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FOOD AND DRUG ADMINISTRATION

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PUBLIC MEETING ON PRESCRIPTION DRUG USER FEE ACT (PDUFA) REAUTHORIZATION

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Welcome and Introduction

00:00:48 **Nana Adjeiwaa-Manu:** All right. Good morning. Can everyone hear me? All right. Wonderful. Good morning and welcome to today's public meeting on the reauthorization of the Prescription Drug User Fee Act or PDUFA. My name is Nana Adjeiwaa-Manu and I am with the Program Evaluation and Implementation staff, and I'm based in the Center for Drug Evaluation and Research. I will be your moderator today.

00:01:13 PDUFA is the legislation that authorizes FDA to collect user fees to support the process for the review of prescription drug products. The current authorization of the program, PDUFA VII, will expire in September, 2027. Preparations are therefore underway to begin the process to reauthorize the program for Fiscal Years 2028 through 2032. The purpose of today's public meeting is to gather input and recommendations from the public in advance of discussions that will occur with the regulated industry. Today's meeting is an important step in engaging with public stakeholders on features of the PDUFA program. We will continue to engage stakeholders throughout the reauthorization process. There is a Federal Register notice out now with details on how to notify FDA if you would like to participate in recurring stakeholder meetings during the reauthorization process. We will provide a link to that notice in the Q&A online.

00:02:20 We have a full agenda for our meeting today. We will begin with Martin Makary, FDA Commissioner who will be providing opening remarks. Andrew Kish, who is the Director of the Office of Program and Strategic Analysis in CDER, will provide background on PDUFA as well as the reauthorization process. We will then hear remarks from the regulated industry trade groups. Following remarks from regulated industry, we will take a short break. After the

break, we will hear public comments from individuals who submitted a request to participate in the public comment portion of this meeting. I will then close the meeting around 11:30 AM.

00:03:03 In the Federal Register notice announcing this meeting, FDA provided four questions to help the speakers frame their comments. The first question was, what is your assessment of the overall performance of PDUFA VII thus far? What current features of PDUFA should be reduced or discontinued to ensure the continued efficiency and effectiveness of the human drug review process? Thirdly, what new features, if any, should FDA consider adding to the program to enhance the efficiency and effectiveness of the human drug review process? And fourthly, what changes, if any, could be made to the current fee structures and amounts to better advance the goals of the agreement, including facilitating product development and timely access for consumers? Please note that policy issues are beyond the scope of the PDUFA reauthorization process. Therefore, comments should focus on process enhancements and funding issues and not on issues of policy.

00:04:05 This meeting is an opportunity for the FDA to listen to public perspectives. FDA will not ask questions nor answer questions raised at the meeting. My colleagues, who will be leading and participating in the reauthorization process, are here in person as well as online. Please know that we are listening and we very much value your perspectives. Further, please keep in mind that you can submit comments to a public docket that will be open until August, 14th. We encourage everyone to submit their perspectives to the public docket for FDA review. We'll post a link to the public docket in the Q&A for this meeting.

00:04:45 A few housekeeping items. This is a hybrid public meeting and we have many people participating virtually today. If your audio or visual connection diminishes, we recommend trying to reconnect through the system. If you experience other technical issues during the webcast, please type your issue into the Q&A online or email

PDUFAreauthorization@fda.hhs.gov. We will have a 15 minute break at about 10:00 AM. If schedule modifications are needed, we will communicate those verbally and post them into the Q&A. For those of you attending the meeting in person, restroom facilities are located down the hall to the right of the conference room. A video recording and transcription of today's meeting, as well as the slides presented, will be published on the FDA website after this meeting. I'll now turn it over to Dr. Makary, the FDA commissioner for some opening remarks.

Opening Remarks

00:05:49 **Marty Makary:** Okay. Good morning. Thank you, Nana. And thanks to the team and Nana for setting things up. There you are. I know you wanted to get a good view here. So, we have at least 10,000 people here in person and millions more joining virtually, I think by rough estimates. So, thank you everybody for being here. This is important. This is a very important negotiation. User fees are critically important and I want to just briefly emphasize our commitment to user fees. I don't know whose idea it was to have user fees, maybe Jacqueline, maybe it was your idea? Take credit because it's a wonderful program. Jacqueline's doing an amazing job. We're lucky to have her here at the FDA. Pre-user fees, the stories that I've heard about boxes of applications being delivered in person to a facility, that companies would not risk using the mail service and so they would deliver the applications themselves, maybe some of you would remember those days, and they would actually see in the back of the warehouse some of the other applications they dropped as far out as a year prior. And that just, I think, symbolized and was emblematic of an era where there was less accountability and less of a structure to get decisions out quickly. And so, the User Fee Program has really transformed the way that we function at the FDA. It started in 1992 as you know, and you're going to hear more from Andrew Kish. Andrew, thank you for being here. It's great to have you. And Grace

Graham here has been a tremendous resource. One of the Deputy Commissioners with a long history on the hill. In 1992, the Program started and they started immediately seeing results, and it's been modified since that first PDUFA, and so we want your input on how to make it better.

00:08:06 We just-- I wouldn't say completed. We're two thirds of the way through a national CEO listening tour. And we were up here, Jacqueline and Vinay Prasad, and myself and others, and we invited CEOs, pharmaceutical companies to come in and we listened to what they had to hear. I'm a big believer in listening. They gave us a lot of ideas. They were not bashful at all. They told us exactly what they think we can do differently. And I would say those suggestions were incredibly informative. Very informative. Some of them had to do with policy and regulation, some had to do with process and procedure, and some had to do with communication. And I would say that what struck me the most was the comment that one CEO made, but it was echoed in the feedback from many that a couple 15 minute calls could save them months of guesswork.

00:09:12 And so, we want to never be satisfied and always seek a better process, but at the same time acknowledge that there's tremendous success and that the tried and true system here has been working well. 50 drugs were approved in 2024. We're probably on track for, I don't know, I'm still learning what I can and can't say in public, but if I had to guess at least 20% higher in terms of the number of drugs we are probably going to approve this year. And in CBER, they had eight-- 11 new biological treatments, many for debilitating and rare diseases, a big priority for this FDA. So, things are moving. We do want to continue to listen. We have intense competition from around the world. If you have been following what's going on with other regulatory bodies, as in China's system of approving drugs, we do have competition. But 34 out of 50 new drugs approved by CDER last year were approved in the United States before

other countries. So, we can continue to be efficient, agile and yet hold to our gold standard of safeguarding the public.

00:10:49 There are many aspects to the FDA. Childhood vaping, mangoes coming across the border, the entire food portfolio, gene editing, CT scanners, the FDA may regulate 20% of the US economy. But this is one of the core functions of the FDA that people understand and people think of. When they think of the FDA, they tend to think of the D first, especially in my field of medicine. And so, I think we have an opportunity now to number one, celebrate the success of the PDUFA Program, and number two, ask how we can make it better?

00:11:36 I'd like to see lower user fees. It'd be a reduced barrier for small companies and individual inventors, and people in academics that may be trying to understand this process, including the capital requirement. But I do believe that we need first and foremost before that goal, a program that works very well. I would say you are the experts in this program and we're here to listen. So, tell us what you think and we are happy to adapt our view. I have always believed that the mark of a good physician and a good human being is somebody who is willing to evolve their opinion as they see new information. Please share with us new information, I look forward to hearing it. And thank you everybody for being here.

00:12:52 **Nana Adjeiwaa-Manu:** Thank you, Dr. Makary. I would now like to introduce Andy Kish, the Director of the Office of Program and Strategic Analysis in CDER to provide background on PDUFA and the reauthorization process.

PDUFA Background and Reauthorization Process

00:13:22 **Andrew Kish:** All right. Good morning, everyone and thanks to the Commissioner for his comments. I've been involved in PDUFA since PDUFA V now. So, we're talking about

PDUFA VIII. It's been a while. I've been at the agency for 15 years and been a part of this program for-- 15 years I've been here. So, I've seen it really change and progress. I'm happy to give some background. I'll talk about a little bit of the history, although I think most of you know that quite well, both in the room and online. Also, give a little overview of the program workload and performance, some information on financials and the fee structure, and then just an overview of the reauthorization process, which we're starting today. Before I jump in, I want to thank everyone who worked to pull this meeting together. Most of them are sitting over there, particularly Emily Ewing for pulling together these slides.

00:14:15 All right, the background. This should look familiar to a lot of you, so I won't get into any details here, but as the Commissioner mentioned, before PDUFA things were not ideal. We had backlogs of overdue applications. We had long review times, we just didn't have the staff to do the work. So, Congress, industry, and the FDA got together and decided to come up with a User Fee Program. That program resulted in a more predictable, streamlined process, which allowed patients to get access to drugs much sooner than before 1992. Overall clinical development time and average time to approval also has dropped under the PDUFA Program.

00:14:59 What does PDUFA do? Introduces fees to help really enhance the review process. So, they're added to appropriated funds, budget authority. It's intended to increase staffing and other resources to speed things up so we have people on hand. User fees pay for a service that directly benefits fee payers. This is what distinguishes it from a tax for those of you who get into the details of OMB.

00:15:27 What do we talk about in these negotiations? It's really around what new or enhanced process FDA or industry might seek in the next five years, or what changes we might seek. We talk about what is technically feasible to do. We also talk about what are the resources required to do that and to sustain these enhancements. I want to emphasize there's no discussion of policy

here. This is a process agreement. Our experience-- And industry colleagues will, I'm sure, chime in when they come up. This really gets detailed. We're talking. Every word, every view. So, our experience is it takes a lot of time to do this and pull it together.

00:16:05 This is a very brief history of PDUFA. I will not go through all of these, but needless to say it has changed quite a bit. It started-- PDUFA I really focused on some core review goals in the pre-market space, and it has expanded over time getting into the post-market space, getting into IT. In VI, we changed the user fee structure. The first time it had been changed since its inception and it got into more of the supporting functions around the program. HR, financial management. Also got into reg tools and some areas that are cutting edge in that space. So, [I'll] spend a little bit more time talking about the last agreement. It was pretty substantial. This was done during COVID. It was done all virtually successfully and congrats to everyone who's involved in that. It was a new challenge thrown at us a couple months before negotiations were supposed to start.

00:16:58 What is in the current agreement? There was a lot of focus on staffing up for cell and gene therapy products, particularly in CBER. That was a big portion of the agreement. We brought in new allergens to the program for the first time. So, the PDUFA goal was applied. Introduced new timelines and performance goals for post-marketing requirements, human factor protocol submissions, use-related risk analysis. We brought in two new meeting types and an opportunity for folks to follow up after meetings. Introduced a number of new pilot programs. We also for the first time got into more of the CMC, Chemistry, Manufacturing, and Controls space and inspection space. We also focused quite a bit on modernizing information technology, particularly in the CBER space, and touched on digital health technologies. As a big agreement, we covered a lot of ground and we're well on our way of implementing a lot of that right now.

