to see this progress continued so that patient generated data can help paint a clearer picture of patient experience and be incorporated into more health care decision making.

We appreciate FDA's consideration of these suggestions and look forward to working with the agency throughout this MDUFA reauthorization. We will be submitting a comment letter to the docket to outline these areas in more detail and look forward to continuing to work to ensure patients have access to new devices in a timely manner and build a stronger, patient centered medical device ecosystem for all. Thank you.

MS. ROTH: Thank you. Thank you very much. And now I would like to turn to Mr. Abrams with Public Citizen.

MR. ABRAMS: Good afternoon. I'm Michael Abrams, health researcher at Public Citizen. And I have no financial conflicts of interest to disclose. Next slide, please. And can I just, ask if it's possible to display the slides large, larger on the broadcast? That might be good.

Regarding MDUFA, Public Citizen has long opposed the basic tenets of this vehicle to fund FDA activities. We believe such user fees, which now, per the graph on the left of the slide, fund well over half of the agency's operating budget, too often cause the agency to place the interests of regulated industry over those of the public.

MDUFA user fees are substantial and growing. You can see the right-hand graph on this slide. The agency, we believe thus should be careful to avoid expanding dependency on direct industry financing as it can compromise their ability to remain objective judges of device safety and efficacy of what we think and what the FDA has said is their primary

mission. Next slide, please.

Per the FDA's own characterization, the agency is responsible for ensuring safety and efficacy of many devices. Furthermore, the agency lauds initiatives under the current MDUFA-5 reauthorization, including the use of more real-world evidence, an idea that sounds smart and practical, but one which, especially under industry finance influence, threatens the credibility and integrity of the medical device approval process.

And performance reviews of the FDA are not reassuring to the public in that regard. Next slide, please.

Here's an example of the so-called MDUFA performance, or MDUFA goal performances, which the FDA formally reports to Congress each year. The list is dominated by benchmarks of particular interest to industry, for example, how quickly decisions are issued on premarket approval applications, PMAs, of course.

But across the 25 goals reported, there's nothing assessing the actual public health consequences of devices, of device review decisions by the agency. Next slide, please.

Moreover, even now, as the FDA prepares for reauthorization, it uses language that underscores our concern that user fees have inappropriately altered the relationship between the agency and the regulated industry such that medical device manufacturers are now viewed as the agency's primary customers.

I'm not sure if you can see my slides there, but these are two directly from the FDA's presentation in preparation for this meeting. And this lexicon -- customers -- we think, is wrong for a regulatory agency and moreover, potentially corrupting. Next slide, please.

As we know from post clearance, post approval, adverse event data and some charts, again, from the FDA I'm showing here demonstrating those kinds of adverse events that do occur. Harm does occur with the use of medical devices at post clearance and post approval.

What we do not know, however, because the performance goals do not mandate it is how often these signals result from bad decisions of the FDA. And the FDA, of course, can make mistakes. Such performance reporting should be essential and dominant, more important than time to review information, which is emphasized in the reports, is to Congress, for example.

More meaningful performance assessments are essential given the challenges of the medical device oversight process and two device case studies highlight this point, which I want to talk about in the next couple of slides. Next slide, please.

The first pertains to trans-vaginal mesh products, non-absorbable surgical implants used to repair pelvic organ prolapse in women. Between '02 and 2011, dozens of these implantable products were cleared for use via the 510(k) process, which does not require clinical testing.

In 2011, Public Citizen petitioned the FDA to ban all such products because of lack of effectiveness and high rates of complication. In 2014, FDA denied our petition.

In 2016, however, the FDA recategorize these meshes in the high risk category, Class 3, and required submissions of PMA, which, in 2019 led to the convening of an advisory committee which reviewed data on new clinical testing for transvaginal meshes still on the market.

The industry's own data at that time revealed that these meshes did not show better success rate compared to native tissue repair. And Public Citizen testified at the February 2019 hearing in this regard, in opposition to the use of these measures and for the following reasons. Next slide, please.

Three to 15 percent of patients receiving these meshes experienced significant adverse effects, the most prevalent of which are listed in the panel on the right-hand side of this slide -- things like serious, debilitating problems, including ongoing or new pain, erosion

exposure and erosion exposure of the meshes.

And, to the second bullet on this slide, 77 deaths were observed related to the use of these methods in the decade between '08 and 2018. The middle arrow on this slide summarizes Public Citizen's review of transvaginal meshes to the 2019 advisory committee -- and let me just read it to you.

Our testimony was as follows: "Because of the FDA's recklessly inadequate actions regarding surgical mesh over nearly a decade, thousands of women have been unnecessarily harmed, many permanently. To prevent further harm, the FDA should reject the pending PMA on these devices."

In fact, in April 2019, the FDA ordered that these meshes measures should no longer be sold. But that was nearly eight years after our initial petition, 17 years post-510(k) clearance.

Clearly, 510(k) process and the FDA's sluggish post-market response to evidence of serious harm failed in this case. And by the way, we should not be surprised that there is substantial lag between the clearance process or the approval process of a harmful device and FDA action.

I've cited in the bottom right of the slide a GEM article recently which found a medium 10-year lag for such a reaction by the agency. Next slide, please.

A second case study involves spinal cord stimulators for pain. In June of this year, Public Citizen released a detailed report -- it's on our website -- examining the FDA's regulatory oversight of these devices over more than 40 years.

That report observed that between '78 and 2019, the FDA cleared 137 510(k) submissions for implantable spinal cord stimulators for pain with external transmitters and power sources.

Between '81 and 2019, the FDA approved six original PMAs for Class 3, totally

implanted stimulators for pain, and even though those approvals were based on very weak clinical evidence.

One of the earliest PMAs was based on a seriously flawed clinical study. Three, later, PMA approvals were based only on published scientific literature from other spinal cord systems, not the ones under review. And even that literature was weak. This is detailed in our report that I said is on our website.

Moreover, for the last bullet on this slide, nearly a thousand PMA supplements, presumably based on many of the inadequate studies noted above, were rapidly approved by the agency over the last 30 years.

From this analysis comes major concern that for many high-risk implantable stimulators, the FDA essentially relied on less rigorous, "substantially equivalent" standard intended instead for moderate risk devices. Next slide, please.

The report that we issued also examined MAUDE data from '04 to 2019 to discern -- concerning adverse event signals related to spinal cord stimulators for pain, revealing hundreds of thousands of these and several hundred deaths summarized and tabulated on this slide.

Surprisingly, though, there was only -- there were no Class 1 recalls issued by the FDA for these devices, finding which states and publicized in the widespread use of these demonstrably risky surgical implantable devices. The next and last slide, please.

Accordingly, and in summary, we make the following recommendations regarding the FDA device approval process. Number 1, seek more discretionary funding rather than user fees to cover essential activities.

Number 2, mandate more randomized controlled trials with definitive end points, especially for high risk, permanently implantable devices.

Number 3, require the FDA to advance performance measures that assess benefit-to-

risk ratios for the devices they clear, approve or reject, emphasizing the public health impact of the decisions that are made and doing so for at least ten years after those decisions are rendered as suggested by the JAMA study.

Number 4, require the FDA to publish technical reviews of PMA supplements for which changes could alter the safety or effectiveness of the device for our work on spinal cord stimulators.

Number 5, require industry to publish and report the number of devices sold in implants. Something that's held back is proprietary and makes it difficult for the FDA or anybody to appreciate the impact of these kinds of approvals and how many are on the marketplace.

Number 6, reject provisions which allow lax standards of review, including PMA approvals based on literature review that's not appropriate. PMA supplements for new device models should go through the full PMA process. Overreliance on post-marketing surveillance instead of more rigorous pre-market clinical trials are completely not appropriate.

And the final recommendation, any federal device legislation proposed should include an override of the Riegel, the recent Riegel v Medtronic Supreme Court decision, which limits a patient's right to sue a maker of a faulty PMA device.

Too often, high risk, permanently implanted devices, among other devices, have insufficient market clinical evidence to provide a reasonable assurance of safety and effectiveness. The device clearance approval process at the FDA, we believe, must involve explicitly to address these insufficiencies.

And my last slide has my contact information. Thank you very much.

MS. ROTH: Thank you, Mr. Abrams. One of the great things about this public meeting is our ability to have a robust dialogue around ways that we can continue to

improve the device safety -- device review program. And so, we really appreciate those comments and that feedback.

And with that, I'd like to turn it to Michael Ward. If you can please continue. Thank you.

MR. WARD: Good afternoon. My name is Michael Ward. I'm the Director of Public Policy for the Alliance for Aging Research. Next slide, please.

The Alliance for Aging Research is a leading nonprofit dedicated to accelerating the pace of scientific discoveries and/or application to improving the experience of aging and health. We are happy to have a longstanding partnership with the FDA to advance its important work on medical devices, including user fee agreements.

