

UNITED STATES OF AMERICA
FOOD AND DRUG ADMINISTRATION

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Center for Drug Evaluation and Research / Office of Communications

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

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September 16, 2026

09:00 a.m. EST

Via Web Conference

Transcript Produced By:



ACSI Connects

1025 Connecticut Avenue, NW, Suite 1000, Washington, DC 20036

<https://acsitranslations.com/>

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Welcome and Introduction

00:00:06 **Nana Adjeiwaa-Manu:** All right. Good morning, everyone. We will go ahead and get started. 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 within the Center for Drug Evaluation and Research. I will be your moderator today.

00:00:32 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, expires in September 2027. Preparations are therefore underway to begin the process to reauthorize the program for fiscal years 2028 through 2032. Today's meeting is an important step in engaging with public stakeholders on the PDUFA program. The purpose of today's public meeting is to share the proposed recommendations for the reauthorization of PDUFA and gather input from the public on the proposed recommendations.

00:01:15 The full text of the proposed PDUFA VIII Commitment Letter can be found on the Agency's webpage. We have also opened a public docket for those who wish to submit written comments. After this public meeting and the close of the public docket, we will revise the recommendations as appropriate and present our proposed recommendations to the congressional committees.

00:01:40 We have a full agenda for our meeting today. We will begin with Grace Graham, Deputy Commissioner for Policy, Legislation, and International Affairs, who will be providing opening remarks. Next, Andrew Kish, the Director of the Office of Program and Strategic Analysis in CDER will provide background on PDUFA and the

reauthorization process. We will then have a series of panels during which FDA will present the proposed PDUFA VIII enhancements. We will also hear remarks from the regulated industry trade groups. These panels will focus on proposed enhancements related to pre-market review, post-market safety, chemistry, manufacturing and controls, finance, and other topics.

00:02:25 We will take short breaks following the post-market safety panel as well as the other topics panel. After the second break, we will hear public stakeholder perspectives from individuals who submitted a request to participate in the Public Comment portion of this meeting. Time permitting, we will hear any additional public comments from in-person meeting attendees. Andrew Kish will then provide closing remarks. 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.

00:03:05 This meeting is an opportunity for FDA to listen to public perspectives. FDA will not ask questions nor answer questions raised at the meeting. My colleagues who are leading and participating in the reauthorization process are here in person as well as online. Please know that we are listening and that we very much value your perspectives. Please keep in mind that you can submit comments to the public docket, which will be open until October 16th. We encourage everyone to submit their perspectives to the public docket for FDA review. We will post a link to the public docket in the chat for this meeting.

00:03:43 Lastly, a few housekeeping items. First, this is a public meeting and it's hybrid in nature, and so we have many folks 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 or email PDUFAreauthorization@fda.hhs.gov. Closed captions are available by clicking the CC button. We have planned two scheduled breaks. If schedule modifications are needed, we will communicate those verbally and we'll also post them in the chat. 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 Grace Graham, Deputy Commissioner, for some opening remarks.

Opening Remarks

00:05:00 **Grace Graham:** Good morning, everyone; and thank you, Nana. Thanks for attending the public meeting on the recommendations for the reauthorization of PDUFA VIII. I want to thank everyone for joining us today, both in person and virtually, as we continue this important process. This meeting marks an important milestone in our ongoing commitment to a transparent, efficient program to review evidence and decide whether innovative new medicines are safe and effective for American patients.

00:05:28 Since the first PDUFA passed in 1992, FDA has utilized PDUFA resources to significantly reduce the time it takes for FDA to review new drugs and biologics, and it has done so while maintaining rigorous standards for safety, efficacy, and quality. PDUFA has increased the predictability of FDA review processes, increased communication during drug development—allowing us to shorten drug development

times as well—and supported a robust environment for innovation. That's demonstrated by great results in 2025, where CDER and CBER approved close to 60 never before approved or marketed in the U.S. medications and biological treatments for a wide range of diseases and conditions. Around half of those were for orphan diseases and one with first-in-class non-opioid pain medication, as examples.

00:06:23 Our 2025 approvals also demonstrate efficiencies in the review process, where we've met our goal dates or exceeded them 90% of the time. And importantly, around 70% were approved in the U.S. before they were approved in other countries. In addition to our reviews, per commitments in PDUFA VII, over the last four years we've published over 15 guidances, multiple public meetings, and published over 30 public reports or documents providing transparency and opportunities for stakeholder and patient industry feedback all along the way.

00:06:57 As that demonstrates, the success of the PDUFA program is not on FDA alone. Participation of patient and consumer groups, industry, healthcare providers, and others is a crucial element, and that's true for the reauthorization as well. Since the initial public meeting held last July—June—FDA has looked at over 60 public comment periods, conducted seven consultation meetings along the way, and posted all of the meeting minutes that we've held in those discussions with industry and public stakeholders, which leads us to today's meeting on the proposed PDUFA VIII user fee reauthorization.

00:07:30 I do want to thank all of my FDA colleagues who have worked tirelessly on the proposed recommendations being discussed today. The teams at CDER, CBER, Office of the Chief Counsel, the team putting together the meeting today and many others

93 have worked around the clock—budget, OPQ here—to get us to this point. And while
94 I know the rest of today will get into some more details from the true experts on the
95 subject, I'd like to highlight a couple themes that stuck out to me as we prioritized and
96 worked through this reauthorization process.

97 00:08:02 First, it will be no surprise that America First is a priority for this administration and a
98 guiding principle and belief that the proposals, recommendations before you today
99 reflect that in a way that both-- Whether you are doing early clinical research in the
100 United States and a proposed fee reduction at the end of the development program, and
101 also making sure that small businesses in the U.S. are the ones who benefit from any
102 potential fee reductions.

103 00:08:31 There's also continued focus on manufacturing, which has been a top priority since I've
104 been at the Agency, starting back in March. Working through the public meeting last
105 September, sort of in parallel with the user fee negotiation process, has given us a
106 great window into what we can do and how we can improve the processes to make
107 sure that the CMC portion of the application is not a lagging indicator. Because I know
108 it is heartbreaking for us, for the patient community, for sponsors, when the clinical
109 looks good, we're ready to approve an application, and there's an issue that comes up
110 on the quality side. We have to be confident the product that is going to be approved
111 and manufactured will deliver on the results the clinical-derived data promises. But
112 however we can remedy that, whether it's by earlier interactions, quickly addressing
113 and discussing them so those delays are minimized or avoided, if at all possible, and
114 really excited about the recommendations here today and look forward to hearing the
115 feedback.

00:09:23 And then lastly, as was mentioned on rare disease, there's been a lot of great work, almost half of the applications approved last year, as I mentioned, but continuing whether transitioning pilot programs into routine practice or having more opportunities for rare-specific patient and other input led by Amy Rick at our Rare Disease Hub, really look forward to continuing that effort. So, I'll stop with those big highlights. I know the team will go into further details today, but we are committed to getting these proposed recommendations—when finalized—to Capitol Hill by the January 2027 deadline and working closely to ensure FDA's ability to collect user fees that fund our staff and key initiatives is reauthorized on time. Failure to do so, as many in this room know, is not an option. Too many patients, healthcare providers, innovators, and families rely on FDA's work facilitating innovation.

00:10:12 So, we appreciate the comments today, those that came in person or attending online and look forward to the partnership and support as we move towards a timely reauthorization. Thank you.

[PDUFA Background and Overview of Recommendations](#)

00:10:24 **Nana Adjeiwaa-Manu:** Thank you, guys. I would like to now introduce Andy Kish, Director of the Office of Program and Strategic Analysis in CDER to provide background on PDUFA and the reauthorization process.

00:10:47 **Andrew Kish:** So, good morning everyone. I'm going to lean down a little bit, a little tall for the podium, but I didn't feel like sitting for longer. For those of you who are familiar with PDUFA, a lot of this will be a repeat. For those that aren't, then maybe some new items. A little bit of history before we get into really what I think

we're all here for is to hear about the specifics of the agreement from the negotiators themselves.

00:11:15 So, a little history on PDUFA. Before it came about, as you can imagine, we had a backlog of applications. Patients were waiting years for us to even pick up an application and review it. So, everyone came together across the stakeholder community, FDA, industry, Congress, and said, "We need to do something about this." And that's the user fee program that started all the user fee programs at FDA, which we have many of. I was told last night there's 18. I don't know if that's entirely true, but I think I could count 10, but there's more apparently.

00:11:49 As a result of PDUFA, we had a more predictable and streamlined process. Patients got earlier access to new drugs, and clinical development time has decreased, and that has been consistent since the inception of PDUFA. So, basically, what is a user fee? These are fee funds that are added to appropriated funds. So, what we get from Congress it's not meant to supplant them. And it's really focused on process and staffing so we can enhance our reviews and the speed of them. By definition, a user fee pays for services that benefit the fee payers. That's what distinguishes it from a tax. So, that's context for our entire negotiations, really, when you think about it.

00:12:37 So, what do we talk about in these negotiations? And we had over 120 of them. We got a lot of face time, which was helpful, and of course a lot of feedback from the stakeholder community through the process, too. So, what do we talk about? We talk about new processes, or enhancing our processes, or modifying them, and what that would look like over that five-year period. What is feasible to do? That's a big part of the conversation. And what are the resources required to do it? Or are they resource-

neutral? There's no discussion of policy, as was already mentioned earlier. That's not something that UFA covers.

00:13:13 It's very detailed, very, very detailed conversations, very detailed feedback, as you can imagine. I won't go through all these because it's getting really long with all the PDUFAs. We filled up an entire slide at this point, so PDUFA VIII, we'll start a new slide for the next one. There's a long history to it. It's basically evolved over time at a summary level, to pretty basic, to more complex. And it's been really instrumental in new drug review in the United States.