00:17:59 What does that convert to in terms of workload? It includes over 250 performance enhancement commitments. What are performance enhancement commitments? That might be an internal FDA term, but those are commitments that aren't review goals. So, there's quite a bit of work that was agreed to. That means 70+ new or updated pilots, programs or processes. 50+ data or list postings to our public website, a number of public meetings and public workshops, new guidances, public reports, and a slew of other commitments. It's a ton of work that we agreed to and that's why it takes quite a bit of time to come up with these agreements.

00:18:41 I'll try to touch on a few of the high points of what's in the current agreement, but won't belabor a lot of them. I'm sure many people have read the commitment letter already. As I mentioned before, CBER was, particularly the cell and gene therapy space, a big focus of the last round and rightfully so since it's an emerging product area. A lot of the agreement was around enhancing staff capacity to handle cell and gene therapy products and engaging with the public in that space. In the pre-market space, a lot of new approaches to improve efficiency, expand communications. As I mentioned before, that included new meeting types, some new guidance and also some pilot programs. Many of these pilot programs also have reviews and public meetings associated with them, and I encourage folks to review those or attend those meetings when they come up.

00:19:34 Also touched on regulatory decision tools, a lot of continuation of what was in VI. Converting pilot programs and pilots into programs, including Model-Informed Drug Development, Complex Innovative Trial Designs. Also, continuing our work in the patient-focused drug development area. Post-market safety continued with a lot of-- Continued to support Sentinel Initiative, including two focus studies in that space and also some new performance goals around REMS. And a new area in PDUFA last round was, as I mentioned before, chemistry manufacturing, and controls. So, it was really around facilitating readiness and use of innovative manufacturing technologies that included improved communications, looking at

how we use IRs, some notification around inspections, more clarity around use of alternative tools, a pilot program trying to get folks ready for their manufacturing when they're on an accelerated clinical development timeline. And we also had a workshop already on manufacturing technologies.

00:20:46 Also touched on digital health and informatics. This was also a big portion of this agreement. As I mentioned before, a lot of it was around supporting CBER's modernization of its IT. Also looking to expand our capacity to really implement DHTs or digital health technologies, including a new DHT framework. Also, additional resources to focus on bioinformatics and also putting out a plan on our IT modernization, some transparency around those efforts, and getting finance, hiring and retention. So, it was a big agreement, it's a lot to get through. Continued focus on financial management and transparency in our finances, and continued focus on our hiring retention of staff. That's been a longstanding area. It started, I think, really in PDUFA V, PDUFA VI. So, we continue to mature our capacity planning capabilities, continue to have transparency around our finances, including having public meetings around our finances. And we did some modifications to fee adjustments to provide funding to retain staff, particularly our highly qualified technical staff. There's a lot of information online if you want to look into the performance data and look at completed deliverables. Here's some links for folks and these will be posted publicly after this meeting. That's typically up to date and you can find some historical data on PDUFA performance also. And for those of you who like to get into the data, you can download it and manipulate it as you want.

00:22:29 Okay. Let's talk a little bit about program workload and performance so far under PDUFA VII. This gives some historical information along with more recent data. There were 128 NDAs and BLAs filed in FY24. And if you look at this graph, it breaks out priority and standard, and then the total. You can see there was a bit of a ramp up in overall applications coming in through PDUFA VI and then, in the past three years in particular, we've seen more variability.

First a little bit of a drop and then increase. This will play into some talking points later, but we'll bring this back up. Something to note. Since 2020, over half of the filed NDAs and BLAs have at least one special designation. What does that mean? It is designated as a priority review, orphan, fast track, breakthrough therapy, accelerated approval, sometimes more than one. This is a fair proxy for complexity of what's coming in. Typically, if you have a special designation, this involves more work, as you've heard us say many times, particularly for breakthrough therapy it's all hands-on deck approach. So, we're seeing more of that in what's coming in the door to us. Folks are taking a picture, so I'll give you a second. We will post this.

00:24:02 Okay. In terms of other workload measures. There's a lot in this program, aside from NDAs and BLAs. When you look at our efficacy and manufacturing supplement submissions, which take up a fair amount of our reviewers' time, we continue to see increases compared to PDUFA V. It just turns out its 32% increase for both efficacy and manufacturing since PDUFA V to where we are right now in the cycle. Something that really consumes a lot of our reviewers' time is INDs, commercial INDs. You could see that is a good sign as drug development, in general, continues to increase. So, under our portfolio in this program, we've seen a 51% increase since PDUFA V in active commercial INDs. So, on average it's nearly 12,000 per year that we're keeping track of. And meetings continue to increase, which you would expect with more INDs. That's when all the formal meetings happen. We continue to see a pretty substantial increase in requests for meetings, managing over 4,500 per year. That's a 58% increase since PDUFA V. So, that's all to really give you a very high level overview that workload is increasing in this program and continues to increase.

00:25:45 There's a number of goals associated of course with these submissions that are coming in. Folks are probably very familiar with these. It includes 42 goals, many of which have pretty aggressive timelines where we are reviewing, for example, applications within eight to 12

months. 90% is our goal and we typically make these, as you can see on this next slide. Some historical here. And for FY24, which is-- Just a note, this is preliminary data, we always update it the next year because there's still some that are pending. So, we do well and we definitely prioritize these important submissions. But we will admit we do have challenges with meeting management and we continue to have challenges with meeting management. It's a large chunk of work, it's very tight timelines and we've done a lot to try to improve on this performance. We've made some incremental improvements, but we're still admittedly not quite making our goals, particularly the past two years. These are the new meeting types where we have done a bit better.

00:27:08 Okay. I'll switch gears over to finance to give you a little bit of background, talk a little bit about the fee structure. [I'll] give everyone a moment to look at this graph. So, as the Commissioner mentioned, user fee revenue is very critical to FDA, to this program. To give the historical here, PDUFA-- When it started, fees paid for 7% of the program. Now they paid for 78% of the program. And hopefully the colors come across for everyone, but the bigger chunk of the graph, the light blue, are PDUFA user fee obligations. You can see how that's grown over time. The gray is non-user fee obligations, that's budget authority. You can also see the spending trigger. For those of you that are familiar with that, that's a requirement by law that we spend a certain amount of budget authority on the program to be allowed to spend User Fee Programs. There're more details on that in our financial report. I encourage you to take a look at it. We also go over that in detail in our public meeting on finance. You can see it's year to year. It's very close to making that trigger early in the program. We've had a bit of a cushion since, and the gap might be closing again. We'll see. So, there's some tight margins we're working in this program. It's a complex program, especially when you're managing multiple user fee programs and the financial folks do a great job there.

00:28:37 Okay, the current fee structure. As I mentioned before, PDUFA VI, we did modernize the user fee structure. The focus was really on a couple of main things here, making sure we have predictable funding, stability, and also focused on administrative efficiency. So, the current structure. We derive 20% of our target revenue. What we bring in comes from application fees. 80% comes from annual program fees. What we have noted is, particularly in the past couple years, that the PDUFA program fee is more predictable and stable compared to the application fee. If you remember the graph where I showed the past three years, that variability, that plays into that unpredictability. So, in 2025, our target revenue was about $1.5 billion and 20% of that came in through applications, 80% through the program fee. What does that convert to in terms of fees? 4.3 million for applications with clinical data, about 2 million without clinical data, and the PDUFA Program fee is 400k.

00:29:44 Something to note and it gets a bit more in the weeds, but I'm sure companies are very familiar with this. As the program does offer a number of waivers for special circumstances where folks don't have to pay fees or pay reduced fees, all this is laid out in the guidance if you want to do some reading on it, but just a quick overview of the types. There's a public health waiver, there's a barriers to innovation, there's a small business orphan designation, and then there's state and federal government entities to get waivers and if there's no substantial work performed on the application.

00:30:25 Okay, so some of you might be saying that the fee is high, and as the Commissioner mentioned, he would like to see a reduction in fees. So, why are we seeing some increases here? And what we've observed is the number of full application equivalents, which is our way of saying those who pay fees are dropping as is the proportion that pays fees. What does that mean looking at this graph? So, total full application equivalents are the blue line, you can see that has dropped in the past three years. And in terms of fee payers versus non-fee payers. Fee payers are less than 50% for four of the last five years. So, run a hypothetical. What does that

mean? The amount of fee payers affects the fee rate. If we didn't have any waivers, and this is not a suggestion in any way, this is purely data, this is what the fee would be hypothetically versus the actual fee. It'd essentially be half. And just to go through this one more time. So, fewer fee payers basically mean those who do pay, they pay more. That's the big takeaway under the current fee structure.

00:32:01 Okay. Touched on the reauthorization process, which we're starting today. We have our public meeting. Thanks to everyone who's attending online and in person. After this, we will then go into starting technical negotiations with industry sometime this fall. We also have the parallel process with stakeholders. We then will have a really relatively short period of time to come together in an agreement with the goal of starting the clearance process in spring of next year. We will then have a final public meeting after the package has been cleared through the various parts of the government and once industry has cleared it, that's typically in the fall of next year, we then have a hard deadline to transmit this to Congress by January 15th, 2027. And then it is in Congress's hands to reauthorize before the current agreement expires on September 30th, 2027.

00:33:03 So, a really small text here. Don't worry about reading it. This is the statute, but just really highlighting in particular a few things where consultation and your input is very valuable. Particularly, the public input, periodic consultation and also some transparency around the negotiations. Just highlight this a little bit more so you can see it. Where are we today? We have our initial public meeting. Thanks to everyone who has signed up for public comment. We also encourage folks to submit their comments to the docket. It closes on August 14th. We also have public stakeholder meetings. This happens during the-- Every month that we have negotiations with regulated industry, we also hold a stakeholder meeting. That FR notice is out. Please, if you fall within those categories and qualify, I encourage you to sign up by August 4th. So, during negotiations, every time we have a negotiation with regulated industry,

we're required by statute to put out public meeting minutes. They will be posted within 30 days of each meeting so that you can keep up to date on what's happening in negotiations through these minutes. Okay, I think that's it for me.

00:34:48 **Nana Adjeiwaa-Manu:** Thank you so much, Andy. We'll now move to remarks from regulated industry. We'll first hear from Annetta Beauregard, who's the Senior Vice President, Science and Regulatory Affairs at Biotechnology Innovation Organization.