On the next slide I will discuss investment in digital health infrastructure. Digital technologies, mobile applications, remote monitoring devices and artificial intelligence serve a key role in the advancement of health care.

The development of these tools has been brisk. The FDA reports 4,200 submissions with digital health considerations during the week before. The role of digital based technologies have been reinforced and strengthened as a result of the COVID-19 pandemic as consumers have experienced heightened hesitancy to receiving in-person services.

The alliance has a longstanding interest in these concerns. As individuals age, they often have elevated needs and face increased obstacles to receiving in person care, such as frailty and limited transportation options.

Older adults also have a higher probability of having one or more chronic conditions. Monitoring key metrics such as weight and glucose levels is vital as sudden changes or fluctuations may provide an early notice that adverse event is likely to occur.

At the same time, these tools require specialized expertise in technology and communications, while also elevating cybersecurity concerns. The FDA and CDRH have

made admirable efforts to adjust and accommodate the evaluation of these digital technologies.

Staff have gone above and beyond to expand expertise in digital health, often in areas outside the scope of their current role. In response to this need, we applaud the FDA's establishment of the Digital Health Center of Excellence this year.

The need to support additional infrastructure is critical. For example, CDRH is currently responding to over 600 inquiries related to digital health per year, with requests exceeding 2,000 per year since fiscal year 2018.

The digital health market size is expected to grow 25 percent year-over-year through 2025. In the next round of MDUFA, the alliance encourages the FDA to prioritize investment in appropriate infrastructure to accommodate both reviews and the ongoing surveillance of digital health and artificial intelligence technologies.

On the next slide is a look at patient access to device benefit risk statements and labeling. Manufacturers are required to include information on product packaging to ensure the safe and effective use of devices and pharmaceuticals.

However, this sensor is generally less accessible for implantable medical device. For example, a patient may require a stent or a pacemaker during the course of their care. However, the surgeon and cure team would physically handle the impact during the procedure, including unpackaging the device from a sterile package.

It is reasonable to expect that the patient information may then be discarded with the other packaging for the device without the patient having the opportunity to review.

An additional issue is that patients may not be aware of the existence of alternative devices, let alone their availability or accessibility for their medical indications. Physicians and hospitals often, and understandably, focus on the implementation of a specific device to ensure maximum faculty and to standardize their supply chain.

However, if patients are made fully aware of risks and benefits among suitable options, they may, in conjunction with their doctor, decide they are more comfortable with an alternate device and care plan.

From the patient perspective, this represents a lost opportunity to learn as much as possible about their device before implantation. The Alliance for Aging Research is interested in exploring strategies for patients to have greater access to labeling information for implantable devices.

We've appreciated the opportunity to work with the Medical Device Innovation Consortium's Virtual Patient Engagement Forum to provide interactive opportunities to engage with relevant stakeholders to learn and share challenges about best practices for communicating benefit risk and uncertainty for medical devices to patients.

TDRH is actively participating in that effort. And the next virtual meeting is on November 18th. The MDIC's communication report, which will be discussed at the meeting, will serve as a guide for the next steps in efforts to provide relevant patient labeling.

We encourage the FDA to utilize the MDUFA due process to explore options that ensure patients have access to label information before a procedure to facilitate shared decision making between patients and their providers.

We anticipate this effort will be patient centered, from focus groups and data collection to support evaluation. As part of this process, we also anticipate that the FDA would work with provider trade associations and clinicians to determine how to incorporate enhanced patient communication about device benefit risks and labeling into their workplace.

Let me move forward to the next slide. We encourage the FDA to utilize its policy authority to ensure appropriate access to device registry data. Patient registries collect post-approval information on outcomes, efficacy and safe. In many cases, CMS has

instituted provider reporting to registries as a requirement when the device is approved under coverage with evidence development status for Medicare.

Registries can also support manufacturers in meeting FDA post-approval data collection requirements. Registries are often posted and operated by specialty medical societies.

However, we currently face a problem with some of these registries as a lack of transparency and ongoing and consistent availability of registry data provides barriers to evaluating outcomes.

For example, the TVT Registry collects data on transcatheter valve replacement and repair procedures. However, the registry has not publicly published data on the procedures or health outcomes in over three years.

Further, federal agencies do not have open access to the data, which is vital for the collection of real-world evidence. In fact, in CMS's proposed national coverage decision for mitral valve repair, the agency said they will continue to assess patient outcomes through evidence published in the peer reviewed literature.

However, waiting for data published in articles in peer reviewed journals, it's a lengthy process. Patients and federal agencies have the right to understand how devices are performing in a timely manner.

Addressing data blocking has been a priority in other areas of health care, and we ask the FDA to prioritize data access for device performance support. We support the same.

The FDA should explore authority either alone or in partnership with CMS to ensure that registries provide regular reports, annually at a minimum, to evaluate outcomes.

Registry data can fill gaps in information that are not available through claims databases. Claim knowledge of public reporting may not be appropriate for all devices if

utilization is limited.

However, federal agencies should have access to registry data to support safety and efficacy monitoring efforts.

On the next slide, the Alliance encourages the FDA to explore a strategic partnership with the Patient-Centered Outcomes Research Institute known as PCORI. Last year, PCORI was reauthorized for ten years. It has an expanded scope in evaluating outcomes for patients and other stakeholders.

This expanded scope includes the ability to examine burden and the economic impact of medical treatments, items and services on patients, families, clinicians, payers and society. This reauthorization comes at an opportune time.

The collection of real-world evidence on clinical outcomes continues to be a priority for the FDA. Other regulatory activity also underlines the essential need to collect RWE.

For example, CMS's recent proposed rule for Medicare coverage for innovative technologies would align Medicare coverage for four years once a device, a breakthrough classification, receives FDA market approval.

Given the increasing demands for RWE and PCORI's ability to investigate and develop data, it makes sense for CDRH to initiate a strategic research partnership to meet reachable goals.

PCORI's mandate also allows studies to measure the relative clinical effectiveness of two or more alternative approaches, including the impact on the cost of care. Enhancing patients' understanding of the relative efficacy of devices and digital health tools will empower patients in their health care choices.

Moving to the final slide, I want to emphasize the Alliance for Aging Research's support for the reauthorization of MDUFA. We encourage the FDA to prioritize infrastructure and expand access to outcomes data in the next round of negotiations. We

look forward to partnering with the agency in this important effort.

In closing, I want to share a quote from Winston Churchill. "Every day you may make progress, every step may be fruitful. Yet there will stretch out before you ever lengthening, ever ascending, ever improving path. You know you will never get to the end of the journey but this, so far from discouraging, only adds to the joy and the glory of the climb." Thank you.

MS. ROTH: Thank you, Mr. Ward. We appreciate you contributing today and all of our panelists.

And now, if I can please turn to Diana Zuckerman, that would be great. Thank you. I think we just need to unmute. There we go.

DR. ZUCKERMAN: Yes. Can you hear me? And are my slides up? Yes, they are. Thank you so much. I'm Dr. Diana Zuckerman. I'm president of the National Center for Health Research. Next slide.

Our center is a nonprofit think tank that scrutinizes the safety and effectiveness of medical products. And we don't accept funding from companies that make those products.

My expertise is based on my post-doctoral training in epidemiology and public health. And as a faculty member, formerly at and researcher at Vassar, Yale and Harvard. I've also worked at HHS, the US Congress and the White House. Next slide.

As we all know, FDA requires evidence that devices are reasonably safe and reasonably effective, and that's defined as having benefits that outweigh the risks for most patients.

So, my focus today is that public health focus of how do MDUFA performance goals and other activities ensure that those criteria are met. Next slide.

MDUFA has provided the financial support that FDA needed to improve the timeliness of reviews and to increase FDA's staff availability for meetings with industry. And

we know that user fees were created because federal appropriations were not sufficient for the essential work of the FDA.

Unfortunately, patients are not included at the table when the MDUFA negotiations and decisions take place. And as a result, most patient centered outcomes are not a focus, as you've heard from other people on this panel.

So, performance data are currently based on speed, but those standards are not -- sorry, those standards are usually that. However, performance data should also be based on other patient-centered outcomes.

And in our experience, MDUFA does not address many issues that are most important to the patients. We work with the next slide.

So, MDUFA should help patients make informed choices. You've heard about that already. Currently, making an informed choice is limited when data aren't available, and it's particularly limited for devices cleared through the 510(k) process because they don't require evidence of safety or effectiveness and almost never require clinical trials.

MDUFA should also support greater scrutiny of De Novo and PMA decisions, as you've also heard. Now, those are usually based on case studies or clinical trials. But they too frequently lack diversity in terms of age, race or men and women. And they often have no comparison groups and therefore can't control for a placebo effect.

So, the real question here is, are user fees sufficient now to support a more thorough scrutiny by FDA staff? PMA fees are much, much lower than -- I'm sorry, yeah -- much, much lower than the PDUFA fees, even for the largest companies such as Johnson & Johnson.

