UNITED STATES

FOOD AND DRUG ADMINISTRATION

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PUBLIC MEETING ON

PRESCRIPTION DRUG USER FEE ACT

(PDUFA) REAUTHORIZATION

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DATE: Thursday, July 23, 2020

TIME: 8:00 a.m.

LOCATION: Remote Proceeding

REPORTED BY: Latrice E. Porter, Notary Public

JOB No.: 4186569

A P P E A R A N C E S

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STEPHEN HAHN, FDA

ANDREW KISH, FDA

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DIANA ZUCKERMAN, National Center for Health Research

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MARC BOUTIN, National Health Council

JEFF ALLEN, Friends of Cancer Research

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DAVID RIDLEY, Duke University

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PATRIZIA CAVAZZONI, FDA

P R O C E E D I N G S

SARA EGGERS: Good morning, everyone. Welcome to the U.S. Food and Drug Administration's public meeting on reauthorization of the Prescription Drug User Fee Act, referred to as PDUFA. My name is Sara Eggers. I'm the director of the Decision Support and Analysis Team, an FDA Center for Drug Evaluation and Research, or CDER. I will serve as today's moderator.

PDUFA is the legislation that authorizes the FDA to collect user fees to support the process for the review of human drugs. The current authorization of the program, PDUFA VI, expires in September 2022. Preparations are therefore underway to begin the process to reauthorize the program for fiscal years 2023 through 2027.

The purpose of today's meeting is to gather input and recommendations from the public in advance of discussions that will occur with the regulated industry leader this fall. Today's meeting is an important step in engaging the public stakeholders on the PDUFA program. We will continue

to engage stakeholders throughout the authorization process.

There's a Federal Register Notice out now with details on how to notify us if you would like to participate in that process. You should be able to see a link to that notice in the announcement section of the meeting platform, which is at the bottom center of the screen. We will cover a lot of ground today. We'll begin with Stephen Hahn, Commissioner of Food and Drugs, who will provide opening remarks.

Andrew Kish, Director of CDER's Office of Program and Strategic Analysis will follow with background on PDUFA and the reauthorization process. We will then have speaker panels providing perspectives, presenting various types of stakeholder groups. Consumer advocates, patient advocates, healthcare professionals, regulated industry, and scientific and academic experts.

Following the stakeholder panels, Patrizia Cavazzoni, the Acting Director of FDA CDER will provide remarks. And finally, there will be a public comment session for those members of the public

who had submitted an online request to provide comment. The format for the stakeholder panels is a series of presentations where each speaker will have 10 minutes to present their organization's perspective on PDUFA.

To help panelists prepare for -- or frame their comments, FDA provided three questions in the Federal Register Notice that announced this meeting. What is your current assessment of the overall performance of PDUFA VI thus far? What current features of PDUFA should be reduced or discontinued to ensure the continue efficiency and effectiveness of the program? And what new features should FDA consider adding to the program to enhance the efficiency and effectiveness of the human drug review process?

Policy issues are beyond the scope of the PDUFA reauthorization process; therefore the presentation should focus on process enhancements and funding issues, and not on issues of policy. As we do have a full agenda, we ask speakers to please adhere to the 10-minute timeframe. Doing so will make the

moderator's job much easier.

Given our virtual format, this meeting will not include questions from FDA to any of the speakers, nor will FDA be able to answer any questions raised at the meeting. Even though you can't see us in person, please know that my colleagues who are leading and participating in the reauthorization process are listening, and we very much value your important perspectives.

Today's meeting is not the only chance to gather public input. There's also a public docket open till August 23rd, and we encourage the public to submit comments. The information is also on the announcements section of the screen -- here on the slide, and in the announcements section.

There are a few housekeeping items. This is the first year that the public meeting is conducted entirely on a virtual platform, as is a necessary response to the COVID-19 pandemic. We thank the speakers for your preparation, and to all participants for your patience as we navigate through this day.

If you experience technical issues during the webcast, please contact us through the tech questions box at the bottom of the screen -- or tech support, I'm sorry. Or email us at PDUFAreauthorization, all one word, at FDA.HHS.GOV. If your audio or visual quality diminishes at any point, we recommend as a first step closing out of the meeting platform and reconnecting through that same meeting link.

We'll have a 15-minute break around 10:45 and a 45-minute break at around 11:45. If schedule modifications are needed, we'll post information on the announcements section of the platform. With that, we look forward to beginning this very important conversation. I will now turn it over to Doctor Hahn for your opening remarks. Thank you.

MAN 1: Okay, I think we need to give Dr. Hahn a few more minutes, so we might want to move to Andy Kish, and he can do his presentation, and we can have Dr. Hahn join us when he's able.

SARA EGGERS: All right, thank you very

much. Then Andrew, if you are ready to provide background PDUFA program and reauthorization process, you can start with that.

ANDREW KISH: Certainly. Thank you, Sara. Good morning, everyone. Actually, I know Doctor Hahn, our commissioner, is extremely busy with the COVID pandemic, and I believe he has actually just joined. So we may be able to have him jump in and give his opening remarks.

SARA EGGERS: Okay.

ANDREW KISH: So how about we give him one more minute. So --

SARA EGGERS: Of course.

ANDREW KISH: -- thanks everyone for their patience. All right, Doctor Hahn, I will turn it over to you now. You can hear us?

SARA EGGERS: Doctor Hahn, if you can make sure that you're off mute.

DR. STEPHEN HAHN: Good morning, everyone. Can you hear me?

SARA EGGERS: Yes, we can, thank you. Thank you very much.

DR. STEPHEN HAHN: I apologize for the technical difficulties. But I want to welcome everyone to today's public meeting on PDUFA. The public meeting process is an essential part of FDA's commitment to public health and our ability to meet future health needs. Providing transparency and public engagement are a vital piece of the PDUFA process. Indeed, all of the UFAs that we participate in.

We hold meetings like this specifically to ensure that we have the opportunity to hear and learn from a broad range of stakeholders. Since the first PDUFA was passed in 1992, we have significantly increased communication during drug development, and the predictability of the FDA review process. This has helped us build an even more robust environment for innovation.

For instance, the FDA has used PDUFA resources to significantly reduce the time it takes to review new drugs and biologics, and it has done so while maintaining our rigorous standards for safety, efficacy, and quality. Since fiscal year '16, nearly

five years after our previous meeting, CDER and CBER have approved over 150 new molecular entities, new drug applications, and biological license applications.

Of special significance over the last several years, many of these advancements, in fact nearly half, 70 of the 153, have been for orphan products or indications for rare diseases. This includes treatments for Batten disease, Fabry disease, phenylketonuria, EPP, and Duchenne's muscular dystrophy.

And after nearly 20 years without new options, the FDA has also approved several treatments for patients with sickle cell disease. I think this illustrates to you what we can do when we work together in partnership between the private sector and government to actually speed great discoveries to patients and consumers.

And that's just a sampling of the progress that we've made so far. In addition, many of these new treatments were for cancer, including several for pediatric cancers. As someone who has

focused much of my professional life on researching and treating cancer, this success has a very personal meaning. It underscores our scientific advance -- how scientific advances are enabling us to develop new and more effective treatments for previously untreatable diseases.

And the PDUFA process plays an important role in this, as you all know. In the most recent year for which numbers are available, fiscal year '19, we reached a new high for priority applications filed, 72, and total applications filed, 166, and again are on track to meet or exceed most of our review performance goals.

In addition to our reviews, per our commitments under PDUFA VI, over the last three years we've published over 30 draft or revised guidances, held more than 20 public meetings and workshops, and published nine public reports. We continue to enhance our regulatory decision toolkit, advancing regulatory science and patient-focused drug development, and structured risk benefit assessment.

These efforts are even more critical

today as we are immersed in the consuming effort to find treatments and cures in response to the COVID-19 pandemic. I'm so pleased that even as our agency is working full steam on our COVID-19 pandemic response across the FDA, many of our staff continue on these efforts, and other mission critical initiatives.

But I want to pause and say that takes two groups to actually make that happen, and my many thanks to the stakeholders here at this public meeting today because they have also very much participated in making sure that's happened. So many thanks to everyone for their terrific work in this area.

As our Center for Drug Evaluation and Research continues to focus on our key role of reviewing and approving new medicines, they are a terrific group of professionals, and of course the success of PDUFA is not the result just of FDA's work as I said.

Everyone's participation, your engagement, today's example of bi-directional feedback, incredibly important, and I encourage you to be very forthcoming with the issues you think that are

before us as we move forward. That's one important reason why we will continue to engage with you, our stakeholders, and through the course of the reauthorization process, as well as today's meeting. And of course this meeting is just the first step. We'll look forward to continuing working with you and to support you as we fulfill our mission.

Thank you for helping us fulfill that mission, and to deliver on the promise of science, with data-driven results and rigorous scientific research and analyses to protect and promote the health of the American public. Thank you again for attending today's virtual meeting, and special thanks to the panelists on today's program. We really do look forward to a productive meeting. Thank you.

SARA EGGERS: Thank you very much, Doctor Hahn. I would now like to invite Andrew Kish to provide background on the PDUFA program and reauthorization process.

ANDREW KISH: Thank you, Sara, and thank you, Doctor Hahn. Again, my name's Andrew Kish. I'm the Director of Office of Program and Strategic

Analysis in CDER, and this morning I'll do a very brief background on the PDUFA and reauthorization process.

So the outline for this briefing, some history on PDUFA, touch on the financial background and fee structure, workload and performance in the program, PDUFA VI commitments -- really just a recap there -- then an overview of the reauthorization process.

So before 1992, timeliness of FDA drug review was a big concern. And in fact, in the late 1980s, some estimates put the median time for FDA to approve a new drug at over 2.5 years, so that's a very large backlog of applications. So PDUFA I was created to allow FDA to collect user fees to add resources, which would allow to add more review staff to eliminate the backlog of overdue applications and improve review timeliness.

In return, FDA agreed to meet specific performance goals. A result of this is a more predictable, streamlined process, patients gained earlier access to new drugs and biologics, and overall

critical development time and average time to approval dropped since 1992.

I do want to note a recent Tuft study looking at the past decade or so. It notes that while FDA review times for approvals continue to drop, there has been an increase in critical development time for certain non-orphan drugs.

So what is the User Fee Program? What is the PDUFA construct? Here are the basics. Fee funds are added to appropriated funds and are intended to increase staffing and other resources that speed and enhance the review process. User fees pay for services that directly benefit fee payers. This is what distinguishes it from a tax.

Fee discussions with industry focus on desired enhancements, in terms of specific activities and aspects of the program or the process for the review of human drugs. So what does that really mean? It means getting into the details around what new or enhanced process FDA would want or industry would take to include in that next five-year authorization.

What is technically feasible to

actually implement, and what resources are required to implement and sustain these enhancements? As previously noted by Sara, there's no discussion of policy in the negotiations. For those of you that are familiar with the commitment letter and have read it, it's rather detailed and it's rather long, so, you know, the experience I believe on the industry and FDA side is the devil in the details.

I'll touch on really briefly the history of PDUFA, and it has evolved quite a bit since 1992. PDUFA I added funds for pre-market review. It really focused on reducing that backlog and setting predictable timelines. PDUFA II shortened review timelines, expanded the scope of the program, what activities are included, slightly, and added more process and procedural goals.

PDUFA III significantly added funding to increase interaction in the first review cycle, and it allowed for limited support of post-market safety for the first time. Getting into PDUFA IV, it increased and stabilized base funding with enhanced pre-market review, and there was a significant

investment in modernizing the post-market safety system.

PDUFA V saw a small increase in base funding for the program. There's a lot of focus on review enhancements to increase communication with sponsors, such as the NME program, the strength and regulatory science in post-market safety, and focus on electronic data standards.

So PDUFA VI, where we are right now, we're in the middle of. It's focused on modernizing the user fee structure, improving HR and financial management. It's created a capacity planning capability, enhanced use of regulatory tools, be it benefit risk, patient-focused drug development, complex, innovative trial designs, model-informed drug development, provided staffing for breakthrough therapy reviews. It focused on communication with industry and explored RWE in regulatory decision-making.

So switching over to the finance, and to give a very brief background. The user fee revenue is critical to the program. The graph that you can

see on the slide right now shows PDUFA program obligations by funding source from 1993 to 2019. These include non-user fee appropriations, so that would be what we call budget authority, we received our budget from Congress, and PDUFA user fee revenue.

As you can see, user fee revenue has outpaced budget authority available for the program. As a point of comparison, PDUFA user fee revenue funded seven percent of the program in 1993. As of 2019, it funds 71 percent of the program.

So the fee structure. PDUFA VI modernized the user fee structure to improve program funding predictability, stability, and administrative efficiency. The new structure eliminated the supplement fees, replaced establishment and product fees with a program fee, and shifted a greater proportion of the target revenue to the new, more predictable, stable annual program fee.

The 2020 target revenue, so what FDA what would like to collect, is over a billion dollars, 20 percent of which should be collected from applications, 80 percent collected from PDUFA program

fees. So the fee types are applications with clinical data, applications without clinical data, and the PDUFA program fee, which is essentially approved products.

Okay, switching over to workload and performance. The fees support review work against a broad set of performance commitments, and those 31 specific review and procedural goals haven't changed much since PDUFA V and PDUFA VI. They're still relatively aggressive. And as you can see from the table, they focus on review times for NMEs and original BLAs, supplements, special protocol assessments, and clinical hold responses, among others.

Despite these goals not shifting, the PDUFA and BLA workload continues to trend upwards in PDUFA VI. You can see from the graph on this slide from 2010 to 2019 the upward trend in number of NDAs and BLAs filed. As the commissioner mentioned, we had a record number of applications in FY19. You can also see the distribution between priority applications and standard applications, and priority applications

increasing over time. Of course, priority applications are quicker reviews.

So despite this, FDA meets or exceeds nearly all review goals. The table on this slide shows -- it's pulled from the 2019 performance report, which is available to you on FDA's website. It shows FDA's performance on most of these major review goals, and you can see the FDA just missed one review goal.

So switching over to meetings and meeting management. PDUFA meeting workload is increasing. As you can see from the graph on this slide, 2008 to 2019, type A, B, and C meetings. Meeting request and WRO, which is written response only, workload by fiscal year. You can really see it particularly in type B and type C meeting requests starting in the end of PDUFA IV, throughout PDUFA V, and so far continues in PDUFA VI. Really an upward demand for meetings with the FDA in this program.

So given the rapid increase in workload and demand for meetings, meeting management is a challenge, and we openly admit that. As you see from this table, also from our PDUFA performance reports,

which is available to you on FDA.gov, you can see our meeting management goals on the left side, and our performance by fiscal year across the horizontal axis.

The numbers highlighted in green are where we were able to make that performance goal for that fiscal year. As you can see, unfortunately those are far outnumbered by those in red where we are unable to meet the goal. So there are review and procedural goals, but there's also numerous commitments.

There's a growing number of enhancements and activities behind the scenes. The FDA is implementing over 200 actions to fulfill PDUFA VI performance enhancements. These include new and updated pilots, programs, and processes, data posting to our website, public meetings and public workshops, new and revised guidances, and public reports.

So I won't go in great detail here, but I want to just recap some of those additional commitments in the PDUFA VI commitment letter. For those of you familiar with the commitment letter, here are some of the major sections in that commitment

letter.

So in regulatory science and expediting drug development, the FDA committed to enhancing communication in the IND phase, committed to integrating its rare disease program staff, and more product specific meetings. There's a number of activities to improve combination product review. Also the FDA committed to exploring real-world evidence in regulatory decision-making.

In regulatory decision tools, there's a number of activities to enhance patient-focused drug development, enhancing benefit risk assessment. FDA committed to launching a pilot in model-informed drug development, also a pilot in complex innovative designs, and a number of activities in enhanced drug development tool and qualification pathways.

In modernizing the FDA drug safety system, the FDA committed to numerous activities to expand the Sentinel system and integrate it in pharmacovigilance activities. Also to improve communication of post-market safety findings.

And for the first time in a PDUFA, FDA

in PDUFA VI committed to management of user fee resources. This included creating a capacity planning capability, modernizing the time reporting programs and practices, and the centers involved in the PDUFA program, and a number of activities to improve financial transparency and efficiency.

Also for the first time in PDUFA, FDA committed to improving FDA hiring and retention of review staff. This included modernizing hiring system infrastructure, augmenting the hiring staff capacity and capabilities, and bringing on contractors to help with the hiring process. The establishment of a dedicated scientific staffing unit. The FDA committed to a comprehensive and continuous assessment of its hiring and retention practices and performance.

Finally, the FDA committed to improving the electronic submission process and the transparency of IT activities. Particularly, this focused on the electronic submission gateway. So I know there's a lot there and I went through it relatively quickly, but that's just to give you a sense of the number of commitments that occur outside of just the review and

procedural goals.

Performance data and completed deliverables are available to the public. Completed PDUFA VI deliverables can be found on the FDA's website. Here is the link in this slide. Also, I want to note FDA released the new PDUFA performance dashboard that allows users to view and download current and historical performance data. This includes much of the data that is in the PDUFA performance reports that we release annually to Congress. Accessing this dashboard can also be found by using this link.

Okay, shifting over to the reauthorization process. I know much of this has already been mentioned, so I'll just recap it briefly. So the big takeaway here is PDUFA reauthorization by statute involves significant consultation. There's prior public input that is required. There's periodic consultation with stakeholders. There's public review of recommendations. And finally, there's transmittal of these recommendations no later than January 15th, 2022 to Congress in the hope of timely

reauthorization.

So where are we today? FDA is required to obtain public input prior to beginning negotiations with regulated industry. That includes holding the public meeting, which we are doing right now, and also to provide a period of 30 days after the public meeting to obtain written comments. As previously noted, the docket is open. We really encourage you to submit your comments. I can assure you every single one of those comments is read.

It also requires periodic consultation with representatives of patient and consumer groups. This has to happen no less frequently than once every month during negotiations with regulated industry. Also note that we have a FR Notice out asking for organizations that would like to participate at public stakeholder meetings to please notify FDA by August 17th.

Okay, what are FDA's priorities going into PDUFA VII? FDA sees the importance of promoting sustainable innovation in drug development, enhancing regulatory predictability in post-market safety,

advancing the regulatory infrastructure for digital technologies and new sources of data, and enhancing the program's operational capabilities, efficiency, and agility. And that's where I'll stop and hand it back to you, Sara. Thank you very much, everyone.

SARA EGGERS: Thank you, Andy -- Andrew. We will now move into the stakeholder panel sessions, comprising series of speaker presentations. And with the all-virtual format, there are no blinking or infrared lights. So to keep us on time with each 10-minute presentation, I will verbally announce when there are about 30 seconds left, and if your comments are not concluded by around the 11-minute mark, I will come back on with a request to wrap up your comments.

Our first session is perspectives of consumer advocates. Our three speakers in this panel are Sally Greenberg from the National Consumers League, Diana Zuckerman from the National Center for Health Research, and Michael Abrams from Public Citizen. So it'll just take a minute. We'll pull each set of slides up. And it looks like Sally, your slides are up, and you should be promoted to be a

speaker by now. So if you are all set, you may begin.