Regulated Industry Perspectives

00:35:22 **Annetta Beauregard:** Good morning. It's very nice to be here this morning and to talk to you about PDUFA. My name is, as mentioned, Annetta Beauregard. I am Senior Vice President at the Biotechnology Innovation Organization for Science and Regulatory Affairs, otherwise known as BIO. And before I dive into PDUFA, I'd like to tell you just a bit more about our organization.

00:35:47 BIO is the premier biotechnology advocacy organization. We represent biotech companies, industry leaders, and state biotech associations in the United States and more than 35 countries around the globe. Our members range from very small emerging start-up biotechs to some of the world's largest biopharmaceutical companies. We are all united by a single goal: to develop medical and scientific breakthroughs that prevent and fight disease, restore health, and improve patients' lives. BIO also organizes the BIO International Convention, which we actually just wrapped up a few weeks ago in Boston, as well as a series of annual conferences that drive partnerships, investment and progress in this sector. Just a bit more about us. We were founded in 1993. We are a non-profit trade association that is currently led by John F. Crowley and our board chair is Fritz Bittenbender from Genentech. We are headquartered right here in Washington DC and represent approximately 1,000 members.

00:36:57 Okay, let's get into PDUFA. As you heard, it was first enacted in 1992 as a bipartisan solution to increase the efficiency of prescription drug review at FDA. Prior to PDUFA, the review process for new drug applications took over two years before medicines were available, and often they were first available in foreign countries before the United States. The HIV/AIDS epidemic really brought this into focus. Today, the average review for new applications is often less than 10 months, and US patients are often the first in the world to receive innovative therapies. Because of that, FDA is considered the regulatory gold standard in the world. PDUFA is an engagement of multiple stakeholders. So, FDA, Congress and industry work together to ensure FDA is resourced appropriately to support the regulatory review process for new medications.

00:38:04 How does it work? PDUFA authorizes the FDA to collect user fees from the biopharmaceutical industry, and then PDUFA establishes performance goals for FDA related to the drug development process, application review, and drug safety. To give you an example, performance goals around sponsor FDA communications have been an iterative process for some time. The FDA and sponsors, we've been working on this for many years, and as you heard from Commissioner Makary just this morning, we're still working on these items and it's an iterative process throughout PDUFA.

00:38:47 It's an important tool with very defined parameters. The PDUFA program ensures adequate resources for the FDA review of new drugs. Those resources enable critical communications between the sponsor and FDA throughout the drug development process. For small biotech companies, this is particularly important. Early and frequent communication, as well as an efficient and predictable review process, can make the critical difference in innovation reaching patients. The PDUFA program is limited to two things: one, allocating resources and two, improving FDA performance in regulatory review and associated staffing. The program cannot be used to alter regulatory policy or FDA statutory requirements, and you heard that

from Mr. Kish as well. The program-- As part of PDUFA, industry receives from FDA a commitment to meet certain industry-wide performance goals. The goals are not tied to a specific application under review. PDUFA fees are never tied to review outcomes. I think it bears repeating. PDUFA fees are never tied to review outcomes. The FDA maintains 100% scientific independence as a cornerstone of PDUFA. It's reauthorized every five years as you saw in the previous slides, and this provides the industry and FDA the opportunity to make changes and add new provisions that will further improve the program. The ultimate goal in this whole process is to adapt FDA's processes to the latest regulatory science to ensure safe and effective medicines reach patients.

00:40:43 This next slide is really a reiteration of what you heard from Mr. Kish. The important piece here is that we've been iterating on PDUFA for more than 30 years. It is an iterative and additive process. At the end of the day, the goal is to ensure FDA staffing and regulatory processes keep pace with scientific innovation, and we've done that every five years. We look back at what is working, we look forward to what is needed, and we have this iterative process. I won't go through each of the PDUFAs because I think you just heard about it, but suffice it to say, you'll see here that as the science evolve, for instance, in the last PDUFA, there was a great deal around cell and gene therapy. There's also a great deal around-- You've seen the breakthrough therapy or the patient focused drug development. Science is pushing us in these directions and we iterate on that in PDUFA.

00:41:43 So, BIO's approach to this upcoming PDUFA VIII. We recognize and appreciate the openings-- Excuse me. We recognize and appreciate Commissioner Makary’s commitment to upholding the gold standard of trusted science, increasing transparency and applying common-sense decision-making. You heard some of that this morning in the opening remarks. Also, the CEO listening sessions as referenced by Commissioner Makary are a great starting point to hear the needs and the wants from industry. BIO looks forward to working collaboratively with FDA,

HHS and other executive and legislative branch stakeholders to ensure a timely reauthorization in this important program.

00:42:32 Our objectives for PDUFA VII are to make sure and prioritize core review activities that ensure safe and effective biotech innovations reach patients faster. As you saw from Mr. Kish slides, the numerous increases in workload and volume. Some goals have been met and some have not, and PDUFA is an important opportunity to address those things. We also want to ensure FDA meets its review activity performance commitments. There are many, as you saw in these PDUFA negotiations and commitments. We want to make sure those are upheld.

00:43:11 Very importantly, we want to increase predictability of the PDUFA review process and financial structure. This is critical for the FDA. It is critical for our companies, particularly small biotech that depends on the predictability of the review process. We want to look at and improve FDA communications, transparency and accountability. It's important to enable innovation to patients in a timely and transparent manner. Sorry about that. Improving FDA communications and transparency. A little more detail here. We want to improve the communications so that we can bring innovative products in a timely manner and have clarity on the regulatory requirements for those innovative therapies. Additionally, we'd like enhancements to how FDA communicates the basis of its decisions to enable greater insights into how America’s biotechnology leaders are using the latest science to improve public health. It's important to note we learn from each other, our competitors, and we learn from the FDA in their decision-making, and the importance of understanding that will advance science.

00:44:34 Improving FDA accountability and predictability. PDUFA is a tremendous tool for ensuring that government regulators are accountable for their performance. We want efficiency and predictability. We also believe that the increase in the accountability for process milestones will add more certainty to drug development, the drug development ecosystem, and spur

additional investment in bringing innovative products to patients. Having a predictable environment includes predictable fees and revenue approaches, and will enhance biotechnology companies' ability to plan for, and invest in, innovation in the United States. Industry depends on that stability and they depend on a well-resourced FDA, staffed by subject matter experts, to conduct the regulatory oversight to bring safe and effective therapeutics to patients. BIO appreciates the opportunity to comment on the importance of PDUFA to bringing safe and effective innovations to patients and we look forward to this reauthorization process. Thank you.

00:45:50 **Nana Adjeiwaa-Manu:** Thank you, Annetta. We'll now hear from Kristy Lupejkis, Vice President and Chief of Staff, Science and Regulatory Advocacy from Pharmaceutical Research and Manufacturers of America.

00:46:17 **Kristy Lupejkis:** Good morning, everyone. Pardon me for a minute while I get accustomed to the slides. Thank you and good morning. My name is Kristy Lupejkis. I am a VP of Science and Regulatory Advocacy at the Pharmaceutical Research and Manufacturers of America or PhRMA. I'm not sure, if you don't mind-- I'm sorry. I'm not sure why this isn't advancing. Please bear with me just for a moment. Press this way. Thank you very much.

00:47:05 PhRMA represents the country's leading innovative biopharmaceutical research companies, which are focused on developing medicines that transform lives and create a healthier world. Together, we are fighting for solutions to ensure patients can access and afford medicines that prevent, treat and cure disease. Over the last decade, PhRMA member companies have invested more than $800 billion in the search for new treatments and cures, and they support nearly 5 million jobs in the United States. PhRMA has been a strong supporter of and participant in PDUFA since its inception in 1992. We appreciate the opportunity to participate in today's public meeting.

00:47:49 America's biopharmaceutical companies are at the heart of a robust R&D ecosystem that develops more innovative medicines than any other country in the world. In recent years, advances in scientific discovery have ushered in a new era of medicine, transforming our ability to treat, and in some cases cure, some of the most challenging diseases, including many cancers, rare diseases, and autoimmune conditions. These advancements are due to the productivity of the US biomedical R&D ecosystem, which is sustained by a policy framework designed to support and advance America's leadership in innovation for new medicines. At the same time, medicine development is a long resource intensive and highly uncertain process. The path to new treatments is rarely straightforward. Fewer than 12% of drug candidates that make it to Phase I clinical trials will eventually be approved by the FDA. On average, it takes 10 to 15 years of research and 2.6 billion to bring a new medicine to market.

00:48:54 FDA approval is rarely where innovation ends. It's just the beginning. Continuous learning about approved products is always part of the process. To support this, we need a modern regulatory paradigm that is able to serve patients by providing timely science-based regulatory decisions. That's why PhRMA and our member companies, along with BIO, support a strong appropriately staffed and science-based FDA, resourced through a combination of appropriated funds and user fees from the regulated industry. For more than 30 years, PDUFA has helped the FDA fulfill its central mission to help protect and promote the public health by ensuring the safety, efficacy, and security of drugs by allowing the agency to keep pace with the increase in the number and complexity of drugs and biologics entering the review pipeline.

00:49:48 America's predictable regulatory environment helps provide patients with more medicine choices than people living anywhere else in the world. However, as you heard before, before PDUFA was enacted in 1992, more than 70% of medicines were first approved outside of the US. As you also heard earlier, the emerging AIDS epidemic in the 1980 sparked demand for faster review times on new treatments and therapies. Patient activists argued that because there

were few treatments for AIDS, new drugs should be reviewed as quickly as possible. Those protests help push FDA, Congress and the biopharmaceutical industry to work together to shorten review times. As other speakers have noted today, PDUFA was created to augment the staffing and funding for the review of new drug applications and meet urgent patient demands for more timely approvals of life-saving medicines. PDUFA continues to play a critical role in strengthening the FDA's ability to ensure the ability of these safe and effective medicines for patients. Since the first PDUFA, the majority of newer medicines are now approved first in the United States, including close to 70% of new medicines in 2024 alone. Overall, PDUFA has helped enable timely access to more than 1000 novel drugs and biologics, including treatments for cancers, cardiovascular disease, neurological conditions, and rare diseases.

00:51:15 The user fee funding provided through PDUFA combined with sufficient congressional appropriations allows FDA to ensure safe and effective medicines are available while helping support FDA as the global gold standard for regulatory review. The program has allowed the agency to keep pace with scientific advancements, meet clearly defined performance goals, and continue protecting public health while encouraging innovation. These critical resources enable the review of complex new treatments while ensuring greater efficiency, accountability, and scientific rigor. The program has brought greater predictability to sponsors through regulatory guidance, improved communication and engagement with the FDA, and advanced new tools and approaches to streamline drug development, including things such as adaptive trial designs and the use of real world evidence and digital health tools, all of which have resulted in faster patient access to transformative medicines.