00:13:50 Okay, so where are we in this reauthorization process? This is laid out in statute and what we've been following. As mentioned, Grace mentioned earlier, we are committed to getting this sent to Congress on time. That is by January 15th, 2027. It's not that far away. To do that, we had to start way back in the summer of 2025 with our public meeting that kicked all of this off. Many of you were potentially there and gave feedback. We then went through a process of getting feedback from public stakeholders while we also negotiated with industry—as mentioned, 120-plus meetings—to come up with the agreement and the recommendations we have to present today.

00:14:38 Today marks our final public meeting. We also have a docket open, so we're really looking to hear your feedback through this process. We then transmit to Congress, and Congress then has essentially nine months to reauthorize; otherwise, it would not be great here, for the FDA or for new drugs.

00:14:59 So, this is the statute. Don't even attempt to read this. I can't even read it from here. It's too small. But what's highlighted is all the public input opportunities, and this is really

184 highlighting where we are today. Again, this public meeting is a big milestone. The
185 docket-- We will read every single comment you put in the docket. We did that with
186 the prior meeting, we actually made-- You'll see some of our recommendations are a
187 result of that. Everything you tell us today is reviewed and thought through. I'd also
188 like to highlight that the meeting minutes that are on our website are very detailed. If
189 you've been an observer of PDUFA in the past, you'll find out these are substantially
190 more detailed than previous ones. Congress told us very specifically to do that. So,
191 there's a lot of detail and information there. If you've been reading them, you pretty
192 much were following the play-by-play of the negotiations.

193 00:16:00 Grace touched on some of this, but just to highlight some of the bigger items you
194 might note in this agreement, prioritizing America First—including a fee incentive for
195 companies that anchor Phase 1 clinical trials in the U.S.—is a big deal. I don't know if
196 anyone did a count of the document, but it's 20 pages shorter, so it's streamlined. It's
197 focused on core review functions. It maintains critical support for our review staff.
198 And as noted by Grace, it introduces a lifecycle approach to addressing manufacturing
199 issues, which is pretty innovative, and it enhances transparency around the program.
200 Other items you may not have noted, unless you did a comparison to the previous
201 letter, is it removed one-time commitments. PDUFA VII had a lot of one-time
202 commitments. Those have been completed, so those are no longer in the document,
203 and also maintains established programs and regulatory science tools structured
204 slightly differently in the past, but kind of grouped together.

205 00:17:05 Themes of the agreement really structured how we negotiated this. So, if you review
206 the minutes, you can review them this way: pre-market, post-market, manufacturing,

and finance. In the pre-market space, it's really a focus on the core review activities and making sure those are stable and we're performing on them. It also enhances communication in the program. This is a common topic, how do we enhance, how we interact, particularly around meetings, and it transitions a lot of our programs and pilots into practice. In the post-market space, we continue to promote safe use of medicines through enhancements to our drug safety system, including Sentinel. Manufacturing, that introduces the lifecycle approach, which our folks will talk about a lot more in a few minutes. And then finance, really enhancing the transparency around the finances and management and also modifying the fee structure to incentivize those clinical trials in the U.S. and a couple other modifications.

00:18:07 So, that's the high level overview. I think we're ready to jump into pre-market.

Pre-Market Review: Proposed Enhancements

00:18:14 **Nana Adjeiwaa-Manu:** Thank you, Andy. We're now going to move on to our panels on the proposed enhancements for PDUFA VIII. As Andy mentioned, our first panel is focused on proposed enhancements related to pre-market review. Mary, Annetta, and Kristy, please join the panelists' table now. Great.

00:18:50 We are first going to hear from Mary Thanh Hai, who is the Director of the Office of New Drugs to provide an overview of the proposed enhancements. Following Mary's presentation, I will introduce the representatives from regulated industry to provide their remarks. Mary, you may begin when you're ready.

00:19:09 **Mary Thanh Hai:** Thank you very much, Nana. I am really excited to be here today. This is a combination of very long resource-intensive negotiation and just really nice to be here with counterparts from industry. We've worked very hard to get to this day

230 today. I'm Mary Thanh Hai. I led the pre-market subgroup negotiations team for FDA
231 alongside with colleagues in CDER, the Office of New Drugs, Office of Translational
232 Sciences, as well as colleagues from CBER. Over the course of four to five months
233 during reauthorization negotiations with industry, we found common ground on
234 proposals that focus on core review activities, enhanced communication in the human
235 drugs review program, and formalizing many of our regulatory science programs. Next
236 slide, please.

237 00:20:03 FDA and industry recognize the importance of the human drug review program,
238 bringing predictability to communications, review processes, and timelines.
239 Streamlining these activities helps improve the outcome of new molecular entities
240 reviewed under the program and the review of efficacy supplements. PDUFA VIII will
241 focus on the first cycle review processes, including interactions during the IND stage
242 that inform the marketing application under first cycle review. PDUFA VIII will also
243 include an assessment of review processes, outcomes, and FDA-sponsor
244 communications during first cycle review that will provide recommendations to, one,
245 help FDA and sponsors limit complete responses for applications that are ultimately
246 approvable; two, also limit missed goal dates; and to limit review clock extensions.
247 The assessment will also provide recommendations on ways to increase effectiveness
248 of FDA-sponsor communications during review. Next slide, please.

249 00:21:09 To increase efficiencies in review and initiation of pivotal studies intended to support a
250 marketing application, there is a commitment to prioritize the review of protocols for
251 studies intended to form the primary basis of an efficacy claim to help ensure
252 applicants receive feedback on critical questions prior to study initiation. The

commitment also includes an assessment not only of the time from receipt of such protocol submissions to the FDA's responses to questions submitted with that protocol, but it's also going to assess the completeness of the sponsor's submission. Was there sufficient information to enable a thorough review, including submission of the statistical analysis plan? Next slide, please.

00:21:56 Formal meetings between FDA and sponsors are critical to ensuring a development program intended to support a marketing application and will contain the necessary data to meet statutory requirements for approval. With evolving science, understanding the biological basis of many diseases, it's not uncommon that a single therapeutic may target multiple indications that span different divisions. Under PDUFA VIII, FDA may grant multi-divisional meetings for sponsors developing investigational products under multiple INDs across multiple therapeutic areas to increase efficiency and alignment across participating divisions. For pre-IND, Type C, Type D and INTERACT meetings only, while sponsors may request a face-to-face meeting and can provide a rationale for this meeting format, if FDA determines a written response to the question is appropriate, justification for that determination will need to accompany that decision. And as in the past PDUFA reauthorizations, there will be a revision to the formal meetings guidance. And there is also a commitment for an assessment of the effectiveness of the multi-divisional meetings as well as written responses and face-to-face meetings. Next slide, please.

00:23:16 PDUFA VIII commitments also focus on expediting drug development and enhancing the use of regulatory science tools. Over the past several decades, we have seen greater investment in developing therapies for rare disease. As a result, we've also seen a rise

in the percentage of new drug approvals for the treatment of rare disease. As you heard earlier this morning from Grace Graham, for the past 10 years now, about half of our new drug approvals are for rare diseases. To continue supporting this important effort, PDUFA VIII introduces up to 10 Rare Disease Innovation, Science, and Exploration—also known as RISE—workshops that build on the success of the rare disease programs in both CDER and CBER and to address key scientific and drug development barriers. In addition, the Rare Disease Endpoint Advancement Pilot that was introduced under PDUFA VII will be transitioned to an established program utilizing existing meeting framework, thus allowing for the discussion of novel efficacy endpoints during drug development and expanding the availability of the program across many therapeutic areas. Next slide, please.

00:24:32 PDUFA VIII will also transition and expand the use of other regulatory science tools, including incorporating the Complex Innovative Design program into standard review practice where sponsors can seek advice through formal traditional meeting requests, expanding access to the Model-Informed Drug Development Paired Meeting Program with a phased transition to Type C-MIDD meetings, eliminating the quarterly cadence and cap on the number of meeting requests. PDUFA VIII will continue to advance patient-focused drug development with publication of case studies on how patient experience data were considered in regulatory decisions and by hosting a public meeting to discuss case studies and facilitate broader dialogue on use of patient experience data in drug development and regulatory review. And finally, the Advancing Real-World Evidence Pilot Program will transition to be an established

program in the human drugs review process and engagement with the Agency through the established formal meetings and review practices. Next slide, please.

00:25:40 And finally, FDA commits to hold a public meeting to discuss best practices for communicating the use of regulatory science tools in drug development and regulatory decision making, and will publish a summary report from that meeting that may include recommendations for increasing transparency and facilitating shared learnings. Next slide, please. Other changes on PDUFA VIII will include sunseting the Split Real-Time Application Review—or STAR—pilot program on September 30th, 2027, given the limited participation from industry during PDUFA VII. And there were sections of the commitment letter that were also streamlined and consolidated. So with that, thank you so much for your attention, and now I'll turn it over to my industry counterparts.

00:26:27 **Nana Adjeiwaa-Manu:** Thank you, Mary. We're now going to hear remarks from Annetta Beauregard, who's the Senior Vice President of Science and Regulatory Affairs from the Biotechnology Innovation Organization. Annetta, please go ahead.

00:26:43 **Annetta Beauregard:** We're going to shift the order just slightly, and Kristy is going to go first.

00:26:47 **Nana Adjeiwaa-Manu:** Okay. I'll introduce you, Kristy, then, really quickly. All right, so we'll hear first from Kristy Lupejkis, the Vice President and Chief of Staff, Science and Regulatory Advocacy from the Pharmaceutical Research and Manufacturers of America.

00:27:03 **Kristy Lupejkis:** Thank you, everybody. Thank you, Nana. Good morning. As Nana said, Kristy Lupejkis with PhRMA. Discovery, development, and delivery of safe and

effective innovative medicines to patients is the core mission of our members. Robust innovation depends on an appropriately funded regulatory agency providing timely science-based regulatory decisions and leveraging modern approaches. That is why PhRMA has been a strong supporter of and participant in PDUFA negotiations since the inception of the agreement in 1992, and we commend and appreciate FDA for holding this meeting to hear stakeholder views.