MAN 1: I was just getting connected to audio real quick.

SARA EGGERS: Okay. So you can imagine this is as though the person's taking that time to walk up to the podium and getting settled. I will use this time to again remind participants that there's important information in the announcements section of the meeting platform, and for anyone, if there are technical issues, you can communicate with us through the tech support.

And again, if you run into technical challenges, try jumping off of the webcast and then coming back on. Okay. All right, we will give Sally a few more seconds to see if we can connect her. Otherwise, Diana, if I can ask you to be on standby and we will move on to you if necessary and come back to Sally. All right, I think we will try to go onto Diana. Diana, are you able to join us through audio?

DR. DIANA ZUCKERMAN: Yeah. Can you hear me?

SARA EGGERS: We can.

DR. DIANA ZUCKERMAN: Can you hear me?

SARA EGGERS: All right, Sally, we will put you on hold. Yes we can, Diana, can you hear us? Can you hear me?

DR. DIANA ZUCKERMAN: Yeah. I can hear you.

SARA EGGERS: Okay. So Sally, be on standby, we will come to you following Diana's. Thank you, Diana.

DR. DIANA ZUCKERMAN: Sure. I'm just waiting for my slides to go up. There we go. Thanks so much for the opportunity to speak today. I'm Doctor Diana Zuckerman, President of the National Center for Health Research. The National Center for Health Research is a non-profit think-tank that focuses on the safety and effectiveness of medical and consumer products. We don't accept funding from the company's that make those products.

My personal perspective is someone trained in epidemiology and public health. I've worked in the field of the safety and effectiveness of medical products for many years, and also worked in

the U.S. House of Representatives and Senate and HHS and White House, so I -- my perspective is really overall, you know, what can we do to improve these programs.

As we all know, FDA approval requires evidence that drugs are safe and effective, and that's defined as having benefits that outweigh the risks for most patients. So the questions I'll be addressing today is, what is FDA doing and what is PDUFA doing pre-market and post-market to ensure that those decisions are accurate?

The big three criteria: safety, effectiveness, and inspections to make sure that the products are being made as they are supposed to be made. For patients the big question is, does it work as it's expected to work? How sure are patients that their medication works and is as safe as the label says? And are those labels understandable? How consistent are they with pre-market data and with the most recent data from post-market surveillance?

The question in my mind is whether PDUFA is patient-centered, and to us, this has been a

shortcoming of PDUFA because performance data are currently based on speed, and you've done a great job of speeding the process and getting more products to market, but performance data should also be based on patient-centered outcome. Because speed and getting new products on the market are only some of the priorities that patients have.

And unfortunately, PDUFA has not addressed many of the issues that are most important to patients. For example, making approval decisions based on biomarkers and surrogate endpoints can certainly speed the process, but they're not clinically meaningful to patients. They can't tell patients if the drug's benefits outweigh the risk. For example, progression-free survival versus overall survival for cancer drugs.

When PDUFA relies on test-tube analyses such as for antibiotics, that can't tell patients if the benefits are going to outweigh the risks of those particular products for patients. And when FDA uses non-inferiority standards, that can result in approving actually inferior drugs. So for example, if

FDA approves Drug B as non-inferior to A, but it's a little bit less effective, and then approves Drug C as non-inferior to B, and then approves Drug D as non-inferior to C, but that drug D may be much, much inferior to Drug A.

So how can PDUFA improve? How good are the safety data for male and female patients at different ages and race and ethnicity, for example? I think FDA's doing a good job of including men and women and males and females, but not so good at including patients over the age of 65, and particularly not doing a good job of subgroup analysis for minority groups.

Another issue that we think PDUFA should help pay for because it's part of the safety issue is whether direct to consumer ads are misleading. We know that they're technically accurate, but they can still be misleading. And what about ads directly to doctors and so on? And another point is that patients want to make sure that those inspections that are being done are thorough, and there's a lot of concern among patients and consumers

about foreign inspections.

And I know that during the COVID-19 pandemic, inspections were stopped for a while. My understanding is the foreign inspections are still not underway. We understand the reasons for that, but it's of great concern and that needs to be -- a solution needs to be found as soon as possible.

How else can PDUFA improve? We believe that PDUFA should support FDA staff to improve safeguards for off-label prescribing. FDA should develop patient materials to explain off-label prescribing and target off-label uses that are known to be ineffective or unsafe.

So that's just a matter of how the money is used, how are these user fees used in additional to the performance? And also are detailing activities and direct to consumer ads, or ads to doctors, directly or indirectly promoting off-label uses that may be harmful to patients. That's another way that performance goals could be improved in a patient-centered way.

How can PDUFA improve the information

available to patients and providers? We think that PDUFA should support more post-market surveillance. We know that some money is used from PDUFA for Sentinel and for other post-market surveillance, but we think that Sentinel isn't the only focus for post-market that's going to be helpful to patients.

We think that PDUFA funding should be used to support FDA staff to create patient booklets, informed consent checklists, and other things that will help patients make informed decisions about new drugs, and that PDUFA should also support FDA Dear Doctor letters and warnings to patients, and by that I mean whether the letters come from industry or the letters come from the FDA directly, FDA staff should be involved in making sure those are understandable, clearly stated, and that they are seen by the people who most need to see them.

Post-market studies are very important, and particularly as FDA has set along the pre-market process, depended more on surrogate endpoints and so on, it becomes more and more important that FDA enforce clinical trial requirements for post-market

studies, and that means funding from PDUFA to make that possible. Because (sound drops) really uses resources.

And Sentinel and adverse event reports and other real-world data can supplement clinical trial data, but it isn't always going to be enough. And particularly, I know this morning we heard about the use of PDUFA for tracking safety signals, and we're concerned that that needs to be done more -- well, more effectively and more efficiently than it's been done so far.

The one other thing I wanted to mention is that, you know, I heard this morning about the fact that PDUFA is supporting meetings with patients and consumers on a regular basis. That information is not available to a lot of patient and consumer groups. We haven't been invited to those meetings. We don't know about those meetings.

It's very important that the patients and consumer and public health groups that are, you know, have a stake -- that we're all stakeholders and we have a stake in how well PDUFA works, and we want

to make sure that those meetings are hearing from everybody, not just the patients that are so closely aligned with industry as has so often been the case.

My final comment is just to say that we support more resources for the FDA. We know that user fees have increased those resources, but those resources will not be helping patients if they are really focused only on speed, and they need to have more focus on those patient-centered outcomes, and the transparency that was mentioned this morning, by including providers, public health advocates, patients, and consumer groups in the process.

We're not at the table for PDUFA, and that's very unfortunate. We appreciate the opportunity to participate in meetings like this, but it's different from being at the table, and for that reason, we hope that FDA can do a better job of including a wide range of patients and consumer groups and public health advocates. Thank you very much.

SARA EGGERS: Thank you, Diana, for your input. If we could ask you to mute your phone. Thank you. Okay. Sally Greenberg is ready, so we

will move on to her, followed by Michael Abrams. So Sally --

SALLY GREENBERG: Sorry for the glitch.

SARA EGGERS: Thank you.

SALLY GREENBERG: Everybody can hear me, I'm hoping. Sorry for the glitch.

SARA EGGERS: We can.

SALLY GREENBERG: Okay, great. On behalf of the National Consumers League, I want to thank the FDA for the invitation to speak to the consumer perspective at this FDA meeting. PDUFA is a critically important law that has helped shape safe and effective drug approvals for millions of patients, and we support its reauthorization with certain caveats discussed below.

The National Consumers League was established in 1899. We are the nation's oldest consumer advocacy organization, and we have a very proud history that tracks closely with the FDA, from our support in 1906 with the Pure Food and Drugs Act, to the more recent FDA modernization act. NCL has been working often alongside the FDA to ensure that

the public is adequately represented and protected, and that our medications are safe and effective.

Before I address the specific question posed for this discussion, I want to emphasize that our remarks are from a consumer perspective. Although the terms are used interchangeably, I want to address briefly the distinction between a consumer and a patient.

First, the patients and consumers may risks -- may weigh risks associated with new drugs differently. A patient suffering from a serious illness is far more likely to take on greater risk, be willing to take on greater risk to get the benefits from a specific treatment. If a consumer has a moderate or mild condition, that may be more risk averse.

The distinction we think is critical to informing our perspective on PDUFA is indeed though an act, which has proved to be very successful in speeding up drug approval. And as the world confronts the COVID-19 pandemic, we're reminded that the global AIDS crisis and activists in the United States pushing

for faster drug treatment approvals to treat HIV were instrumental in getting the first PDUFA law passed in the early 1990s.

That said, a number of new drugs approved under PDUFA, especially for rare diseases, have come with astoundingly high prices, which we want to point out could be a barrier for patient access. So that's something that we need to all as a society be paying attention to.

I'd now like to turn to the first question posed for the meeting, what is your assessment of the overall performance of PDUFA VI thus far? NCL wants to be sure that in the quest to reduce barriers to new drug approval, the FDA, through the PDUFA program, doesn't lose sight of the importance of the agency's mission of protecting and promoting the health of patients and consumers.

NCL strongly believes that the patients and consumers deserve a drug approval process that provides timely access to safe and effective drugs, while reducing exposure to harmful medications that pose undue risk. We recognize that PDUFA must balance

the needs of consumers who are concerned about serious side effects with the concerns of patients who may be facing a life threatening illness where time is of the essence.

Thus, while it's important to have an efficient and timely approval process, there is still, in our view, sometimes too little emphasis on performance goals aimed at improving safety and efficacy of drugs, and at times too much emphasis on speed.

In 2020, the United States GAO analysis of 637 new drug approvals submitted from fiscal years 2014 to 2018 indicated that FDA has largely met its performance goals for reviewing new drug applications and biologics license applications with the help of funding through the PDUFA program.

According to the FDA's 2019 report, the agency had completed over 1,600 reviews and met the majority of performance goals, which is very impressive indeed. The FDA meets these performance goals by completing its review and issuing an action letter for a specified percentage of applications

within a designated period of time.

In fiscal year 2018, FDA approved 89 percent of priority applications for NDAs and BLAs within the first cycle of review. Performance goals are intended to protect patients from the risks of pharmaceutical drugs, not just to speed those drugs to market. We want to be sure that there are adequate safeguards in PDUFA VI.

In addition, four years ago, NCL expressed its concern that -- to the FDA that PDUFA VI does not address the agency's limited capacity to support the review of post-marketing safety issues until the end of fiscal year 2022. NCL urges the agency to continue to make this post-marketing review a priority and speed up the timeline for this.

NCL supports the continuation of provisions in PDUFA VII that enhance patient and caregiver perspectives in drug development and decision-making. I cannot stress enough the importance of giving patients a voice. I've attended several of these workshops and they really provide a very unique opportunity for patients to come forward

and be part of the discussion as drugs are under consideration at the FDA.

We believe that the FDA benefits from this input tremendously, but that to be free of any suggestion of industry influence, an FDA patient workshop travel fund would be money well spent, and it would enable many more patients to come to Washington to be part of these discussions.

We are impressed with FDA's efficiency in meeting goals and delivering largely safe and effective drugs to consumers. We would also like PDUFA VII to consider how the PDUFA process can help improve representation of patients of color in clinical trials. There are certain medical conditions present in African Americans and other communities of color, and diversity in clinical trials is a critical approach to addressing that disparity.

Despite accounting for 12 percent of the population, African American patients represent only five percent of clinical trial participants. Similarly, Hispanic or Latino patients account for 18 percent of the population yet represent only one

percent of all clinical trial participants. Adequate representation in clinical trials is vital due to existing evidence that patients of different backgrounds can have varying outcomes using the same drug.

And I think it's especially true during this COVID pandemic, that we're all -- the scourge of the pandemic that we're all suffering from, it's really revealed racial disparities, and we have learned that a medication that might work exceedingly well for a Caucasian patient may not be suited for an African American patient or vice versa.

So these discoveries help inform provider treatment plans for patients and impact overall health outcomes. We encourage the allocation of user fees to go toward the assessment of the diversity present in clinical trials to inform the approval process. Health disparities in drug treatment and access should be reviewed, and a comprehensive plan developed to address them.

Now I'm moving to question three, which are what new features should FDA consider adding to

the program to enhance efficiency and effectiveness of the human drug review process? NCL commends the FDA for the enhanced benefit risk assessment actions that have implemented under PDUFA VI. However, we continue to urge FDA to consider our recommendations regarding off-label prescribing.

We suggest greater attention to the use of medications prescribed for off-label uses and the influence of direct to consumer advertising of prescription drugs. We also have suggestions for additional features. NCL believes that a portion of PDUFA funding should be directed toward examining the safety of off-label prescribing to address consumers' lack of awareness and understanding of the practice.

We can do this through Sentinel, and we think it would contribute very strongly to our understanding the use and health and safety implications of off-label prescribing. NCL also thinks it's imperative that FDA have staff and resources to oversee the direct to consumer drug ads, and to ensure that they are accurate and not misleading before they read the public.

We strongly believe FDA should seek the authority to require that all DTC ads undergo review before public dissemination, and we recommend that user fees be allocated to support the hiring of additional staff to review this DTC ads.

The COVID-19 pandemic has caused disruptions in foreign travel, which is a key aspect of inspecting drugs manufactured in other countries. The public really does rely on the agency personnel to help assess quality, safety, and availability of medicines for Americans, so we suggest PDUFA VII funds be used to support FDA's efforts exploring additional ways to safely conduct inspections at our ports and in production in other countries.

NCL also encourages that PDUFA VI funds -- VII funds be allocated to the development and review of COVID-19 vaccine efforts, like Operation Warp Speed. Operation Warp Speed's ambition of delivering 300 million doses of safe and effective COVID-19 vaccine requires that funds go to the hiring and retention of personnel that will help support review of those vaccines.

NCL has worked closely with adverse reporting programs, like FDA MedWatch, to help gather accessible messaging and resources for consumers. We see the immense value that post-market surveillance has for consumers and encourage great allocation of resources to help fund staff and support programs like FDA MedWatch, the Sentinel program, and post-market studies.

In conclusion, although we convene today as stakeholders, we are all both patients and consumers who rely on the FDA and the pharmaceutical industry to work closely and thoughtfully and carefully in approving new drugs for the public. PDUFA has been a tremendously important law and it has got -- brought many effective and safe drugs to the public much more quickly.

So we support the act, we support PDUFA VII, and with the caveats noted above. As advocates, NCL will continue to work collaboratively with other non-profit organizations, the FDA, and industry stakeholders to ensure that consumers and patients have access to the safe and effective drugs and

treatments they deserve. Thank you for your time and for inviting us to be part of this discussion.

SARA EGGERS: Thank you, Sally. Okay, we have Michael. We'll tee up Michael. So if you could walk to the podium, please.

MICHAEL ABRAMS: Thank you. Hope you can hear me okay.

SARA EGGERS: It's a bit -- let's try that again. Why don't you test is one more time?

MICHAEL ABRAMS: Can you hear me? Testing, one, two, three.

SARA EGGERS: It's just -- it's rather quiet.

MICHAEL ABRAMS: I will try to speak up. How is that? Is that better?

SARA EGGERS: That is wonderful. Thank you, Michael.

MICHAEL ABRAMS: Very good. Good morning and thank you for hosting this meeting to everybody at the FDA who's working so hard on this. I'm Michael Abrams, a researcher at the health and research group of Public Citizen, a non-profit

consumer advocacy organization with more than a half a million supporters nationwide.

Since 1971, we have advocated on a broad range of federal issues, including those concerning the FDA. And we do not receive contributions from industry, and thus have no conflicts of interest to disclose. Regarding PDUFA, Public Citizen has long opposed the basic tenants of this vehicle to fund FDA activities. I want to be clear about this.

We believe such user fees, which now directly fund well over half of the agency's operating budget as we have heard, too often cause the agency to place the interests of regulated industry over those of the public. Simply stated, Public Citizen continues to strongly oppose in fact any government agency being funded directly by the industry that it regulates.

Nevertheless, I am pleased to be here, and we do have advice for PDUFA VII that I'll provide. And it includes provisions that we think will better promote the mission of the FDA and the public health

interests of the U.S. population. Certainly, the stakes are substantial, as we have heard. And we've seen displays like this previously but let me just briefly review them.

In 2019, the FDA's obligated user fee revenues for activities related to human drugs exceeded a billion dollars, supports the efforts of more than 4,000 full-time professionals. The chart here just shows again the number of NDAs and BLAs that have been reviewed over the years. And you see this distinctive increase -- you see increases in priority applications that were reviewed as well.

Part of the theme of my presentation today is to remind us all that more is not necessarily better. Moreover, per the FDA's actual budget from -- again, data from 2019, 64 percent, and we actually heard from Andrew that it was 71 percent or so, of the money focused on human drugs actually comes from user fees directly from industry.

The FDA submits annual reports to Congress of course. Here are three exhibits from a recent 2019 performance document. The left table

lists -- and we saw this again from Andrew -- it lists hundreds of meetings that have occurred, shows that the FDA professionals are being timely, scheduling -- generally scheduling gatherings on time, completing follow up activities.

All laudable, notable, important, what we expect from a professional organization such as the FDA. The right two charts present PDUFA performance data that typically garner the most attention however, especially since PDUFA was spawned.

Both charts show annualized data indicating that over the last 10 years -- these charts end in 2018 -- and the top right chart shows that application reviews on average, the median review times are about seven months for priority drugs and about 11 months for standard drugs.

The chart below on the right shows that the priority review of drugs -- that over half of them are approved if they're priority drugs, and in fact, well over half are approved in the first cycle. So, you know, all good things suggesting efficient approval pipelines.

But from a consumer perspective on such data presentation, and my colleagues who presented before me indicated this, they seem to avoid the opportunity to assess more how PDUFA actions have actually impacted on human health. We believe that instead of these kinds of presentations, which are certainly important, the consumers want to know more about whether truly beneficial drugs have emerged, and whether bad or questionable drugs were approved in a given cycle.

How many and how fast is important, but quantitation of health gains and harms is essential. One immediate approach to collecting data about the quality of a review cycle in the near term is to survey experts who directly contribute to the decision making process.

This is a very busy slide. I don't expect you to read it all. But I want you to know that such surveys should afford FDA reviewers the opportunity to provide anonymous comments on the agency's review process every cycle. Past anonymous surveys conducted by Public Citizen and others,

including the HHS Office of the Inspector General, have revealed that a substantial proportion of expert FDA reviewers have been concerned about the FDA review process since PDUFA has been spawned.

And results from these two surveys -- I'll just highlight a couple. In 1998, 64 percent of medical officers felt increasing pressure to approve new drugs by virtue of PDUFA. And in the early 2000s, 36 percent of CDER reviewers said that they were not confident in FDA decisions regarding drug safety.

And these concerns persist in the era of PDUFA VI, in both the lay and academic publications. Again, this is a busy slide, but I'll review some key points. The slide offers notable points made by a 2018 ProPublica report and a 2020 JAMA study.