And 510(k) fees are miniscule and can't support careful scrutiny of those products. Next slide.

Since a picture is worth a thousand words, here are a few photos of devices that

were cleared for market as substantially equivalent. The first is a spinal system which, you can see, is very different from its predicate.

The company added or modified parts and the new complex systems were not tested prior to clearance. Next slide.

This slide shows diathermy devices for pain. And the photo on the left, you can see the device is so large that the patient is inside the device. So, how is that substantially equivalent to the device on the right that's small enough to put on top of a person's knee or elbow? Next slide.

This slide asks the question, is FDA comparing apples and oranges in their 510(k) process? Actually, apples and oranges are much more similar than most predicates are today, the cleared devices, because apples and oranges are both fruit.

They're both round, about the same size and they're both nutritious with some of the very same vitamins. That's much more similar than many of the devices cleared through the 510(k) process. Next slide.

So how can MDUFA improve? When good data are lacking prior to clearance or prior to De Novo or PMA decisions, then post-market surveillance is especially important. But device user fees have been inadequate to support excellent post-market surveillance. Next slide.

MDUFA could be used to ensure that clinical studies are large enough and long term enough. Staff could use MDUFA resources to determine if there are solid safety and effectiveness data for male and female patients of different ages and different races and ethnicities.

That's the diversity issue you've heard about previously. That's very, very important. And MDUFA for funds could be used to increase staff who review directed consumer ads and other promotional activities to make sure they're accurate and not misleading. Next

slide.

This slide's upsetting. It shows a two-year-old whose face was so horribly swollen because of the off-label use of Infuse bone cement. Infuse is a device whose labels specifically says that use in children is dangerous.

So why did the company sell it to a children's hospital? And what did FDA do about it? Next slide.

Well, FDA did put important information on their website that lists the risks. But instead of calling the product Infuse, they called it "Certain recombinant proteins and synthetic peptides that may be used as bone graft substitutes."

This is an example of information that is not understandable to patients and family members and in some cases, not to doctors either. So MDUFA could and should be used to provide better warnings to doctors, patients and parents about dangerous off-label uses. Next slide.

MDUFA should support FDA staff to develop patient and provider materials, to explain off label risks and to target off-label uses that are known to be ineffective or unsafe as food. And the FDA should use MDUFA funding to determine if detailing activities, direct to consumer ads or ads to doctors directly or indirectly promote inappropriate off-label use. Next slide.

Prior to allowing devices on the market, MDUFA should provide support for FDA staff to create patient booklets, informed consent, checklists and other patient materials that can be considered part of the labeling process but are directly given to patients, which, of course, labels often aren't for devices.

MDUFA should also support comprehensive post-market surveillance, and MDUFA should support things like FDA Dear Doctor letters, warnings to patients when risks are discovered and other materials that are really directed to patients and consumers. Next

slide.

My last slide focuses on the need to increase user fees to support post-market surveillance. These user fees should help support enforcement of clinical trial requirements, when those are included.

They should use them to evaluate data from adverse event reports, from registry data and other real-world data. You've heard a lot about real-world data today, and I would just reiterate what some others have said, which is that it should supplement but not replace controlled clinical trials.

In summary, the term performance goals is a misnomer because MDUFA performance standards are currently based only on speed and industry access to FDA staff. Now, those are important, but performance standards should also be based on more patient-centered outcomes, such as patients having fewer symptoms, improved quality of life and overall survival.

And they should be supporting short-term and long-term safety and side effects information and clearly defined warnings and contraindications. MDUFA user fees should support FDA's scientific and decision-making staff to meet upon request with consumer and patient advocates who are concerned about safety and effectiveness standards, either in general or regarding specific products.

So, it shouldn't only support meetings with industry. This is essential at all stages of the pre-market and post-market process. And these advocates should represent all patients and consumers, not just those recruited by industry or by organizations funded by industry.

User fees should also be used to improve inspections. This has become even more important during the pandemic because FDA inspections have been reduced and delayed because of the pandemic.

As noted previously, two of our key concerns are, number one, patient consumer

advocates should be at the table during the do for negotiations between industry and the FDA.

We greatly appreciate meetings like this one today. We appreciate the briefings that we've had after closed door meetings. But that doesn't replace us being at the table during the meetings.

And number two, MDUFA fees should be increased to generously support post-market surveillance and the enforcement of post-market study requirements.

And in summary, MDUFA performance goals need to be more patient-centered by including specific metrics pertaining to safety and effectiveness, both pre-market and post-market, and improving patients' and consumer advocates' access to meet with FDA decision making officials.

And this will be a great step forward and helping to make sure the safeguards are there that patients and consumers deserve. Thank you so much for the opportunity to speak to today.

MS. ROTH: Thank you very much. And now I would like to turn it over to Mr. Paul Conway from the American Association of Kidney Patients. Thank you.

MR. CONWAY: Thank you very much. And it's an honor to be speaking with you and my previous panelists. Let's see, next slide. Yeah, there you go. Thank you very much.

Just a minute on my personal background. So, I am a kidney patient. I've been a patient for 40 years, including three years of home dialysis and for the past 23 years, living with a gift of life from a young man who was cut down early his life, a kidney donation and I was his recipient.

I'd like to speak to you today on a couple of different levels. One, as the chair of Policy and Global Affairs for the American Association of Kidney Patients, which is the largest kidney patient organization in the United States.

And then I would also like to give a perspective here, as somebody who has worked in federal public policy and state public policy for a large number of years under four presidents and three governors and, especially from the advocacy standpoint, what it actually means to be both a patient and advocate and a policymaker and the implications of what has already occurred with MDUFA.

My perspective from the kidney community at large is drawn from several different positions that I hold, one of which is on the Kidney Health Initiative Board.

But just as importantly as the chair of the Patient Engagement Advisory Committee for the FDA, I'd also like to mention the fact that the AKP is very closely involved with the FDA through the community engagement program, and we've had a tremendous amount of input from our rank and file members into that process. Next slide.

So I think it's important, as we discuss these issues, to step back and see how much ground has actually been covered, at least in the field of kidney advocacy and in devices that serve kidney patients.

So prior to the advent of FDA weighing in on the device side and actually creating pathways in structure for PPI and PROs and RWE, getting the patient perspective across to federal policymakers and the researchers and other stakeholders that were involved was quite random.

Many times it depended on the personality or the individual interest of somebody inside of an agency or somebody in industry or at an academic level, a researcher.

What's important about this is that it has all changed, and that has changed dramatically, at least for kidney patients, because in the past, many times at decision tables, lobbyists and other industry representatives would characterize patient reported outcomes or patient insights.

It would not be the patient that was actually describing it directly, nor the advocacy

organizations bringing all of their tools to bear for patient insights and patient opinion to deliver to agencies. It was very unstructured.

What the FDA has been able to do, at least in the field of kidney patients, kidney advocates and all kidney stakeholders, is actually create structure, certainty and a very clear signal that patient insights and patient experiences are valued and that the data that's collected from patients will actually be used in deliberative decision making.

And that had been a very clear signal that was not missed by industry and it was not missed by anybody in the health care ecosystem. And I think that FDA's work in MDUFA has sent a very strong signal.

And I'll show you how it has set off a chain reaction across, I believe, the federal agencies and many other stakeholders that patients and advocates work with and medical professionals in kidney medicine. Next slide, please.

One of the first places that you actually see the impact of FDA's work -- and again, much of this under MDUFA -- is the impact that it has had on patients and their professionals, the medical professionals that patients choose to be their primary care doctors or their specialists.

And I think it's been quite apparent for a very long time, many decades, among patients in their medical teams, that the unique insights that patients were bringing that were non-clinical were important. But how this information was actually collected and communicated by medical professionals or by patients was again, somewhat unstructured.

But inherently, I think that medical professionals and patients knew that the insights that they were experiencing and seeing could actually make for better products.

And as FDA has worked diligently over the past ten years, and especially the past five or six years, what it has done is it has changed the nomenclature in the practice room between doctors and patients, because doctors are much more inclined now to encourage

patients to get involved in clinical trials, to get involved with advocacy organizations, and to make certain that the unique insights they have are being shared.

Same, too, for medical professionals. Medical professionals have been very engaged with the FDA, the American Society of Nephrology and the Renal Physicians Association, in encouraging FDA's involvement with their professional societies and with patients.

So practically, what does this mean? It means there's been a change in the white jacket on one side of the table and the paper dress or the paper jacket that a patient is wearing.

There's much more of an effort for clear communications and much more of an effort we're seeing with patients and professionals to work together to inform the process on medical devices. I think that's unique and it's a direct impact of the leadership that FDA has had in MDUFA. Next slide, please.