00:27:40 As you heard today, for more than three decades, PDUFA has helped create a predictable regulatory environment which helps U.S. patients be provided with more medicines than anywhere else in the world. The PDUFA VIII Commitment Letter reflects the shared goal of FDA and industry to continuously improve regulatory efficiency, embrace emerging science, and ensure that the U.S. remains the global leader in biomedical innovation.

00:28:05 At a time when scientific innovation is rapidly advancing and international competition is intensifying, we believe PDUFA VIII will continue to help facilitate and sustain the predictable, efficient, transparent, and science-based FDA regulatory review process that patients, industry, and the broader healthcare ecosystem depend upon. To achieve this, as you heard, PDUFA VIII includes initiatives intended to reduce avoidable delays by providing more timely FDA feedback during drug development and review, and helping identify and address potential issues before they slow patient access to new treatments.

00:28:40 This includes some key enhancements that we also want to highlight as important tools to enhance FDA-sponsor interactions and review efficiencies and improve transparency in the regulatory review process. The agreement includes a commitment,

as you heard, for FDA to prioritize the review of pivotal clinical trial protocols, which will help ensure timely FDA-sponsor interactions and feedback, and in turn reduce uncertainty and enable sponsors to finalize clinical trial designs with greater confidence, helping ensure studies undertaken align with regulatory expectations and thus avoiding delays.

00:29:15 We'd also like to highlight the multi-divisional review meeting to streamline development of products with multiple indications. We believe that memorializing this meeting in the PDUFA VIII agreement will help drive more efficient engagement between sponsors and FDA, and potentially reduce duplicative discussions and the number of individual meetings a sponsor would otherwise need to request of the Agency. In addition, the agreement will improve transparency by providing sponsors with greater visibility into information requests issued later in the review cycle, allowing both parties to better distinguish between routine clarifications and larger, more substantive issues that could affect the review timeline or regulatory outcome.

00:29:55 Similarly, PDUFA VIII reinforces FDA's commitment to timely communication regarding labeling review as applications approach their PDUFA goal dates, providing sponsors with greater clarity on outstanding labeling issues, facilitating resolution of comments, and supporting timely regulatory action. Enhancements like these build a more predictable and transparent review process from trial design through labeling finalization, reducing avoidable delays while helping ensure that safe and effective medicines reach patients sooner.

00:30:27 Finally, as you heard, PDUFA VIII builds on prior PDUFA agreements and continues to enhance transparency and accountability in the program. As mentioned, the

agreement includes an independent third-party assessment to evaluate FDA review performance and identify potential opportunities for enhancements to further refine the Agency's regulatory review processes and help ensure the program continues to deliver results for patients. The assessment findings will be available for public comment and can help inform any changes to practices as well as informing the next PDUFA negotiation. Taken together, we believe that the PDUFA initiatives will help enhance the consistency, quality, and timeliness of FDA-sponsor interactions while helping facilitate first cycle review and approvals and reduce review times for new drugs and biologics, all while maintaining FDA's standards for safety and efficacy. Thank you.

00:31:19 **Nana Adjeiwaa-Manu:** Thank you, Kristy. All right, Annetta, we will turn it over to you.

00:31:24 **Annetta Beauregard:** Good morning, everyone. Annetta Beauregard. I lead Science and Regulatory Affairs for BIO, the Biotech Innovation Organization. We are a trade association that represents over a thousand members from small, medium, to very large. And I just want to make a few comments that for all drug review, an efficient and predictable regulatory process can make a critical difference in innovation reaching patients. For small biotech, dependent on limited- and time-constrained investment, it has the potential to be the difference between the ability to pursue innovative treatments for patients or not. BIO's very proud of this negotiated PDUFA VIII agreement. I want to take a moment just to thank my FDA colleagues and industry colleagues who generously gave of their time and expertise over months in this process. I think we all are proud of the outcome.

390 00:32:30 PDUFA VIII retains the processes, the timelines, the metrics, and reporting on
391 application review activities from previous reauthorization, but it also strengthens the
392 predictability and timely review. I won't repeat what Mary and Kristy so carefully
393 conveyed. I'll just highlight a couple of things from a BIO perspective, the third-party
394 assessment. It'll look at the quality and efficiency of the biopharmaceutical regulatory
395 review with a focus on first cycle review outcomes. We very much support this
396 assessment. We've done this before, meaning the PDUFA process, which at this point
397 feels like one and the same, the we and the PDUFA. We've done this before with great
398 outcomes and we look forward to this exercise again.

399 00:33:20 As you heard from Mary and Kristy, PDUFA VIII expands existing and adds new
400 initiatives to advance regulatory science tools. These are opportunities to have
401 training, share best practices, public meetings, all opportunities for the biotechnology
402 ecosystem to learn and progress together. For maturing regulatory science tools, we
403 look forward to transitioning from pilot into standard practice. This opens up so that
404 these regulatory innovations are not constrained by the pilot or by its size. And so we
405 very much look forward to that transition.

406 00:34:00 I do want to emphasize that for the 10,000 identified rare diseases, there are far too
407 few FDA-approved treatments or therapy. And so we support the Rare Disease
408 Endpoint Advancement Program. We look forward to it proceeding in PDUFA VIII
409 and the cap being raised year over year, as Mary described, and then transition into a
410 Type C meeting.

411 00:34:29 And finally, PDUFA VIII further improves FDA-sponsor communication, which is the
412 cornerstone of a predictable and efficient regulatory review. Emphasizing the

importance of early, often, and transparent communication is cornerstone to an efficient regulatory review and we're very much supportive of the changes that we've made in PDUFA VIII. Thank you.

Post-Market Safety: Proposed Enhancements

00:34:52 **Nana Adjeiwaa-Manu:** Thank you, Annetta. And thank you Kristy and Mary for your remarks. We're now going to move on to our second panel, which is focused on proposed enhancements related to post-market safety. Amy and Ryan, please join the panelists table now. All right.

00:35:42 We are going to start off our panel by hearing from Amy Ramanadham, who is the Director of Drug Safety Operations. She will be providing an overview of the proposed enhancements related to post-market safety. Following Amy's presentation, I will introduce the representatives from regulated industry to provide the remarks. Amy, we'll turn it over to you.

00:36:03 **Amy Ramanadham:** Thank you, Nana. Good morning. I'm Lieutenant Commander Amy Ramanadham, Staff Director for Drug Safety Operations in the Office of the Center Director. I had the pleasure of leading the post-market safety subgroup. Members here of that subgroup, which included both colleagues from CDER and CBER-- It worked. Okay. So, our post-market safety subgroup was both regulatory and industry members. We negotiated a commitment under PDUFA VIII to provide continued resources to maintain the high quality and large quantity of data available to support the Agency's pharmacoepidemiology needs. Sentinel 3.0 is FDA's planned modernization of the Sentinel Initiative, the Agency's large-scale post-market medical product safety surveillance system.

00:36:55 The vision for the Sentinel 3.0 is to provide a more modern and efficient system for detecting safety signals and generating evidence to support regulatory decision making. So, overall, the section has been streamlined compared with previous versions of the letter. And so in particular, we have streamlined the reporting metrics associated with Sentinel. So historically, if you've studied past commitment letters, FDA issued a comprehensive Sentinel report every five years, which included detailed descriptions of our program and its activities. So, going forward, FDA will make reporting metrics available on an annual basis to provide greater visibility into how Sentinel is being used for regulatory purposes.

00:37:39 Also, we will have engagement with industry. FDA has committed to holding meetings with industry twice a year to discuss Sentinel 3.0. These meetings will provide an opportunity to share updates and hear industry feedback. And finally, a goal is to explore the potential for establishing a process under which sponsors may voluntarily submit what we're calling a "concept brief," describing the sponsor's proposed approach to evaluation of a safety issue that could be subject of a post-marketing requirement under Section 505(o)(3) of the Food, Drug, and Cosmetic Act.

00:38:18 So with this, industry is committed to continued resources to support this work. These resources will support the underlying data infrastructure, but importantly, they'll support the additional staff that we need to conduct these data analyses. So, an investment in both infrastructure and analytical capability will be important to the successful implementation of the commitment.

457 00:38:41 **Nana Adjeiwaa-Manu:** Thank you so much, Amy. We will now hear from Ryan
458 Kaat, who is the Deputy Vice President, Law from the Pharmaceutical Research and
459 Manufacturers of America.

460 00:38:53 **Ryan Kaat:** Thanks, Nana; and thanks, Amy. Good morning, everyone. As
461 Nana mentioned, my name is Ryan Kaat. I'm a Deputy Vice President and Assistant
462 General Counsel of Law at PhRMA. I want to briefly underscore a few items that Amy
463 mentioned earlier that will help enhance and modernize FDA's post-market safety
464 system, recognizing that effective post-market surveillance relies not only on FDA's
465 ability to identify emerging safety signals, but also on clear expectations and timely
466 engagement with sponsors on how to evaluate and respond to those signals.

467 00:39:22 As you heard, one key piece of the PDUFA VIII agreement is centered on
468 strengthening the FDA Sentinel Initiative, as well as the Agency's ability to use real-
469 world data to inform post-market decision making. Throughout the course of PDUFA
470 VIII, FDA will continue to build and enhance the Agency's safety and surveillance
471 capabilities with the aim of reducing the need for post-marketing studies through
472 implementation of the Sentinel 3.0 system. PDUFA VIII will provide resources to
473 expand the scale and quality of the data available to FDA, modernize the underlying
474 infrastructure, and help ensure FDA reviewers have necessary training and tools.

475 00:40:00 As Amy highlighted, PDUFA VIII also lays the foundation for enhanced engagement
476 between FDA and sponsors on potential post-marketing requirements for non-
477 interventional studies. FDA's commitment to exploring a voluntary process for
478 sponsors to submit proposed approaches to evaluating safety issues that could become
479 the subject of a post-marketing requirement would allow methodological

considerations to be discussed before approval. This would potentially reduce uncertainty, enable more efficient study design and implementation if FDA does in fact require a post-marketing requirement.