00:52:13 Going forward, it's important that all stakeholders work together to further build on the success of previous PDUFAs to allow for continued support of FDA's vital role in medical product review. PDUFA VIII can help ensure US drug development and review processes are timely, consistent, and rooted in sound science. This includes ensuring that the FDA Human

Drug Review Program continues to do the following: serve as the Global Gold Standard Review and the US authority over regulatory decision making on safety and efficacy of medical products. Advance decisions that are patient-centric, evidence-based, and take into consideration the full range of current scientific knowledge and technological progress. Adhere to clear, transparent established review timelines that meet or exceed current PDUFA timelines while prioritizing essential review activities. Foster predictability and consistency for sponsors to understand regulatory expectations. Facilitate the most timely and effective reviews. Ensure supply chain security and work with sponsors to help ensure a steady supply of medical products. Embrace new methods in medical product development appropriately and consistently across modalities and therapeutic areas. To speed up and reduce the cost of development, submission and review. Apply regulatory flexibilities that align to broad patient needs while weighing the benefits and risks of medical products. Ensure regulatory review is driven by and assessed against metrics-based outcomes, including key performance indicators, public reporting of relevant review timelines and accountability measures. And finally, engage directly and continually with the public and relevant stakeholders to provide proactive, timely, and accessible information on regulatory processes and approval, as well as emerging safety information to maintain the public trust.

00:54:10 PDUFA VIII can also build on specific initiatives included in previous PDUFAs that are intended to help provide greater efficiency, transparency, and accountability in the Human Drug Review Program. This includes pulling through prior PDUFA commitments and translating previously funded regulatory science initiatives and pilots into practice. PDUFA VIII can also focus on facilitating first cycle review of new applications and related performance goals to expedite availability of new medicines. The program should also be used to help FDA optimize available staffing and resources by supporting new efficiencies in the Human Drug Review Program and streamlining regulatory review processes.

00:54:50 In conclusion, medicines in the biopharmaceutical pipeline provide hope for potential future treatment options for patients who have not found success with existing therapies. The US leads the world into the introduction of new medicines thanks in part to the FDA's Human Drug Review Program and the supportive resources provided by both congressional appropriations and industry user fees. PDUFA VIII should be used to help ensure FDA remains the global gold standard for regulatory review, while helping bring more innovative medicines to patients in need. PhRMA looks forward to working with FDA, patient groups and other stakeholders to advance our PDUFA VIII agreement that strengthens America's world leading innovation ecosystem to address our most pressing health challenges. Thank you very much for your time.

00:55:53 **Nana Adjeiwaa-Manu:** Thank you, Kristy. We'll now take a brief break before continuing with our public common portion of the meeting. We'll reconvene in 15 minutes.

00:00:38 **Nana Adjeiwaa-Manu:** Hello, everyone. Welcome back to our PDUFA public meeting. As a reminder, if you experience technical issues during the webcast, please type your issue into the Q&A or email PDUFAreauthorization@fda.hhs.gov. Also, please keep in mind that you can submit comments to a public docket that will be open until August 14th. We encourage everyone to submit their perspectives to the public docket for FDA review. You can find a link to the public docket in the Q&A. Before the break, we heard from FDA and regulated industry. Our next session is dedicated to public comment. Before this meeting, FDA invited everyone who registered for this meeting before June 16th to send an email indicating if they would like to provide public comment at the meeting. Today, 19 people will provide public comments on the perspectives of patients, consumers, healthcare professionals, scientific and academic experts, regulated industry and others. Each speaker will have three minutes to provide their comments. It's my responsibility to notify speakers when they have reached their time limit. I'll invite each participant to speak one at a time. Our first speaker is

Juliana Reed from Biosimilars Forum. Juliana is joining us virtually. Juliana, you may unmute and begin when you're ready.

Public Comment

00:02:10 **Juliana Reed:** Thank you and thank you for the opportunity to speak today, but most importantly, thank you to all the people at the FDA who support the review and approval of the biosimilars in the US. We appreciate all the work you do. I'm Julie Reed, I'm the executive director of the Biosimilars Forum, the Trade Association of the biosimilars industry here in the US. While the biosimilars User Fee Program will not be negotiated until after the PDUFA User Fee Program is finalized, it's important that during PDUFA careful consideration is taken to any decisions that will impact the BsUFA program and be communicated to our industry. This year we're celebrating the 10th anniversary of the first biosimilar approved in the US, and today we have 71 FDA approved biosimilars in the US.

00:03:09 Right now, the US has created over $56 billion in savings and we have the opportunity to increase those savings to over $200 billion in the next 10 years, if we can continue to develop biosimilars in an efficient manner that reflects the scientific expertise of the OTBB and our industry. Today, there is a biosimilar void in which less than 15 of the over 100 brand biologics will be developed as biosimilars. Today it takes seven to nine years and over $200 million to develop a biosimilar and the market is not working. Now is the time to evolve the review process inside the FDA and to improve efficiencies so that our industry can continue to be viable, and our companies and the patients can continue to have biosimilars and reduce the cost of healthcare in the US. Thank you.

00:04:16 **Nana Adjeiwaa-Manu:** Thank you, Juliana. Next, we have Kaylin Bower from On a mission from multiple sclerosis. Kaylin is also joining us virtually. Kaylin, you may unmute and begin when you're ready.

00:04:31 **Kaylin Bower:** Good morning and thank you for taking the time to hear me speak and give my public comments as the Founder and Director of a patient advocacy organization that focuses on multiple sclerosis. I was originally going to talk about an issue regarding multiple sclerosis this morning, but I changed course at the last minute. So, one of the questions we were told we could address is regarding current features of PDUFA that could be or should be reduced or discontinued, and we heard Commissioner Makary this morning talk about the gold standard being associated with safeguarding the public. So, in this vein, I would like to speak quickly and hopefully succinctly about the provision of accelerated approval that is connected with PDUFA. I would like to use the FDA's approval of a drug for Duchenne muscular dystrophy called ELEVIDYS as my very short case study. This was approved by the FDA despite the fact that the clinical review team did not recommend approval. That conclusion was overridden by the current-- At the time, Dr. Peter Marks the Director of CBER.

00:05:44 Just very recently, last month, June 24th, the FDA issued a safety communication. Very, very unfortunate news that there were deaths of two young patients who had taken ELEVIDYS that were non-ambulatory, that passed away and their deaths were believed to be attributable to their taking of ELEVIDYS. So, this brings me to these points regarding accelerated approval that pertained to the multiple sclerosis community, as well as all other patient populations and communities. Will future FDA accelerated approval be like ELEVIDYS and could they possibly have the same outcome? Will they appear to cause more harm than good? That was the case with ELEVIDYS. And the argument of the FDA following the gold standard of science and evidence, and scientific rigor is questionable in some of these approval decisions. There is concern in the patient advocacy community that some provisions connected to

PDUFA such as accelerated approval appear to have possibly lowered the bar for the substantial evidence of effectiveness that is a statutory requirement. This is obviously very debatable, but again, in conclusion, I would just like to represent the views of my organization and our members that we have concerns about accelerated approval and some of the outcomes of some of the FDA's approval decisions where accelerated approval was utilized. Thank you.

00:07:14 **Nana Adjeiwaa-Manu:** Thank you, Kaylin. Our final virtual speaker is Irene Ulrich from the Center for Science in the Public Interest. Irene, you may unmute and begin when you're ready.

00:07:26 **Irene Ulrich:** Thank you. Good morning and thank you for the opportunity to speak today. I am a Senior Policy Scientist at the Center for Science in the Public Interest, a consumer advocacy organization that has worked to advance public health for over 50 years. As FDA begins negotiations for PDUFA VIII, I want to highlight two points for consideration. First, we are concerned that PDUFA will be used to weaken FDA's longstanding substantial evidence standard for drug approval, as Kaylin just mentioned. The standard has already been weakened over time through the PDUFA reauthorization process. For example, the FDA Modernization Act, which reauthorized PDUFA in 1997, allowed approval of some products based on a single adequate and well controlled investigation instead of the accepted practice of requiring two studies. Recent statements from HHS leadership, including Secretary Kennedy and Deputy Secretary Jim O'Neill suggest support for further loosening of effectiveness requirements, perhaps even approval of products before effectiveness is established.

00:08:27 At FDA, Commissioner Makary has emphasized accelerating cures, which appears, based on an assumption, that promising early study results will translate into actual clinical benefit. The data show this is often not the case. A 2014 study found that only one in 10 investigational drugs entering Phase I are ultimately approved, and we heard this highlighted by PhRMA's

presentation this morning. Nearly 40% of drugs that reach Phase III are never submitted for approval at all. This is further supported by a 2017 FDA report documenting 22 cases where positive Phase II study results were not confirmed in Phase III and two drugs even worsened the condition they were intended to treat. Meanwhile, and as others have noticed, FDA is already the fastest major regulator in the world. Over half of all new drugs in the world are first launched in the US with FDA's review times on average being two to four months shorter than peer agencies. Yet PDUFA has historically been a vehicle to introduce expedited programs and pilots that risk diluting the substantial evidence standard and observational data suggests that approval through these pathways may be associated with increased post-marketing safety related actions. We urge FDA not to add any more in PDUFA VIII. Speed should not come at the expense of scientific rigor.

00:09:48 Second, and as we heard from industry earlier, FDA must improve transparency. Many documents are vital to public health and are often delayed or only accessible through FOIA requests. Even when disclosures are required, timelines are inconsistent. For example, approval packages for efficacy supplements often take months or years to appear online, if at all. To truly fulfill its stated commitment to radical transparency, FDA should proactively release more of this information and reinvest in FOIA capacity either through appropriated or PDUFA funds. Doing so is not a bureaucratic inefficiency, it is a foundational step toward restoring transparency and rebuilding public trust in the agency. Thank you.

00:10:29 **Nana Adjeiwaa-Manu:** Thank you, Irene. The remainder of our public common speakers are joining us in person. Our next speaker is Patricia Kelmar from US Public Interest Research Group. Patricia, we look forward to your comments.

00:10:44 **Patricia Kelmar:** Thank you. I'm Patricia Kelmar. I'm with US PIRG, the Public Interest Research Group. We're a 50-year-old consumer advocacy organization working to achieve

high value healthcare, which means good cost and great quality. The FDA's mission is to protect health and President Trump has committed to increased government transparency. The PDUFA reauthorization process should meet both of these goals, both putting public health and safety at the center of new drug approvals in a fully transparent process. We urge you to actively seek out and value the public input as you build the new iteration of user fees.