So the other arena in which there's been impact here is in government and industry. And essentially what the introduction of PPI and RWE and PROs has done is it has given policymakers, whether they were elected or appointed, the ability to say that beyond rhetoric patient insights are actually valued within the agencies and within the decision process, that the recommendations and the policies that they are making are actually informed by the constituents they've been appointed or elected to represent.

We have seen this at AKP, in Congress and across HHS and other federal agencies where the reference to the work of the FDA under MDUFA and for patient engagement is center-most in the discussions as an example of how it should work.

We've been very pleased about this. It gives us great credit to be able to say that our patients, as kidney patients, are involved in the front end of medical device development and that they're actually informing the devices that they're going to live on.

For example, dialysis machines are now machines that can be used at home using

smart technologies for dosing and communications back and forth that patients are actually at the table.

You've also seen this in the advent of Kidney X, the prize incentive program for incentivizing new medical devices and new treatments in kidney medicine. The fact that patients are actually involved, that the Kidney Health Initiative that the Patient Family Partnership Council is involved in at the table with manufacturers and developers is something that has given policymakers, I think, a great deal of optimism.

But more importantly, it has inspired the patient community to get much more engaged than they had been before. Next slide, please.

So how has this actually translated in impacted patient advocacy organizations? And this is something that I think might be missed, but I think it's something that has to be put on the table as a positive because FDA actions, under MDUFA, have not happened in a silo absent any impacts on how advocacy organizations operate.

I'll tell you, for example, the American Association of Kidney Patients in the past 24 months, we've been approached and worked with over 134 companies who are contemplating coming into the kidney space for devices or for diagnostics.

And what they're trying to do is get their head around how do how do we engage patients, because they know that the FDA has put a premium on seeing that level of engagement and having it affirmatively displayed by companies.

And so, what are these companies asking us when they meet with us? They're asking for assistance and study design, on protocols, consent forms, trial recruitment efforts, targeted patient surveys, cognitive interviews, online video focus groups.

All of it is designed to gather patient insights, talk to patients about what they would view as a relevant patient reported outcome, what some of their actual practical experience has been. What this has done to us is it has completely changed our operations in terms of

our staffing, our internal responsibilities and our systems.

At the same time, during the same 24-month period, we've had over 263 contacts with the federal government, not all of them in HHS -- other agencies, DoD, the VA, HSRA -- similar, looking for patient insights in what we would recommend as better inclusion of patients to come closer to modeling within those agencies what FDA has already done and is doing.

So, I think the agency deserves a tremendous amount of credit for the impact that you've had not only in industry, but also across the government and in patient organizations. Next slide, please.

This is one thing that we survey quite a bit. It's an issue among patients, I think. I don't think it really matters if you're kidney patients are not.

It's the sense of idealism that patients have of wanting to give back and to have their insights help improve the lives and limit suffering for others that may come behind people them or people that they'll never meet.

So, we surveyed our patient membership back in June at a survey level of 900 participants, and we ask this question regularly. It's gone up every single yea.

And the core of the question is, if you believe that your insights and your experiences were valued and could actually impact discovery and science and innovation in devices, would you be more willing to participate in clinical trials?

And this year was the high watermark, 94 percent. And part of that is informed by what our patients, not just did AKP, but across the ecosystem in kidney medicine are seeing in terms of federal agencies moving forward led by the FDA.

And I think it's very important for patients to understand that not only do they have this unique experience, but that there is actually an avenue that they can assert their idealism and assert their voice and have it heard and make an impact in terms of improving

the lives of others. Next slide, please.

I referenced the change in our operations. If you take a look here under research, all of the text that's in red, those are all new operational capacities that the American Association of Kidney Patients has stood up in order to respond to industry and researchers in academia who are trying to get a better handle on how to work with patients and collect PPI, RWE and formulate PROs.

Literally one-third to almost 40 percent of our operational capacity has been shifted to meet the research and industry needs to gather insights from the largest patient kidney patient organization in the United States. We have substantial databases.

But what that has done to us internally is it has made us wiser, more efficient, but actually armed with many, many more capacities to help inform what industry is doing to be responsive to FDA. We think it's a great thing. Our patients love it because they are at the table. They're not ignored. We don't think it's in balance, but we do think that patients are being listened to and helping create safe medical devices and have an impact on the future of medicine. Next slide.

So that's true in research. It's also true in our engagement. We've set up an entire nationwide program of kidney patient ambassadors under the American Association of Kidney Patients. These are influencers who are online and in their communities, people who are well respected.

They work within churches and nonprofits among many, many patients. They're quite diverse in the populations and also people who are not online to encourage them to be involved in the FDA process. And I put all of this out because these are the implications of good sound policy under MDUFA that has put patients at the center.

We believe patients are actually at the center at FDA. We don't necessarily view it as industry at the center. We think we are equal partners at the table. In terms of the look

ahead, some of these things may actually fall within the realm of MDUFA and some of them are also implications outside of MDUFA.

But I think it is important to discuss these. We would recommend that the FDA keep going forward and expand patients at the table in terms of all the deliberations and back those types of efforts with formal policy and guidance.

We think there is an opportunity, expand research in the science of patient insights. And the FDA is a leader in this. We believe that there's a huge generation or a large number of researchers, the next ones up to be the most prominent in medical journals that could actually benefit with closer engage with the FDA on patients science and to make that a priority and have more published so there's more data to pull from for RWEs and PROs and PPI.

We think there's an opportunity also for the FDA to educate other federal agencies on what they are seeing and the unique ways which they have engaged patients and the substance that has come out of those engagements.

We think there's a very good opportunity to also align with other federal agencies. There was a previous mention of PCORI. The American Association of Kidney Patients has participated in all 17 kidney studies that have been funded by PCORI over the past ten years.

But in the initial years of PCORI, many of those research efforts were focused, and many of those dollars, went to research institutions as opposed to patient advocacy organizations or to put a premium on involving patients.

That's the exact opposite of what the FDA has done, in our opinion. FDA put the patients first and the institutions kind of come along and see what's happening. But we think there is an effort to better align with organizations like PCORI.

And we also think there's a very strong opportunity to better align with CMS because

you can have a tremendous amount of effort done from a regulatory standpoint and have patients at the table and then you get to the end of the line.

And if something is approved by the Food and Drug Administration, it goes over to CMS and some of their folks may not have the same level of expertise or understanding of what the patient reported outcomes and the real-world evidence were that got that device approved.

And so then you're going to have an advocacy community that's very interested in having it funded, and they simply may not understand the amount of ground that has been covered.

The last item I would put here is it is a very good opportunity also to educate non-government organizations. And in particular, I think there's a very good opportunity to educate the fine folks at ICER, the Institute for Clinical and Economic Research, whose existing evidence thresholds are quite high.

And they are not that favorable towards patient reported outcomes, real-world evidence and patient insights. And this is a disadvantage to patients because many of the decisions that are being made by payers are actually informed by non-government organizations like ICER.

But the problem with that is the access to innovation can be stifled if one set of organizations is strictly looking at economic impact and cost and federal regulatory agencies are actually putting the patient at the center and their insights, and those are not being captured by or listened to by payers and those who advise payers.

We think that is where the future is, is to have a fusion of those efforts. So, at the same time that you take a look at clinical effectiveness, you are actually anticipating where innovation can go, have more insights be gathered, and that some of those decisions that might be made strictly on economic grounds could actually evolve and be better

representative of where patients are and patient experiences.

Overall, listening to the other panelists, again, I think the FDA has shown tremendous work. There are a lot of opportunities to pursue and we just have the finest words possible for FDA's efforts under MDUFA. We fully support reauthorization, and we consider ourselves a loyal and good partner to the fine public servants at the FDA.

And we'd like to thank you, because absent FDA's leadership, we're not quite certain that kidney patients would be in the position that they are now to advance kidney medicine alongside the medical professionals who will help us keep going and stay alive.

In the course of 40 years I've had heart stents. I've been on medical devices. I understand safety issues and I understand issues with regard to clinical trials and patient acceptance and risk.

I think all of us who have been involved as kidney patients understand these issues. But this is the first time actually, in my experience as a public policy professional within the past ten years that I've seen a federal agency listen, adapt, apply and then become actually leaders in the field.

And again, in the areas of PPI, RWE and PROs, I think full credit should go to the FDA, and we're very optimistic about what we would see over the next iteration of MDUFA. So, thank you very much on behalf of the American Association of Kidney Patients.

MS. ROTH: Thank you, Mr. Conway. Thank you for your support both today and for -- and now, if I can please turn to our final panelist for the Dedicated Consumer and Patient Perspectives presentations, Leanne West, who's the chief engineer for Pediatric Technologies at Georgia Institute of Technology and the president of the International Children's Advisory Network.

Leanne, thank you for being with us today. We really appreciate it.

MS. WEST: Thank you for having me today. So, what she said, I'm Leanne West. I'm

the president of the International Children's Advisory Network. We are a nonprofit dedicated to promoting the pediatric patient voice in health care.