00:40:33 Ultimately, we believe these commitments will bolster FDA's ability to rapidly identify and evaluate potential safety signals, improve the sufficiency of the Active Risk Identification and Analysis—or ARIA—that in turn can help reduce the need for post-marketing studies and advance and expand the role of real-world evidence in assessing the safety and efficacy of medicines.

00:40:53 As with other PDUFA VIII initiatives, we believe these enhancements will contribute to a more efficient, streamlined review process that can help expedite patient access to new medicines. Thank you for your time and I will now turn the discussion over to Annetta.

00:41:08 **Nana Adjeiwaa-Manu:** Thank you, Ryan. Annetta, please go ahead.

00:41:12 **Annetta Beauregard:** Thank you. As Amy and Ryan outlined, PDUFA VIII continues to support the Sentinel Initiative. FDA's real-world data-based active surveillance system for drugs is important for identifying and researching safety signals. With the rapid expansion of technology and the ability to mine large data sets, it's critical that FDA and industry continue to learn from real-world data. Exploring the ability to evaluate a safety issue that could potentially be the subject of a post-market requirement, as Amy described, is an endeavor. We look forward to partnering with FDA and learning and sharing information in continued public meetings. It benefits the entire biopharmaceutical ecosystem and patients. Thank you.

502 00:42:03 **Nana Adjeiwaa-Manu:** All right. Thank you so much, Amy, Annetta, and Ryan for
503 your comments. We are now going to take a brief break before continuing with our
504 panels. We will be reconvening in 10 minutes, so it'll be at 9:53. Thanks so much
505 everyone.

506 00:53:15 Good morning, everyone. We will get started in just one minute.

507 **Chemistry, Manufacturing, and Controls: Proposed Enhancements**

508 00:53:50 **Nana Adjeiwaa-Manu:** All right. Welcome back, everyone. As a reminder, if you
509 experience technical issues during the webcast, please type your issue into the Q&A or
510 email PDUFAreauthorization@fda.hhs.gov.

511 00:54:07 We will now continue with our panels on proposed enhancements for PDUFA VIII.
512 Larry Lee, who is the Deputy Director of the Office of Pharmaceutical Quality, will
513 provide an overview of the proposed enhancements related to chemistry,
514 manufacturing, and controls. Following Larry's presentation, I will introduce the
515 representatives from regulated industry to provide their remarks. Larry, you may begin
516 when you're ready.

517 00:54:33 **Sau Larry Lee:** Hey, good morning, everyone. Today, I want to talk about what we
518 have proposed under the PDUFA VIII to really improve how FDA engages with
519 industry on manufacturing facility issues and why that matters for American patients.
520 And before I start my presentation, I really want to acknowledge my industry
521 colleagues. I think we spent a lot of time together, almost several months, to really
522 jointly develop this proposal and make sure that we still be able to provide the new
523 medicines to American patients and from quality facilities.

00:55:12 So, before I start describing this proposal, let me give you a little bit of background. I would like to point out that product quality is the foundation of our drug safety and efficacy for every dose delivered to patients. And I also want to point out that a drug can only work as intended if it is manufactured consistently and correctly. This is reflected in the data. Most drug recalls and drug shortages in the United States are primarily driven by manufacturing and product quality problems. Ensuring that drugs are made in a quality facility is therefore a critical part of FDA's public health mission.

00:56:02 And with that context, let me describe what problem we are trying to resolve here and what we are trying to improve from a PDUFA perspective. When a drug company submits a marketing application, an NDA or BLA, FDA reviews not only just the clinical data, but also the manufacturing facility where the drug is made. This often includes a physical inspection of these facilities, a pre-approval inspection—or a PAI—for drugs and a pre-license inspection—or PLI—for biologics. When significant manufacturing deficiencies are identified during these inspections, FDA may issue a complete response letter, meaning that the application cannot be approved in that review cycle. The industry then needs to adjust the deficiencies and resubmit the application.

00:57:12 When that happens, I want to emphasize that both FDA and industry need to invest significant resources and time into another review cycle and possibly additional re-inspection, and patients will need to wait longer for access to new medicines. The data shows that facility-related complete response actions are not uncommon. Under the current framework, opportunities for FDA and industry to communicate about manufacturing topics are quite limited in the context of drug applications. There is

currently no structured mechanism for early discussion of facility readiness for commercialization as well as for inspection before the submission, and no formal pathway to discuss inspection findings and potential corrective actions before a final decision is made.

00:58:20 Both FDA and industry recognize that this is really the problem statement, right? And we also recognize that earlier and more transparent communication on facility topics could really help prevent these deficiencies or facility-related deficiency from becoming robust to approval. And this is exactly what PDUFA VIII CMC Facility Lifecycle Program aims to improve. So, next slide. Oh, I can change my slides. Okay.

00:59:02 So, under the PDUFA VIII, we have worked really hard together to agree to implement the CMC Facility Lifecycle Program, a set of new structured engagement opportunities that can occur before, during, and after the application assessment so that facility issues can be identified and addressed early rather than becoming a reason for complete response action.

00:59:35 There are few new features I would like to highlight here. The first one is the CMC Facility Pre-submission Meeting. Before a company submits its application, it can request a single dedicated meeting with FDA, specifically focused on the manufacturing facility that will be included in the application. This meeting would typically happen three to six months before the submission, and topics that can be discussed under this meeting include the company's manufacturing supply chain, the relationships between different facilities, any manufacturing and compliance risk associated with these facilities, lessons from previous inspection by FDA or other

regulators, as well as readiness for PAI and PLI. And then we also will be able to also talk about the inspection, whether that will be an inspection during the review cycle.

01:00:48 I want to emphasize that this really gives both FDA and the applicant an early shared understanding of the facility landscape, and more importantly, an opportunity to discuss any risk mitigation if needed. While there is still plenty of time to address potential issues before the application is filed, this is a proactive step that benefits both sides. Industry can better prepare for the inspection if we have one, and FDA can conduct a more informed and efficient facility evaluation.

01:01:30 And the second one is the Post-PAI and PLI Meeting or post-inspection meeting. We have to admit that even with a very good preparation, sometimes inspections can identify, still identify deficiencies. And under the current framework, once FDA completes an inspection and identifies issues that may lead to a complete response action, there's no formal structured meeting pathway to discuss those findings before the final action date. And PDUFA therefore introduces a post-inspection meeting available after FDA completes a PAI or PLI for original NDAs and BLAs. When FDA determines that the inspection observation may result in a complete response action, the applicants can request this meeting to discuss the findings and the potential corrective action they plan to take.

01:02:42 And this meeting is really all about transparency and also being proactive. This gives FDA an opportunity to provide specific and very actionable feedback and also gives the applicants the clarity of what needs to be addressed. The ultimate goal of this meeting is really to determine whether the corrective actions can realistically resolve the outstanding facility issues within the current review cycle. And to further support

592 this, FDA may carefully consider extending the review goal dates by up to three
593 months if this facility issue can really be fixed within this timeframe. And hopefully, I
594 think what we are trying to do is when there is a reasonable likelihood that the new
595 information provided or the new approach provided by the company could resolve the
596 outstanding facility issue and lead to the approval without any additional review cycle.
597 As you can see, we are really committed to make sure that we approve the drug as
598 soon as possible, but still coming from good-- Quality facilities.

599 01:04:12 And third, the post-action meeting, which is not in the slides here, but even with these
600 enhanced engagements, there may still be facility deficiencies that warrant a complete
601 response action. The PDUFA VIII also introduced a structured post-action meeting
602 after the CR action on the application. This is really to discuss and gain understanding
603 of these deficiencies that should be corrected before the application can be approved.
604 And this is a vision to enable resolution of our issues ahead of the next review cycle.
605 As you can see, this is really a comprehensive approach to cover different stages of the
606 review program. And together, we believe that these measures address the issue from
607 both ends. The pre-submission meeting supports early shared understanding and better
608 preparation on both sides.

609 01:05:16 The post-inspection meeting really creates a structured, transparent pathway for FDA
610 and industry to discuss inspection findings and enable the industry to take corrective
611 action before a final decision is made. And this expected result is fewer facility-related
612 complete response actions, fewer additional review cycles, but more importantly,
613 faster access for American patients to safe, effective and high quality medicines from
614 quality facilities.

615 01:05:58 And we will also publish draft guidance describing how this will work in practice, and
616 we will also conduct a third-party assessment and a public workshop to evaluate its
617 effectiveness and identify further improvements. We understand that this is sort of a
618 new program and new approach. I think it's very important that we continue to get
619 feedback from our stakeholders. More importantly, from the industry so we will be
620 able to continue to make refinement and improvement to this program.

621 01:06:37 And in summary, PDUFA VIII CMC facility lifecycle program is all about building a
622 more collaborative and transparent process between FDA and industry around
623 manufacturing facility readiness and address issues in a very proactive manner. By
624 creating a structured opportunity to communicate earlier and more openly, we, FDA
625 and industry, can work together to reduce delay and ultimately to get safe, effective
626 and high quality medicines to American patients more efficiently. And thank you.

627 01:07:22 **Nana Adjeiwaa-Manu:** Thank you for your presentation, Larry. We will now hear
628 remarks from Annetta Beauregard from Biotechnology Innovation Organization. And
629 following Annetta's remarks, we will hear from Ryan Kaat from Pharmaceutical
630 Research and Manufacturers of America.

631 01:07:39 **Annetta Beauregard:** Thank you. And just to reintroduce myself, I'm Annetta. I
632 lead Science and Regulatory at BIO, the Biotechnology Innovation Organization. And
633 I-- Larry very accurately summarized the problem statement, but it bears repeating on
634 the why for the CMC change.

635 01:08:02 Anytime a drug is approved, but it's not approved on the first-cycle, that means that a
636 patient is delayed from receiving a drug that FDA ultimately determined was safe and
637 effective. Looking at this issue, we took a data-driven approach to negotiations. As

Larry summarized, it's clear CMC is a driver of first-cycle complete response and an area that we need to work together to improve. The lifecycle approach and the two meeting types that Larry described are designed specifically to address these complete responses and therefore mitigate delays in getting treatments to patients.