00:11:28 First, expand and ease public engagement in new drug approvals. Although past commitment letters have mentioned better patient engagement, the next User Agreement should make it central. You're under increasing industry pressure to move swiftly to approve new drugs, but speedy approvals must be balanced against the public's desire and FDA's mission to ensure safety and efficacy of new drugs before and after they hit our pharmacy shelves. Significantly broaden who's at the table and implement less intimidating ways than this for the public to express their concerns about new drugs and get answers to their questions. You can invite these new voices by working with other agencies such as HHS and CMS, regional leaders, the Consumer Product Safety Commission, and other agencies that have really strong public outreach and stakeholder lists. Conduct outreach through community and faith leaders and use normal communication methods, emails, public service announcements, and social media to invite regular engagement. Utilize surveys and informal community listening sessions. When seeking public input, please use plain language. These slides were filled with acronyms that the public just can't engage in and understand. Please pose clear questions so regular folks, caregivers and patients can engage easily. Current methods, such as registered notices, formal comments are intimidating and they exclude a lot of people who have important things to say.

00:13:05 Second, improve the public's ability to be relevant during the PDUFA process. People can't weigh in on things that they don't know about. The public needs to understand what's happening in FDA's discussions with industry. How else can we stand up for the public interest? Timely, complete summaries of private meetings must be shared before stakeholder

meetings. I understand that these deadlines that were listed on these have passed away oftentimes where we don't get the information in a timely way to react during the PDUFA process. We want to come prepared to engage constructively and those summaries should use plain language and offer sufficient context so we understand the elements at stake in these private negotiations. And because patients, caregivers, and even their physicians can't attend workday meetings, we need alternative ways to hear and provide input.

00:13:59 Finally, more user fees should be directed to post-market monitoring and new drug applications should include a company's past history of post-market compliance. No drug company that's failed to follow through on confirmatory trials for their other medications should be granted the benefit of accelerated approvals for their next medication. Patients who take these expedited drugs place their trust in a system that should at a minimum track and learn from their experiences. We're eager to collaborate with you so the public as a genuine partner can be assured safe and effective treatments with full transparency and accountability. Thank you.

00:14:43 **Nana Adjeiwaa-Manu:** Thank you, Patricia. Next, we have Amanda Berhaupt from the National Center for Health Research. Amanda, you may approach the podium.

00:14:54 **Amanda Berhaupt:** Thank you. Good morning. I'm Dr. Amanda Berhaupt, Health Policy Director at the National Center for Health Research. I appreciate the opportunity to speak on behalf of our nonprofit think tank. At NCHR, we scrutinize the safety and effectiveness of medical products and we do not accept funding from companies that make those products or entities with a financial interest in our work. Prior to my current position, I worked here at the FDA and for the United States Senate. I want to begin by thanking Commissioner Makary for his remarks about prioritizing patient safety when discussing user fees at the GDUFA meeting last Friday. The appropriated funds for FDA are not sufficient to support all of its critical

work, so we understand the agency needs user fees to get safe and effective medical products to market in a timely manner. User fees are vital to ensure reviewers have subject matter expertise, institutional knowledge, adequate time, and uninterrupted access to the FDA library with peer reviewed research among other scientific resources.

00:15:56 User fees have mainly supported faster reviews and more frequent meetings between the FDA and the sponsors to address concerns about their applications. I want to emphasize that this is not what's most important to patients. Their greatest concern is to have access to safe and effective medical products to treat, maintain, and promote their health. With a renewed focus on transparency at FDA, will patients and healthcare professionals be represented at user fee negotiations? At minimum, they deserve to watch the negotiations virtually and in real time if they are not participating. In the past, summaries and minutes of negotiations have been too vague, which has prevented key stakeholders from providing input.

00:16:46 To date, the performance goals in the commitment letters have outlined metrics for meetings and timelines and pre-market reviews. These goals benefit industry and may indirectly benefit patients as well, but are not patient-centered and do not focus on safety or efficacy. We urge the agency to include performance goals with metrics on quality post-market surveillance, including confirmatory studies with clinically meaningful outcomes. This is especially important when drugs are approved based on data from short-term studies with a small sample size or based on surrogate endpoints instead of measures for how a patient feels functions or their overall survival. Patient advocates, public health researchers and professionals without industry ties need representation during negotiations to ensure that there are performance goals that directly benefit patients and consumers.

00:17:41 The public's trust in the FDA has been eroded. PDUFA needs to show that user fees will do more to ensure that drugs are safe and effective in ways that matter to patients. Speed should

be secondary because when drugs are ineffective or unsafe, patients lose confidence in their relationships with their doctors and the FDA, and they seek advice from other sources like social media and where they may find erroneous and harmful advice. Thank you.

00:18:11 **Nana Adjeiwaa-Manu:** Thank you, Amanda. Next, we have Mary Hilley from Humane World for Animals. Mary, please approach the podium.

00:18:25 **Mary Hilley:** Hello, my name is Mary Hilley and I'm speaking on behalf of Humane World for Animals and Humane World Action Fund, formerly known as the Humane Society of the United States and Humane Society Legislative Fund. Thank you for the opportunity to comment on the reauthorization of PDUFA. We will be submitting more substantial written comments so I will be briefed today. We have been pleased to see the recent efforts by FDA to advance non-animal testing methods through the publication of the roadmap to reducing animal testing and preclinical safety studies, as well as the recent workshop co-hosted with the National Institutes of Health to reduce animal testing.

00:19:05 The reauthorization of PDUFA provides an opening to proactively advance some of the agency's recommendations as outlined in the roadmap and we encourage FDA to consider how best to do this. For example, we recommend that FDA consider a way to prioritize review of investigational new drug applications that include data from non-animal test methods. This aligns with one of the recommendations in the roadmap to consider incentives for companies that utilize NAMs. For instance, fast track meeting requests and regulatory reviews. Incentivizing submission of non-animal data will not only encourage more drug sponsors to utilize them, but also help reviewers to become more familiar with non-animal data. Toward that end, we also encourage PDUFA fees to be directed towards training FDA reviewers on non-animal approaches. Regulatory scientists need ongoing training and skills to enable them to effectively and confidently assess non-animal data derived from complex in-vitro models

and artificial intelligence for example. This request perfectly aligns with one of the roadmap recommendations that says, in order to consider-- In order to successfully transition from animal testing to non-animal approaches, FDA must ensure its reviewers and scientists are well-versed in NAM technologies and open to novel types of evidence. It further states that the agency will commit to providing training workshops for staff. This would be a good use of PDUFA fees.

00:20:42 We also encourage FDA to utilize PDUFA VIII as an opportunity to encourage transparency and data sharing. Reluctance to openly share data has long been recognized as a significant issue that slows drug development. The roadmap encouraged FDA and other agencies under ICCVAM to compile shared databases of toxicology and immunogenicity that include both animal and human data from various sources and called out FDA's vast amounts of data that could be used to inform AI models and to conduct retrospective NAM analysis.

00:21:16 Initially, PDUFA VIII fees could be dedicated to the creation of an internal database of non-animal data that FDA reviewers can use for training purposes, but ultimately, we see this being extended to become the open access repository described in the roadmap. Finally, we encourage FDA to utilize PDUFA VIII fees to create guidance for NAMs. This idea included in our May, 2024 citizen petition was also called out in the roadmap that FDA will update or create guidance documents that articulate how NAMs can be used in various development programs. PDUFA VIII offers the ideal opportunity to develop this guidance that specifically provides information about how NAMs acceptance will help drug sponsors more easily and incorporate these approaches into their evaluations and submissions, and provide additional clarity about how these new approaches can be used.

00:22:11 Thank you for your time and attention. Humane World for Animals and Humane World Action Fund would welcome the opportunity to work with FDA to help advance non-animal

methods and encourage the agency to use PDUFA VIII as a vehicle for progressing the goals outlined in the roadmap. Thank you.

00:22:28 **Nana Adjeiwaa-Manu:** Thank you, Mary. Next, we have Annie Kennedy from EveryLife Foundation for Rare Diseases. Annie, please approach the podium.

00:22:46 **Annie Kennedy:** Good morning. My name is Annie Kennedy and I'm honored to be here today on behalf of the EveryLife Foundation for Rare Diseases. The US Rare Disease community comprises an estimated 30 million Americans, more than 50% of whom have pediatric onset conditions with significant unmet need. We are grateful to FDA for the rigor and regulatory flexibility you would deploy when evaluating safety and efficacy of life saving therapies.

00:23:17 Just as previous user fee agreements and the recent establishment of the Rare Disease Innovation Hub have yielded great strides for the rare disease community, we have identified four key areas of opportunity to advance rare disease therapy development as we look to PDUFA VIII. They include: one, expanding PDUFA VII pilot programs. Thanks to the agency's swift implementation on pilot projects initiated in PDUFA VII, such as the START and RDEA pilot programs improvements are occurring both in processes to advance innovative endpoints and in the speed and structure of regulatory review. PDUFA VII also led to comprehensive NASEM and GAO studies related to rare disease. Looking to PDUFA VIII, we hope the opportunities stemming from these investments will be applied to PDUFA VIII considerations. Further, we urge the dissemination of data, case studies and other learnings resulting from the PDUFA VII pilots.

00:24:22 Second, evolving patient-focused drug development by co-creating processes that build upon the impact of the PFDD movement we can transform PFDD meetings from a single point in time to a pathway for ongoing engagement as the ecosystem shifts, thereby enhancing the

transparency of how patient experience data is used in regulatory decision making. PDUFA VIII could be transformative for the PFDD movement.

00:24:53 Third, the establishment of the science focused drug development meeting mechanism. Building on the success of the externally-led PFDD workshop model, the establishment of a new mechanism for community engagement around scientific and regulatory challenges will provide an opportunity for developers, regulators, scientific experts, and patient advocates to systematically discuss specific development considerations in particular rare diseases.

00:25:23 And finally, innovations and post-market data collection. More than 250 drugs have been approved through the accelerated approval pathway. Still, for many rare disease communities, the pathway remains out of reach despite being one of the only viable routes of bringing a treatment to market. To better achieve the intent behind the accelerated approval pathway and to ensure we learn from real world applications of a treatment, we must innovate regarding how FDA uses post-market data, this includes opportunities to enhance the collection and application of real-world evidence within the post-market environment to include the deployment of digital tools and technologies.

00:26:08 Thank you for considering the concerns of patients and community partners. We look forward to continuing to collaborate alongside you to advance PDUFA VIII that catalyzes progress in the rare disease therapy environment. Thank you.