ProPublica's investigative journalist wrote this statement, and I'm going to quote directly from this reporting. "The FDA is increasingly greenlighting expensive drugs despite dangerous side effects and inconclusive evidence." Moreover, in that same article, Doctor Janet Woodcock, of course the

longtime director of CDER, said this, "Clearly, accelerated approval has greater uncertainty." Okay?

In addition, policy and medical researchers have observed, I think somewhat amazingly, that at the FDA there has been a culture, "of built-in fear of regulation," at the FDA. And one former FDA medical team leader actually said this, "You don't survive as a senior official at the FDA unless you are pro industry."

These points demonstrate that pharmaceutical largesse is at least somewhat ensconced at the FDA in a way that negatively impacts on the agency's mission. Studies and surveillance of the FDA's review and approval process have revealed negative impacts on PDUFA. In 2014, the Health Affairs report by Frank and colleagues studies over 700 new drug approvals between 1975 and 2009 and divided them between those which were approved pre and post PDUFA.

They then searched for negative events attached to each approval drug in two forms: either the issuance of a black box warning or the drug's

removal from the marketplace. What they found is summarized on the graph that I'm showing you here. During the first four years both pre and post PDUFA, drugs experienced about a five percent probability of warning or withdrawal.

But beyond that point, they split. Post-PDUFA approvals always performed more poorly than drug approvals before the law was implemented. Additionally, we know from simple reporting data pictured here, adverse event reporting data, that since the 1990s, serious events and even deaths have increasingly been linked to pharmaceutical use.

I show this graph not to infer causality, but instead to remind us that these simple trends, just like the simple trends we saw from Andrew and from others, of inclines in how quickly drugs are approved don't really tell us what we need to know. Consumers and the FDA need to know if and how these adverse event trends and other indicators relate to changes in the drug -- the review process.

Such analyses should be regularly used to assess the performance of the PDUFA program and

presented to Congress and the public. Identifying those correlations of course require advanced data processing methods that we know are on the FDA's radar screen. Other folks on the dais with me mention some of those. The Sentinel real-world data analytics initiatives, for example.

Public Citizen supports those initiatives, and they're important, but only as tools to complement the FDA's principle and statutory role as a gatekeeper for new drug products. The gatekeeping function, by contrast, must be reliant on rigorous randomized trials.

And so just on to a summary slide at the end. Accordingly, Public Citizen strongly advocates for the following to be important touchstones for this PDUFA reauthorization process. More taxpayer supported spending for the agency to decrease its user fee dominance and dependence. More adherence to pre-market requirements for at least two large randomized blinded trials, with definitive clinical endpoints rather than surrogates and shortcuts.

Requirements that the FDA have independent organizations conduct anonymous surveys, like the ones I described. Surveys of reviewers after each review process. Establishment of the FDA authority to order drug recalls, rather than being purely initiated by industry. Direct the FDA to create regulations that allow generic drug manufacturers to update product labeling and safety information.

Establish opioid specific regulatory framework. This is important. The opioid crisis has not gone away. And by the way, we also very much support the idea of looking more at other subgroups, disparity subgroups, as my cohorts here on the dais suggested as well. And then require the FDA to assess benefit to risk ratio linked to drug approval actions; that should be central to the performance reports that are submitted.

And finally today, we caution against any provisions that might either loosen restrictions of off-label promotions, or create time limited provisional approval pathways, or pathways that extend

manufacturing monopoly placing powers -- of course, the latter of which can greatly increase cost to consumers.

In summary, Public Citizen believes that future PDUFA-related legislation must enable the FDA to reassert its ethos as a strong gatekeeper for new drugs that are effective, safe, and truly advance human health. And there's my contact information and thank you very much. We look forward to working with you over the next two years.

SARA EGGERS: Thank you, Michael. That concludes our session on the perspectives of consumer advocates. We will now move into a session on perspectives from the vantage point of patient advocates. Our four speakers in this session are Rachel Sher, from the National Organization for Rare Disorders, Marc Boutin, from the National Health Council, Jeff Allen, from Friends of Cancer Research, and Cynthia Bens, from Personalized Medicine Coalition.

We will take a break following this session. And as we saw, if we have challenges with

the order, we might switch up the order, but it looks like Rachel, your slides are up, and if your video and audio -- audio and/or video if you want is ready, you may begin.

RACHEL SHER: Okay. Can you hear me?

SARA EGGERS: We can, thank you.

RACHEL SHER: Great. Hi, I'm Rachel Sher, Vice President for Policy and Regulatory Affairs at the National Organization for Rare Disorders, or NORD. Founded in 1983, NORD represents over 320 rare disease patient organizations, and the over 30 million Americans who are struggling with a rare disease. We are committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient services.

I want to begin by thanking the FDA for invited us here today. Our participation is a testament to the commitment of FDA and industry to the idea that rare disease patients deserve to be partners throughout the drug development process. FDA's user fee programs have been a tremendous success, permitting FDA to maintain its gold standard while

also conducting efficient reviews of the products patients need.

Great strides have been made under PDUFA VI with respect to rare diseases, including various public meetings and workshops, guidances on rare diseases and patient-focused drug development, reviewer training to aid in rare disease drug review, and the creation of important web resources.

Today I will address these four areas that NORD hopes will be incorporated into the PDUFA VII agreement. There are over 7,000 rare monogenetic diseases that currently do not have a treatment. With recent advances in science, these conditions are prime candidates for gene and cell therapy. The Center for Biologics Evaluation and Research, or CBER, will be the epicenter of review and approval of these innovative cell and gene therapies in the coming years.

There are over 900 active investigational new drug applications, or INDs, in-house at CBER as of the end of last year. As this chart demonstrates, over 200 INDs were submitted in

2018 and then again in 2019, a doubling of submissions just since 2017. Projections show that over the next 10 years, we will see 40 to 60 launches of new gene therapies, with 15 to 30 of these in the next five years.

This oncoming increase threatens to overwhelm current resources at CBER. Currently, CDER has about five times as many staff as CBER. To continue the progress that CBER has made in important but resource intense programs, like INTERACT and RMAT, and to keep us with the demands of increasing submissions, additional staff will be critical.

But CBER's needs go beyond new FTEs. Given the increase in regulatory submissions and the complexity of the data likely to be associated with the scientifically complex biological products, modernization of the center's information technology infrastructure will also be critical to ensuring that CBER is well positioned to address these challenges.

We need to recognize though that any proposed user fee increases cannot occur until the reauthorization of these programs in law, which

Congress is not poised to do until September 2022. CBER needs additional resources now. The workload is enormous, and if additional resources are not provided, NORD is concerned that a backlog will develop.

NORD will be acting alongside partners like the Alliance for a Stronger FDA to pursue congressional appropriations for CBER's critical work prior to the reauthorization. PDUFA VII also presents a prime opportunity to build upon recent innovation and investment in the development of a groundbreaking rare disease initiative, the Rare Disease Cures Accelerator.

NORD applauds FDA for spearheading this important project, which will establish a scientific collaborative approach to the accelerated development of therapies across rare diseases. The Rare Disease Cures Accelerator, or RDCA, as FDA has described it, is compromised of three interconnected goals and components. Rare disease characterization, development of standard core sets of clinical outcome assessments and endpoints, and support of clinical

trials in rare disease populations.

NORD is proud to be a partner in the first component of the RDCA. Led by the Critical Path Institute, or C-Path, and NORD, the RDCA-DAP, the Rare Disease Cures Accelerator Data and Analytics Platform, is an FDA-funded cooperative agreement that will create a resource through which researchers and drug development -- developers can access data about rare diseases and how they progress, leading to new insights about those diseases.

We will also provide a way to develop new tools and processes to improve clinical trial design and empower the rare disease community. Ultimately, RDCA-DAP will contribute to more efficient and effective clinical trials and more rapid and cost effective development of new drugs.

NORD and C-Path are also collaborating on another FDA-funded cooperative agreement to advance the second component of the RDCA, supporting the development of standard core sets of clinical outcome assessments, or COAs, that measure impacts most important to patients.

The Rare Disease COA Consortium is aimed at accelerating the development of new therapies by creating and curating a public resource of information on available COAs that have been identified as potentially fit for purpose as endpoint measures in treatment trials across multiple rare diseases.

This project will also support researchers in the generation of new, high quality, high utility data, and will inform the design of clinical trials for rare disease drug development. In addition to this work with C-Path, NORD is partnering with the Northwestern Clinical Outcome Assessment Team on an initiative to develop COAs on physical function for use across both common and rare diseases.

The third component of the RDCA, the subject of FDA's recent request for information, is aimed at creating a global rare disease clinical trials network to support improvements in the design, conduct, and completion of clinical trials in rare disease populations.

NORD believes that the coordination of

the three components of the RDCA initiative has the potential to bring critical innovation to rare disease drug development space, and common disease drug development alike. Additional and sustained funding from PDUFA VII would contribute to the long-term success of the program and its goal of bringing treatments to patients faster.

NORD greatly appreciates the FDA -- the efforts by the FDA to incorporate a patient experience into the regulatory process. NORD has been honored to work closely with FDA on two externally led patient-focused drug development meetings, including one on TKD last September, and an upcoming meeting on Krabbe's disease.

Along with the patient affairs staff at FDA, NORD has also conducted nine listening sessions on a variety of disease states. NORD worked to bring the patient community together for these meetings to present their stories and experiences to the FDA. We have heard time and again from patients how much it has meant to them that FDA has been willing to listen.

But more can be done. Patients should

have a greater understanding of what impact their stories and data had on the FDA review process. This can be accomplished by establishing a more robust feedback loop with the patient community. NORD stands ready to help identify how best to articulate such impacts to the patient community so that patients understand the value of their participation and seek to continue to be a part of this process.

Additionally, in PDUFA VII, NORD urges that additional PDUFA resources be directed to ensuring patient-focused drug development plans are discussed within all FDA review divisions early in the drug review process to allow for ample consideration of the patient experience.

The COVID-19 pandemic has presented significant challenges for the rare disease community. But in the midst of this difficult time, a bright side has been that telemedicine has taken hold in an unprecedented manner, a goal long sought by many rare disease patients.

Given the scarcity of rare disease specialists, patients and their caregivers are usually

forced to take time off work and travel great distances to see their providers. The same is true for participation in clinical trials, where trial sites are often distant from the patient's home.

FDA has responded to this changed world by issuing strong and clear guidance to industry on the conduct of clinical trials during the pandemic. The pandemic has revealed new ways to achieve the goal of ensuring clinical trials continue, while simultaneously allowing patients to participate in a safe, and when necessary, remote way.

PDUFA VII resources should be directed toward ensuring these learnings are memorialized and carried forward in guidance or regulations that can facilitate broader adoption of the decentralized clinical trial model. Critical to the goal of creating an ecosystem where clinical trials can be effectively decentralized is increased acceptance of real-world evidence, which can be produced by digital technology, such as wearable devices and remote monitors.

However, for effective uptake of these

tools, FDA needs to assess and validate them. NORD believes this work should be a top priority for the agency, both in and out of the context of COVID-19, so that patients can actively participate in clinical trials with fewer burdens.

Thank you again for the opportunity to speak with you today. NORD stands ready to remain a constructive partner to the FDA and to our industry partners throughout the PDUFA reauthorization process. We encourage anyone with interest in any of the initiatives that I mentioned more to visit our website at www.rarediseases.org. Thank you.

SARA EGGERS: Rachel, thank you. And next up is Marc. Marc, it looks like your slides are up, so if you're ready to begin, please go ahead. Thank you.

MAN 1: Marc, we can't currently hear you. You can check to see if the audio icon at the top, your phone or microphone icon, to see if you can connect that way.

SARA EGGERS: Okay, so we'll see if we can give him another few seconds for Marc. If not,

Jeff, can we ask you to be on standby? Oh, I think we hear Marc.

MARC BOUTIN: Can you hear me?

SARA EGGERS: We can. It's a little bit inconsistent. Let's try again.

MARC BOUTIN: So I apologize for that. Hopefully you can hear me okay. Thank you so much, Sara, for the opportunity to be here. My name is Marc Boutin. I'm the CEO of the National Health Council. The council was created by patient organizations for patient organizations 100 years ago. We focus on systemic issues that are important to all people with chronic conditions, with a heavy focus on ensuring meaningful and affordable access to high value, high quality care, and driving innovation.

The CEOs of the non-profit organizations control our governance but have invited representatives from all stakeholders within the health ecosystem into membership, which includes the biopharmaceutical, device, diagnostic, generic, payer, provider, researcher, and family caregiving communities.

I want to take a moment and reflect on PDUFA VI. From our perspective, this has been a historic agreement. It has created fundamental change in terms of how we engage with patients. Going back to PDUFA IV, the patient community came to FDA and said, we really needed to understand benefit risk from the perspective of patients. We needed to ensure that products were developed with that perspective in mind.

And FDA has listened. And in PDUFA V we started to really look at how we could engage with patients. And just a couple of weeks ago, we had the first patient engagement guidance for drug development released anywhere globally. It's part of a huge cultural phenomenon where people are saying in every aspect of their lives, we want customization.

We want our homes customized. We want our cars customized. And increasingly, people are saying they want their health customized. And in order to do that, all of the various surrogates in health, researchers, regulators, drug developers, need to fundamentally understand what the patient and family caregiver perspective is.

And with the release of this guidance, we've had a sea change in how we develop products and how we think about releasing them into the marketplace. Huge cultural shift. And one aspect I think really needs to be underscored. The FDA's done a terrific job with this, but it's part of a cultural shift.

We've really inspired the beginning of this. We're beginning to put the frameworks together. But culture change is hard, and it's just beginning, and we need to reinforce it moving forward. But what FDA does here has implications for the entire health ecosystem.

While FDA does not regulate the practice of medicine, its focus creates significant opportunities for the entire ecosystem and how we can deliver care more effectively, more efficiently, and care that reflects the outcomes that matter most for patients.

In PDUFA VII, we are really interested in a variety of elements that will further elevate the voice of patients. When you think of the

opportunities for digital clinical trials and real-world evidence, huge, huge opportunities to learn more and really understand how products work in the real world for the lives of real people.

But recognize real-world evidence, and even the use of digital clinical trials, is not a substitute for engaging the patient. You have to engage the patient in the design of these clinical trials, in how you're going to look at real-world evidence, and how you're going to interpret it.

You know, I meet a lot with experts in augmented intelligence, and they'll tell you, we are so sophisticated. We know the moment the child takes the wearable off during the clinical trial and puts it on the dog. That's great. But they do not know why the child took the wearable off in the first place. We can help you understand that, interpret it, and develop better digital clinical trials to get better data that is more useful.

We are excited to see the movement with knowledge monitoring systems at FDA. We want to ensure that the great outcomes, the knowledge we're

learning about what patients care most about, is captured effectively and disseminated so it does not have to constantly be replicated.

And of course, there's a huge need for additional FDA staff. We're hearing from many folks as they engage with the FDA. They want more opportunities to have conversations and really figure out how to develop plans to systematically and consistently engage patients and family caregivers. We need more resources on the FDA side as we continue to learn and improve in this space.

But I want to focus most of my time on patient centered core outcome sets. It's been raised a few times already, and we're really, really excited about this. It really is an opportunity to take patient engagement to the next level. But when you think of core outcome sets now -- and let me step back for a minute.

For our perspective, patients in a core outcome sets are agreed upon, standardized sets of outcomes that at minimum should be collected and reported on. There are a number of entities, like

CNTP, ICHOM, and COMET, that are working extensively in this space. And in fact, the FDA has begun several pilots looking at core outcome assessments.

Currently, the emphasis of core sets of clinic outcome assessment measure, or the emphasis is on measure development. It usually begins with an environmental scan of literature, previous clinical trials, and existing measures. Unfortunately, patients had very little involvement in the development of existing measures.

We're getting a lot better at incorporating the patient perspective into the measure selection and into the development and moving into the core sets of measures. But the reality is, we really need to do a better job. Most of these core outcome sets have really focused in on how we can use them in clinical trials, and to an increasing extent of real-world evidence studies.

What we would like to propose is that we think of it a little bit differently. We need to think about how we develop patient centered core outcome sets. And to do that, we really need to begin

at the frontend of engaging patients and other stakeholders to really identify what are the outcomes that matter most. Then we can do the environmental scan to see what exists.

But we really need to focus in on identifying those outcomes first, and then move to the measure selection. When you think of many of the measure selections, as I said earlier, that have been developed in many cases, in fact most cases, without patient input. And they're really focusing in on things that may not be the outcomes that are most important issues to patients.

Our goal here has really got to be patient centricity at its core. Core outcome sets serve as a foundation for a wide range of activities beyond research and trials. It can include care provision, quality measurement, real-world evidence, policy, value-based payment -- a whole core of elements.

What is really exciting is there is a clear opportunity to focus on the outcomes that matter most to patients, and then look at how we get to the

right measures and the endpoint selection. And to do that as a group.

Part of why this is so important from a patient perspective is because of this cultural movement to engage us, not only in drug development, but in other types of research and delivery system design, quality measures, the patient community is being asked over and over to engage with different entities to answer very similar questions.

We really need to figure out what are the core outcomes that we need to focus on so that we can better maximize our capacity and produce better results. It leads to huge opportunities for the FDA to get everybody on the same page by standardizing terms, methods, and approaches.

It allows us to foster multi stakeholder and multidisciplinary collaboration, promote innovation in method development, and to convene stakeholders to identify our infrastructure needs.

So our big ask is to really continue the major cultural phenomenon and shift in patient

engagement that has begun with PDUFA IV, V, VI, and now moving into VII, to really focus in on patient centered outcomes -- or patient centered core outcome sets. With that, I will turn it back to you, Sara. Really appreciate the opportunity to be with you today.

SARA EGGERS: Thank you very much, Marc. And we will move into the presentation by Jeff. Marc, if you are still there, I think you have shut your red -- make sure your red cam is shut off. There you go. Jeff, if you're ready, you can go ahead. Thank you.

JEFF ALLEN: All right. Thank you, Sara. Can you hear me okay?

SARA EGGERS: Yes, we can.

JEFF ALLEN: Okay. Thanks so much. Well, I'd first like to thank the FDA for hosting this meeting in a creative format, and for the invitation to participate with you all today to provide our thoughts on the current PDUFA program and enhancements that could be made moving forward.

In terms of the first question

regarding the assessment of the current program, as the previous speakers have each noted, this has been a multi-year process that has been continued to be built upon and taken many steps to achieve improvements and overall access to new medicines.

Originally, it was established to alleviate the backlog for drug applications a number of years ago, something that has been consistently kept up with, and has provided an important component of ensuring timely access to new medicines. In the end, it's been able to result in a more predictable format for submitting applications and the timing that new medicines can make it onto the market and become available to the patients that need them.

By setting up firm goal dates, this has become something that has been allowed to set up numerous different process management techniques that have improved operations. And obviously, this program supplies critical funding that augments these operations and personnel opportunities. And it's created a more predictable and efficient and accessible process through doing them.