01:08:45 As Larry described, the pre-submission meeting allows sponsors and FDA to get comfortable with the manufacturing plan. The post-inspection meetings allow for issues that might lead to complete responses and therefore a delay in getting patients access to safe and effective drugs to be resolved. BIO is proud to support this type of FDA-sponsor collaborative approach. I want to thank Larry personally and the FDA team and my industry colleagues for championing this change. Thank you.

01:09:22 **Ryan Kaat:** Thanks Annetta. And I'd just like to second and third Larry and Annetta's statements. It was a really productive and professional negotiation. I think it was clear everyone in the room had the American patient top of mind and we believe the commitment-- The facility lifecycle program really does benefit the American patient. So, with that, I'll further highlight some of the new aspects of this CMC facility lifecycle program.

01:09:48 We too at PhRMA believe this is an important PDUFA VIII initiative that will support modernization of FDA's approach to CMC review by promoting earlier, more transparent engagement between FDA and sponsors. As Larry discussed, manufacturing facility issues identified late in the application review process or during inspection can often result in complete response letters, additional review cycles and avoidable delays in bringing new medicines to patients. This new program recognizes

that many of these issues can be better addressed through proactive communication before they become barriers to approval.

01:10:23 Notably, we want to highlight a key feature of the program in that it establishes two dedicated opportunities for engagement to proactively identify and resolve facility issues before the anticipated first-cycle action date. This represents an important shift toward preventing deficiencies before they happen rather than addressing them only after they have contributed to a delay or a complete response action. We believe PDUFA VIII will also improve transparency and predictability around FDA's expectations for manufacturing facilities.

01:10:53 As you heard earlier from Larry and Annetta, FDA will publish guidance describing the facility readiness attributes that should be met before a facility evaluation or inspection supporting an NDA or BLA. This will help sponsors better understand expectations and prepare facilities for inspection. Applicants will also have the opportunity to request a CMC facility pre-submission meeting, the first of two new meeting types to discuss manufacturing facilities for a proposed application, creating an additional mechanism to identify potential concerns before submission.

01:11:23 The CMC facility lifecycle program also is intended to address challenges sponsors face when FDA identifies manufacturing facility issues during a preapproval inspection. These inspections can occur later in the review cycle and ensuring that sponsors and FDA have a shared understanding of any identified deficiencies and how they may be addressed can help facilitate first-cycle reviews. To that end, sponsors now have the ability to request a post-inspection meeting, the second new meeting

type, to discuss the findings and assess if there are corrective actions that are responsive and may support approval of the application.

01:11:58 Finally, Larry mentioned a critical component of this facility lifecycle program, which is an independent third-party assessment of this new initiative and a public workshop midway through the PDUFA VIII cycle. In keeping with my colleague Kristy's statement earlier on the pre-market panel, this builds on the theme throughout PDUFA VIII of enhancing accountability and transparency in the review program, including ensuring that any new enhancements are assessed to see if they are helping as intended. And the public workshop will serve as an important mechanism for both FDA and industry to share learnings to help improve the new program going forward.

01:12:32 Overall, we agree with FDA and believe these commitments will help create a more proactive, predictable, and collaborative approach to CMC facility oversight. By providing earlier opportunities to discuss facility readiness and resolve potential issues, the facility lifecycle program will help reduce avoidable review cycles and delays, improve manufacturing readiness, and increase the likelihood of successful first-cycle reviews, which is ultimately to the benefit of American patients. Thank you and I will now turn it back to FDA.

01:13:00 **Nana Adjeiwaa-Manu:** Thank you Ryan, Annetta, and Larry for your remarks.

Finance: Proposed Enhancements

01:13:04 **Nana Adjeiwaa-Manu:** We are now going to move on to our next panel, which is focused on proposed enhancements related to finance. Josh, Steve, Kristy, and David, please join the panelists table now. Josh Barton, who is the Staff Director for the Resource Capacity Planning in the Office of Finance, Budget, and Acquisitions will

provide an overview of the proposed enhancements related to finance. Following Josh's presentation, I will introduce the representatives from regulated industry to provide their remarks. Josh, I'll turn it over to you.

01:13:55 **Josh Barton:** Thanks and good morning. Thanks everyone for coming out today. Before I get started, I'd just like to acknowledge all the staff efforts that went into getting this agreement done. While there's a few of us speaking up here today, there's many people behind the scenes that helped to get us to where we are today with this agreement. So, thank you all.

01:14:17 In terms of the finance group, the goals we really had for the finance group were to ensure stable and sustained funding for the PDUFA program, especially for the staffing of the PDUFA program while also being able to manage reasonable fee amounts. So, a quick lay of the land, I've got four slides. The first speaks to proposed changes to the commitment letter in regards to the finances, and the latter two will speak to proposed changes in the statutory language.

01:14:47 So, in terms of the commitment letter, there's a big theme on financial transparency, and this is really adding for the most part additional topics to be addressed in both the five-year financial plan that's published every year, as well as the annual financial report. So, that includes additional reporting in the five-year financial plan regarding the consolidation of shared services, which is ongoing. And it also adds an index of finance and personnel-related reporting to help external audiences navigate data provided in various reports.

01:15:23 We acknowledge there's many different sources of data information related to the finances and personnel out in various reports and on the website. And so, this is really

728 to help sort of provide a user guide to the differences and the commonalities in those
729 data.

730 01:15:43 In the annual financial report, this includes new reporting on the operating reserve
731 tracking, reserving and reporting, which I'll speak a little bit more about in the
732 statutory section. And it also adds additional reporting on personnel compensation and
733 benefits as well as operating expenses. So, there'll be a little bit more detail in those
734 data in the financial report.

735 01:16:10 This section also adds a new annual technical staff meeting between the FDA and
736 industry each year. And so, this is intended to provide an opportunity to discuss
737 PDUFA fees and finances, answer questions, help enhance understanding of the status
738 of the finances for the program. And we also commit to publishing meeting minutes,
739 so there'll be some documentation on the topics and questions discussed in those
740 meetings on the FDA website after those meetings.

741 01:16:48 In addition, in the commitment letter, there's a commitment to commission a third-
742 party assessment to evaluate the operations of the PDUFA program with a goal of
743 helping to identify efficiencies realized and whether those efficiencies should be
744 reflected in the PDUFA revenue amounts. This is a study that will be published on the
745 FDA website in 2029, and this will also feed into a detail in the statutory section,
746 which I'll speak to in a second.

747 01:17:25 So, in terms of proposed statutory changes, as you may be aware, the way that the fees
748 work is that first there's a process to set what we call the annual target revenue for the
749 year, and then that annual target revenue is divided up into the fees to set the actual fee

amounts. So, the first slide speaks to the revenue framework, setting that annual target revenue, and then the next slide will speak to some changes on the fee side.

01:17:56 So, for PDUFA VIII, there is a base reduction that will be implemented. This is approximately about \$50 million out of a roughly \$1.5 billion program that will be implemented starting in FY28. And that really accounts for some of the consolidation of shared services that is ongoing. The strategic hiring and retention adjustment, which was introduced in PDUFA VII, will be sunsetted as was intended in the PDUFA VII agreement.

01:18:31 There is some modification to the capacity planning adjustment in that it will not be applied until FDA restaffs to a certain level of scientific and technical expertise, and then limits the maximum increase of the CPA to 3% per year. And again, I'll talk to the certain level of scientific and technical expertise in a second. There's a reduction in the maximum balance of the operating reserve from 14 to 12 weeks, and that will be phased in over the first three years of the program.

01:19:10 And then, the introduction of this operating reserve tracking, reserving and reporting, which sets aside funds for restaffing and retaining scientific and technical expertise in the PDUFA program. And the concept here is really to ensure that the payroll levels from FY25, after adjusting for inflation and a few other changes in the organization, will really be the benchmark that we'll be working to fund the program to. And if we're not at that level, that's what limits the ability of using the capacity planning adjustment. So, we really shouldn't be using the capacity planning adjustment until we are at that benchmark.

772 01:19:55 The proposed statutory changes also provide for a new enterprise performance
773 adjustment. And so, this is related to that enterprise performance assessment I spoke
774 about in the prior slide. And this will provide a decision point for the FDA to adjust
775 program revenue amounts, if warranted, to account for savings from program
776 efficiencies. So, this is a potential adjustment that could first be implemented in fiscal
777 year 2030.

778 01:20:33 On the fee structure side, a couple updates here. This updates the fee structure. So,
779 sponsors could pay a fee equal to half of the full application fee in place at the time if
780 they anchor their Phase 1 clinical trials in the United States. There's also the
781 introduction of a fee for the first non-orphan supplement to an orphan-only product,
782 and that would be equal to half of the application fee. And there's also some updates to
783 target the eligibility for the small business waiver to be available for U.S.-based
784 companies, which is defined as companies organized under the laws of any state.

785 01:21:18 So, with that, I think that's all we have here and I'll turn this back to Nana.

786 01:21:24 **Nana Adjeiwaa-Manu:** Thank you, Josh. We will now hear from Kristy Lupejkis,
787 who is the Vice President and Chief of Staff, Science and Regulatory Advocacy from
788 Pharmaceutical Research and Manufacturers of America.

789 01:21:36 **Kristy Lupejkis:** Thank you, Nana. Thank you, everyone. And first I want to start by
790 thanking Josh for the presentation and FDA again, as we worked through this
791 negotiated agreement, appreciated the effort of all. PhRMA recognizes that
792 maintaining a world-leading regulatory system requires not only continued investment
793 to ensure FDA has access to a workforce with the expertise necessary to keep up with

the pace of science, but also responsible stewardship of resources to ensure allocation to areas of critical programmatic support for regulatory review.