00:26:22 **Nana Adjeiwaa-Manu:** Thank you, Annie. Next, we have Pamela Gavin from the National Organization for Rare Disorders. Pamela, please approach the podium.

00:26:40 **Pamela Gavin:** Good morning. It's great to be with you today. My name is Pam Gavin. I'm the CEO of the National Organization for Rare Disorders, also known as NORD. NORD is the longest standing advocacy organization for the one in 10 Americans living with rare

diseases. As an independent 501C3 nonprofit, we're dedicated to serving individuals with rare diseases and the organizations that support them, of which there are 355 and about members of NORD. Over 95% of the known 10,000 rare diseases lack an FDA approved treatment. Continued investment in FDA's regulatory processes is essential for addressing these unmet needs. FDA's User Fee Programs have successfully supported efficient product development and review that meets FDA's gold standard while accelerating treatments for rare disease. I'll address three key areas NORD supports incorporating into PDUFA VIII to build upon prior successes.

00:27:50 First, NORD supports earlier and more frequent patient engagement to further the shared goal of efficiently bringing safe and effective treatments to market. FDA should build upon the existing patient-focused drug development framework to provide clarity about how and when sponsors may incorporate patient organizations into their development programs. Externally-led PFDD meetings should occur earlier to best support successful drug development. FDA should utilize patient listening sessions to proactively educate and prepare patient communities for these engagement opportunities. NORD, with its unique experience facilitating these meetings, we stand ready to support FDA in this important work.

00:28:38 Second, we encourage FDA to fully resource the work of the Rare Disease Innovation Hub. The hub can facilitate meaningful improvements in rare disease, therapeutic development and review through collaboration across the agency, thereby encouraging regulatory science developments and alignment between centers. The hub also serves as an important role in engaging with partners outside of the agency. If appropriated-- If appropriately resourced, excuse me, the hub could help facilitate efforts with partners such as NORD’s Rare Disease Centers of Excellence to develop rare disease biomarkers and endpoints, and leverage diverse and decentralized sources of real world data.

00:29:25 Finally, we must make progress in addressing the needs of patients with rare diseases affecting very small patient populations through more systematic and proactive use of existing authorities and regulatory flexibilities. Challenges, including the infeasibility of conducting randomized controlled trials in many cases are significant and warrant a solution. NORD supports a right-sized approach that fosters innovation and accelerates treatment access while meeting FDA's evidentiary gold standard.

00:30:08 I would be remiss if I didn't emphasize the importance of a well-resourced FDA in supporting both existing processes and programs as well as fueling innovation to sustain the US' leadership in rare disease treatments. I want to thank the FDA for convening this meaning and its commitment to partnering with patients throughout the drug development process. NORD stands ready to collaborate with FDA, industry and other stakeholders to develop PDUFA VIII commitments that support those impacted by rare diseases. Thank you.

00:30:50 **Nana Adjeiwaa-Manu:** Thank you, Pamela. Next, we have Keith Desserich from the Cure Starts Now Foundation and the Pediatric Brain Tumor Consortium Foundation. Keith, please approach the podium.

00:31:07 **Keith Desserich:** Thank you for the opportunity to provide input on the reauthorization of the Prescription Drug User Fee Act. I also want to applaud the FDA for its new directions and focus on rare diseases. I'm speaking not just as an advocate or an organizational leader, but as a father. My daughter Elena was diagnosed with a type of cancer called diffuse intrinsic pontine glioma at the age of six. Like thousands of families before us, we were told that there was no hope, there were no drugs approved for this cancer, no clinical trials and no treatment. We were told to just go home and make memories. They told us we had less than five months. Five months. Sadly, my daughter understood this and she knew that there was nothing that we could do. Each day we would watch this horrible cancer take something else from her. First, it

was her sight, then her voice, then her ability to walk. Eventually, it took her ability to breathe and to swallow. All the while her mind remained intact. It's a particularly cruel disease. Still, she's not the first child, nor will she be the last. I hope that through these comments, I, as a father that has lost my child, can represent the magnitude of the rare and terminal diseases that affect our children, for they must be treated differently. In the end, all we wanted was hope. Sadly, we were offered none. Elena died nine months later without a single targeted FDA approved treatment available to us, and that was nearly 20 years ago, but unfortunately nothing has changed.

00:32:59 In an effort to change this, my wife and I have built the world's largest foundation focused on these aggressive pediatric tumors and have helped fund and create nearly 200 trials to help close this gap. This is why I value good research and I treasure trial safety. Still, we are just one part of the process and we need the help of the FDA and the support from initiatives like PDUFA to save our children fighting rare and terminal cancers. This is an opportunity we cannot miss.

00:33:31 DIPG brain cancer is universally regarded by pediatric neuro-oncologists as one of the most aggressive and devastating childhood cancers. About 300 children in the US are diagnosed each year. Median survival remains under one year. Sadly, fewer than 10% survive beyond two years. Yet, in four decades, little to no therapies have earned FDA approval for DIPG brain cancers, and this is for a cancer that is often referred to as a homerun cure cancer, meaning that if we can unlock effective treatments here, the insights may ripple across all of oncology. I can see no better place to focus our attention and our investment than a cancer that may offer us a cure for all.

00:34:17 We are not lacking an interest, scientific promise or community engagement. The reality is that the system is not built for rare terminal and pediatric diseases. Traditional drug pathways

rely on large trials, extended timelines and endpoints that don't apply to ultra rare, fast moving cancers. While I reserve my specific recommendations for the written comments, I want to emphasize in the verbal comments that children like my daughter don't have the luxury of time. They need innovation now and they need big changes like the cure for cancer that we have to do by thinking big. We thank the FDA for its ongoing commitment to innovation and we stand ready to collaborate in building a system that offers real hope, real options for children that are fighting these diseases. Thank you.

00:35:09 **Nana Adjeiwaa-Manu:** Thank you for your comments, Keith. Next, we have Alexander Naum from Generation Patient. Alexander, please approach the podium.

00:35:22 **Alexander Naum:** Hello, my name is Alexander Naum and I'm the Policy Manager at Generation Patient, a patient advocacy organization representing the 25 million young adult patients living with chronic and rare diseases in the United States. Generation Patient is independent of all private healthcare industry funding. We hope that FDA will offer more seats to the table for independent patient advocacy groups like ourselves. In order to foster transparency in PDUFA reauthorization negotiations, we ask that the public have access to the commitment letter during all stages of negotiations so we have the opportunity to provide public comments. In addition to ensuring the public's participation in these negotiations, I want to emphasize that over half of all young adults manage at least one chronic condition, and that number has only increased in recent years. Young adults must be distinguished as an age group separate from pediatrics, adolescents, and older adults as FDA is considering reviews for products and new initiatives to aid in the development of new drugs.

00:36:17 As young adult patients, we have distinct physiological differences. This includes differences in hormonal shifts, metabolic processing, and varying immune responses, which may affect the clinical efficacy of drug interventions, or at worse lead to unexpected adverse events.

Unfortunately, clinical trial and post-clinical trial data often aggregates young adult patients with other age groups or fails to have adequate young adult participation. This is problematic for trials concerning conditions such as inflammatory bowel diseases where the peak onset is now an adolescence.

00:36:51 In addition, we ask FDA to scrutinize adult participation in the drug clinical trial process for conditions that impact young adult patients and emphasize the importance of including data that cannot help identify potential side effects that are unique to our age group. For example, when we're viewing FDA's adverse events reporting system, the young adult age group is aggregated together with other age groups, reporting data between the ranges of 18 to 64. For post-marketing commitments, we ask that FDA consider requiring public reporting that addresses the potential for differing adverse events in young adults.

00:37:25 One step for achieving this is by finalizing the agency's guidance and diversity action plans. Another step is requiring trial sponsors to submit clinical trial diversity action plans to FDA ahead of key pivotal studies, as well as including in the final guidance considerations for recommended age groups and intended enrollment targets that specifically include young adults where clinically relevant. FDA should also include analysis of age-related data and integrated review documents for new drug applications. Finally, we ask that FDA commit to promoting drug development that include young adult populations, including through public meetings and other opportunities. Thank you for your time and for amplifying the current and next generation of patient priorities in PDUFAs reauthorization.

00:38:10 **Nana Adjeiwaa-Manu:** Thank you, Alexander. Next, we have Amalia Guinee, from NYU Langone MS Center. Amalia, please approach the podium.

00:38:23 **Amalia Guinee:** Hello all and thank you so much for having all of us here today and hearing our comments and our stories. My name is Amalia Guinee, and over the summer of

2018, I suddenly became paralyzed at only 16 years old. My parents watched on as their bubbly, happy, active girl, lost the ability to move, open her eyes and speak. After spinal taps, MRIs, CAT, PET scans, and any other tests that you can think of, it was determined that I have multiple sclerosis, something no one ever expects to hear of a child. Thanks to the many doctors, especially Dr. Lauren Krupp and nurse Jennifer Abate out of NYU Langone, I'm here before you today. But finding a treatment that would work for me was incredibly difficult. The main reason being that most of the options were not designed for children like me. They were designed for adults.

00:39:23 Every new treatment we tried felt like a shot in the dark hoping it would make me better instead of sending me backwards. After three months in the hospital, something finally stuck and worked, I could finally begin to live a normal life. But I was lucky. Some kids don't get the somewhat immediate turnaround. I appear before you today as a somewhat normal 23-year-old because of my treatments. Some kids have to wait to get that medication that's going to let them live life like a normal child. Some kids have to wait in hospital rooms while their friends start school, hang out, play sports, and just live life like normal kids while a trial awaits to be approved. Sara Loud, who's appearing on Zoom today knows this reality all too well. She's with the Accelerated Cure Project, a nonprofit working to speed up research and fight for patients with MS. They recently submitted a comment to this docket highlighting real actionable ways you can help kids who are still waiting so they can have safe proven options, so they can just be kids.

00:40:30 Most of these drugs are known to be safe for adults. It's absolutely heartbreaking that children and their families are forced to wait eight to nine years for life-changing drugs to be approved. Insurance and money should not be the first priority, the children need to be. There's absolutely no need for these long wait times. I understand even with my minimal knowledge that medicine needs to be tested before usage. I get that, but you have to understand that a kid

only gets one childhood and that timeframe is in your hands. All we ask is that you restructure the approach for trial drugs for pediatric patients. Thank you.