While the PDUFA process provides essential funding, we certainly are strong advocates for public funding through the typical congressional appropriations approach as well. But in the absence of that, the user fee program has enabled a number of different scientific programs to continue to accelerate, in addition to the benefits that have been provided in terms of access.

This has provided critical support for programs like improvements in safety surveillance technology and techniques over a number of different years, as well as setting up new scientific programs that can inform future product development in order to make them safer and more effective in the long run.

In looking at a case study, I think it's important to recognize the breadth of different products that are regulated by the drug division at FDA. In this slide, I've depicted a timeframe specific to oncology, which you can see in the green bars on the right hand side.

And the years of this current period of -- for PDUFA, the green bars represents the goal times

that have been set up, both in terms of the standard review process of approximately 10 months, as well as the priority review process of six months.

And in each of the years of the current PDUFA, you've seen that the oncology -- the review of oncology drugs has regularly met these performance metrics, and in fact, exceeded them by approximately about 30 -- of about 30 days.

It's important to note that this is about the review of the product. The time in which the final application has been submitted to FDA in order for them to assess the merits of the application provided to them. This is not necessarily about the development of the product, the standards of which have not changed in a number of decades.

But in this instance, it is also important to note that for individuals who -- many of these products have been brought to individuals that previously had no therapeutic options. And in these instances of addressing unmet medical needs, time certainly matters.

In terms of a few key components of the

prior PDUFA program that I've highlighted here that were put into place during the last reauthorization, I've noted several programs that we have seen advance quite quickly in a very favorable fashion.

The first being the role of -- to advance the role of patients and their experiences, and this has been able to set forward a process allowing for funds to be devoted for the creation of numerous different guidelines that the FDA has propagated, the formation of both internally and externally patient-focused drug development meetings to help provide additional insight into the experiences of patients, as well as various pilot programs that have come out of this work.

The second is these past PDUFA programs have provided essential fundings to support the continued success of the breakthrough therapy designation. During this time, FDA -- since the inception of the breakthrough therapy designation as a whole, the FDA has approved well over 300 different breakthrough therapies that have been designated, and over a 150 different products have been approved

through this expedited mechanism for drugs that show an unprecedented activity very early in development, and transformative potential, in order to accelerate the completion of their development process.

During this specific PDUFA period, since the -- since PDUFA VI has been enacted, this includes over 100 different designations that have been supported through this additional funding. In addition, PDUFA VI provided additional fundings toward the qualification and the use of drug development tools.

While this still continues to be a work in progress, and as one of a scientific nature, which requires multiple years of research, to be able to allow additional fundings an guidelines to be established for the uniformity, the qualification, and the validation of new measures that can help identify safety signals earlier and signs of efficacy sooner in order to help identify the most promising compounds that can continue through development.

And finally, the use of real-world evidence is a growing field that FDA has been able

through these fees that have been collected for this -- and applied toward this particular program, to propagate guidance documents, including their recent framework on the different use cases of how to develop high quality real-world evidence and apply it to scenarios of safety monitoring and looking at long term benefits of products over time.

In addition to thinking about what can be done to enhance many of the programs that have been included in past PDUFA reauthorizations, it's important to recognize that while the current pandemic has put challenges on numerous individuals, all of us, particularly those that are patients that have to adjust how they access care, as well as the entire health system as a whole.

But are there things that we can learn from this in thinking about what the future of development of new medicines can look like? Things like clinical trial design and the different considerations that may be needed in response directly to COVID-19, given the high proportion of patients particularly in fields like oncology, where these

patients may be more susceptible to severe infections due to immune -- having compromised immune systems due to the treatment and the underlying disease.

How to think about different clinical trial designs that maybe need to be applied, including things like the loosening and broadening of eligibility criteria in order to ensure that a diverse set of patients are represented into trials moving forward.

In addition to thinking about ways to accelerate the setup processes, things that have been strongly paid attention to in the context of developing new therapies toward COVID-19, looking at things like shortening IRB reviews, and how different sponsors can work directly with the FDA on pre-planned modifications and amendments to existing studies.

In addition, the use of master protocols as a way of creating more efficient trial designs that enable multiple different products to be tested within the same protocol in order to speed the efficiency of setting up these protocols, as well as the adoption of more remote services and the

application of decentralized trials.

Things like remote consultations or sending more medications directly to patients have been strategies that have been deployed recently and may inform the future of drug development, and thereby making it more -- making clinical trials accessible to more patients in the long run.

In terms of thinking about PDUFA VII moving forward, I've listed six ideas here of areas that we'd be very interested in seeing be part of the discussion as they move ahead. The first, looking at efficiency pilots to explore how they might be expanded.

I've noted two here that have been deployed already by the Oncology Center of Excellence at FDA, including a program around real time review in order to streamline the different components of application review in a more cohesive and horizontal manner, as well as global coordination.

As drug development has become a much more global enterprise and clinical trials are recruiting patients from across the globe, having

alignment between different global authorities is important in order to streamline those trials and make sure that they are consistent and able to be applied broadly.

The second are on cell and gene therapy. With a growing pipeline of products, additional support will be needed in order to hire and allow the experts in this field to be part of FDA review processes to be able to be applied to a growing number of products.

Similar to this, manufacturing innovation and readiness, techniques that can be -- include advancements in technology to speed and improve the quality of manufacturing, as well as biomarkers and diagnostics, which are -- continue to be a growing component of the drug development process.

While they are regulated outside of CDER, they are important in order to try and streamline the processes to the fullest extent possible, as well as individualized drug development, where new technologies are being developed where

doctors are able to identify patients within their hospital and develop drugs for them right there.

This is reusing the potential need for new -- a new framework to evaluate the safety and efficacy of these products, as well as the continued progress in real-world evidence in order to ensure long-term benefit of new drugs. So thank you for the chance to join the meeting today. I look forward to being part of the discussion forward. I hope everyone stays well and safe. Thank you.

SARA EGGERS: Thank you very much, Jeff. Our final speaker of this session is Cynthia, and after Cynthia we will take a break. So Cynthia, if you are ready, your slides are coming up. You're not -- I don't think you have slides. Is that correct?

CYNTHIA BENS: No slides. No, no.

SARA EGGERS: Great, then go ahead, Cynthia. Thank you.

CYNTHIA BENS: Thank you, Sara. Good morning everyone. It's an honor to join you today. I'd just like to take the opportunity to thank FDA for

inviting me to share some insights on the importance of the prescription drug user fee program and advancing personalized medicine.

As Sara mentioned, my name's Cynthia Bens, and I currently serve as Senior Vice President of Public Policy at the Personalized Medicine Coalition. The Personalized Medicine Coalition is an education advocacy organization that has more than 200 members from across the healthcare spectrum. We're all working together to advance personalized medicine in ways that benefit patients.

We define personalized medicine as an evolving field that uses diagnostic tools to identify specific biological characteristics to help determine which medical treatments and procedures will be best for each patient. By combining this information with an individual's medical history, circumstances, and values, personalized medicine allows doctors and patients to develop targeted treatment or prevention plan.

The prescription drug user fee program is a critical source of funding that ensures the

timeliness of drug reviews, encourages innovation in drug development, and promotes initiatives at the FDA that leverage the best science. Having a well resourced, focused, and flexible FDA is essential to achieving personalized medicine, and our mission as a coalition to bring it closer to all patients who need it.

The Personalized Medicine Coalition has documented that personalized medicines account for more than 20 percent of the FDA's new drug approvals each year. These approvals have sharply increased since the Coalition first started looking at approval trends in 2005. At that time, personalized medicines only accounted for approximately five percent of newly approved therapies.

There have been notable regulatory firsts since the last PDUFA reauthorization, including the approval of the first cell and gene therapy, NF1 therapy, and the first tissue-agnostic therapy. Activities taken by FDA in recent years have fostered a favorable environment for innovations like these, and we believe this progress will continue under PDUFA

VII.

Our analyses have also shown that successes in personalized medicine product development is not just occurring in oncology anymore. There are lessons learned from part of the treatment in oncology that are being applied in drug development for an increasing number of diseases.

We believe that enhancements included in the user fee reauthorization that advance the future of personalized medicine are going to yield benefits for a wide range of patients, including those patients that currently have unmet medical needs.

There are three main areas that I'd like to emphasize in my remarks that should be the focus of discussions leading up to PDUFA VII. These are targeted staffing needs to perform drug review, additional considerations for advancing the use of real-world evidence and real-world data, and the use of digital health tools to support personalized medicine.

PDUFA VI and the 21st Century Cures Act both included provisions to help FDA develop and

maintain a capable and well trained staff to fulfill the agencies mission to protect and promote public health while meeting the challenges posed by an increasingly complex regulatory landscape.

While FDA has made progress, we understand that there are still challenges with the tracking and retaining of expert staff. PDUFA VII should focus on where there are still staffing gaps, and the Personalized Medicine Coalition supports adequate staffing levels at the Center for Drugs and Center for Biologics that can be achieved in PDUFA VII.

For as long as medical researchers have been discovering genes that contribute to particular diseases, there's been interest in developing ways to repair abnormal genes or introduce new genetic material directly into cells to treat or prevent disease. Since 2012, 10 cell-based therapies or direct gene therapies have been approved by the FDA to target a variety of diseases, ranging from metabolic and rare neuromuscular disease and more common cancers.

FDA finalized the CBER guidances for the development and assessment of gene therapies earlier this year in anticipation that by 2025 it'll be reviewing and approving between 10 and 20 cell and gene therapies each year.

Cell and gene-based therapies have the potential to yield unprecedented improvements in clinical outcomes in some disease areas, and it continues to be a very important area for the Personalized Medicine Coalition and our members.

The Personalized Medicine Coalition is particularly concerned with the size of the workload facing CBER as a result of the need to evaluate increasing numbers of new cell and gene therapy products.

We've already called on Congress to provide the FDA with the budget authority appropriations necessary to deal with issues, but realistically, meeting the FDA's staffing needs in this area will take funding outside of the appropriations process. So in order to continue much of the exciting progress we've already seen in this

area, we believe that attention needs to be paid in PDUFA VII to increasing CBER staff.

Real-world evidence can provide valuable insights drawn from information about individual's lifestyles, disease biology, and treatment outcome. Thanks to new technologies and data science approaches, real-world data can be harnessed as a powerful complement to traditional clinical trials.

Real-world data applications can provide new ways to track disease, allow for optimization of treatment approaches, and capture insights about patient populations to accelerate clinical development. We believe the use of real-world evidence can help transform the future of personalized medicine, but only if the information can be combined and aggregated in ways that inform answers to questions that truly meet patient needs.

PDUFA VI made initial improvements of the agency to enhance the use of real-world evidence and real-world data. The Personalized Medicine Coalition commends the FDA for recognizing real-world

evidence and real-world data as a strategic priority, and for its framework that it released on real-world evidence.

The 21st Cures Act also acknowledged how real-world data could generate evidence and accelerate our understanding of which patients can benefit the most from new medicines. Specifically, that law directed the Secretary of Health and Human Services to establish a program that evaluates the potential use of real-world evidence to support new indication approvals and satisfy post-approval study requirements.

We understand that there's a lot happening organically within the individual review decisions to get reviewers comfortable with the science and ways that real-world data can inform drug review. We'd encourage this to continue, and that the FDA should continue to host workshops and facilitate FDA participation in other forms where staff can educate themselves.

The agency noted in its framework that there is more data available to inform medical

decisions than ever before, but the agency needs to provide clear guidance on appropriate -- on the appropriate collection of data and evaluation of this information.

We agree with the statement, and we've identified some areas that should be given additional attention. The future of personalized medicine will increasingly rely on the ability to continuously leverage high quality regulatory-grade data.

The Personalized Medicine Coalition would support additional staffing, resources, and guidance in PDUFA VII to allow the agenda to make further transformations in the use and acceptance of real-world evidence beyond early phase trials, and for purposes beyond demonstrating product safety.

One issue to be mindful of is the aggregation of large volumes of data over time, and one of -- it's one of the most valuable characteristics of real-world databases. Real-world databases cannot be single use, as it limits a data set's full potential.

There are multiple ways that data can

be used to support research, development, and regulatory approval, included hypothesis generation or providing supplemental evidence to the existing companion diagnostic or label expansion.

We recommend that FDA consider addressing, as part of PDUFA VII, the repeated use of real-world databases for regulatory submission. Clear guidance on acceptable surrogate clinical endpoints and methods to establish equivalence to patient enrollment criteria and defining the clinical comparability between real-world data and the intended use population of a product are two areas where we would have interest.

Further, stakeholders could benefit from increased visibility into FDA's experience with real-world evidence and real-world data as the space continues to evolve. We'd encourage FDA to disseminate learnings from real-world data submissions while protecting sponsors' proprietary and confidential information. This type of transparency will allow manufacturers, researchers, and other health data organizations to more efficiently leverage

real-world datasets.

And finally, we know that FDA is committed to its Technology Modernization Action Plan. The initial phase involved updating the agency's computer hardware, software, data, and analytics. The Personalized Medicine Coalition knows that much of what we're highlighting in this portion of my remarks won't be possible without the fundamental steps laid out in the TMAP.

PDUFA VII should resource the FDA to rapidly move beyond near-term steps, so full implementation of actions in the plan, particularly those that focus on data application solutions, the chief (sound drops) direct engagement with stakeholders and other government agencies.

The ubiquity of mobile information devices such as smartphones, as well as advances in sensing technologies and self-management platforms have been important tools for personalized medicine. A growing number of ongoing clinical trials feature the use of wearables and environmental sensors to learn how to deliver real-time care to patients.

Digital health platforms like wearables and mobile apps can help us gather information and also capture the patient experience, which is a critical perspective that we've heard a lot about on the two panels that have gone so far today.

People can report detailed information about their symptoms, treatment burden, quality of life, and other experiences, actively and passively documenting their health in detail in real-time, and this is in ways that go far beyond standard tests performed episodically in the doctor's office.

Digital health technologies really hold the potential for enhancing trial efficiency, parallel to the delivery of real-world care, and provide personal insights at the point of care. But as adoption of digital health technologies increases over the next generation we need to evolve and incorporate approaches such as decentralized clinical trials.

Decentralized trials utilize telemedicine, including remote patient visits and monitoring, to enhance recruitment, incorporate diverse patient populations within community settings,

and maintain the physician-patient relationship, as well as they hold the potential to reduce trial timelines.

Decentralized trials provide more patients with access to investigational therapies, while also generating more data to inform scientific understanding. Importantly, such approaches increase patient participation in research, and can make it easier for diverse populations and patients in difficult geographic regions to access trials. Recognizing --

SARA EGGERS: Cynthia, you're out of time.

CYNTHIA BENS: Okay. So PMC believes that FDA should accelerate the use of decentralized clinical trials, especially now since healthcare delivery has radically changed as a result of COVID-19. There's a growing acceptance and availability of telemedicine and remote patient visits that are important in this area.

Guidance regarding digital health technology issues, including the acceptance of

decentralized trials, should be considered as part of PDUFA VII, and we'd ask the FDA to consider any guidance barriers that it can remove to allow for greater participation in novel clinical trials, and enable the collection of information on off-label and approved uses of therapy.

I'll close by thanking you again, and if there are any questions, people are welcome to reach out to me. My contact information is on the Personalized Medicine Coalition website, and my colleagues at PMC look forward to continuing to engage in the stakeholder process as the year goes on. So thank you.

SARA EGGERS: Thank you very much, Cynthia. That concludes this session. We will now take a break. Breaks are very important, especially so for virtual meetings. So I will ask everyone to be back at 11:05, and then we will maybe make up some time in the agenda.

And just want to note, there might be some testing of some audio and visual during the break, but that is just part of the break; it's not

part of the meeting. So we look forward to seeing everyone back at 11:05. The speakers for the next session, of the healthcare professionals, if you could please make sure you're back a few minutes early. Thank you.

(Break)

Okay, welcome back from break, everyone. I'd also like to welcome any participants who have joined since we made introductory remarks and remind all participants that it is an entirely virtual public meeting to gather input on the Prescription Drug User Fee Act, or PDUFA program.

If you have technical questions, please use the tech support pod that's at the bottom of your screen. Again, if you run into technical issues, try shutting off, closing out of the meeting and jumping back in on the same link. We -- there also is information in the announcements about how everyone can participate, provide additional comments or continue to participate through this process through our public docket.

And with that, we will move into

session 3, hearing from the healthcare professionals, or Panel 3, of the Health Care Professionals Perspectives. Our two speakers are Karin Bolte from the American Pharmacists Association, and Patrice Harris from the American Medical Association. Karin, it looks like you are ready, so I will jump off the webcam and you can take over. Thank you.

KARIN BOLTE: Great, thank you so much. Good morning, everyone. I'm Karin Bolte, Director of Health Policy at the American Pharmacists Association. APHA represents pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in improving medication use and advancing patient care across all practice settings.

APHA thanks FDA for inviting us to provide our perspective on the implementation of PDUFA VI to date, and to offer some considerations as work begins on PDUFA VII. APHA believes that FDA has made good progress on PDUFA VI's goals. For fiscal year 2018 and 2019, to date, FDA met or exceeded the 90 percent performance level for 11 of 12 review performance goals.

There is room for improvement in first review cycle approvals however. While 89 percent of approved priority applications were approved on the first cycle in fiscal year of 2018, only 61 percent of standard applications were approved on the first cycle. Improving first cycle approval should be an area of focus for PDUFA VII.

Improving predictability of FDA funding and resource capacity planning utilization. Changes in the PDUFA VI fee structure have improved the predictability of FDA funding, simplified user fee administration, and enhanced the flexibility of financial mechanisms to improve the management of PDUFA program funding.

APHA is pleased to see that FDA has collected 100.1 percent of the total Plan's target user fee revenue through the first two years of PDUFA VI. It is critical that FDA continues to be a good steward of its financial resources. We are encouraged by FDA's resource capacity planning and modernized time reporting implementation to date.

Moving forward, we urge FDA to fully

enable its RCP capabilities and to adopt its proposed capacity planning adjustment methodology to better assess the sustained workload and PDUFA resource needs. As FDA begins to consider PDUFA VII, we urge the agency to include the following areas in the commitment level.

Continuing FDA's focus on hiring and retaining highly qualified staff. PDUFA VI includes several commitments to improve the hiring and retention of critical review staff through modernization of the FDA's hiring system, augmentation of hiring staff capacity and capabilities, creation of a dedicated function focused on staffing the program, reporting on hiring metrics, and a comprehensive and continuous assessment of hiring and retention.

On April 13th, Booz Allen Hamilton published an interim hiring and retention assessment report that noted continued deficiencies in FDA's recruiting, hiring, and retention functions. While APHA appreciates the improvements FDA has made, and the action plans the agency has developed to address specific issues identified in the report, more

progress needs to be made. For this reason, APHA believes that it is imperative that PDUFA VII maintain FDA's focus on hiring and retaining highly qualified review staff.