And pediatric centricity is really one of the main components of the JSI, so we greatly appreciate everything the FDA has been doing. So what I'm going to do is tell you a little bit about ICAN and our kids and then give you some examples of some of the interactions that our kids have been able to have with the FDA over the last few years.

And then I'm going to end with a video of one of our kids telling you what her experience was like talking at the FDA just so you can really understand the impact that's being made on these kids and when know they're really being listened to by someone who can really make a difference. Next slide.

So, we have 28 chapters on four continents, one virtual chapter, because we believe that the voice of every child, everywhere matters. Next slide.

So, ICAN -- again, what we're here for is to really empower the pediatric patient to share their voice by putting them where they need to be to tell their stories. One of those locations is the FDA, industry, and other activities, conferences, professional conferences.

Most of our kids are age 8 to 18, about 90 percent have some sort of medical diagnosis, but there are some without a medical diagnosis. And we think they're important, too, because they represent the child that might get diagnosed with something later in life.

And we will work with any organization that wants to have the input of our kids in whatever they're doing. Next slide.

So, when you work with us, you can now have your product kid reviewed and kid approved. Once you give us feedback and make changes, you can use our seal of approval.

And that let's everybody know that you're really making an effort to include the pediatric patient in what you do, whether it's looking at consent and assent, educational materials, medical devices and anything else. Next slide.

So, our kids are the expert. We have them talking at conferences and with industry and groups like the FDA and AAP. And our kids know that when we have them speak, they're speaking with people who they know can make a difference.

And so, our kids are always very, very excited to be able to share their voice at these types of activities. Next slide.

So, here are some comments from some of our industry sponsors. These are just some examples of some of the things that they say about working with our kids. And this is really all a part of MDUFA requiring that industry put the patient first or suggesting that they put the patient first.

And so, here are just some of the comments. There is no better way to be truly patient-centric than talking with kids, that giving children a voice leads to better clinical trials for enhanced recruitment and retention, and that they walked away with very concrete ways to change the way they were doing things in clinical research.

So, those are just some examples of what industry can get out of listening to the patient. Next slide. So, I snapped this screenshot from the FDA, the patient engagement video, and we are very, very proud to be partners with the FDA.

MDUFA really encourages these partnerships with patients and both with the FDA and industry. And it has created a culture of patient engagement in all aspects of health care, wellness across the entire product lifecycle from inception all the way to when it's being used publicly. Next slide.

So, one of the first things we did with the FDA was to do a survey of our kids so that they did really better understand what our kids were like. And so, these are just a couple of different questions.

Do you use a medical device to treat your managed disease? What difficulties do you have with the device? And what can be fixed to make your life better? So, they really

wanted to get to know the patients. Next slide.

So, as I said earlier, our kids are the experts at what they do and what it's like to live with the condition. So, a couple years ago, we had two of our youth, now in college, present at the Patient Engagement Advisory Committee on their medical device they invented. Next slide.

This is Paige, and she came to the FDA at a patient and caregiver connection town hall to let people know about ICAN and to let them know that there is a way to connect with the pediatric patient. Next slide.

We also had several kids speak at the FDA on a panel on pediatric clinical trial endpoints for rare diseases. And I list the conditions that these kids had just so you can see them, but I also want make a point of saying that these are real kids, real people. They're not just a condition.

So, Regina plays the cello. And Anya started a hands-on STEM program for girls in rural areas. Audrey sings in her school choir. Olivia really -- is really good at golf. And Logan has been named the best of the best at his school in chess. Next slide.

They also had Isabella, kind of a boxed in green, come and speak in February at the FDA on the workshop to share perspectives on emerging technology. And I got to read this next thing, because this came from her mom.

"So, it's been a little rough for Isabella the last 12 to 18 months. She's in heart failure and we'll be going on the transplant list shortly. With that said, her FDA event was amazing and gave Isabella something to look forward to, which really means the world to us."

Okay, next slide. So, I told you that most kids are age 8 to 18. And this is Dakota, and she is actually older than that because we just started to program for kids who were 19-plus who kind of aged out of ICAN or were interested in health care and want to stay

involved. So, again, here's Dakota. She works in public health now. And she spoke at the FDA in September about her experiences living with a digital health technology. Next slide.

This is Rhiannon from our D.C. chapter who spoke at the FDA on Rare Disease Day in April of this year, and this is probably my favorite picture of any child at ICAN because you can just see how excited she is and how proud of herself she is that she got to speak at the FDA where she knew she was making a difference.

And so, next slide, so the FDA also invited Rhiannon back to make a video to help the FDA staff better relate to the kids that they saw. I'm not going to show you that video, but what I am going to show you is a video from our conference this past summer, which had to be virtual.

Hopefully, next year we'll get to the in-person in France. She's going to -- she spoke at our last conference and she talked about her experience speaking at the FDA. And again, I just want to say that this is -- this opportunity is really, really impactful to these kids.

And so, what we're going to do now is I'm going to play the video. It's about three and a half minutes long, I think. But it's all Rhiannon talking. And I just hope that you really understand the value that MDUFA is giving these kids who live with these real-world issues. Do you want to play the video now?

(Video playback)

MS. PERRY: I'm Rhiannon Perry (ph.). I'm 17 years old and I'm from Manassas, Virginia. Recently I had the opportunity to join the FDA summit regarding ICAN and the opportunity presented to me was a gift because I was able to use my experience to help others.

This summit was important because I feel as though, as a patient, sometimes it can be difficult to understand and feel as though others around you are there to help you and to feel as though you're connected to others during this time, or people who understand

what you're going through.

And while some of the people at the FDA weren't necessarily patients, they did have a strong understanding of everything that was going on. And not only that, but they were working towards improving the experience of a pediatric patient, which was really important.

And another part that was important to me was just shining light on certain issues that aren't always talked about. And for me, I feel like the experience was such a great one to be able to use my past knowledge or my experience and my time in the hospital to improve the time for other patients and to work along with that.

My hope for the future is that this platform will be able to expand and not only give me the opportunity to explain things -- I feel comfortable with it, I'd like to change, but to also expand that to other patients and give them a voice.

I also hope that one thing can change is giving patients more accountability and more control over things. Personally, I feel like one of my biggest challenges during my treatment or any treatment that I've endured is just the loss of control and not feeling as though anything is in your hands, because when you have your health issues, there's nothing that you can really do to control it other than taking your medication and doing the things that are asked of you.

But giving patients a little bit more control and talking to them about the things are going on and having them more engaged in their treatment, can definitely improve the experience. And I know that from just being able to be a part of my transplant experience and, you know, just coordinating my medicines and coordinating my appointments and looking at things and not 100 percent having control over everything, which is an aspect of that, which can improve the patient experience.

Thank you for giving me the opportunity to share in my experience. And I'm looking

forward to all of the changes that have been made and all the efforts and continuing this process with you guys again. Thank you.

(End of video playback)

MS. WEST: Thank you. I just want to thank the FDA for all the activities that they've included our kids in. We really, really appreciate it.

We think MDUFA's great at making things pediatric-centric. And one thing that Rhiannon said in her talk was that she -- being able to talk like this kind of gave her some control over things that she couldn't really control, and that helped her feel better.

And I think that that's a large part of why these kids do this. And then I know also just, altruistically, because you really want to help the next person who comes along. So, we thank you.

MS. ROTH: Thank you. Thank you for sharing those perspectives with us. And thank you to all of our panelists this afternoon.

Our next and final segment of the meeting will be the traditional open public comment period. I'm thrilled that we received so many requests to provide comment here today.

And before we begin, I just have a few housekeeping items. First, I will now ask our speakers to unmute. We've got a long lineup. So just maybe you can come on and off it, if that makes more sense for you, depending on what's happening, your location. But if you can at least be ready to unmute, that would be fabulous.

And in order to provide time for everyone who wants to speak to participate, we're respectfully requesting everybody try to limit their remarks to five minutes.

If, because of time constraints, any individual organization has additional feedback that isn't able to be covered today, we hope you'll provide written comments to the docket so that your views can also be considered as part -- as we begin negotiations through that

forum as well. The docket is going to remain open for an additional 30 days until November 27th.

With that, I'm going to start by turning first to Laura Koontz from Flatiron Health. And then just quickly, I'll just list all the names, but then also come in and out to make sure we stay on track.

We've got Laura Koontz from Flatiron Health, Maria Gmitro from TrackMySolutions, Madris Tomes from DeviceEvents, Dylan Simon from EveryLife Foundation, Linda Radach from the USA Patient Network, Lisa McGiffert from Patient Safety Action Network, and John Owen from CDISC.

So, without further ado, Ms. Koontz, if I can turn it over to you. Thank you.

MS. KOONTZ: Great. Thank you so much. Good afternoon and thank you for the opportunity to comment on the success of MDUFA-4 and to recommend enhancements for MDUFA-5.