00:41:14 **Nana Adjeiwaa-Manu:** Thank you, Amalia. Next, we have Janet Krommes from Doctors for America. Janet, please approach the podium am

00:41:31 **Janet Krommes:** Thank you, Director Kish and valued FDA staff for allowing us to come and speak before you today. My name is Janet Krommes, I am the Chairperson of Doctors for America's FDA Task Force. Doctors for America is an organization that is nonpartisan, composed of 27,000 physicians. We take no industry funding and we teach physicians to be able to be the voice in the room for our patients. I speak today first and foremost as a clinician. Having started the practice of medicine before the first PDUFA, I have seen two profound changes.

00:42:08 First, the explosion of new groundbreaking medical products and drugs that have been no less than miraculous, but at the same time the shrinking of evidentiary standards for approval. Our main concern is that the quantity and rapidity of drug approvals is a problem for clinicians and patients when approval studies do not answer the two basic questions, is it truly safe enough? Is it truly better enough? An example of this problem is Xeljanz, a JAK inhibitor that was improved for rheumatoid arthritis. It was eight years before the major risk factors were determined, and that was three years after the full implementation of the Sentinel Initiative.

00:42:48 PDUFA VII improves on the post-marketing risk management through expansion of REMS and also increased reliance on the Sentinel Initiative. We are concerned about funding cuts particularly to Harvard where Sentinel Initiative is based as it may affect the entire Sentinel network. The initiative has important and ongoing work to address current limitations, which include outcome identification and semantic interoperability, and we'd also like to see the

initiative continue to make progress to provide efficacy data, which is as clinicians an important goal.

00:43:26 Surveillance measures can be relied on, but they take time. Clinicians must prescribe, or avoid prescribing as I did with Xeljanz, drugs before those signals are known. Clinicians must decide based on smaller, shorter, often single arm studies or surrogate marker results. For that reason, there will be instances when there still is a need for confirmatory clinical trials and other measures to reduce risk to patients. PDUFA has increased the use and focus on real world evidence, but there are inherent biases such as selection bias and others that can incorrectly influence conclusions. Clear guidance and establishment of best practices is evolving, but critical questions such as access to patient level data remain to be addressed and more direct publicly available feedback is needed on the use of real world evidence when it is applied to regulatory decisions.

00:42:34 PDUFA VII increases the interactions between sponsors and the FDA at all stages of the approval process. This is intended to save time and resources, but can result in an even greater industry influence at the expense of other stakeholders. We agree with the concept of improved communication, but approval decisions should be transparent and should engage outside experts and stakeholders. In terms of changes to the current fee structure, we'd like to see more emphasis on transparent communication at all phases of product development and also more investment in post-marketing surveillance. Thank you again for the opportunity to bring the views of Doctors for America to this forum.

00:45:09 **Nana Adjeiwaa-Manu:** Thank you, Janet. Next, we have Dathan Hamann from Saguaro Dermatology and Contact Dermatitis Institute. Dathan, please approach the proteome.

00:45:20 **Dathan Hamann:** Good morning, everybody. PDUFA team members, thank you for the opportunity to speak today. My name's Dr. Dathan Hamann, and I'm a dermatologist and I'm

here to call attention about how PDUFA fees and the process of regulating patch test diagnostic allergens affects my patients. Contact dermatitis is a chronic inflammatory skin disease. It is one of the most common reasons that Americans seek dermatologic care. Allergic contact dermatitis is a type IV hypersensitivity reaction and it resembles a poison ivy-like eruption with intensely itchy and inflamed skin. It can cause substantial impairment in quality of life, including chronic itch, chronic pain and loss of productivity and work, but atypical versions of allergic contact dermatitis may mimic other inflammatory skin diseases such as atopic dermatitis, and this can lead to a misdiagnosis. Failure to diagnose correctly these patients may lead to unnecessary, long-term systemic treatment with immunosuppressants or immunomodulatory drugs.

00:46:28 Under diagnosis of allergic contact dermatitis represents substantial patient harm. When patients are accurately diagnosed and can avoid their allergens, allergic contact dermatitis is one of the very few chronic inflammatory skin diseases that is curable. But our ability to diagnose allergic contact dermatitis is being undermined by a regulatory crisis. Patch test allergens are not therapeutic substances. They're diagnostic and they're not administered orally or parenterally, but they are intended to elicit an immune reaction. Thus, they're biological products as defined in Section 351 of the Public Health Service Act. The American Contact Dermatitis Society recommends for routine testing at least 90 allergens. There are only 35 allergens that currently have CBER licenses and enjoy FDA oversight. Thus, physicians who perform patch testing must routinely use unlicensed allergens and no new diagnostic patch test allergens have been approved by FDA in over a decade. Why is this? There are two main reasons. The first is that there are disproportionate requirements for approval of these low risk and high benefit allergenic diagnostic products, and second are recently added PDUFA fees.

00:47:51 The framework for regulating biological products, like a therapeutic drug that alters the immune response is simply not suitable for a patch test allergen, where dozens of unique

allergens are applied to the skin on one patient on one day. Furthermore, allergenic products were historically exempt from PDUFA associated fees because their public health value was high, their risk was low, and their profitability was low. However, new fee requirements for all allergenic products were introduced in 2022, and the application of these to diagnostic allergens makes their future in jeopardy. Today, I urge the team to reinstate PDUFA fee exemptions for patch test diagnostic allergens, and start a process with the American Contact Dermatitis Society to adjust the requirements for approving future past patch test allergens so that they can be proportional to their high value and low risk. My patients deserve a diagnosis. Thank you.

00:48:52 **Nana Adjeiwaa-Manu:** Thank you, Dathan. Next, we have Zoe Bilis from Biocom California. Zoe, please approach the podium.

00:49:04 **Zoe Bilis:** Good morning and thank you to the FDA for the opportunity, excuse me, to share our perspectives on the reauthorization of PDUFA. My name is Zoe Billis and I'm the regulatory policy manager at Biocom California, the largest trade association representing the entire life science ecosystem of California. Our membership encompasses biotech, pharmaceutical, medical device and diagnostics companies of all sizes, as well as research universities and institutes, CROs, investors and service providers. Biocom California has always been a strong supporter of the FDA's mission, and we are dedicated to ensuring that the agency has the necessary resources and staff to review and approve lifesaving products for the more than 12,000 life science establishments in our state. The PDUFA program has been critical to improving the timeliness of reviews, supporting innovation in drug development, and enhancing engagement with patients, providers, and the industry at large. PDUFA VII specifically made great strides in advancing the use of real-world evidence and supporting scientific dialogue among many other initiatives.

00:50:15 We believe that PDUFA VIII can build upon this great work by enhancing the following five main areas. Number one, consistency in review practices across FDA divisions. Many divisions within CDER and CBER already employ high quality review practices, but oftentimes sponsors have reported inconsistencies in the feedback received. We recommend strengthening reviewer training by sharing best practices internally and increasing education on the existing authorities and available flexibilities to support a more consistent regulatory approach. Number two, high quality written responses. Reviewer training should also incorporate lessons learned and skills for developing robust written responses. This would enable learnings from one product review to be leveraged in others. Number three, the establishment of milestones and performance goals for substantive labeling comments. We suggest that these milestones establish a timeframe that allows for meaningful labeling discussions to occur between the FDA and sponsors. Number four, increased transparency and communication for inspections. Building upon the PDUFA VII commitments, we suggest including earlier discussions between the FDA and sponsors to determine the timing and sites for inspection. And last but not least, number five. A framework for the utilization and acceptance of primary disease biomarkers as endpoints. In rare disease drug development, the role of primary disease biomarkers is critical to understanding and evaluating the disease process and drug response. While we appreciate that the FDA accepts these biomarkers as endpoints, we recommend the establishment of a widespread framework outlining criteria for their utilization and acceptance.

00:52:10 Thank you again for the opportunity to comment on behalf of Biocom California and its members. Our detailed comments will be submitted to the docket and we really appreciate and applaud the FDA and its staff for their hard work and dedication to ensuring that patients continue to have access to safe and effective therapies. Thank you.

00:52:20 **Nana Adjeiwaa-Manu:** Thank you, Zoe. Next, we have Curt Hamann from Smart Practice. Kurt, please approach the podium.

00:52:43 **Curt Hamann:** Thank you, team PDUFA for the opportunity to share recommendations on the solution needed to ensure the availability of safe, effective, and licensed patch test allergens, a critical priority because 20% of Americans will experience an allergic contact dermatitis in their lifetime. Diagnostic patch test allergens are regulated by CBER because of their intended topical elicitation of an immune reaction that is needed to confirm a contact sensitization. Smart Practice has received 35 allergen licenses by CBER over the last 35 years, far short of the core and extended series that are recommended by the American Contact Dermatitis Society for patients that deserve a diagnosis. In 2022, PDUFA VII removed the fee exemption for allergenic products, a very discouraging discovery by our team as we are the only company that has submitted a type IV patch test application to CBER in the last 30 years. $4 million BLA fees and $400,000 annual maintenance fee per allergen will ensure that there will be no additional submissions made to CBER. The annual maintenance fee itself exceeds the annual revenue of each of these patch test allergens. Patch tests are performed once in a lifetime in a patient to elicit a reaction, used to counsel the patient to avoid the substance and cure their allergic contact dermatitis. A single use diagnostic test has no recurring revenue as there is with a therapeutic drug, which is why over a dozen pharmaceutical companies have exited the patch test market over the last 30 years. The fee exemption needs to be reinstated for the diagnostic patch tests in order to have a future of regulated products in America.

00:54:50 The current CBER requirements for these diagnostics are disproportionate to their low risk and high benefit profile for patients. Requirements need to be differentiated from therapeutic drugs and from biologics. This can best be accomplished by harmonization with medical licenses that have been issued in the European Union. Over 200 licenses have been granted to smart practice in the member states in Europe, the majority by the Paul Ehrlich Institute in Germany.

A key feature to the regulatory requirements, which we believe CBER should adopt, is acceptance of real world data from the literature as sufficient evidence of safety and efficacy. Together with state of the art validated analytical methods and robust stability programs, licenses could be efficiently submitted and reviewed to CBER. We would further recommend the acceptance of GMP certificates issued by the Danish and German authorities to mitigate the CBER expense of duplicate audits.

00:55:52 Finally, a progressive regulatory path forward is needed to preserve diagnostic patch test availability while CBER regulation is pursued in order to prevent a healthcare crisis of undiagnosed patients caused by allergen patch test unavailability in America. Thank you.

00:56:13 **Nana Adjeiwaa-Manu:** Thank you, Kurt. Next, we have Marcia Howard from Consumer Healthcare Products Association. Marcia, please approach the podium.