Enhancing the use of real-world evidence. APHA commends FDA for its commitment to enhancing the use of real-world evidence in regulatory decision-making. We appreciate the publishing of FDA's framework for real-world evidence, and its May 2019 draft guidance on submitting documents using real-world data and real-world evidence.

APHA recommends that FDA build upon this momentum by incorporating RWE commitments in PDUFA VII. In addition, APHA urges FDA to include pharmacists as a key stakeholder in this process because pharmacists are highly accessible healthcare providers and have been collecting, analyzing, and using RWE in their practice settings for many years.

Enhancing the incorporation of the patients' voice. As part of PDUFA VII, APHA supports the continued development of approaches and processes for incorporating patient reported outcomes in

regulatory decision-making. We welcome the June publication of the first of four patient focused stroke development guidance documents addressing how stakeholders can collect and submit patient experienced data and other relevant information from patients and caregivers for medical product development and regulatory decision making. APHA urges FDA to include pharmacists as a core member of integrated review teams during drug development and application review where a sponsor intends to use PROs as part of the development program.

In addition, APHA urges FDA to consider how PROs reported to pharmacists can be incorporated, as pharmacists are easily accessible to patients and collect PRO data through the provision of pharmacy services such as medication therapy management, disease management, and patient counseling.

Post-marketing drug safety. APHA believes that a larger proportion of PDUFA VII user fees should be directed to post-market surveillance. Performing active, diligent post-marketing pharmacovigilance is critical for proactively

identifying possible areas of concern for medications and ensuring the ongoing safety of medications post approval. APHA commends FDA for its commitment to develop a more robust and rigorous Sentinel Program.

Sentinel plays a critical role in providing proactive surveillance through a distributed data approach that can't be replaced by AERS, REMS, or other surveillance systems that retroactively collect data.

Addressing drug shortages. APHA appreciates FDA's and CDER drug shortage staff's efforts to address our nation's drug shortage problem, including early notification requirements, expedited inspections and reviews of manufacturing sites, the establishment of an agency drug shortages task force and stakeholder listening session, and the publication of FDA's October 2019 report examining the root causes of drug shortages and potential solutions.

Despite these advances, drug shortages continue to occur, especially in the context of COVID-19 where we have seen shortages of critical drugs used to treat COVID-19 patients. For this reason, APHA

urges FDA to continue to focus on alleviating drug shortages as part of the PDUFA VII reauthorization.

APHA calls for widespread development of redundancy and risk mitigation strategies in the manufacturing process to ensure reliable and consistent availability of safe and high-quality drugs. APHA also urges greater transparency, accuracy, and timeliness of information and notification to healthcare professionals regarding drug shortages and anticipated shortages, product quality and manufacturing issues, supply disruption, and recalls.

Biomarkers and pharmacogenomics. APHA supports advances in the utilization of biomarkers and pharmacogenomic markers. As part of the patient's healthcare team, many pharmacists integrate pharmacogenomics into their practices to achieve optimal medication use, outcomes, and safety. As medications have become more complex and personalized, patient counseling and education regarding medication regimens are imperative to successful patient outcome.

Pharmacists have more medication

related education and training than any other healthcare provider, making them best suited to provide medication related consults and services, based on a patient's genomic information. As we move into the next iteration of PDUFA, APHA supports the inclusion of pharmacogenomic analysis in the drug development, approval, and post-marketing surveillance processes.

APHA also encourages FDA and stakeholders to consider incentives to support enhanced coordination of care with pharmacists to ensure adequate patient access to education and ongoing support to improve medication adherence, safety, patient self-management, and understanding.

In closing, APHA again thanks FDA for the opportunity to provide our initial thoughts on PDUFA VII. We look forward to continuing to work with FDA, manufacturers, and other stakeholders as the reauthorization process continues. Thank you very much.

SARA EGGERS: And thank you, Karin. And now we will have Patrice, and I believe Patrice

has webcam as well.

PATRICE HARRIS: Am I --

SARA EGGERS: Just pause for one moment. We're having a hard time. We don't hear.

PATRICE HARRIS: Sorry.

MAN 1: Try again, Dr. Harris.

PATRICE HARRIS: Hello. Yes, can you --

MAN 1: Good to go.

PATRICE HARRIS: -- hear me?

SARA EGGERS: Yes, we can.

PATRICE HARRIS: Okay. Fantastic. Well, good morning. Thank you for the opportunity for the American Medical Association to offer comments on PDUFA VII. I do have a slide presentation this morning, and we will move forward. First, a little bit about the American Medical Association. We are the largest physician advocacy organization in the United States. We represent physicians nationwide and we develop policy through our House of Medicine. We meet twice a year to develop policy that will become the policy of the American Medical Association.

We address the most pressing healthcare

issues in our country. Just to highlight a few that we are addressing right at this moment, we are working through our Center for Health Equity to make sure that equity is centered in the work of the American Medical Association and in our work with partners. Since 2014, I have been the chair of the AMA's Opioid Task Force where we are looking deliberately and with a focused effort and attention to the opioid epidemic.

We just released our 2020 progress report, and certainly now realize, as do we all, that we are in the midst of a broader epidemic and not just those overdoses that include opioids. We also recently established a pain care task force as well as a newly formed cannabis task force. The AMA thanks the FDA for the invitation to provide our perspective and commends FDA for facilitating the dialog among many stakeholders to improve the drug approval process and maintain safety for our patients.

The AMA has longstanding policy that supports an adequately funded FDA. By the way, this policy goes back to 1978, and that's prior to the institution of user fees. The AMA has supported

previous PDUFA authorization, based on the primary purpose to make the drug approval process as efficient as possible, of course without compromising standards for proof of efficacy and safety. Thus, the AMA has a strong interest in the future of PDUFA and the AMA, again, is pleased to present its views at this meeting.

The AMA has reviewed FDA's FY2018 and FY2019 performance reports to Congress for the Prescription Drug User Fee Act. We believe certainly there has been progress. It is clear that PDUFA has been highly successful in reducing application review times for drug and biological products. The extended range of activities for which FDA could use prescription drug user fee revenue, including post-market safety activities and adverse event data collection systems has also been useful.

Advancement in FDA's regulatory science program including the release of the framework for FDA's Real-World Evidence Program and continued efforts on FDA's Sentinel events are commendable. Now, certainly COVID-19 has caused many challenges for

us all, and the FDA is no exception. Certainly, staff responsibilities have had to shift to a response to the pandemic.

Inspections of foreign and domestic drug manufacturing facilities have been on hold. Deficiencies in the drug supply chain is amplified and certainly there has been disruption of clinical trials. And following the pandemic, the FDA will have residual challenges related to clinical trials to face, and so the AMA urges flexibility and cooperation with clinical trial sponsors to find workable solutions, solutions that are customized, and certainly not a one-size-fits-all approach.

Certainly, as you consider the next iteration of PDUFA, we believe there should be a focus on health equity. It is critically important to collect and share more accurate data related to race and ethnicity, and we certainly have to make sure there are requirements for clinical trials to accurately resemble patient populations.

Now I do want to say that representation in clinical trials is not necessarily -

- or lack of a diverse representation in clinical trials is not necessarily that drug sponsors are unwilling to diversity participants, but certainly this area will require focus and intention.

It is also important to note that members of minority groups are often reluctant to participate. They lack access to trials. They may lack the time and the resources to participate. But AMA has strong policy that resources be provided to community level agencies that work with those underrepresented groups who are not proportionally represented in clinical trials to address these issues of lack of access, distrust, and lack of patient awareness of the benefits of trials in their healthcare.

Now strengthening the supply chain to ensure an uninterrupted supply of essential medications that are safe, meet standards for quality, and are beneficial to health should be seen as a public health priority. Drug shortages remain an ongoing public health concern in the United States and unprecedented demand due to large numbers of

critically ill patients with COVID-19 is worsening the situation.

It is ideal for physicians to be able to use first line medications, those that are considered more effective and have the fewest side effects. Shortages force physicians to make adjustments to use second- or third-line medications. Those medications cost doctors and nurses a lot of time and certainly are not beneficial and helpful to our patients. AMA urges innovation. We urge manufacturing processes to be innovated away from batch manufacturing, which has been used and largely unchanged in the U.S. for the past 50 years to continuous manufacturing.

We urge establishment of redundancy plans. We urge increased transparency to maintain a strong and safe supply chain. Regulators need to know where medicines and ingredients are manufactured and how they pass through the supply chain.

The CARES Act took some steps, but certainly more can be done, including expanding global reporting requirements for indicators of drug

shortages requiring drug manufacturers and ingredient suppliers to monitor and report on their capacity and ingredient quality and providing incentives to manufacturers for developing a shortage mitigation plan.

The AMA is very concerned about medication quality and safety for our patients. We have a Council on Science and Public Health and they currently have this topic under study. We also want to make sure that we adequately conduct drug safety inspections abroad. GAO outlined a number of deficiencies in the FDA surveillance of foreign drug manufacturing, including the agency alerting drug manufacturers in advance that it is planning an inspection.

We certainly want to make sure that we, along with the GAO, raise concerns and certainly continue to identify issues with foreign drug inspections as a high-risk issue and certainly requires attention. As we -- as FDA implements these tracking systems, certainly those tracking systems should be evaluated as we go along in real time and

course correct as needed.

We also need to continue the modernization of the drug safety system and the use of novel techniques, including real world evidence, to maximize the usefulness of tools used for collecting adverse event information at various points during the product life cycle.

Our AMA will certainly support the Food and Drug Administration's efforts to evaluate and facilitate implementation of effective tracking systems for pharmaceuticals and our AMA supports legislation making the production and distribution of counterfeit pharmaceuticals a felony.

So in conclusion, because of its past success, the AMA strongly supports the reauthorization of PDUFA in 2022. The AMA believes PDUFA reauthorization is critical to sustaining the improved performance of the FDA in expediting new drug and biological products to patients.

These user fees should continue to be tied to specific performance goals negotiated with the pharmaceutical industry and should not be considered

as an offset for any proposed funding cuts for the agency or be mixed with general operating funds. We look forward to continue to work collaboratively with the FDA and other stakeholders. Thank you.

SARA EGGERS: Thank you so much, Patrice. That concludes the panel on Health Care Provider Perspectives, and we thank all the speakers that have given their perspectives so far. We will now move into Session 4, the Regulated Industry Perspectives. Our two speakers are Lucy Vereshchagina from Pharmaceutical Research and Manufacturers of America and Cartier Esham from Biotechnology Innovation Organization.

Following this session, we'll take a 45-minute break for lunch. So I think Lucy has some slides that are being pulled up. Again, we think of this as the walk to the podium. So we can see Lucy. We don't see the slides yet, so we'll give that just a few more seconds. And, Lucy, you want to test that we can hear you?

MAN 1: Can you see the (inaudible) right now, so you may need to check the phone or

microphone icon at the top of your screen and see if you can connect to audio that way.

LUCY VERESHCHAGINA: Can you hear me now?

SARA EGGERS: Yes, we can. And I'm not sure why --

LUCY VERESHCHAGINA: All right, good morning --

SARA EGGERS: -- (sound drops) slides. Can we go -- we'll get the slides up as soon as we can, if you want to get started. Would that be --

MAN 1: We have the -- we see the slides on our screen, I think, Sara.

SARA EGGERS: Okay.

LUCY VERESHCHAGINA: I can see the slides. Thank you.

SARA EGGERS: All right. So that's just me. Go ahead, Lucy, please.

LUCY VERESHCHAGINA: All right. Good morning again, everyone. I'm Lucy Vereshchagina, Vice-President of Science and Regulatory Advocacy at the Pharmaceutical Research and Manufacturers of

America or PhRMA. PhRMA is a trade association that represents America's leading innovative biopharmaceutical research companies which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives.

Over the last 20 years, PhRMA member companies have invested more than $900 billion in the research for new treatments and cures including estimated $79.6 billion in 2018 alone.

It's been great to hear continued support for the PDUFA program in general and patient centric innovation from previous speakers. Discovery, development, and delivery of safe and effective innovative medicines to patients is a core mission of our members with more than 8,000 medicines in development around the world, 74 percent of which are potentially first in class.

The pipeline of biopharmaceutical promise is extraordinary and new developments in medical and fundamental science including immunotherapy and cell and gene therapies hold the

promise of treating debilitating diseases such as Alzheimer, cancer, diabetes, many rare disorders. Fulfilling this promise depends on the modern regulatory paradigm that is able to serve patients by providing timely science based regulatory decisions.

That is why PhRMA and our member companies are supporting a strong, appropriately staffed, and science-based FDA resource through a combination of appropriated funds and user fees from the regulated industry. For nearly 30 years, PDUFA has helped the FDA fulfill its central mission to help protect and promote public health.

By allowing the agency to keep pace with rapid increase in the number and complexity of innovative drug biologics entering the new pipeline. PhRMA has been a strong supporter of and participant in PDUFA since its inception in 1992. As many speakers noted today, PDUFA has played a critical role in strengthening the FDA's ability to regulate safe and effective medicines for patients.

The new molecular entity program that was established under PDUFA V continues to meet its

goal of increasing the efficiency and effectiveness of the first review cycle and decreasing the number of review cycles necessary for approval. In 2019, FDA approved 48 new molecular entities including 21 for orphan drugs for rare diseases.

Last year, FDA met 100 percent of their PDUFA review goals and 90 percent of those drugs were approved in the first review cycle. And this year, in addition to all the great work under PDUFA, FDA is also at the forefront of the response to the COVID-19 pandemic. FDA has acknowledged impacts of the current public health emergency on formal meetings and user fee applications in the recent guidance on these topics.

The agency has been working with the biopharmaceutical companies to facilitate their efforts to accelerate the development of safe and effective COVID-19 therapeutics and vaccines, and in the response to the current pandemic, FDA and the industry are utilizing new approaches to clinical trials for safety inspection, drug review, manufacturing, and supply chain security to support

continued innovation and inform rapid regulatory decision making.

There's a pressing need for FDA and the industry to identify actions taken during the COVID-19 pandemic and evaluate their effectiveness and applicability to innovative drug development beyond the public health emergency declaration. For example, FDA has been utilizing technology to communicate with sponsors by holding virtual sponsors and advisory committee meetings to maintain continuity of operations.

PDUFA VII can include revisions and commitments that help address licensure from FDA and sponsors developing COVID-19 drugs and vaccines. For example, industry and FDA could benefit from more predictable, timely engagement and better communication during drug development, additional priority on innovative drug development and manufacturing approaches including needs-based inspections and enhanced infrastructure at the agency.

Many speakers today mentioned the importance of patient centered drug development. It's

important that all stakeholders work together to further build on the successes of previous PDUFA, including initiatives on novel drug developments tools, trial designs, use of patient perspective in regulatory decision making, and use of real-world evidence.

Scientific advances are shaping our understanding of the causes of the disease creating new avenues of research, exploration, and discovery. New and powerful tools including adaptive trial designs, advanced statistical methods such as patient statistic digital health technologies and new real-world evidence have the potential to expedite drug development and ultimately patient access to new therapies.

Specifically, digital health technologies has been a powerful tool for industry regulators, health professionals, and patients in the response to the current pandemic. Sponsors have incorporated telehealth into clinical trials, virtualizing clinical trial visits, and collecting data remotely.

Digital health technologies such as digital health products, artificial intelligence, machine learning, present significant opportunities to support clinical trials and decentralized or virtual clinical trials. In PDUFA VII, PhRMA will support establishment of a flexible and scalable global framework for digital technology development and build upon the lessons learned from COVID-19 pandemic.

Rapid advances in information technology and beta science have enhanced ability to use unprecedented volumes of data to generate timely insights on the use, benefits, and risks of medicines. PhRMA believes that real-world evidence, for example, can be used for demonstrating effectiveness, either on its own in come circumstances, or in combination with other data.

Real-world evidence can enable more efficient drug development programs for additional uses of drug, provide more robust information about the benefits and risk of new medicine after approval, and ultimately lead to more timely access to innovative, safe, and effective medicines to patients.

Additional initiatives will be needed in PDUFA VII to provide even greater priority to sponsors to help increase use and regulatory acceptance of these tools and approaches. PDUFA VII should be used to further modernize regulatory evidence generation and increase transparency and promote stakeholder learnings around acceptable uses of innovative approaches for regulatory decision making.

Finally, for the agency to keep pace with rapid pace of scientific advances, it must be able to deploy the most modern technologies and expertise to review criteria nature sensitive developments. PDUFA user fees help ensure that the FDA Human Drug Review Program staffing resources and infrastructure is robust and able to support efficient drug review and development.

PhRMA commends FDA for completing key financial deliverables from PDUFA VI, including implementing staff time reporting and establishing new capacity planning methodologies. FDA also recently released a third-party interim assessment of hiring

and retention for public comments, which provided specific recommendations and we believe that they should be completed prior to start of PDUFA VII in October 2022.

And finally, information technologies and other critical infrastructure component underpinning success of Human Drug Review Program and PDUFA VII should build on ongoing efforts to establish formal data and technology modernization framework and this framework and related infrastructure enhancements will support new data and technology initiatives, including cloud-based submissions.

So in conclusion, the United States leads the world in the introduction of new medicines, thanks in part to FDA Human Drug Review Program, and PDUFA VII will ensure that the agency keeps pace with scientific discovery and helps bring the next generation of safe and effective new medicines and potential cures to patients, and PhRMA looks forward to working with all stakeholders and with FDA patient groups to enhance the existing program and make improvements where appropriate.

And the last thing, just to emphasize that the timely reauthorization of PDUFA is important to maintain the high level of Human Drug Review Program while creating predictable and timely regulatory review framework needed to support future biopharmaceutical investment. Thank you for your time and thank you for the opportunity to participate in today's meeting.

SARA EGGERS: Thank you very much, Lucy. And finally, we have Cartier and after Cartier, we will take a break for lunch.

CARTIER ESHAM: All right, can you hear me okay?

SARA EGGERS: We can. Go ahead, Cartier.

CARTIER ESHAM: Trying to advance the slides, here.

SARA EGGERS: There might be a little bit of a lag, but it's with the arrow buttons.

CARTIER ESHAM: (sound drops) seem to be working.

SARA EGGERS: We can try it on our end.

CARTIER ESHAM: Okay, if you'd just advance the slide, please. Okay, let me -- okay, good morning. My name is Cartier Esham. I'm the Executive Vice-President of Emerging Companies and Senior Vice-President of Science and Regulatory Affairs at BIO. Appreciate the opportunity to give this presentation today to share with you all our proposed recommendations for the reauthorization of PDUFA, all of which are designed to ensure ever more effective and patient centric processes.

BIO is the world's largest trade association, representing biotechnology companies, academic institutions, and state biotechnology centers and related organizations across the United States and more than 30 other nations. While our membership includes most of the large biopharmaceutical companies, the vast majority of our members are pre-revenue small companies.

All of our members are working to deliver the next generation of biomedical breakthroughs to improve the quality of patient care and find treatment for diseases where there are

currently no therapeutic options.