I'm Laura Koontz, Director of Regulatory Policy at a Flatiron Health and a Roche stockholder. Flatiron Health advances the understanding of how real-world data derived from electronic health records can improve patient care and inform decisions about cancer, product development and access.

We provide software and services to cancer clinics across the United States and create the identified datasets for cancer research.

We work to realize the full potential of real-world evidence to support the development of oncology treatments, including precision medicines and diagnostics, to improve patient access to effective therapies and care, and to facilitate enrollment in clinical trials.

RWE can complement evidence from clinical studies in evaluating safety and effectiveness of medical devices. It can help fill critical evidence gaps by capturing the

experiences of patients who are typically included in clinical studies, such as people with rare conditions or rare genetic mutations.

We expect that the use of RWE will grow as new sources of data become available and methods evolve to analyze and derive insights from these data. Flatiron applauds CDRH's work in implementing the real-world evidence provisions of MDUFA-4.

Its 2017 guidance, the use of real-world evidence to support regulatory decision making for medical devices and the center's participation in drafting the MDIC framework applying this guidance to in vitro diagnostics.

This work lays important foundations for understanding how and when RWE from a variety of sources can provide clinical evidence to support regulatory decisions.

Looking forward MDUFA-5, we encourage FDA to consider programmatic enhancements to facilitate and/or capture and use of RWD for regulatory review IVDs.

Specifically, we encourage FDA to, one, convene stakeholders and submit and develop standards for better capture transmission and linking of data; two, conduct pilot projects exploring how EHR derived RWD can be leveraged to support IVD reviews and, three, maintaining the Q-submission mechanism as a way for data and analytics organizations to get valuable FDA feedback.

I will address each of these points in a bit more detail. So, the first, convening stakeholders to develop data standards for better capture, transmission and linking of data. FDA's 2017 guidance notes that, "In order to use RWD, the device must be sufficiently identified with the level of detail necessary to address regulatory question."

In practice, this has meant that real-world datasets must contain details about the laboratory, the test, the platform used and the test result. We've learned through this pandemic how difficult it is to capture, transmit and link all of these data.

Meetings of the Reagan-Udall EHR Evidence Accelerator have focused on challenges

such as the lack of device information, capture and laboratory information systems and have transferred this information to electronic health records and other systems.

We hope the FDA will facilitate discussions between device manufacturers, developers of lab information systems and EHRs to find technical solutions to enable better capture and linking of complete patient laboratory and clinical data.

Two, conduct pilot projects exploring how EHR derived RWD can be leveraged to support IBD reviews. In parallel to the work I just described, pilot projects around the use of EHR derived RWD for IVD submissions can help FDA explore how and when the data that currently exists in real-world data sets can be leveraged in research and regulatory submissions, with the goal of ultimately advancing patient care.

And three, maintaining the Q-submission mechanism as a way for data and analytics organizations to get valuable FDA feedback. We believe is critical for data and analytics organizations that generate RWE and the tools that are used by a range of sponsors to obtain timely and actionable agency feedback.

The Q-sub mechanism codified in previous MDUFA negotiations is an ideal way for these types of organizations to engage with the agency. Through these meetings organizations can obtain the regulatory certainty necessary to drive investments towards tools that have the greatest potential to help speed patient access to effective products.

We urge the FDA to continue prioritizing feedback through this mechanism now and in MDUFA-5. Again, we thank you for the opportunity to contribute our input and look forward to continued participation throughout the MDUFA reauthorization process.

MS. ROTH: Thank you. And now if I can turn it to Maria Gmitro?

MS. GMITRO: Yes, I'm wondering if you can see my slide presentation. There it is. Thank you. You can advance to the next slide, please.

Good afternoon. I want to thank you for the opportunity to speak. My name is

Maria Gmitro and I am the Director of Community Outreach and Patient Advocacy for TrackMySolutions.

I have not been paid to speak today. I am a former educator and currently co-founder and president of the Breast Implant Safety Alliance. I serve on several collaborative communities. I am also a harmed patient, which is the drive for my involvement. Next slide, please.

Through personal and professional experience, I've learned the hard way that new does not necessarily mean safe. Innovation can be important, but so is accountability and quality.

Before I dive into my speech, I want to make my recommendations clear. With the next round of funding, I urge the FDA to do the following: Involve patients and public health experts from the start, increased funding for post-market surveillance efforts, such as analyzing adverse event or it's implementing better device tracking and alerting and increasing communication, issue more mandatory recalls over voluntary and overall become more patient focused with more patient involvement. Focus on quality. Next slide, please.

Adverse events increase as devices are rushed to market. I'm going to use breast implants as an example, so you can advance to the next slide, please.

DeviceEvents uses information from FDA's public database. The frequency of adverse events has increased. However, 450,000 non-public summary reports submitted to the FDA from 1997 to June of 2019 were hidden from the public. Next slide, please.

My question to you is, how can health care professionals and patients make informed decisions without more accurate data? Post-market surveillance is crucial. Next slide, please.

Another issue to address is device tracking recalls and patient provider alerting. Device recalls drive the need for UDI utilization and better device tracking. The recent

recall of a particular breast implants is evidence of this problem. Next slide, please.

In 2019, Allegan recalled particular textured breast implants due to risk of cancer. This Class 1 recall is the most serious as it may cause injury or death. As shown in these headlines from Fortune, Allegan lost track of thousands and thousands of patients and more lives were lost. Next slide, please.

Device tracking and recall alerting is vital to patient safety. Why is a system not already in place? Next slide, please.

I work with patients daily, and there are many serious issues. They don't know the exact device info or the UDI. They're unable to locate their implant ID card. Devices are often kept much, much longer than medical records.

The public is not always aware of recalls. They may find out on social media or a commercial. And doctors and patients are not aware that they can file an adverse event report. And when they do, it is often less accurate because the device is not linked to a UDI. More patients are becoming harmed. However, this problem can be solved. Next slide, please.

Again, here is the summary of my recommendations for the next round of funding that I spoke about at the start of the presentation. Please involve patients, invest in post-market surveillance, focus on quality. I'm here to remind you to focus on quality. Next slide, please.

Patient safety should always be the top priority. As a harmed patient and breast implant, Cancer BIA-ALCL survivor and patient advocate, Terri McGregor said, "Engage with your patients because they are the ultimate stakeholders. They pay with their lives." Next slide, please.

I appreciate all the recent communication and collaboration with the FDA. Thank you again for the opportunity to speak today. And I look forward to the FDA considerations

on this matter. Thank you.

MS. ROTH: Thank you very much. Now I'd like to turn to Madris Tomes from DeviceEvents, please.

MS. KINARD-TOMES: Hello. Thank you for allowing me to speak today. I do see my slides, so I appreciate that. Thank you. So, go ahead and advance to the second slide.

So, my name is Madris Kinard, and I am the founder and CEO of DeviceEvents. I previously worked as a public health analyst for the FDA and have expertise in adverse event reporting as well as you need device identification or UDI. Next slide, please.

MDUFA is primarily used to fund pre-market approval and clearance activities in CDRH. There has long been pressure on the FDA to get innovative devices to market more quickly. New does not always mean innovative. Next slide, please.

This graph shows how adverse events have increased steadily as the number of devices on the market has increased. We are now well over a million reports per year. And 2020 is on pace to exceed 2019.

One of the things that's important to think about with this is that two-thirds of all device recalls began as an adverse event report. The reading of these reports as critical. Next slide, please.

Adverse event reports are still the primary mechanism to identify signals or patterns of problems with medical devices. So, MDUFA funding does not pay for post-market surveillance reviewers. They are paid through the congressionally approved FDA budget.

Post-market surveillance funding needs to keep pace with pre-market MDUFA funding in order to even just keep up with the current device issues. Next slide, please.

As a public health analyst at FDA from 2012 to 2014, I observed there were approximately 65,000 adverse event reports per month to review.

When the FDA furloughed government employees in 2013, the post-market

surveillance division was reduced to one analyst who was part of the public health service. One employee was left to review 65,000 reports. The pre-market division, funded by MDUFA continued working through the furlough. Next slide, please.

As of 2014 East, each post-market surveillance analyst was reviewing between 10,000 and 20,000 thousand reports per year. Two analysts had to leave before one replacement analyst could be higher.

When 80 new scientists were approved for hire at CDRH, they were all designated as pre-market and paid for with MDUFA funding. Congressional funding to the FDA is not keeping pace with MDUFA hires. Next slide, please.

If pre-market approvals continue at this pace, post-market surveillance of these devices needs to also keep pace. So how can we do this? Next slide, please.

There are now over one million reports per year being submitted to the FDA, specifically to the device division. FDA and CMS efforts to require the UDI on claims and electronic health records has stalled somewhat due to COVID-19, as well as technological and regulatory complications.

So, here's what we see when the MDUFA funding doesn't help to fund post-market surveillance and doesn't do what it needs to do to ensure safe devices prior to approval or clearance.