00:56:25 **Marcia Howard:** Thank you. Good morning. I'm Dr. Marcia Howard, Vice President of Regulatory Affairs and Quality at the Consumer Healthcare Products Association, or CHPA. CHPA is the leading US-based trade association for manufacturers of non-prescription or OTC medicines, OTC medical devices and dietary supplements. The federal register notice announcing this meeting, invited stakeholders to answer four questions and to provide any other pertinent information stakeholders wish to share. Our comments provide relevant information about the process by which PDUFA reauthorization and alignment is achieved.

00:57:07 The consumer healthcare industry currently has no meaningful input on the performance measures, fee and meeting structures, and other criteria that is negotiated during the PDUFA for reauthorization process. Yet, OTC medicines approved under new drug applications are subject to nearly all of the provisions contained in PDUFA. CHPA must be given an equal seat on the industry negotiation team. In the past, our request to join the negotiations have been denied. Our members bring self-care options to consumers to save $7 for the US healthcare

System for every $1 spent on OTC medicines. We are asking FDA to correct this oversight and formally include CHPA in the PDUFA negotiation process.

00:57:56 The consumer healthcare industry is separate and distinct from the pharma industry, and most OTC companies no longer have divisions within the traditional prescription drug companies. For the last 40 years, the norm is for new molecules and strengths to become non-prescription market products to be approved under a new drug application or NDA process, which is funded by the PDUFA system. OTC switches are also fully governed by PDUFA and we bring a unique point of view compared to prescription drugs because our products focus on the consumer as the end user. Given the critical role RX to OTC switch plays in driving public health, it is imperative that the OTC industry is meaningfully included in upcoming PDUFA reauthorization discussions, and CHPA looks forward to FDA assistance with bringing our request to fruition. Thank you for your time and attention.

00:58:59 **Nana Adjeiwaa-Manu:** Thank you, Marcia. Next, we have Gil Roth from Pharma & Biopharma Outsourcing Organization. Gil, please approach the podium.

00:59:13 **Gil Roth:** Hi, I'm Gil Roth. I'm the president of the Pharma & Biopharma Outsourcing Association or PBOA, a nonprofit trade group representing Contract Development and Manufacturing Organizations or CDMOs. CDMOs play a significant role in the US drug supply chain manufacturing an estimated 40% of total prescription finished doses in the US and an even greater share of Drug API and biologic drug substances. Our members provide services to innovator and generic drug companies, large molecule and small molecule products, and cover the largest companies in the world down to the smallest of startups. As we all celebrate the new drug approvals of recent years that PDUFA has brought about, bear in mind that CDMOs have also supported the development of a substantial majority of drugs approved by the FDA over the last decade. And CDMOs actively invest and reinvest in

onshore and domestic capacity more than 7 billion over the last five years alone. Our members and their peers empower innovation by enabling biotech startups to focus on R&D without having to invest in their own facilities, and non-US startups often work with our members to facilitate US launch of their new drugs.

01:00:29 Now, we believe that CDMOs have important ideas to bring to the PDUFA discussion, particularly about inspections of facilities serving multiple sponsors or pending approvals, streamlining processes to more rapidly approve expanded or new capacity and more. For example, developing a process for CDMOs to interact directly with FDA related to specific sponsor filings or cross filings with similar needs. And we'll submit more of these through the docket, and I hope to serve-- PBOA can serve as a resource in these upcoming negotiations. We support a strong PDUFA program that provides a certainty of review timelines, issuance and publication of guidance, especially for new drug modalities and appropriate hiring of drug review and support staff, all to help assure high quality effective medicines reach patients. And while there's been some discussion today and in recent months about adjusting the funding model for PDUFA, discussing financial structure, et cetera, we want to make sure that any changes to that structure don't unwittingly damage the robust infrastructure of facilities and laboratories that the CDMO sector has built to support the US biopharma industry. So, everyone at FDA, thank you for your opportunity or for this opportunity to speak today, and I hope we can be involved in PDUFA VIII going forward. Thanks.

01:01:53 **Nana Adjeiwaa-Manu:** Thank you, Gil. Next, we have Reshma Ramachandran from Yale Collaboration for Regulatory Rigor, Integrity, and Transparency, and Yale School of Medicine. Reshma, please approach the podium.

01:02:10 **Reshma Ramachandran:** Thank you for the opportunity to provide comments on PDUFA VIII. My name is Reshma Ramachandran. I'm a practicing Primary Care Physician at Yale

School of Medicine, where I co-direct the Yale Collaboration for Regulatory Rigor, Integrity, and Transparency. We research the balance that FDA aims to strike between timely access and ensuring that novel medical products are truly safe and effective for our patients and clinicians. Without a doubt, user fees have been instrumental in enabling FDA to have sufficient capacity to review an increasing number of new medical products in a timely manner. Over time, FDA's reliance on and the scope of user fees have also increased substantially. This has raised concerns whether FDA is able to sufficiently negotiate user fee agreements that are centered around patients and not just that of regulated industry. We share these concerns and ideally would like to see FDA have more independence in its funding to ensure that its priorities are aligned with the role of protecting patients and public health.

01:03:06 However, absent a significant increase in congressional appropriations coupled with large scale layoffs and departures at FDA, PDUFA remains necessary to ensure sufficient capacity at FDA for its crucial regulatory activities. However, as FDA leadership, we consider the role of user fees. There's also an opportunity to revisit and reform PDUFA to increase transparency and promote patient-centeredness. First, the lack of transparency during PDUFA negotiations has hindered public engagement as negotiations take [place] largely behind closed doors between FDA and industry with only limited meeting minutes publicly posted afterward. Additionally, PDUFA’s engagement with public stakeholders occur separately from negotiations with industry, despite no discussion of things that are commercially confidential or considered to be trade secrets, and these are structured as listening sessions where attendees provide input without access to the details of the commitment letter being negotiated between FDA and industry. Although under law, PDUFA calls her monthly meetings with public stakeholders, only six meetings were held during the 18 month PDUFA VII cycle compared to the over a hundred meetings held with industry.

01:04:14 Several steps can be taken to enhance transparency and promote public participation. At a minimum, FDA could ensure that meetings with independent public stakeholders are held monthly, as required under statute. FDA should also publish comprehensive meeting minutes and details of negotiations to allow for public stakeholders to meaningfully weigh in on negotiations. Moreover, the agency could directly solicit public stakeholder input on specific issues under consideration in their negotiations with industry. More broadly, rather than keeping the engagement with industry and public stakeholders separate, FDA should instead include public stakeholders in their negotiations with industry. Additionally, while PDUFA performance goals have been traditionally focused on metrics and pilot programs intended to streamline drug development and review, other steps can be taken to promote patient-centeredness and enhance public trust in FDA and its decisions.

01:05:06 As a performance goal, FDA could annually report the number and names of drugs approved under traditional and accelerated approval based on validated and unvalidated surrogate endpoints respectively. This would make clear to the extent which novel endpoints other than clinical outcomes that directly measure how patients feel, function and survive are being used to support FDA approval. FDA could also report the completion rate of required post-market safety studies and the time required for the completion, as well as whether studies results led to FDA safety actions, such as new black box warnings, safety communications to prescribers and the public, and withdrawals of drugs found to be unsafe. Reporting such patient-centered measures could motivate FDA to act within a timely manner once results of required post-market studies evaluating efficacy and safety are available. For over three decades, FDA, industry and Congress have agreed that user fees are needed to provide the agency with critical resources to ensure that patients have timely access to truly safe and effective innovation.

01:06:05 We at Yale CRIT welcome the opportunity for meaningful reforms to the PDUFA process to recenter user fees around the mission of FDA in protecting patients and public health. We look

forward to the opportunity to partnering with the agency as it initiates PDUFA VIII negotiations. Thank you for the time.

01:06:22 **Nana Adjeiwaa-Manu:** Thank you, Reshma. Our final public common speaker is Emily Anderson from Physicians Committee for Responsible Medicine. Emily, please approach the podium.

01:06:37 **Emily Anderson:** Hello, I'm Emily Anderson. I'm with the Physicians Committee for Responsible Medicine, a nonprofit organization with nearly 1 million supporters. I work with a team of scientists, physicians, and lawyers to advance more effective, efficient and ethical medical research and product testing. We also collaborate with a variety of industry, government, and scientific stakeholders. Through PDUFA VIII, we urge FDA to enhance the use of new approach methods or NAMs as regulatory decision tools in drug development and review. NAMs include advanced in vitro systems such as organs on chips and computational models such as AI. These technologies are helping make nonclinical testing more predictive for humans, improving efficiency and drug evaluation while avoiding animal testing. We appreciate the recent FDA roadmap on reducing animal testing and preclinical safety studies. This makes it clear that the agency seeks to phase out animal tests and transition toward more human-based systems. The following PDUFA enhancements to accelerate the use of NAMs can help achieve FDA's goals.

01:07:40 So first, we urge PDUFA VIII to commit to updating guidance to ensure they clearly and practically allow for the use of NAMs. Industry requires certainty about which methods can be used in regulatory applications. FDA should ensure that its guidances are flexible to accept all nonclinical approaches, including in vivo, in vitro, and in silico, and provide clarity about how NAMs can be used. Second, we urge the FDA to accelerate the qualification of NAMs through the ISTAND Drug Development Tool Qualification Program. ISTAND provides a critical

pathway for the evaluation of new NAMs tools, but ISTAND has not successfully qualified a single tool since the program launched in 2020. So, PDUFA VIII should expand the capacity of ISTAND by providing dedicated staff to support applications progressing through the program and establishing benchmarks for the number of tools the agency aims to qualify each year. Third, we urge PDUFA VIII to commit to providing training workshops for FDA reviewers on interpreting NAMs data to help build expertise and improve reviewer consistency. It's essential that FDA staff are well-versed in NAMs to avoid unnecessary delays in applications or requests for additional data, simply due to lack of familiarity. And lastly, we urge the FD to provide incentives to sponsors that use NAMs applications to help overcome the historical reliance on animal testing as the default approach.

01:09:06 A PDUFA VIII commitment that expedites the review of NAMs applications and provides meetings on NAMs suitability would instill further confidence in FDA's willingness to accept NAMs and would help support FDA efforts to accelerate the adoption of human relevant methods. Our written comment will provide more detail on these requests, and we hope PDUFA VIII continues to build on the great progress that FDA has made in integrating human relevant technologies and drug evaluation for timely drug review and patient access to safe, effective and innovative medicines. Thank you very much.

Closing Remarks

01:09:56 **Nana Adjeiwaa-Manu:** Thank you, Emily. That concludes our public common session and our meeting today. Thank you to all of the speakers who took their time to share their comments with us. Thank you all for attending, both in person and virtually. A final reminder that the public docket to provide written comments will be open until August 14th. Thank you, and we hope that you enjoy the rest of your day.

[End of the recording.]