As Lucy mentioned, this is an incredibly successful program that has and will enable the FDA and industry to continue to advance more patient centric and effective approaches to drug development, review, and life cycle management. I will underscore Lucy's statements on the importance of learning from tools and methodologies that have been deployed during this pandemic, so we can advance broader utilization of those that prove to be of benefit to patients and are more effective and efficient.

To reiterate, there are three main objectives, in addition to the Evergreen position that we want to ensure FDA has the ability to hire, retain world class personnel, and those include continuing to optimize the current program and processes; two, to ensure science based and effective post-approval requirements and activities; and third, to develop new initiatives that will best prepare us for the future.

I'm going to highlight a few additional areas that BIO and PhRMA will be proposing and

discussing this fall. The investment in and development of cell and gene therapies and other advanced biological products has and is continuing to grow at a rapid pace, as denoted on this slide. With these products, comes increased demand on CDER resources including expert personnel, additional meetings and engagement with the FDA.

It will also require clear regulatory pathways to enable the acceptance of innovative approaches to product development and production. BIO looks forward to working with the FDA to proactively plan for the future, for future gene therapy -- gene and cell therapy submissions and think differently about how to conduct those product reviews. Those are focused on dedicated recourses to bolster CBER's infrastructure that will share adequate resourcing and enable efficient review management practices as well as effective scientific dialog and engagement planning.

Further clarification of expedited pathway evidentiary standards will also be a topic -- a focus of discussion. For example, understanding the

key learnings from the first year of the RMAT Program. We'll also be looking to ensure the acceptance of advanced manufacturing processes that are critical to the success of cell and gene therapy product development and approval.

It is imperative that industry and the FDA proactively plan for future cell and gene therapy submissions today to ensure those therapeutics are available for patients and families tomorrow. We will also be working to continue to enhance scientific dialog between FDA and sponsors. BIO recognizes the many ways in which FDA has worked to support communication between agency and sponsors, for example through the issuance of guidance documents, organization of public meetings, and providing opportunities for product specific discussion.

BIO appreciates stakeholder acknowledgement both on industry, patient organizations, and regulators of cases where a well-understood development pathway may be chosen due to the existing precedent that even in cases where innovative approaches may ultimately be a better

choice for patients, sponsors, and regulators.

We believe opportunities exist for sponsor-FDA interactions to have focused discussions on innovative approaches in the context of product development. In addition, our goals for PDUFA VII will include seeking analysis and establishment of processes and best practices to approve efficiency and effectiveness of FDA-sponsor meetings.

Best practices can ensure FDA-sponsor interactions are as efficient as possible and, if properly done, could serve to decrease the amount of meeting requests. Among other things, we'll be working to establish best practices that include establishing a mechanism for sponsors to obtain clarifying questions following milestone meetings to ensure clarity and improve efficiency, lean mapping to enhance approaches relating to submission and review of meeting materials, as well as processes to ensure that decision making among review team and other FDA experts are efficiently communicated to sponsors.

We also believe that the establishment of communication plans early on in drug development

and review could serve to optimize FDA and industry engagement.

Looking to continue to build upon a successful new molecular entity review program, which has accomplished its goal of increasing the number of products approved after only one cycle of review, we will be encouraging the FDA to consider additional structured timelines for both sponsors and FDA for predictable communication around labeling and post-market requirements and commitment processes as well as pediatric study plans.

The current review processes for determining PMRs and PMCs in some instances create significant investment and resources. We want these processes to be based in science and ensure that there are mechanisms for sponsor and the agencies to discuss and/or reevaluate the feasibility, scientific basis, and need for particular existing post-approval requirements and activities as new science becomes available.

As many have mentioned, it's also going to be critically important that we continue to advance

modern manufacturing quality and inspection methods and methodologies and processes. Manufacturing and quality play a vital role in the drug development process in ensuring timely access of these medicines to patients. Processes should be established that promote scientifically based approaches and timely regulatory decision making on manufacturing and chemical and manufacturing control issues.

Earlier communication for manufacturing supplement review would increase the efficiency and effectiveness of the first cycle review of these important submissions. Facilitating the use of innovative manufacturing technologies for both products and development and those that are current commercially available, would enable critical and much needed efficiencies to manufacturing capacity and capabilities, something this pandemic has taught us is vitally important.

This must also address the needs of enabling effective and quality manufacturing of advanced biologics. And lastly, enabling risk-based approaches to preapproval license inspections would

create a more efficient and risk based inspection paradigm.

In closing, again, we would like to -- we really appreciate the opportunity to talk with you all today, not just the FDA, but all the stakeholders that have been speaking today, and look forward to continue to work with you throughout this process over the coming years. So thank you very much, and with that, I'll turn it back over to the FDA.

SARA EGGERS: Thank you very much, Cartier. That concludes our session on the regulated industry perspectives. We will now take a break for lunch and we will stick with our agenda, so we'll -- the webcast and the meeting will resume at 12:30. Our session following will be the scientific and academic perspectives, and I'll ask the speakers at that session to make sure you're back a few minutes early.

There may be some technical testing or other things that happen on the webcast, but that's all part of the lunch break, so we will, again, start at 12:30. Thank you very much.

(Break)

SARA EGGERS: All right. It is 12:30 by my clock, so I would like to welcome everyone back to this virtual public meeting to gather input on the Prescription Drug User Fee Act or PDUFA program. If you were not here for the opening remarks, the purpose of this meeting is to gather input and recommendations from public stakeholders the FDA can consider as we move into the next phase of reauthorization of the PDUFA program for the fiscal years 2023 through 2027.

If you have technical questions, you may write in the tech support box or you may email PDUFA reauthorization, all one word, at FDA.HHS.gov. And again, as a first step, if you run into issues, we recommend just exiting out of the webcast program and coming -- reconnecting in the same link.

Now if you would like to contribute further input to today's meeting or throughout the process, the announcements page -- announcements section of the webcast information has that information. You can also see on the screen here how you can find that. You can google PDUFA in regulations.gov and find that.

So our next session and our last stakeholder session is to hear scientific and academic perspectives. Our four speakers are Kathy Giacomini from University of California, San Francisco; Aaron Kesselheim from the Harvard Medical School, Brigham and Women's Hospital; David Ridley from Duke University; and Russ Altman from Stanford University.

Kathy, you are first on deck, so if you'd like to bring up your webcam. Your slides, I believe, are on here, and then you may begin.

KATHY GIACOMINI: Okay. Sara, can you see me?

SARA EGGERS: Yes. We can see you and hear you.

KATHY GIACOMINI: Great. Okay, so first of all, I'd like to thank the organizers for inviting me to this panel. As we all know, the FDA is the premier regulatory authority in the world. It not only approves drugs and a myriad of other medical products, but it has a very important research mission. That mission is the public health mission: generate new knowledge that speeds innovation that

makes medicine safer and more effective.

The knowledge gained from the research informs FDA guidances, standards, policies, and practices as well as their approval and monitoring process. In this short presentation, I would like to strongly advocate for the use of PDUFA funding to support collaborative academic FDA mission driven research. To this end, I will describe research conducted by the FDA funded Centers of Excellence in Regulatory Science and Innovation, CERSI.

These are funded by the various offices and centers at FDA, including CDER and CBER with oversight from the Office of Regulatory Science and Innovation, ORSI. FDA supports four CERSIs including on at the University of Maryland, one at Johns Hopkins, and two multi-campus centers, Yale University-Mayo Clinic and ours, the UCSF Stanford CERSI.

I am co-PI with Russ Altman, also on this panel, at the UCSF-Stanford CERSI. All of these centers conduct mission critical research which are collaborations between academic scientists and FDA

scientists. This works extremely well as FDA leverages the research powerhouses of academia to advance their mission.

Today, I'll highlight a few examples of collaborative research conducted by our CERSI and funded by the FDA, and I think you'll see that funding the CERSIs represents a quadruple win for the FDA as they gain important new knowledge; for academic scientists, it gives us an opportunity to work on an important problem with large effect on patients; for drug developers, it helps inform and improve the drug development pipeline; and most importantly, for the public as it provides them with better, safer drugs in a more rapid timeframe.

So my first example of research supported by our CERSI is a research project conducted by Steve Goodman at Stanford working with FDA scientists at CDER and that partnership is important. The project is focused on improving the methodologies for clinical trial design and analysis. Currently and very simplistically, what we have two of three clinical trials show a significant difference between

the new drug and standard of care on the primary outcomes of, let's say, P less than or significant value less than 0.05, the drug is approved.

But what if three trials are all not significant but with P less than 0.08 and in the right direction? Should FDA simply throw that drug out or should they consider that drug for approval? And how can the data be pooled and analyzed? In other words, how can we establish improved statistical framework to allow more flexible clinical trial designs and analysis and pave the way to approval of safe and effective drugs?

My second example, also shown on the slide of a collaborative FDA supported research project is focused on how can we improve electronic data collection systems for clinicians and health care providers who either participate or would like to participate in clinical trials but currently find it too burdensome. Clinicians participating in clinical trials are burdened with two electronic data entry systems.

They first have to enter data for

caring for patients in the normal electronic health record, but they also, if they're participating in a clinical trial, have to complete a second set of data entries for the clinical trial database for that same patient. It's too much for many healthcare systems and many physicians who already have enough paperwork to do.

That burden excludes many smaller hospitals and healthcare systems that cannot afford to pay for extra help. That means patients who want to enroll in clinical trials and may actually benefit from those trials at these places are simply excluded. It results in healthcare disparities and an unequitable effect on the American public.

Our CERSI through CDER is funding an outstanding faculty member at UCSF, Laura Esserman, a breast cancer surgeon, and her team to work with FDA scientists to harmonize Epic, one of the major electronic health record systems, with clinical trial databases and entry systems so there will be one point of entry where clinicians can enter the data and have it populate both the electronic health record and the

clinical trial database, making it so much easier for physicians even out in rural communities or poorer urban areas to participate and greatly accelerating clinical trials and expanding the access for all Americans.

The third collaborative study I would like to highlight is one which exemplifies how a project that was completed by our CERSI informed an FDA guidance which is currently being used by drug developers, changing drug development and approval process. I think everyone out there is aware of drug-drug interactions and how serious they may be, causing huge problems in drug safety.

Many of you will remember the interaction of one of the early statins, cerivastatin, Baycol, with a fibrate, gemfibrozil, which resulted in or contributed to the removal from the market of cerivastatin many years ago because of life-threatening drug toxicity. The Office of Clinical Pharmacology in CDER at the FDA, through research collaborations in this case with my laboratory and others have worked to develop and standardize in vitro

methods to predict clinical drug-drug interactions more accurately.

While not perfect, these methods have greatly improved the ability of drug developers to predict clinical drug-drug interactions and therefore to carry out targeted clinical DDI studies or drug-drug interactions studies, rather than many multiple clinical drug-drug interaction studies that inform the labeling of the drug, indicating which drugs can be used safely together and which drugs should be avoided.

Results of this research were used to inform a new FDA guidance published in 2019 on in vitro studies to predict DDI, or drug-drug interaction.

So in closing, as you can see, I'm a strong advocate of funding mission critical collaborative academic FDA research through CERSI resulting in quadruple wins for FDA, for academic scientists, for drug developers, and most importantly for patients. Thank you.

SARA EGGERS: Thank you very much,

Kathy. We will now move on to Aaron. Kathy, if you want to close out of your webcam. I think Aaron's joining. There we go. Thank you, Kathy. And hi, Aaron.

AARON KESSELHEIM: Hi, Sara, and thank you very much. And thank you very much for the opportunity to talk to the group today. My name is Aaron Kesselheim. I'm a internal medicine physician and lawyer and a professor of medicine at Harvard Medical School where I run the Program on Regulation, Therapeutics, and Law, which is one of the largest and most prolific research groups in the country that is focused on issues relating to regulated medical products and pharmaceuticals.

And I just wanted to state up front that neither I nor anybody in our group has any personal financial relationships with any pharmaceutical company, and in fact, here you can see where we get some of our researching from.

So today I want to just talk briefly about the Prescription Drug User Fee Act and some of the changes that have occurred in the FDA drug review

process since then, since its passage originally back in 1992. The Prescription Drug User Fee Act ensures that the FDA has sufficient funding to conduct its essential activities effectively and efficiently, and user fee legislation over the years has contributed to the more rapid evaluation and approval of new drugs and it funds the generation of important evidence after drug approval as well.

And here you can see a figure from a New England Journal article led by one of my colleagues at PORTAL, Jonathan Darrow, looking at the standard application time and priority application time for the amount of time that the FDA takes to review drugs since passage of the User Fee Act in 1992. And as you can see, FDA review times have fallen substantially, such that now the FDA is the fast -- if not the fastest, among the fastest regulatory agencies in the world.

And since that time, user fees now grow -- user fees have accounted for greater and greater fraction of the FDA's budget, now accounts for about 40 percent of FDA's funding and about -- actually 75

percent of funding for new drug reviews.

Another thing that has emerged in concert with the passage of the user fee act and its renewal every five years have been various expedited pathways intended not only to expedite the FDA's review of products but to expedite their clinical testing as well, and there are the four major ones. Some people consider the orphan drug designation to be a fifth, but I'll just focus on these for now.

The fast track pathway, for example, which was created out of the crucible of the HIV epidemic and crisis in the 1980s allows drugs to be approved potentially on the basis of a single Phase 2 trial. That was added in 1988 and formalized as part of the Prescription Drug User Fee Act renewal as part of the FDA Modernization ACT in 1997.

The accelerated approval pathway allows drugs to be approved on the basis of a biomarker or surrogate measure that is only reasonably like to predict clinical benefit. About half of drugs now are approved based on surrogate measures or biomarkers, but the accelerated approval pathway allows the

biomarker surrogate measure to be only reasonably likely to be linked to actual clinical benefit. It's supposed to be applied only to serious or life-threatening illnesses.

Same with the priority review pathway, which shortens FDA review time to six months. Priority review is supposed to be attached to drugs that offer a therapeutic advance. And then finally, most recently, the breakthrough therapy designation was added in 2012 for drugs treating serious or life-threatening diseases, and again, the effect -- to get a breakthrough therapy designation, you only have to show an effect based on a change in a biomarker or some kind of predictive toxicology.

What we've seen over the years is that more and more drugs qualify for these expedited development pathways. Here you can see the trends over time until 2013 for application of expedited review to new drugs, and we split them, then, into first in class and non-first in class drugs.

The first in class drugs you can see there in the dotted red line and the non-first in

class drugs in the blue line, showing that first in class drugs, drugs that are more innovative and supposed to meet unmet medical need have qualified consistently for these expedited pathways, but it's been an increase in the application of these pathways to non-first in class drugs that has really driven their increasing use over the years.

And this is the experience in the most recent PDUFA reauthorization. You can see that among the new drug approvals, drugs qualifying for expedited pathways now account for about 60 to 70 percent of new drug approvals and that's been continuing to increase slowly over the more recent year.

And I think that that's led some people to ask whether these products truly are the most innovative meeting unmet medical need and really do -- whether all of these products are supposed to qualify for these pathways or whether the exceptions starting to -- are starting to swallow the rules.

Another trend that has evolved along with growth in these expedited pathways is the emphasis on -- and the emphasis on review speed has

been an increase of reliance on surrogate measures including biomarkers for new drug approval. And as I said, surrogate measures -- drugs approved based on surrogate measures now account for half or more of new drug approvals.

It's important to recognize that surrogate measures have a really important role in the evaluation of new drugs. You can use surrogate measures to identify drug safety problems sooner. You can identify surrogate measures to predict efficacy or identify direct treatment for patients more precisely to incentivize drug development by predicting likely efficacy years earlier.

But of course, that requires that the surrogate measure be validated as being connected to an actual clinical end point, because as clinicians and patients, that's what you want the drug to provide is actual clinical benefit. But I think there's been concern that there's been an increased growth in unvalidated surrogate measures and their use in approving a new drug. If valid -- surrogate measures aren't validated, then they can lead to approval of

drugs that don't work as intended or that can have safety issues that outweigh their benefit.

So for example, the FDA now publishes, as a result of the 21st Century Cures Act a table of surrogate end points and in that table, it lists the disease, the surrogate endpoint, and type of approval that's relevant, whether it is traditional approval or accelerated approval. Remember, accelerated approval is for surrogate endpoints that only meet -- that only are reasonably likely to be related to clinical endpoints.

And so we looked at breast cancer which is listed in this surrogate endpoint table as being associated with -- the surrogate endpoints that are useful in breast cancer include objective response rate, progression free survival, disease free survival, event free survival, pathologic complete response, and then we actually looked in the literature for association studies to see whether or not those surrogate endpoints are connected to actual clinical endpoint, and unfortunately what we found is that the association between those endpoints and

actual clinical endpoints is not strongly correlated in most cases.

In fact, the only strong correlation we found was for disease free survival in HER positive breast cancer, which is a particularly virulent form of breast cancer. And one of the end points, event free survival, we couldn't find any studies of validation at all.

One of the ways that we addressed this issue of broader use of surrogate measures is by requiring or encouraging that these measures be confirmed after the drug's been approved in post-market studies and intended to confirm the effect that you see in a surrogate measure. And that's the way we allow drugs to be approved and get to patient while still trying to ensure that we ultimately do follow up on how those drugs actually work.

Unfortunately, there's been limitations with our ability to get those confirmatory trials done and numerous reviews have shown that there are problems with enforcing these requirements.

In some cases, they may be -- the FDA

may give long time horizon, so in the case of a tuberculosis drug that was approved in 2012, the FDA gave 10 years for the manufacturer to complete the confirmatory trial, and in some cases, they may be delayed and in one recent muscular dystrophy drug, for example, approved in 2016, there was a recent report in January of 2020 from the FDA suggesting concern about the lack of initiation yet of a confirmatory trial which is due in 2022.

Post-market requirements for accelerated approval drugs are even more important because they're only reasonably likely to be connected to an adverse outcome. And we did a review of drugs -- of accelerated approval cancer drugs and found that about 50 of them were shown to confirm their benefit, but when you actually look at the post-approval study that confirmed the benefit, only 15 of those studies tested an actual clinical outcome, whereas the rest of them tested -- again, tested surrogate measure and 19 of those surrogate measures were the same surrogate measure that was used in the preapproval study leading to the accelerated approval in the first place.

So what do you do about all this? Well, I think it's important to recognize that PDUFA is important to provide adequate funding to ensure that the drug regulatory system serves the public effectively.

In a different political climate, maybe adequate public funding would be preferred in place of user fees to allow the FDA to continue its current performance levels while promoting maximum confidence from the public that the public -- that the FDA is getting the funding for doing its critically important work, not from the industry that it's regulating.

But in addition to that, we need to, if we're going to move forward with PDUFA as is, we need to make sure that we do have a process for identifying promising drugs in development and getting them out to patients that need them. However, I would submit that multiple expedited pathways are inefficient and confusing and, in future PDUFAs, should be streamlined to a single pathway.

And we need to be vigilant about the possibility that expedited development will lead to

drugs that actually have risks that outweigh their benefit, and that is -- that the chance of that is increased when a drug is approved based on an unvalidated biomarker or surrogate endpoint.