You can see the number of adverse events for the 10 years to 2010. And then you can see those now. Thank you for advancing the slide. I missed that. There are now up to over one million reports this year and the year hasn't finished. Next slide.

So, what needs to happen now? CDRH needs to increase the number of post-market surveillance analysts to keep pace with the number of devices on the market. As an IT person, I know that good technology helps, but it does not replace the need for analysts to read the reports. Next slide, please.

If CDRH wants to prioritize innovation over safety and effectiveness while approving or clearing new devices, then they need to be just as willing to strengthen enforcement actions when a signal is found indicating that a device might be more risky than initially thought.

CDRH needs to utilize mandatory recalls more readily than they currently do. As you may know, most are voluntary. Next slide.

CDRH needs funding to improve signal identification technology and not rely solely on NEST, which has numerous third-party dependencies such as device registries and EHRs.

Finally CDRH needs to utilize moratoriums when possible if post-market surveillance studies are more than one year late. The theory of MDUFA makes sense. The scope of MDUFA needs to expand and needs improvement.

My contact information is on the last slide, and I really appreciate your time today so that I may speak.

MS. ROTH: Thank you, Madris. And now if we can please move to Dylan Simon from the EveryLife Foundation.

MR. SIMON: Thank you so much for your time today. Good afternoon. My name is Dylan Simon with the EveryLife Foundation for Rare Diseases. The EveryLife Foundation for Rare Diseases is a nonprofit, nonpartisan organization dedicated to empowering the rare disease patient community to advocate for impactful, science driven legislation and policy that eventually is the equitable development of an access to lifesaving diagnoses, treatments and cures.

The inherent nature of rare diseases can make them difficult to diagnose with small patient populations and limited investment in medical research and device development. Efforts to increase research and development are ongoing.

But according to the Institute of Medicine report, those reports "clearly focus on

drugs and biological products. Devices and the need for devices are much less frequently mentioned in journal articles and stakeholder conversations."

In a joint FDA/NIH report from 2018 called The Unmet Medical Device Needs for a Patient with Rare Diseases states that, "Device development for rare diseases significantly lags behind orphan drug development."

I can say in the report 77 percent of clinicians cite a need for entirely new diagnostic and/or therapeutic devices while 64 percent dissatisfied with existing diagnostic and/or therapeutic devices.

There's a need to continue to grow the number multiplies to be able to the rare disease community to improve both therapeutic and diagnostic options for the entire community. It is through this lens I offer comments here today.

As we plan for MDUFA-5, we have identified a number of priority areas for the consideration. They fall from from the following four categories.

First, building upon patient engagement efforts and approving the use of patient experience, data and decision making; second, maximizing digital health opportunities for the diagnosis and treatment of rare diseases; third, efficient, cross-center collaborations and finally, improvements such as for rare diseases, device development through the humanitarian use device program.

To save time, I would highlight a few key points in those areas. First, CDRH had been a leader in committing to robust patient engagement through the Patient Advisory Committee and the Patient and Caregiver Connection programs.

In addition, the advancements in conducting the use of patient contact information is directly attributable to the Center's commitment to meaningful incorporation of patient experience in the -- process.

Even with this great progress, there are areas CDRH can continue to improve upon.

We recognize the difficulty of maintaining commitment to patient engagement activities during the COVID-19 pandemic.

I urge you to work with communities to identify new ways to convene additional methods to ensure that diverse and inclusive populations are heard and the safety of participants is protected.

Similar to our comments at the PDUFA public workshop, we encourage CDRH to help ensure the robust data gathered through your patient engagement activities and the use of patient preference studies and regulatory submissions is optimized for maximum benefit of the community.

The information can inform outcome measure development, identify unmet needs and encourage further investment by developers and patient organizations while also informing patients that have value and access decisions following approval.

We urge you to consider instituting a standard reporting mechanism for how patient experience or preference data is informing the review of devices that are approved. In addition, we hope to collaborate with you also on orphan drug products to encourage and support the conduct of patient preference studies for all the rare disease devices.

Lastly, we encourage you to further efforts to educate the valued community members on CDRH's commitment to patient engagement and patient preference studies, including identifying the most effective way to present this information to the advisory committee members as a part of your review.

Streamlining how patient preference is presented and then provide some focused content area, training will be a relatively simple way to encourage additional developers to include such information in their submissions.

Next, I'd like to call attention to an important unmet need, the development of novel devices for rare and ultra-rare conditions. Humanitarian use of a device program has long

aspired to help bring much needed devices to the rare disease community.

There is great promise in device drug combination for rare disease treatments. Earlier engagement and clarification on which commission combination products are eligible for an interpretation of the probable benefit standard will help to bring much needed treatment to the community.

We do not have a specific policy to move forward today on this issue. We urge you continue reviewing the program and gathering stakeholder feedback to update and modify the program as needed.

Finally, I want to thank you all for the great work that is occurring at CDRH around digital health. We are excited for the launch of the Digital Health Center of Excellence and to see all the great work the center will do in setting international standards on the issue.

We urge you consider the needs and preferences of those with rare diseases as you continue to build on this network. Artificial intelligence and machine learning hold great promise for assuring a diagnostic odyssey. So many with rare diseases in this space.

Additionally, CDRH should consider how these AI tools can be used to accelerate development for rare diseases. Other digital technology devices have the potential to connect people with rare diseases to care and clinical trials that were otherwise unattainable.

We hope that you will engage with the rare disease community including patients and caregivers who would use new digital health tools and specialists treating patients with rare diseases as you build out appropriate regulatory framework so you can identify unique perspectives, unique possibilities that might be required for those populations.

In closing, we are grateful to the FDA for your leadership and continued commitment to placing patients at the heart of product development. We look forward to continuing to collaborate, innovate alongside with you to ensure the needs of the rare disease community

are met going forward. Thank you again for your time.

MS. ROTH: Thank you, Mr. Simon, if I can now turn to Linda Radach from USA Patient Network? Thank you.

MS. RADACH: Good afternoon. My name is Linda Radach. I'm also speaking for Penny Burau in representing the USA Patient Network, an independent voice advocating for safe, effective and accessible medical treatments. Next slide, please.

We have no disclosures. Our topic is MDUFA-5 from the consumer's perspective. MDUFAs is misdirected in mission. FDA is charged with assuring safe and effective medical treatments. Next slide.

A question today, how is MDUFA working? The answer depends upon which mission is being served and the metrics used to evaluate success. Industry wants speed to market. Patients need safety and effectiveness.

FDA seeks quality review processes. Patients need access, but they also need product quality and reliability. The focus of FDA and industry is on rapid response times. Patients seek positive outcomes. How does this disconnect with FDA mission and consumer needs protect Americans? Next slide.

Clearly, timeliness and efficiency and pre-market are insufficient to protecting consumers. Although sales of medical devices have grown at an annual rate of 9 percent for the past decade, industry growth has come at tremendous human cost.

Serious patient adverse events reported to the FDA have grown at a rate which is about twice as fast as the increase in the overall medical device market. Clearly, industry has abundant resources to produce safe and effective devices to end the spiral of medical harm destroying the health of millions of Americans. Next slide.

To answer the question, FDA and industry give themselves an A. However, nowhere in the FDA's stated mission is speed to market even mentioned. The goals for the FDA is

routinely negotiated in MDUFA, are diametrically opposed to the needs and expectations of consumers.

Given the rising level of patient harm and users of the medical devices give the program and the FDA industry partnership a failing grade. Next slide, please.

To improve MDUFA, safety and effectiveness must be prioritized. Balancing pre and post-market activities through increased funding will yield improved post-market data, which is fundamental to device improvements and innovation.

Safety and effectiveness data is available in adverse event reports must be required for all predicate devices used in 510(k) submissions and as part of the clinical data used in all NEST evaluations.

In the absence of rigorous premarket safety and effectiveness studies, it is inexcusable to have adverse event data available and not apply it to pre-market decisions. Next slide.

It is standard care for patients receiving a vaccine to be given information on what, when and where to report an adverse event. The same information as well as risk benefit, composition materials and off-label use information must be given to all patients with any medical device. Next slide.

MDUFA should be focused on goals which would create a medical device ecosystem that prioritizes patient outcomes by re-centering the medical device industry on the pursuit of quality and increasing the presence of the patient voice at all stages and levels of the total product lifecycle. Next slide.

Negotiated efficiency goals support, timeliness, but speed does not promote excellence. In building the business case for medical device, quality McKinsey report found that CEOs believe loss of time to market and use of high-quality materials reduces profits.

This perception is at the root of poor patient outcomes, a lack of objective

information and increasing expensive, serious quality events such as recalls. On average, such events cost $2.5 billion to $5 billion per year. In the last 10 years, one company per year has seen a 10 to 13 percent drop in stock prices.