01:22:08 Since enactment, as you heard, PDUFA has helped FDA remain the gold standard for regulatory review. However, as always-- And as Andy said in his earlier presentation, it's important to note that user fees supplement, but do not replace congressional budget authority supporting this program. Over the last 34 years, PDUFA reauthorizations have focused on expanding FDA's scientific expertise and workforce, modernizing its review infrastructure and building the specialized capabilities needed to evaluate increasingly complex therapies.

01:22:40 Prior PDUFAs have also focused on further refining the financial structure and related reporting, which we heard from some of those initiatives today from Josh, while further ensuring resources are allocated where they provide utility. This focus ensured programmatic stability and helped sustain the human drug review program. Those investments have helped establish FDA as a global leader in regulatory review and positioned the agency to review cutting-edge medicines with the rigor and efficiency that the work requires.

01:23:10 As the program continues to mature, PDUFA VIII will continue to help ensure FDA has the resources to recruit and retain the staff necessary to conduct timely and predictable reviews. At the same time, as you heard, the agreement emphasizes operational efficiencies and continuous improvement so that user fee resources are directed where they provide the greatest value in supporting high-quality scientific review. We believe PDUFA will also help control the financial growth of the PDUFA

program, which is important for sustainability and increased predictability of user fees by limiting new commitments and reallocating resources.

01:23:45 As you heard earlier, this includes further refinements to inputs used in the annual fee setting process to align fees with actual costs. Importantly, PDUFA VIII also, as you heard, includes enhanced reporting commitments on the use of user fee resources and FDA restaffing efforts. As noted, an independent third-party assessment is also included to identify additional efficiencies achieved by the agency and their potential impact on programmatic resourcing.

01:24:12 This will be important not only to understand the state of resourcing supporting the human drug review program, but also to help identify any impacts to drug review of the FDA's ongoing move to the shared services model. Taken together, these PDUFA VIII financial enhancements will help ensure that investments in the user fee program strengthen FDA's review capacity, ultimately resulting in timely review and patient access to safe and effective new medicines. Thank you very much.

01:24:38 **Nana Adjeiwaa-Manu:** Thank you, Kristy. We will now hear remarks from Steve Berman, Vice President, Science and Regulatory Affairs Strategy from the Biotechnology Innovation Organization.

01:24:49 **Steve Berman:** Thank you very much. It is my tremendous honor to be here talking to you all today, much as it was my honor to be able to represent the biotechnology industry during the negotiations. I'll begin by apologizing to my FDA colleague that I will be discussing finances while wearing a tie, which is in violation of the ground rules that we set out. And I bring that up to sort of acknowledge the tremendous amount of work and close collaboration that went into this agreement.

839 01:25:20 And as I reflect on the 127 negotiation sessions that turned into the 54-page
840 commitment letter draft document, I identify three themes that I think really capture
841 the spirit and the technical content of the negotiations and the agreement. And these
842 three themes persist throughout the entirety of the document covering pre-market,
843 post-market, CMC, all of the other areas, but are especially reflected in the finance
844 section. And those three themes that I identify are stability, transparency and maturity.
845 And I'll talk to each of those in turn here as they relate to the finances.

846 01:26:02 In terms of stability, I'm quite pleased that the PDUFA VIII agreement includes a
847 recognition of the importance that technical staff plays at the FDA and provides for the
848 resources required for the FDA to be staffed at the level required to conduct its
849 regulatory activities. Continuing on with the theme of stability, there are changes to
850 how the fees are calculated, specifically the capacity planning adjustment changes and
851 changes to the sunseting of the strategic hiring and retention adjustment. And we
852 think that contributes to the stability of the program as well.

853 01:26:38 Finally, under stability, I do want to highlight something that Josh mentioned, the
854 ORA TRR, the operating reserve adjustment, tracking, reserving, and reporting
855 mechanism. We think that that really provides stability to ensure that FDA has all of
856 the resources it requires, all of the financial resources it requires to acquire and to
857 retain the technical resources that it needs to get its regulatory obligations met.

858 01:27:05 With respect to transparency, we're very excited on the enhanced reporting that is
859 called for in PDUFA VIII, including reporting on the impact of the shared services
860 model, the simple reform model that is being rolled out as we speak. And finally for
861 transparency, we're also excited for the possibility that the technical staff meetings

bring to have meaningful ongoing discussions between the regulator and the regulated industry.

01:27:33 With respect to maturity, I want to highlight the enterprise performance assessment.

This is a new feature in PDUFA VIII that wouldn't have been possible had we not had the previous seven PDUFAs setting us up for success here. What the enterprise performance assessment allows us to do is to ensure that the program is right-sized for its needs. That is to say, where there are efficiencies that can be recognized to have those efficiencies translate into the financial components of the commitment.

01:28:05 So, those are the three themes that I see reflected throughout the entire commitment letter, stability, transparency, and maturity and how they are manifested in the financial pieces and [I am] very excited to see the PDUFA VIII process continue and to see the impact from 2028 to 2032. Thank you.

01:28:25 **Nana Adjeiwaa-Manu:** Thank you, Steve. We will now hear from David Spangler, Senior Vice President, Legal Government Affairs and Policy from the Consumer Healthcare Products Association. David, you may begin.

01:28:38 **David Spangler:** Good morning. Yes, as was just stated, I'm David Spangler with the Consumer Healthcare Products Association. We represent over 65 manufacturers of non-prescription or OTC medicines, as well as dietary supplements and OTC medical devices. We were pleased to be included for the first time in the PDUFA negotiation discussions since an OTC with a full NDA with clinical data is subject to an application fee.

01:29:07 Acknowledging our interests are more limited than the overall PDUFA program encompasses, we took part in those portions of the discussions of the steering

committee meetings where we had direct interest in the topics at hand, some of those included finance. We also took part in a non-prescription drug product subgroup. You're not going to see anything in the goals letter specific to that, but we were able to gain clarity on a number of items around processes for non-prescription NDAs that are reflected in the meeting minutes.

01:29:42 We believe that the recommendations overall presented today are very fair, very appropriate. We look forward to supporting PDUFA reauthorization in the next Congress, and again, we're pleased to take part.

01:29:56 **Nana Adjeiwaa-Manu:** Thank you, David, and thank you Kristy, Steve, and Josh, for your remarks as well.

Other Topics: Proposed Enhancements

01:30:03 **Nana Adjeiwaa-Manu:** We are now going to transition to our final panel, which is focused on proposed enhancements related to other topics. Andy, please join the panelist table now. Andy Kish, Director of the Office of Program and Strategic Analysis in CDER, will provide an overview of the remaining proposed enhancements. Following Andy's presentation, I'll introduce the representatives from regulated industry to provide their remarks. Andy, you can begin when you're ready.

01:30:47 **Andrew Kish:** All right. Thanks, Nana. So, this won't follow the order of the commitment letter. It's kind of the grab bag of other things that we want to highlight. So, many of you who are familiar with PDUFA VII, I imagine most of you are. A big part of that was cell and gene therapy. And in that agreement, there's a significant investment and commitment to staff up in cell and gene therapy and our expertise and review staff.

908 01:31:18 What PDUFA VIII does is it maintains that commitment in terms of investment and a
909 commitment on the FDA side to maintain and restaff that expertise to be available to
910 do those reviews and provide guidance to industry.

911 01:31:33 Okay. So, allergenic extract products might sound very minor to you, but we heard
912 quite a bit in the initial public meeting about some of the challenges with
913 epicutaneous-test diagnostic products and getting in the market in the U.S.,
914 particularly with PDUFA fees. We listened, we had discussions in the negotiations,
915 and we came to an agreement to propose exempting those products from the PDUFA
916 program and also from the fees beginning in PDUFA VIII, which is really to
917 encourage continued development of these products and availability in the U.S.

918 01:32:13 I'm not sure why there's a strikethrough the title. I don't think that was purposeful.
919 Please don't read into that. So, transparency and hiring retention of review staff for the
920 human drug review program. If you're familiar with previous letters, there's always a
921 section that says, what are we going to do in terms of hiring and noting progress in
922 hiring. Because of the structure of this agreement, we're really reprioritizing existing
923 funding, and finance touched on that a little bit, and restaffing to a certain level.

924 01:32:53 So, there's no new hiring, there's reprioritization and there's a need to be transparent
925 about that progress and restaffing and prioritization, some of that, prioritizing some of
926 that hiring, particularly around model-informed drug development, rare diseases,
927 facility lifecycle and Sentinel. So, that's what this commitment's about in that section
928 of the letter, and we will continue to provide updates on the web and our progress.

929 01:33:21 Okay, technology. Technology was a big part of PDUFA VII. It's really meant to be a
930 one-time investment to help FDA modernize its IT infrastructure relative to the

PDUFA program. As with most IT investments, it's big investments infrastructure-wise meant to be one time, not for perpetuity. I don't know if that's the case in your companies, but that's the intention here. So, reflecting that there's less commitments in this space, PDUFA VIII, because really we made the big investment in VII, but there are commitments to continue to be transparent on our progress in IT modernization.

01:34:02 That includes continuing our quarterly meetings with industry to provide updates, continuing to engage in pilot testing of systems that impact you all, maintaining data standards information and regularly updating that information on our website, and also a commitment to continue to engage on the international front, which some of you may be familiar with what we're doing with ICH and other bodies in terms of helping some convergence on international standards and potentially technology. I think that's the grab bag, that's everything. So, I'll turn it over to Nana.

01:34:42 **Nana Adjeiwaa-Manu:** Thank you, Andy. We'll now hear remarks from Steve Berman, Vice President, Science and Regulatory Affairs Strategy from the Biotechnology Innovation Organization.

01:34:53 **Steve Berman:** Thanks Andy for setting me up to discuss the grab bag. I'm happy to begin by discussing cell and gene therapy and the enhancements in PDUFA VIII there. Obviously, cell and gene therapy represents an exciting modality for bringing treatments and cures to patients. And we are very pleased to see that PDUFA VIII includes a recommitment to this field to honor the investments made in previous cycles and to both maintain and restaff the capacity FDA needs to ensure that these innovations reach patients.