This will be a good use -- a good opportunity for thoughtful use of real-world evidence after the drug is approved, and so I would recommend that PDUFA funds go towards formal reassessment of the safety and efficacy of new drugs approved based on surrogate measures after a time of three years on the market. Pull together all the evidence and make reassessments to understand what we now know -- formally, what we now know and whether or not the labeling needs to be updated or whether or not, in extreme measures, the drug actually shouldn't be on the market.

Thank you very much.

SARA EGGERS: Thank you, Aaron. We will now have David.

DAVID RIDLEY: Thank you, Dr. Eggers. I'm David Ridley. I'm a health economist at Duke University's business school. I'm also affiliated

with the Duke Margolis Health Policy Center. I've received funding this year from the Gates Foundation, the Wellcome Trust, and while I haven't received any drug industry funding this year, I have in the past. The views I'll express are my own.

I'll be showing some slides, I think. I don't see them yet on my screen. My (inaudible) are --

SARA EGGERS: Ah --

DAVID RIDLEY: -- not cabled. Oh, Karin sees them. Okay.

SARA EGGERS: David, we can advance them, if you tell us.

DAVID RIDLEY: Okay, and I see them now. Okay. Sorry about that. So I interact with the FDA in a couple of ways. First of all, I was the lead author of the priority review voucher paper that created some extra work for the FDA, which the FDA has done very well, but also added some user fees for the FDA. I'm also a regular user of FDA data.

First thing I want to say is thank you. FDA plays a vital role and does it well. The FDA has

managed the priority review voucher program well. The priority review voucher program is not perfect, but the FDA administers it well. Priority reviews have been consistently about six months. The voucher user fees are quite sensible. Initially, they were excessive, $5 million in 2012, but now they're appropriate, I think, at about $2 million in 2020, and the FDA has used very reasonable criteria as they've added tropical diseases for eligibility.

Also want to talk some about the FDA data. FDA shares many useful datasets, but there's much more to do, I think, in terms of data access and transparency. So first, a positive example. Earlier this year, FDA staff released some great data on new molecular entities, also BLAs for a long period of time in a very easy to use format. I think Dr. Kathleen Miller was involved in that and I salute FDA for that, that transparency and those great data.

Here's a negative example. These are shortages data over the years. These are screenshots of the Internet archive. Because FDA, as far as I know, doesn't maintain the data or at least doesn't

make the data available, so if you want to see historic data on drug shortages, you need to go to the Internet archive and hope they've taken a snapshot in a given month.

Unfortunately, these are in HTML format, which change all the time, and really formatted very poorly so it makes it almost -- makes it really impossible to do machine learning. I don't want to dig too down in the weeds, but I'll just give you an example here. You see rows and columns with no data. You see changes in the columns. Sometimes, it's company and product as separate columns; sometimes, they're the same column.

Often over on the right there'll be the name of a company and in terms of machine learning, you can't tell whether that's a company that actually has the drug or is also in shortage. And sometimes, that's all messed up. So again, these data are accessed through the Internet archive which is not FDA and just takes an occasional snapshot. It's HTML format, inconsistent headings, and really just can't be read by machines.

Why does this matter? Because drug shortages matter. In fact, Dr. Janet Woodcock and Dr. Marta Wosinska wrote an important paper about how one of the main problems with drug shortages is a lack of data, a lack of information. Which are the problematic companies? Which companies aren't investing enough in quality and reliability? And we should be able to see that in the data, but we can't do the analysis because the data are a mess, and so I think this is important for researchers and for society.

So, proposal. Please, please, please don't post data on the web in HTML format, especially HTML format that's changing over time. Please post it in a database and please maintain historic data. Now sometimes, posting data will be imperfect, but just include some caveats with this. And in order to align incentives, I think it'd be worthwhile to create a data tsar that reports to the commissioner.

That way, someone is motivated to make sure that good data are available to the public and that person would be evaluated on access and

transparency to existing data and new datasets.

Certainly, FDA staff and lawyers will have some concerns. What if there are errors and what if we're sued? I think that's a really minor concern relative to the potential benefits. Just include some caveats. Include some contact information for FDA staff that can interact with the researcher and have an iterative process where you communicate and refine the data.

Second possible concern is that these are commercially sensitive, but most of the data I'm talking about have almost no commercial sensitivity. In fact, the FDA shortages data I'm talking about were public at one time. They've just been poorly formatted and poorly archived.

Greater data transparency would benefit the FDA. I think the -- would refine the data, would create opportunities for interaction with researchers, in some sense, would be crowd sourcing assignments from Congress. Congress is very concerned about data shortages, for example, want more work in that area. More work could be done by the public if the data were

more accessible, more transparent, better quality. Also, obviously, benefit society.

Again, back to the drug shortages example, we need to know -- we need research on which drugs tend to be in shortage, which companies tend to have drugs in shortage. Okay. I'll wrap up. Again, I think the FDA is doing really good work, but could make some improvements, one of which is improving data access and sharing and part of -- and creating a data tsar would be sure that someone is responsible for getting that done, so ideally, that person would report to the commissioner.

Thanks for this opportunity.

SARA EGGERS: Thank you very much, David. And finally, for this session, we have Russ.

RUSS ALTMAN: Hi, there. Can you see and hear me? I have no slides.

SARA EGGERS: Yes, we can. Thank you.

RUSS ALTMAN: Great. Thanks everybody, and hello. Thank you to the organizers for inviting me and thank you to my colleagues who really did a great job with their comments. My name is Russ

Altman. I'm a professor at Stanford University.

I'm a general internist, but I'm also a researcher in informatics, data science, and AI, and I would like to urge in the next PDUFA that there be a robust research program in the area of AI, data science, and informatics, which I think is starting to revolutionize drug development -- drug discovery, development, safety, efficacy monitoring, and surveillance.

Little bit about my background is I'm an associate director of the Stanford Institute for Human Centered AI, which is devoted to ensuring that AI technologies serve humanity in positive ways, which many people have concluded is not a default. I'm also co-PI if the UCSF-Stanford FDA supported CERSI, Center of Excellence for Regulatory Science that Dr. Giacomini just mentioned a few minutes ago which really is focuses on mission driven collaboration between FDA scientists and academics.

I define regulatory science as science that generates new knowledge critical for the FDA mission. It helps them do their job better, faster,

more efficiently. And as you all know, I think, the area of data science and AI and informatics is exploding. In the San Francisco Bay Area where I live, there are well more than 100 startups looking at ways to use biological and health data for aspect of drug therapy diagnostics and prognostics and monitoring.

In terms of some -- just a couple of examples of projects in this area that our CERSI has done, mostly to get you fired up about the possibilities, text processing to read FAERS reports, the adverse event system, in order to score their likely value. We want to make sure we can put the most important reports in front of FDA reviewers in a prioritized way and as quickly as possible.

Methods to model the impact of mutations in target protein, especially for cancer medications where, for example, the kinases can have lots of mutations that could change the efficacy of these drugs, we can use computational models and we have to model the effects of these mutations.

Integration of medical records with

research protocols so that every patient on a drug becomes not only a patient who's being monitored and documented in the medical record, but also becomes a trial participant. Similarly, we have projects that use medical records to ask questions about drug effects in real time in terms of tracking drug response, efficacy, and side effects as it happens.

There's also projects we have in discovering biomarkers, complex biomarkers not obvious to the human eye or the human brain, but validated to be complex combinations of OMICS measurements, perhaps also clinical biomarkers to create these complex biomarkers that can very, in some cases, accurately track important drug efficacy and safety markers.

And finally, of course, in all of this, there's the issue of making sure that these algorithms are used fairly and without a bias; or if there is bias, that it's well characterized and policy mechanisms can be used to correct for it. These algorithms have hit the world very quickly and they're not fully characterized in some cases and we have to make sure that the FDA has the knowledge and the

competencies that it needs internally and through collaboration to make sure that biases and the behavior of these algorithms is well managed.

So I want to say that the FDA deserves great credit for recognizing that the academic world wants to assist them. They created this CERSI program which I think deserves the support it has gotten and I think you could argue a larger network of researchers. I can tell you that not only for the knowledge base but for the workforce, our students are uniformly excited to participate in these research projects and to learn about careers in regulatory science, and I think that this could then create the next generation of workers who are ready to do this.

When we think about data in medicine these days, we think about the electronic medical record and population health data sources, so that's part of this discussion. We also think about genomics and other molecular measurements, often at a large scale. And then we think about sensors and wearables. And even though I'm mentioning some devices and some algorithms, I think these all impact drug discovery

development and monitoring of efficacy and safety.

So I think the regulatory science agenda is wide. I think there's a tsunami of new things that will be coming to the FDA and I think we should proactively prepare FDA scientists, both with their knowledge base and their workforce to be ready for this tsunami. There will be novel drugs that were invented and discovered in unusual ways, often based on AI technologies, to the extent that the FDA has to be ready to understand where these come from and adjudicate them.

They'll be -- these new drugs will be based on novel technologies in terms of cell-based therapies, gene replacement therapies, as well as small molecule and biologics. In many of the cases, the data collected about these new modalities will be complex and will require computational analysis making sure, for example, that our cell-based therapies have expression and proteomic and metabolomic profiles that are stable and predictable that essentially will become a computational challenge.

These drugs will come at a novel pace.

There may be updates and learning, kind of a learning healthcare system, as we look at their effects, the best ways to use them, and so I'm imagining a much more dynamic than previous pace of watching drugs and making changes to their use or to the regulations of their use, perhaps at a pace and at a kinetics that is perhaps unprecedented.

So we have to be ready for that and finally, we will require novel regulatory processes. I think it's obvious for following the effects of these drugs, understanding their impacts, and then modifying regulations and recommendations for their use by physicians.

So to conclude, I think there is a huge upside to this new world of data science, AI, and informatics enabled drug discover and use, but I think it creates challenges. I think the FDA has recognized these challenges and has already put into place programs, but I think that those programs must continue and probably should expand -- definitely should expand.

FDA scientist education and protected

time for research, collaborative and otherwise. Collaborators in academia are standing by ready to work together. There is a need for distributed FDA presence at all the pockets in the country where there is a need to have discussions, and we've heard about this in earlier sessions.

The pre-meetings become critical for these new constituencies that have not been the traditional developers or enablers of drug discovery. Global awareness, because this is a global world and so harmonization with other regulatory entities of computational expectations and AI expectations.

And I want to end with the final port, which is this research agenda in AI and data science must have an agenda for bias detection and remediation and interpretability to make sure that we don't leave groups behind that have historically been subject to disparities and injustices because of default assumptions that are really not fair.

So the fairness aspect of the application of algorithms, obviously, must be an important research agenda at the FDA and elsewhere.

So those are my thoughts and I want to thank the organizers again.

SARA EGGERS: Thank you so much, Russ. And this concludes our stakeholder panels. I want to personally thank, on behalf of myself as moderator and my tech colleagues, thank you for all of the presenters. This is -- there's a lot we threw at you and you -- commendable the amount of work you put in to make your points clear, concise. I think that you were all successful in that.

We are going to move into remarks from Patrizia Cavazzoni, FDA CDER acting director. But let's take a bio break for about 6 minutes and resume promptly at 1:15 to have those remarks and that will keep us on the agenda. So again, we will come back at 1:15. Get up, stretch your legs, and grab a cup of coffee.

(Break)

SARA EGGERS: Welcome back, everyone, from a brief break. We -- this is Sara Eggers from CDER and we've concluded our series of stakeholder sessions and we will now have Patrizia Cavazzoni, FDA

CDER's acting -- center director to provide the remarks. Thank you so much, Patrizia.

PATRIZIA CAVAZZONI: You're welcome. Thanks, everyone, for coming today. I'm delighted to be providing some closing remarks to this very informative and very important meeting that kicks off the next cycle of PDUFA discussions.

This program is critically important to FDA, and as we have seen during the pandemic, it's also very resilient program that has continued to perform under very exceptional circumstances, both for the public, industry, and all stakeholders as well as, obviously, FDA.

What we have heard today are a number of themes, some of them cross cutting, and we've heard from speakers, for instance, a call to focus on modernizing clinical trials, providing incremental review capacity for emerging cell and gene therapy products. We've heard a call to continue to advance modern manufacturing, having a greater focus on the security of the drug supply chain, and provide greater transparency on the drug supply chain. These are

things that obviously have come even more to the forefront during the COVID-19 pandemic.

We have also heard about the need to support modernization of FDA's data and IT infrastructure including knowledge management and we heard continued support and -- for the development and -- of regulatory decision-making tools such as clinical outcome assessments as well as patient focused drug development tools.

We have heard from consumer groups that they would like to see PDUFA's performance not be measured by speed alone but also on quality and public health as well as patient centered outcomes. From patient groups -- from consumer groups, we have also heard a support for post-market safety activities under PDUFA including Sentinel, Real-World Evidence, timely safety reviews, and an expansion of safety surveillance activities.

And from the academic and scientific groups, we have heard a call for a need for greater data transparency and publication of data. Need to modernize clinical trials, and also to explore the

numerous expedited pathways and reliance on surrogate endpoints makes sense and for revisiting efficacy of products after a number of years on the market.

So very robust, very important things that really preamble what will be a very robust and meaty series of discussions in the months to come. As I mentioned earlier, the PDUFA program continues to function despite very exceptional circumstances during the global pandemic. We have continued to meet or exceed nearly all PDUFA application goals.

First cycle approvals rate remain high, and in addition to performance goals, as you heard from the commissioner, we continue to publish guidances and hold public meetings and workshops around various topics to advance regulatory science and drug development, and this is despite the fact that we unfortunately -- we cannot hold these meetings in person, so we have had to obviously rely on technology, but I think that we have really risen to the challenge without missing a beat.

Over the last three years, FDA has piloted a complex innovative designs and modeling for

direct development programs and we -- it was good to hear that there is ongoing interest in advancing this regulatory science and decision-making modalities. And we also facilitated important conversations around real-world evidence and advancement of patient-focused redevelopment.

In addition, we have stood up the potential first in government resource planning capacity -- resource capacity planning capability that utilizes continuous time reporting against activities and advanced predictive analytics to understand the future workload and to predict resource needs so that we can get to a point where resources are available at the right time and against the right activity. This will really represent a major enhancement for the program.

FDA sees the value in advancing a number of areas. We think that the program should continue to promote sustainable innovation in drug development. We also are committed to enhancing regulatory predictability and post-market safety.

We also understand that it is important

to advance the regulatory infrastructure for digital technology and new sources of data and there are lessons learned from the COVID-19 pandemic that we are going to take very seriously and we hope that will provide new insight on how we can leverage these technologies to support the modernization of clinical trials.

And last but not least, we are interested and committed to enhancing operational capabilities, efficiency, and agility. So we look forward to the timely reauthorization of this critical program and to the future meetings to continue to seek input from all stakeholders so that we can continue to grow and advance this critical program. Thank you.

SARA EGGERS: Thanks, Patrizia. We are now going to move into the final session of today's meeting, the Open Public Comment. This is another important mechanism to engage the public in conversation. Please keep in mind that FDA will not be responding to comments, just as we couldn't respond to comments throughout the day, but they are included, they are important, and they will be part of the

public record.

To facilitate a transparent process, we encourage the speakers to note any financial interests that you have related to your comment. If you do not have such interests, you may state that for the record, and if you prefer not to supply this information, you can still provide your comments. We have collected online requests for comments as part of the meeting registration process, and we have five people signed up.

Each speaker will have five minutes to speak, and as I did with the earlier speakers, I'll verbally announce when there's 30 seconds remaining and then shortly after the five-minute mark. I will -- the earlier speakers stayed on time fantastically well, and so I entrust that I'm going to have an easy moderating task to close out this.

The speakers will be in this order: Robert Falb, Paul Melmeyer, Nicole Mahoney, Annie Kennedy and --

ROBERT FALB: Hello?

SARA EGGERS: -- Marta Wosinska. So

when I -- I'm going to ask everyone who's on the open public comment to stay muted until I call your name to begin your comment. And if you're having any technical issues, please let us know or we'll figure that out and then we'll just move to the next person and come back to you once those issues are resolved.

So with that said, Robert Falb is the first one up for public comment, and you may begin.

ROBERT FALB: Hi. Can you hear me?

SARA EGGERS: Yes, we can. Thank you.

Robert FALB: Thank you. good afternoon. I am Robert Falb and I'm the Director of Policy and Advocacy for the Alliance of Regenerative Medicine, or ARM. In light of the time constraints, I'll provide a brief overview of our PDUFA recommendations. Our formal comment letter will be more detailed.

ARM is the leading international advocacy organization dedicated to realizing the promise of regenerative medicine and advanced therapies. As the voice of the sector, representing more than 350 members worldwide, ARM appreciates the

support that FDA has provided in advancing the development of cell and gene therapies and appreciate the opportunity to offer our perspective today.

Increased funding for additional CBER reviewers. Over the next several years, regenerative medicine, including cell and gene therapies, will be brought to market at a rapid pace. When PDUFA was last reauthorized in 2017, ARM calculated that there were 580 developers conducting more than 480 clinical trials globally. Just three years later, we now estimate that there has been a 60 percent increase in the number of developers, now numbering approximately 950 and they are conducting more than 1,000 clinical trials worldwide.

Indeed, FDA leadership stated last year that based on the assessment of the current pipeline and the clinical success rates of these products, the agency expects that it would be approving 10 to 20 cell and gene therapy products a year by 2025. In order to meet this challenge, FDA needs more properly trained staff with the expertise to evaluate these applications.

Therefore, ARM's priority recommendation is that the user fee program funding be appropriately designed to ensure FDA has the necessary resources to recruit, train, and retain CBER reviewers.

Prosecuting unregulated stem cell clinics. Mirroring the growth in the regenerative medicine sector, there has been, regretfully, a significant increase in the number of unregulated stem cell clinics marketing non-FDA approved products. It has been estimated that in 2009, there were two stem cell clinics in the United States, but by 2017, that number had grown to more than 700.

Indeed, in 2017, the agency announced that it would adopt a risk-based enforcement policy targeting the worst of the bad actors, and ARM applauded that action. Nonetheless, the continued increase in the number of clinics providing unapproved and potentially unsafe treatments leads ARM to conclude that a risk-based enforcement approach is not robust enough to adequately regulate these businesses.

Therefore, ARM recommends that the

agency dedicate increased resources to establish and implement strong, swift, and consistent legal action against these questionable clinics and prosecute those that are in violation of the law.

Improvements to the INTERACT meeting process. We appreciate the agency's formalization of the pre-pre-IND meeting in the form of INTERACT meetings which particularly important to developers of cell and gene therapies as they provide an opportunity for the product developer to discuss important issues with FDA early in the development cycle.

This PDUFA reauthorization provides ARM the opportunity to ask for more impactful INTERACT meetings.

Need for additional regulatory CMC flexibility. ARM applauds FDA for embracing novel approaches to clinical development, including from trial designs, analysis, and end points to speed the availability of new treatments for serious or life-threatening diseases to address unmet medical needs. Expedited programs have successfully compressed clinical development and regulatory review timelines.