McKinsey found that the pursuit of quality across the total product lifecycle resulted in cutting the costs of recall events in half and boosted the revenues by $3.5 billion. Next slide.

Industry's cost cutting practices of seeking cheaper materials and less costly suppliers is backfiring, as evidenced by the dramatic rise in patient harm. Industry must get out of their silos and create cross-team development processes, adopt long-held quality practices used by other major manufacturers, seek materials biocompatibility expertise from other areas of study, and select the highest quality materials. Next slide.

A pervasive presence and increased responsiveness to the patient voice should be a hallmark of quality. The equation for listening to patients must be balanced between groups who are willing to take greater risks and the more cautious, perhaps harmed patients. As MDUFA-5 is negotiated patients along at the table. Next slide.

The medical device ecosystem must protect public health by prioritizing safety and effectiveness through an equal balance in post-market and pre-market activities and pursuing product quality and reliability. This is the only ecosystem which works for all the stakeholders. Thank you.

MS. ROTH: Thank you. If we can now turn to Lisa McGiffert from the Patient Safety Action Network.

MS. McGIFFERT: Thank you. My name is Lisa McGiffert. I'm with a Patient Safety Action Network, which is a network of individuals and organizations working to end medical harm.

I have 30 years' experience as a consumer advocate on health issues -- 17 of those

years have focused on patient safety. FDA's mission relating to medical devices is to be, "responsible for protecting the public health by assuring the safety of efficacy and security of various products, including medical devices."

And that should be the priority in the MDUFA negotiations. My experience as a consumer advocate has led me to understand that the health care system rarely connects the dots between prevention, treatment, risks and benefits.

Unfortunately, medical devices, especially implants, are a good example of this. Implants are unlike any other medical products. If something goes wrong, patients must have surgery to remove them. They cannot simply quit using them.

This requires an enhanced attention to safety by the FDA. Doctors and their patients have little useful information about what led to approval or clearing of devices, or about post-market experiences and the overall quality of implants.

They need this information in a timely manner to make responsible medical decisions. Fees are commonly used by government to fund licensing and oversight of various industries and professions. They are not typically controlled by the industry or professionals paying them.

The current focus of MDUFA is clearly on pre-market speed to market, and our biggest concern is that these fees are not used for critical post-marketing surveillance activities.

Since most of these devices have not been thoroughly studied in the clearance process, it is essential to focus on what happens after they are put into patients. This is especially true for commonly used implants such as cardiac devices and joint replacements.

I could find no reference in the law that restricts using MDUFA fees for post-market surveillance. Who is around the MDUFA table? And where is the table? Are all stakeholders represented such as experienced and informed public interest advocates,

physicians and payers, all who are independent from the medical device industry?

Negotiating only with industry means only their interests will be on the table. These other affected parties need to be in the negotiation room at the table to get fair results for all parties regarding how these funds are used.

And where is the public? Negotiation should not be conducted behind closed doors. This should be treated like all other FDA business, in public meetings, so all can see why certain agreements were made.

There is nothing in the law that I can sign that restricts bringing other parties into the process. And we ask that MDUFA-5 change these dynamics.

Adverse event reporting is an essential part of real-world evidence that might not be picked up in medical claims or records. MAUDE is the only direct interface between the FDA and patients and health care providers. It should be well-funded and technologically updated regularly to be more user friendly in the reporting and searching process.

Public outreach should be enhanced, including to doctors who implant and use devices on their patients. Doctors should be encouraged to look at MAUDE before making their practice decision.

Summary reporting to MAUDE should not be allowed. All adverse events should be publicly visible. We also recommend that post-market surveillance should be well-funded, government controlled and responsive to the public interest, not industry run, controlled or oriented.

Patient engagement should include all types of patients -- those who are satisfied, those who are harmed, those desperate for help, and general public who may need an implant later. They all have different levels of acceptable risk and expectations.

We need more rigorous oversight and follow through on post-market requirements like post-market studies typically required as a condition to clearance or approval. We need

more communication to the public and medical providers regarding early signals of problems with specific devices.

Transparency is essential to safety. Recall activities should kick in earlier and more frequently, with more pressure on makers of problem devices to pull products back and fix the problem.

Thank you very much for this opportunity to speak and we look forward to working with the FDA as MDUFA advances.

MS. ROTH: Thank you, Ms. McGiffert. And now if we can please turn to John Owen from CDISC?

MR. OWEN: Hi. Good afternoon, everybody. My name is John Owen. I am the head of Product Research and Developments at CDISC.

But CDISC is Clinical Data Standards Interchange Consortium. And it was formed 1997 by a group of Volunteers and incorporated as a nonprofit standards development organization in 2000.

CDISC developed standards to represent data from preclinical, clinical and device research. The drivers for development of CDISC standards, amongst others, are regulatory requirements. For example, the requirement to submit data in CDISC formats for FDA, CBER and CDER and so the Japanese -- CDISC is 450 global member organizations, and we rely on volunteers from these and other companies to develop consensus based standards. CDISC to the standards, are free to download from the CDISC website. And also included in the CDISC library it has machine readable connected standards. Next slide, please.

I just want to introduce four of the foundational standards from CDISC? So, we have our CDISC national data collection standards; our STDM standards, which are used for organizing data in a tabular format, maximizing predictability of our data.

We have our outcome standards which define key effectiveness and safety analysis

data sets and also XML technologies for day to transfer. All of these standards are underpinned by CDISC controlled terminologies and use of the four standards allows traceability of data from data collection through to analysis. Next slide, please.

CDISC has also created seven domains to represent device specific data are based on these SDTM structures. The Medical Devices Implementation Guide, includes domains that will be used for identification of devices; device properties that are very over the study; device in use as in pertaining device measurements and settings; device exposure detailing the subject's exposure to a medical device on the study; device related events such as device malfunctions, device tracking -- for example, shipment deployment, return.

And finally, a relationship dataset linking a subject to devices that they've been exposed to. Use of these device domains has also been shown in some of the CDISC therapeutic area user guides for data such as cardiovascular and diabetes. Next slide, please.

In the 2014 -- presentation done in 2015 CDISC Interchange Poster, various CDRH challenges were identified. CD standards have solutions or can help with many of these issues.

Today, I'm just going to focus on data trial challenges. Next slide, please.

So, to the first point, organizing device related data in tables using the CDISC SDTM standards and the subsequent representation of the analysis of the data in the CDISC guidance standards are both transmissible in a variety of formats, including, for example, such transport files.

This allows data to be supplied to CDRH in electronic, machine readable -- to the second point, the CDISC standards developed to represent adverse event data in a standardized format, including device related adverse events, allows for standardized reporting of these data using, for example, data visualization tools to assist review.

When a standard, consistent data structure is expected, these tools can be reused across different submissions. For the third points, the CDISC -- analysis standards allow key effectiveness and safety analysis to be defined.

The analysis of the data can be easily described using these standards, allowing for easy interpretation and understanding of how the data are analyzed and how the results are traceable from data collection.

And finally, for the last points, understanding the data structures submitted is key to the understanding of the data. The CDISC defined XML and defined PDF formats that are provided along with submitted data sets allow for reviews to easily understand the data that's being submitted in terms of tables, variables, code lists, as well as descriptions of how the data were analyzed, providing clear definition of the data.

Other CDRH requests and solutions are available as supplemental slides to this presentation. But unfortunately, we haven't got time today to go through them.

So, if you go into the final slide, please, so CDISC can help CDRH. Summarizing the points on this slide, when CDISC standards are applied to data, there is predictability built in and the potential efficiencies, benefits in collection, submission and review of data and the daring to findability, accessibility, improper interoperability and reuse principles or the fair data principles for digital assets.

When data is received in a known format, reviewers can spend less time trying to decipher the structure of the data and more time on in-depth exploration of the data, including ad hoc analysis, cross-study comparisons, for example, with the potential to reduce reviewers having to re query sponsors about the data.

When we speak the same CDISC language, regulators, sponsors and ultimately patients all benefit. Next slide, please.

Finally, I'd just like to say thank you and CDISC appreciates the opportunity to speak

at this meeting.

MS. ROTH: Thank you, Mr. Owen.

And with that, we have reached the end of our agenda for today. I want to say thank you again to all the presenters and to the rest of the participants who joined us via the webcast. We look forward to engaging with all of you further as the negotiation process proceeds. And have a great afternoon. Thank you.

(Whereupon, at 2:40 p.m., the meeting was concluded.)

C E R T I F I C A T E

This is to certify that the attached proceedings in the matter of:

MEDICAL DEVICE USER FEE AMENDMENTS FOR FISCAL YEARS 2023 THROUGH 2027

October 27, 2020

Via webcast videoconference

were held as herein appears, and that this is the original transcription thereof for the files of the Food and Drug Administration, Center for Devices and Radiological Health, Medical Devices Advisory Committee.

SHAYLAH LYNN KISER

Official Reporter