953 01:35:33 We're excited for specific callouts in the commitment letter regarding training,
954 regarding communication both internally and externally and a recommitment to
955 maintaining FDA's ability to respond to emerging science in this important area. I'll
956 talk briefly about hiring. If you're familiar with past commitment letters, you'll see that
957 the hiring section of this commitment letter looks a little different. I hope that nobody
958 misunderstands that as a focus away from hiring.

959 01:36:09 It is critically important for FDA to have the staff needed to conduct its regulatory
960 review activities. It always has been and that will continue through PDUFA VIII. I
961 think speaking to the maturity of the program, it is reflected slightly differently in this
962 commitment letter, but is no less important, particularly in the areas that are explicitly
963 called out. So, MIDD, rare diseases, manufacturing and post-market. Critically
964 important for FDA to have the resources required to conduct its regulatory review
965 activities there.

966 01:36:42 And then finally, with respect to technology, we are very excited to see the
967 continuation of regular touchpoints between the FDA and regulated industry and the
968 public as the FDA continues its modernization journey. The convergence and adoption
969 of global standards will help ensure efficient drug development globally so that
970 patients can receive the benefits of modern innovations.

971 01:37:13 And so, I'll just wrap up my thoughts here, reemphasizing how the entire commitment
972 letter from pre-market to post-market to CMC to finance to our grab bag of other
973 topics really does help ensure that the FDA has the tools it needs to ensure stability,
974 transparency and maturity for the next five years. And we are very excited for its
975 reauthorization. Thank you.

976 01:37:39 **Nana Adjeiwaa-Manu:** Thank you, Steve. We will now hear from Kristy Lupejkis,
977 Vice President and Chief of Staff, Science and Regulatory Advocacy from
978 Pharmaceutical Research and Manufacturers of America.

979 01:37:51 **Kristy Lupejkis:** Thank you again, Nana, and thank you everyone. And so, I'm
980 going to further underscore some points on initiatives that both Andy and Steve raised.
981 As discussed, we also recognize that cell and gene therapy products continue to
982 present highly specialized scientific and regulatory challenges. PDUFA VIII builds on
983 the significant cell and gene therapy review enhancements made in PDUFA VII, as
984 you heard from Andy, by preserving FDA's institutional expertise while transitioning
985 completed one-time initiatives into ongoing agency practice. We believe that this will
986 help ensure that FDA continues to have the specialized expertise necessary to support
987 the review of increasingly complex biologic products.

988 01:38:32 Another important area within the agreement that Andy mentioned speaks to
989 continuity between the cycles for important initiatives, such as the information
990 technology enhancements. PDUFA, as you saw, continues to build on prior PDUFAs
991 by maintaining a structured cadence of meetings between regulated industry and FDA
992 to discuss improvements to the regulatory IT systems underpinning a prescription drug
993 review in the U.S.

994 01:38:56 This can include agency enhancements, as you saw, to IT systems supporting the
995 process for sponsor submission of a marketing application for review and related
996 FDA-sponsor interactions, as well as FDA internal IT-enabled process changes that
997 streamline reviewer experience and reduce unnecessary delays in regulatory decision-
998 making.

999 01:39:15 Echoing remarks from earlier again, we also recognize that FDA's ability to deliver
1000 timely, efficient regulatory review depends on maintaining a strong and appropriately
1001 staffed workforce, which as you saw in PDUFA VIII, we believe will support.
1002 Restoring and retaining critical review expertise will be essential to helping ensure that
1003 FDA maintains predictable review timelines.

1004 01:39:37 Restaffing through resources provided through PDUFA VIII should prioritize hiring
1005 review staff, as you heard, while ensuring FDA has the scientific, clinical, regulatory,
1006 and operational expertise necessary to support the review of increasingly complex
1007 medicines and emerging technologies. Maintaining adequate staffing is also essential
1008 to preserving the depth and quality of FDA's scientific review, sustaining institutional
1009 expertise, and ensuring that sponsors and American patients can continue to rely on a
1010 predictable U.S. regulatory system that supports innovation and helps FDA maintain
1011 its leadership as the gold standard for regulatory review.

1012 01:40:14 So, in conclusion, I want to thank FDA again for the opportunity to participate in
1013 today's meeting and all stakeholders who have and will provide their valuable
1014 feedback. As we heard for the last 34 years, PDUFA has been integral in making
1015 America the global leader in new medicine approvals and giving U.S. patients earlier
1016 access to innovative treatments. The program supports a proven framework that helps
1017 patients, supports innovation, and strengthens America's regulatory ecosystem.

1018 01:40:41 PDUFA VIII will continue to help ensure that the agency keeps pace with the rapid
1019 rate of scientific discovery, continue to help the U.S. maintain competitiveness in the
1020 global pharmaceutical market and allow the next generation of safe and effective new
1021 medicines and potential cures to be brought to patients. Since 1992, Congress has

1022 reauthorized PDUFA six times with strong bipartisan support. As we heard before,
1023 PDUFA VII expires on September 30th, 2027. Congress must move quickly to
1024 reauthorize the PDUFA VIII program. Without it, American patients and innovation
1025 will fall behind. Thank you.

1026 01:41:16 **Nana Adjeiwaa-Manu:** Thank you Kristy, Steve, and Andy for your remarks. We
1027 will now take a brief break before continuing with public stakeholder perspectives. We
1028 will reconvene in 15 minutes. Thank you.

1029 **Public Stakeholder Perspectives**

1030 01:58:36 **Nana Adjeiwaa-Manu:** Hello, everyone. We'll get started in a minute. I'd also like
1031 to invite the FDA negotiating team to come to the panelists table please.

1032 01:59:44 All right. Welcome back to our PDUFA public meeting. As a reminder, if you
1033 experience technical issues during the webcast, please type your issue into the Q&A or
1034 email PDUFAreauthorization@fda.hhs.gov. Also, please keep in mind that you can
1035 submit comments to a public docket, which will be open until October 16th. We
1036 encourage everyone to submit their perspectives to the public docket for FDA review.
1037 You can find a link to the public docket in the chat.

1038 02:00:17 Before the break, we heard from FDA and regulated industry. Our next session is
1039 dedicated to public stakeholder perspectives. Before this meeting, FDA invited
1040 members of the public to request to make a verbal statement at today's meeting.
1041 Today, 22 people will provide public comments on the perspectives of patients,
1042 consumers, healthcare professionals, scientific and academic experts, regulated
1043 industry, and others. Each speaker will have two minutes and 30 seconds to provide
1044 their comments.

1045 02:00:49 It is my responsibility to notify speakers when they have reached their time limit. I
1046 will invite each participant to speak one at a time. Virtual speakers will be invited to
1047 unmute after I introduce them. In-person speakers will approach the microphone and
1048 provide their remarks after I introduce them. We will start with our virtual speakers.
1049 The first speaker is Steve Wosahla from Children's Cancer Cause. Steve, you may
1050 unmute, turn your camera on and begin when you're ready.

1051 02:01:22 **Steve Wosahla:** Great. Thank you so much. And as the leader of a patient advocacy
1052 organization, Children's Cancer Cause, I greatly appreciate the collective efforts that
1053 have gone into PDUFA VIII, and we strongly believe that PDUFA is vital to the
1054 FDA's work in evaluating and improving new therapies, and ensuring that relevant
1055 drugs are studied in children.

1056 02:01:46 Cancer in children represents over 200 specific malignancies with rare patient
1057 populations. And unlike therapies for adult cancers, we recognize that biopharma
1058 companies are challenged to develop treatments because of the small populations for
1059 clinical trials, their cost and ability to generate enough revenue for a viable
1060 commercial market. So, how to safely and effectively treat these very small patient
1061 populations depends on continued and robust federal funding, and a strong FDA
1062 supported by PDUFA.

1063 02:02:23 I think over the past decade, PDUFA has enacted into law the Research to Accelerate
1064 Cures and Equity (RACE) for Children Act, and the RACE Act requires adult cancer
1065 drugs that are molecularly relevant in pediatric cancers be evaluated in children. The
1066 RACE Act has stimulated an increase in early pediatric oncology studies, and we
1067 continue to believe that FDA should require sponsors to fully evaluate in pediatric

1068 trials all adult agents that demonstrate reasonable evidence of efficacy and safety in
1069 early phase studies.

1070 02:03:03 Today, we face a dilemma that drugs that are approved for adults and show promise in
1071 children may not be studied further because they're not viable, but the delineation
1072 between drugs for adults and those for children is becoming obsolete as we better
1073 understand the unique biology of children. Future cures lie in studying combination
1074 drugs, repurposed drugs, and public-private partnerships to address the promise of
1075 emerging treatments.

1076 02:03:31 And in closing, I would say that children's cancer treatment, which has been marked
1077 by decades of improved survival outcomes, but still progress is hampered due to
1078 persistent and late toxicities of treatment. We're really now in an era of precision
1079 medicine and promise, and with an increasing understanding of genetics, specific
1080 biomarkers and drug targets, the promise of safer and more effective therapies
1081 portends a promising future. A robust and continuing commitment through PDUFA, as
1082 we've discussed today, will enable the FDA to support these future advances. Thank
1083 you very much.

1084 02:04:09 **Nana Adjeiwaa-Manu:** Thank you, Steve. Next, we have Mark Yale from
1085 International Pemphigus & Pemphigoid Foundation. Mark, you may unmute and begin
1086 when you're ready.

1087 02:04:24 **Mark Yale:** Thank you, Commissioner and FDA leadership, and thank you for
1088 the opportunity to comment on PDUFA VIII. I am speaking on behalf of patients
1089 living with rare autoimmune blistering diseases, including pemphigus and pemphigoid.
1090 These diseases are rare, chronic, heterogeneous, and potentially life-threatening.