Equally important, is enabling flexibility in CMC components of development and review to bring gene and cell therapies to patients faster. Unfortunately, challenges with CMC review present a bottleneck. FDA has acknowledged this, that CMC review of gene therapy product applications account for approximately 80 percent of the time and the 20 percent remain for clinical review.

Therefore, ARM recommends that FDA better utilize and define regulatory flexibility during CMC reviews of cell and gene therapy products while maintaining the agency's rigorous approval standards.

Greater use of patient insights in the drug development review process. As has been noted, cell and gene therapies hold immense promise for patients with serious conditions, but these therapies also leverage rapidly emerged science, present new development challenges, and add complexity to treatment decisions for patients and their families.

We strongly support enhanced patient engagement of patients in the process and recommend

that FDA convene a dedicated session to present and discuss patient experience data directly from patients, patient advocacy groups, and sponsors in the context of a drug development program.

Utilization of real-world data and real-world evidence --

SARA EGGERS: You're at the end of time.

ROBERT FALB: ARM supports FDA's efforts to expand the use of real-world data and real-world evidence. Therefore, ARM recommends that FDA hold a public meeting to focus specifically on the unique issues associated with the use of real-world evidence for cell and gene therapies.

And finally, lessons learned from COVID-19. COVID-19 pandemic has impacted virtually every element of society. Within FDA, it has forced the reevaluation of what previously had been standard practices and procedures and required process changes. ARM recommends that FDA develop and publish report containing an analysis of pandemic related disruptions to standard processes, policies, and procedures and

modifications adopted to address the disruptions and evaluation of best practices. The report should be published and made available to public -- for public comment.

In conclusion, the regenerative medicine sector is the next frontier in the fight against some of society's most devastating diseases and disorders. Cell and gene therapies have begun to demonstrate their power to improve patient lives, but there is still much work to be done. ARM is looking forward to continuing the work with FDA to address the policies needed to continue positive advancement of the sector so that these cutting-edge treatments can meet their potential and be accessible to patients in need. Thank you.

SARA EGGERS: Thank you, Robert. We'll go with Paul next, and I have faith that (sound drops). Feel free to turn on your webcam.

PAUL MELMEYER: All right, very good. Can everyone hear me? Can everyone hear me?

SARA EGGERS: Yes, we can.

PAUL MELMEYER: Okay, perfect. Thank

you so much. Good afternoon, everybody. I'm Paul Melmeyer. I'm the Director of Regulatory Affairs at the Muscular Dystrophy Association. We serve over 250,000 individuals with 30 -- 43 neuromuscular diseases including some better-known neuromuscular diseases such as ALS, Duchenne muscular dystrophy, and spinal muscular atrophy as well as some lesser known and incredibly rare conditions such as mitochondrial myopathies and myositises.

In addition to funding research and operating over 150 clinical care centers across the nation, we also advocate for policies to accelerate the development and regulatory review of meaningful, safe, and effective therapies for our community, and that's why I'm here today.

I want to start by echoing many of the comments and sentiments from our patient advocacy organization colleagues made this morning. The greatest priority for MDA during the user fee reauthorization is to ensure a well-resourced agency can adequately review the products for out community, and that really starts with much more robust funding

for gene- and cell-based therapeutic reviews.

As Rachel Sher at NORD mentioned this morning, the number of applications arising for CBER and CDER cell based therapeutic review division have been increasing substantially while resources have not been able to keep up entirely, so what we're asking for is for the user fees for this current PDUFA VII cycle to keep up with the innovation that is reaching CBER in the form of gene- and cell-based therapies.

We're very privileged. We already have one gene- and cell-based therapy for a neuromuscular condition on the market today. That's Zolgensma for SMA, but there are many more coming and we don't want for those gene therapies to potentially be delayed in reaching our patients.

We also want to echo sentiments on decentralized trials. It's very difficult for the neuromuscular disease community to travel to clinical trials. Oftentimes, mobility (inaudible) neuromuscular diseases, and that makes, of course, traveling through air travel to clinical trial sites as well as other accessibility challenges very

difficult, but we recently did a survey in which we found 29 percent of individuals with neuromuscular conditions who have not participated in a clinical trial, they didn't do so because the trial sites were too far away.

Now of course, in rare diseases, 29 percent, that's a very important cohort of those individuals that we're losing. So we further encourage a decentralized clinical trial paradigm to be established through the next user fee reauthorizations.

We also are advocating for further evolution of integration of patient voice. We're very pleased to see the first patient focused drug development guidance finalized earlier this summer and now that the instructions are out there from this guidance and other draft guidances that are out there, as well as the discussion documents in this current iteration of the user fee reauthorizations, we're also asking for the next iteration of user fee reauthorization to include further assistance for patient organizations to actually collect the data.

Now that they know how to do it, they oftentimes need some consultative services, perhaps that FDA could provide in the next user fee reauthorization, as well as financial assistance. We don't want patient organizations to have to decide between the incredibly important basic and translational research funding that they fund, especially in rare diseases, and have to choose between that and collecting data on patient experiences or patient preference information.

Now these are just some of the topics that were discussed by our colleagues earlier. There are others in which we would like to see included within the conversation for this user fee cycle. One would be on N-of-1 therapies and creating a regulatory pathway through this user fee process that allows for FDA to better define and more seamlessly review N-of-1 products. We know N-of-1 products are gaining prominence in the neuromuscular disease therapeutic development atmosphere, and we're hopeful that a more structured and predictable approach from FDA can be considered during the user fee reauthorizations.

Investigational products. Access to investigational products outside of clinical trials are also important to our community, especially for those that don't have any other better option, and that's where extended access comes into play. And we know that Project Facilitate over in the Oncology Center of Excellence has been very successful thus far. We've already seen data showing how successful it could be. We'd ask that that project perhaps be expanded into, at the very least, neurology if not further from there.

Finally, the Rare Diseases Program has been very impactful within both CDER and CBER, but with the reorganization of the Office of New Drugs as well as a different structure over in CBER, the current structure of the rare diseases program as defined by our current user fee program may not fully have kept up with the evolution and FDA structure, so it also requests that the rare diseases program and the way in which it is integrated within both CDER and CBER be considered as part of this user fee structure.

That's all. Thanks.

SARA EGGERS: Thank you very much, Paul. Next, we will go to Nicole Mahoney. Nicole, are you able to -- are you unmuted?

NICOLE MAHONEY: Yes, I am unmuted. Can you hear me?

SARA EGGERS: Yes, we can.

NICOLE MAHONEY: Thank you very much. Good afternoon. I'm Nicole Mahoney, Senior Director for Regulatory Policy and an employee of Flatiron Health. For financial disclosures, I'm also a Roche stockholder. Thank you for the opportunity to comment on the success of PDUFA VI and recommend enhancements for PDUFA VII from our vantage point and area of expertise.

Flatiron Health is dedicated to advancing our understanding of how real-world data derived from electronic health records can improve patient care and inform decisions about cancer therapy development and access.

We provide electronic health record and practice management software and services to cancer clinics across the U.S. and create deidentified

research datasets to accelerate cancer research. Our vision is to realize the full potential of real-world evidence to support the development of oncology treatment, including precision medicines, improve patient access to effective therapies and care, and facilitate patient enrollment in clinical trials.

Real-world evidence can compliment randomized clinical trials, the gold standard evidence base for regulatory decisions by filling critical information gaps for patients typically excluded from traditional trials, including those with rare conditions. We expect the use of real-world evidence to grow as new sources of data become available and methods to analyze and derive insights from them evolve.

Flatiron applauds the success of PDUFA VI in advancing patient focused drug development and accelerating understanding of how and when real-world data from a variety of forces can support regulatory decisions. We look forward to forthcoming guidance and continued partnership with FDA. PDUFA VII provides opportunities to build on the success to

date, explore what is possible with respect to real-world evidence, and address challenges identified under PDUFA VI.

We offer the following four recommendations for your consideration. One, ensure that the learning from real-world evidence submissions to the agency are captured and shared broadly, including how real-world evidence is generated and used by sponsors and incorporated into FDA's decision making. We encourage FDA to work with sponsors to share key takeaways, obviously in ways that protect proprietary and confidential information.

Two, issue targeted real-world evidence guidance that builds on lessons of PDUFA VI, clarifies the clinical and regulatory circumstances where real-world evidence may be acceptable, and addresses current limitations on its use, including but not limited to methods to establish causal inference, including ways to address bias and confounding and development and use of real-world evidence endpoints.

Three, establish new pathways for FDA to work with the technology companies who are

generating real world data and analytic tools that are used by a range of sponsors, to enable patient centered drug development. Regulatory certainty through formal meetings would drive investments towards technological tools with the greatest potential to help speed patient access to effective therapies.

Four, continue to build on FDA's efforts to promote a learning health data ecosystem by modernizing the use of technology and increasing capacity to inject and analyze data as described in the technology modernization action plan and working with external stakeholders to help establish a robust real-world data ecosystem. PDUFA VII provided an opportunity for FDA to continue promoting high quality data capture at the point of care by setting clear expectations around the data and technology standards the agency would find most useful.

Thank you again for this opportunity to contribute. We look forward to continued participation through the user fee reauthorization process.

SARA EGGERS: Thank you, Nicole. Next we have Annie.

ANNIE KENNEDY: Hi, can you hear me?

SARA EGGERS: Yes, we can. Go ahead, Annie.

ANNIE KENNEDY: Good afternoon. I'm Annie Kennedy with the EveryLife Foundation for Rare Diseases, but actually I'm here today representing much more than just our nation's rare disease community. More than a year ago, a group of colleagues and I came together to reflect on all that had yielded from the PDUFA and 21st Century Cares Initiative and to together think about what was needed going forward.

Within moments of our first gathering, we all agreed that our communities have benefitted significantly from our patient focused drug development movement and thus, we grew to refer to our efforts as the PFDD work collaborative.

Our PFDD work membership includes the National Psoriasis Foundation, the Amyloidosis Research Consortium, the Longevity Foundation, the

Michael J. Fox Foundation for Parkinsons Research, the COPD Foundation, the Lupus Foundation of America, the ALS Association, the National Eczema Association, the Medical Research Fund, Parent Project Muscular Dystrophy, and the EveryLife Foundation for Rare Diseases.

We have reconvened with the leadership of Faegre Drinker Consulting and the Kith Collective. Together, we represent a broad array of patient communities with a diverse expertise in patient engagement.

Collectively, we've led eight FDA-led patient focused drug development workshops, eight externally led PFDD workshops, two meetings that predated the PFDD terminology that included significant FDA engagement, two patient community led draft guidances, numerous patient preference studies that have been incorporated into clinical development and regulatory review, and most notably, a few formerly stark disease bases transform into robust therapeutic pipelines.

In assertive transparency, many of our

PFDD Works members' efforts are supported through collaborations with biopharmaceutical industry organizations. It is through this lens of our PFDD Works collaborative that I offer some comments here today.

First and foremost, we thank you. Today our patient community organizations are working within the ecosystem as trusted conveners of industry, agency partners, and academia to help advance PFDD in an open and precompetitive environment. To that end, as we lean in to PDUFA VII, we have identified a number of priority areas to further this expansion.

We actually include four categorical areas which include transparency, authenticity, consistency, and comprehensiveness. For the sake of time today, I'm just going to highlight two of these priority areas and some key points to each of them.

Transparency. As our organizations and others continue to make significant investments of time and community resources to develop robust patient and caregiver data, we support continued efforts to incorporate this data early and target identification

and clinical trial design and to seek additional opportunities for both sponsors and regulators to share how this information is utilized.

We applaud the agency's implementation of the patient experience data checklist and we encourage further expansion of this application and its use through the sponsor agency and patient community engagement. Further, we recognize the immense resources that have been collected through the PFDD workshop, its narrowly led meetings, and voices of patient reports and we urge that additional resources be made available to the agency to further support PFDD innovation.

These could include supporting cooperative agreements that include the patient community to use PFDD data in critical areas such as the development of core sets of clinical outcome assessments that are shown to be meaningful to patients and caregivers and supporting activities that center on obtaining caregiver input in drug development and expanding the role of the caregiver in regulatory science.

And the next area is comprehensiveness. Perhaps most importantly, we recognize that the principles of patient centered, data driven product development must be applied across the entire continuum. We encourage efforts to reduce the barriers between regulatory approval and market access, a gap which is emerging as a second valley of death in the lifecycle of therapeutic development.

To that end, as core outcomes are developed, they could be created with consideration of outcomes of importance to stakeholders all throughout the development pipeline and must include patient community involvement to ensure that these outcomes are collected which are meaningful and of value to both patients and caregivers.

And we also encourage the advancement of opportunities to support label determinations that are made based in whole or in part on patient experience data and the availability of such date to inform decision making beyond the regulatory environment.

In closing, our PFDD Works partners and

the communities that we represent are grateful to the FDA for your leadership and continued commitment to placing patients at the heart of product development and we look forward to continuing to collaborate and innovate alongside you. Thank you for all of your efforts.

SARA EGGERS: Thank you, Annie. And finally, we have Marta.

MARTA WOSINSKA: Great. Thank you. Can you hear me?

SARA EGGERS: Yes, we can.

MARTA WOSINSKA: so good afternoon. My name is Marta Wosinska and I'm a consulting professor and Deputy Director of the Duke Margolis Center for Health Policy at Duke University. I am pleased to present comments on behalf of the Duke Margolis Center. No conflict of interests to disclose.

So our center has experienced working with FDA on implementing PDUFA VI. Under a cooperative agreement with the FDA, our center has worked with the agency to advance the patient focused drug development program, RWE, or real-world evidence,

and the benefit with framework assessment across the drug development lifecycle.

Today, I would like to sketch out how the Duke Margolis Center sees the most productive direction for PDUFA VII. That direction is informed not only by our cooperative work with the FDA, but also by lessons learned from our center's experience with our collective national response in the development of therapeutics to treat COVID-19.

I would say there are three lessons from COVID that we see as applicable to PDUFA. First, we need to draw on a range of data sources and evidence to get a more complete picture of a product's safety and efficacy. Second, we need to build our evidence on strong transparent data collection practices and data infrastructure. And third, strong stakeholder collaboration is necessary for being able to make the first two happen.

Together, these three lessons show us that it is possible and frankly necessary to develop a more efficient and adaptive approach to evidence generation. So let me walk through each one of these

lessons in more detail. Let's start with the first lesson, the need to bring together a range of data sources and evidence.

What we're finding is that to answer COVID-related disease and treatment questions in a more efficient way, we need a broad spectrum of evidence generation approaches. On the clinical side, we have seen a broad range of approaches to trials, from large, simple trials like the U.K.'s recovery to more traditional clinical studies like those found in the NIH's active collaboration.

We have leveraged trial networks and master protocols to reduce overall data collection burdens, to integrate data collection and care delivery, to reduce barriers to site recruitment and trial involvement, and to increase collaboration between early stage practical trials and more traditionally structured studies.

On the real-world data side, we're seeing how RWD can help answer questions around the use of repurposed treatment as well as those that have come to market under emergency use authorization.

COVID has highlighted now these information sources complement each other and collectively help us make informed decisions.

As we receive new information from clinical trials and from real-world evidence, and as we gain a better understanding of COVID itself, we're bringing the totality of evidence to bear to help us understand the benefits and risks of different treatment.

The second lesson from the COVID response has been the importance of strong transparent data collection and infrastructure. Through COVID, we are seeing the importance of sharing and reporting mechanisms for trials, the importance of collecting and linking high quality real-world data, the importance of leveraging novel data sources such as patient generated health data, and the importance of making use of post-market safety surveillance systems like Sentinel.

And the third lesson from our COVID response is that multi-stakeholder collaborations are critical to the success of the first two lessons

around evidence generation. There are numerous examples in COVID where unprecedented stakeholder collaborations have helped advance the development of COVID-19 therapeutics.

Groups at UCSF and UPMC are finding ways to reduce operational burden of coordinating across trial size and the individual trials themselves. Groups like (inaudible) are identifying pathways for industry including small biotech firms to quickly scale up their research effort and plug into platform trial. FDA is working directly to engage data holders' inquiries of their real-world data in collaboration with the (inaudible) Foundation in advancement of cancer research, the agency is bringing together a range of data organizations, researchers, and others to rapidly access diagnostics and treatment.

This COVID-19 evidence accelerator represents and unprecedented collaboration bringing expertise and resources from across the research community. Here at Duke Margolis, we -- our RWE collaborative brings together experts to develop

recommendations to build a learning healthcare system model in the U.S. that's heading for regulatory decision making.

PDUFA VII presents an opportunity to learn from and build on all this success, but doing so will require us to further strengthen FDA's workforce and institutional capabilities. Here are three ways to strengthen those capabilities. First, we need to recognize the greater demands on FDA's time. The greater demands on FDA's time means the need for more experts at FDA from data scientists and patient statisticians to decision scientists.

Second, FDA needs not just more FTEs, but also continued investment in IT, data, and knowledge management systems. FDA's technology management action plan and visions of technology can support all of the principles we talked about earlier, helping the agency draw multiple evidence course, building out its data infrastructure, and promoting stakeholder collaboration.

And third and last, FDA will need to break down organizational barriers and silos to

advance regulatory science and innovation. FDA should leverage lessons learned from structural changes as seen in the Office of New Drugs and the Oncology Center of Excellence.

So with these strategic goals in mind, we look forward to submitting formal comments on how such activities could be operationalized in PDUFA VII and we look forward to continued discussions in the months to come. Thank you very much.

SARA EGGERS: Thank you very much, Marta. And thank you to all the public commenters. This concludes our public meeting on the PDUFA reauthorization. We have heard directly from 20 individuals representing a variety of stakeholders and reiterating Dr. Cavazzoni, FDA very much values all the input that has been generated from today's discussion and we look forward to receiving further comments to our docket.

Again, anyone from the public is welcome to contribute to the docket and we encourage that. the meeting information will all be posted on the PDUFA VII webpage that is put in the Announcements

pod after our webcast. The meeting is -- we also welcome feedback on the meeting, so you may put any final comments in through the tech support chat box or send an email to PDUFA reauthorization at FDA.HHS.gov.

And I would also like to point out the efforts of Graham Thompson, Patrick Zhou from CDER's Office of Program and Strategic Analysis, and the meeting technical staff, (inaudible) Williams, Philip Dylan, and Richard Barnes for the tremendous behind scenes work to prepare for the meeting and to assure its smooth running. And with that, I will close the meeting and please enjoy the rest of your afternoon. Thank you.

(Whereupon, at 3:58 p.m., the proceeding was concluded.)

CERTIFICATE OF NOTARY PUBLIC

I, LATRICE E. PORTER, the officer before whom the foregoing proceedings were taken, do hereby certify that any witness(es) in the foregoing proceedings, prior to testifying, were duly sworn; that the proceedings were recorded by me and thereafter reduced to typewriting by a qualified transcriptionist; that said digital audio recording of said proceedings are a true and accurate record to the best of my knowledge, skills, and ability; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

LATRICE E. PORTER

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SONYA LEDANSKI HYDE

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