1091 Patients can experience painful skin and mucosal lesions, severe itching, difficulty
1092 eating and swallowing, sleep disruption, fatigue, impaired functioning, and significant
1093 emotional and financial barriers, and many also face serious toxicity from prolonged
1094 corticosteroid treatment.

1095 02:05:06 For patients with autoimmune blistering diseases, these challenges are not simply
1096 getting treatments reviewed faster. We need a regulatory system, a system that can
1097 recognize what meaningful treatment benefits actually look like for patients with rare
1098 and heterogeneous diseases. We strongly support the next generation of patient-
1099 focused drug development, but patients' experience data must move beyond being
1100 collected to being demonstrably used.

1101 02:05:40 For patients, meaningful treatment and benefit is more than fewer blisters. It includes
1102 relief from pain and itching, control of oral disease, and the ability to eat, speak, and
1103 sleep normally, and have improved quality of life and functioning, reduced treatment
1104 burden and corticosteroid exposure, and sustained disease control. We therefore
1105 encourage the FDA to increase transparency and answer a fundamental question, what
1106 did patients say? How was the information evaluated, and where did it influence
1107 endpoints, trial design, benefit-risk assessment or regulatory decisions?

1108 02:06:20 The Rare Disease Endpoint Advancement Program offers an important opportunity to
1109 develop endpoints that capture the full patient experience, and patients and patient
1110 organizations should be involved early in the process, not after endpoints have already
1111 been established. We also strongly support expanding the Rare Disease Innovation
1112 Hub and RISE workshops. The hub can create consistent opportunities for patient

1113 organizations to identify systemic barriers, contribute patient and natural history data,
1114 and help shape endpoint and trial design.

1115 02:06:56 Importantly, lessons learned must translate into broader FDA review practices. For
1116 ultra-rare diseases, FDA should support fit-for-purpose evidence generation while
1117 maintaining rigorous standards, including innovative trial designs, registries, natural
1118 history studies, real-world evidence and patient reported outcomes. Finally, these
1119 initiatives depend on experienced FDA staff and retaining rare disease expertise and
1120 institutional knowledge must be a priority.

1121 02:07:34 Ultimately, PDUFA VIII should not be judged only by how quickly therapies are
1122 reviewed. It should be judged by whether we become better at developing and
1123 recognizing treatments that provide meaningful benefits to patients. Patients should
1124 not simply be asked what matters to them. Our experience should help define how
1125 treatment benefit is measured, how trials are designed and how the FDA determines
1126 meaningful progress.

1127 02:08:00 So, thank you for listening to me on behalf of autoimmune blistering disease patients
1128 and our perspective. We do look forward to working with the FDA to build a rare
1129 disease regulatory system that is rigorous, innovative, transparent, and surely
1130 responsive to patients.

1131 02:08:18 **Nana Adjeiwaa-Manu:** Thank you, Mark. Next we have Tingting Zhang from
1132 Here2Care. Tingting, you may unmute and begin when you are ready.

1133 02:08:28 **Tingting Zhang:** Hi, thank you for the opportunity to speak. I'm Tingting Zhang, a
1134 cancer survivor and patient advocate representing a group of stakeholders working on
1135 assessing treatment toxicities to improve supportive care in cancer. The group includes

1136 patients and caregivers from advocacy organizations, oncologists, nurses, and
1137 researchers in data sciences, health systems and toxicology.

1138 02:08:52 With the recent approval of effective yet toxic cancer drugs, there's a groundswell of
1139 concerns over patients' quality of life affected by the toxicities. Extensive supportive
1140 care needs with these treatments are also putting pressure on our health systems,
1141 especially our healthcare providers. The current publicly available adverse event
1142 reporting from passive monitoring has its limitations, which is why Sentinel was
1143 launched in 2008 with funding for PDUFA. However, few patient advocates or clinical
1144 researchers were aware of the value of Sentinel prior to our discussions.

1145 02:09:33 Encouraged by PDUFA VII commitment M.2.a.iii, "By the end of FY 2025, FDA will
1146 publish on its website an update on facilitation of public and sponsor access to
1147 Sentinel's distributed data network to conduct safety surveillance." I inquired through
1148 FDA's public engagement staff about access to Sentinel August of last year amidst the
1149 uncertainties.

1150 02:10:00 I'm grateful that a response was relayed by the Oncology Center of Excellence within
1151 two weeks. "FDA doesn't have direct access to patient partner data and does not keep
1152 the data in-house at FDA." This creates a challenge for FDA to provide public or
1153 sponsor access to data housed behind data partners' firewalls. Nevertheless, the
1154 Sentinel system has explored options to address the intent behind this commitment.

1155 02:10:29 We followed the suggestion and met in November with the Innovation in Medical
1156 Evidence Development and Surveillance program at the Reagan-Udall Foundation for
1157 the FDA. However, as "Sentinel lacked the funding to maintain this resource as an

1158 ongoing pathway for external investigators and formal partnerships," the same
1159 challenge exists for the foundation.

1160 02:10:56 We need sustainable funding for engagement so that the public can better appreciate
1161 the value of the enhanced Sentinel system, hopefully with population level summary
1162 available to the public. Thank you.

1163 02:11:12 **Nana Adjeiwaa-Manu:** Thank you, Tingting. Next we have Megan Miller from
1164 Critical Path Institute. Megan, you may unmute and begin when you're ready.

1165 02:11:23 **Megan Miller:** Good morning, and thank you for the opportunity to comment on
1166 the draft PDUFA VIII Commitment Letter. Critical Path Institute or C-Path is an
1167 organization that de-risks and accelerates drug development through advances in
1168 regulatory science by bringing together regulators, industry, academia, patient groups,
1169 and other stakeholders in the pre-competitive space. Over the last two decades, this
1170 collaborative work has led to dozens of new innovative drug development tools, 22 of
1171 which have received formal FDA acceptance.

1172 02:11:56 Our comments today focus on Section L of the draft letter, expediting drug
1173 development and enhancing the use of regulatory science tools. C-Path strongly
1174 supports the commitment to invest PDUFA resources in FDA review, training, and
1175 implementation activities related to drug development tools, including provisions that
1176 support FDA review of novel digital health technologies and biomarkers specifically.
1177 However, digital health technologies and biomarkers are just two of several examples
1178 of the actionable tools that accelerate drug development.

1179 02:12:30 Clinical outcome assessments, quantitative models, new approach methodologies, and
1180 other innovative approaches also play an increasingly important role in improving

1181 clinical trial design, endpoint assessment, and evidence generation, helping bring
1182 effective treatments to patients more quickly. FDA has already established multiple
1183 pathways to support the development and regulatory acceptance of these tools, but
1184 their successes depend on timely and actionable predictable reviews.

1185 02:13:01 For this reason, C-Path recommends that PDUFA VIII explicitly support FDA
1186 capacity to review and advance drug development tools broadly rather than limiting
1187 this commitment to digital health technologies and biomarkers. We also encourage the
1188 establishment of timelines, performance measures, and impact assessments for these
1189 activities. Together, these additions would create greater predictability in tool review
1190 and benefit innovators, sponsors, regulators, and ultimately patients.

1191 02:13:31 The bottom line is that if we want innovative drug development tools to accelerate the
1192 development of new therapies, FDA must have the resources needed to evaluate them.
1193 Thank you again for the opportunity to provide input today, and we look forward to
1194 our continued collaboration.

1195 02:13:46 **Nana Adjeiwaa-Manu:** Thank you, Megan. Next, we have Reshma Ramachandran
1196 from Yale Collaboration for Regulatory Rigor, Integrity, and Transparency. Reshma,
1197 you may unmute and begin when you're ready.

1198 02:13:59 **Reshma Ramachandran:** Hi everyone. Thank you for the opportunity to provide
1199 comments. My name is Reshma Ramachandran. I'm a physician and researcher, and
1200 Assistant Professor at Yale School of Medicine, and I also co-direct the Yale
1201 Collaboration for Regulatory Rigor, Integrity and Transparency. We appreciate the
1202 hard work that's been undertaken by the FDA team to negotiate and secure resources
1203 for the agency amid continued uncertainty of agency capacity.

1204 02:14:22 As noted, the devil's indeed in the details, and we have three specific areas where we
1205 would appreciate clarification from the FDA. First, with regard to the commitment to
1206 have third-party review provide recommendations to the FDA about how to reduce
1207 complete response letters, miss goal dates, and also review clock extensions, we would
1208 ask that this also be coupled with transparency. Prior analyses including by the agency
1209 have found that the primary drivers of CRLs are CMC and facility inspection
1210 deficiencies and/or clinical efficacy and safety deficiencies.

1211 02:14:52 These are appropriate reasons to issue a CRL, but given the focus of the third-
1212 party review to provide recommendations to reduce CRLs, we are concerned that
1213 this may create an incentive to reduce CRLs even when there may be good reason
1214 to issue them. Thus, we would urge the agency to, at the minimum, also release
1215 the reasons for why CRLs are being issued to target recommendations toward
1216 administrative reasons for why such denials are issued rather than important
1217 regulatory reasons that protect patients.

1218 02:15:18 Second, further transparency is necessary regarding FDA's efforts with Sentinel
1219 3.0 and post-market surveillance. Repeatedly during the public stakeholder
1220 meetings, we had asked for clarification of Sentinel 3.0 on par with what was
1221 provided to industry, and publicly available details on government contracting
1222 websites have been thin about details related to Sentinel 3.0. The commitment
1223 letter now commits to biannual meetings only with regulated industry to provide
1224 updates, and so we would ask that these meetings also be made public and with
1225 the inclusion of public stakeholders as well.

1226 02:15:49 Third, it's unclear whether or not the America First initiatives included with the
1227 agreement will be successful as it can be easily gamed and costing the Agency
1228 user fee funding that could be redirected towards other critical regulatory
1229 activities. Our analysis of 2024 and 2025 new drug approvals found that over 80%
1230 already had at least one Phase 1 trial that was hosted in the U.S., all of which
1231 would now receive the fee reduction under the new incentives that have been
1232 proposed.

1233 02:16:16 Based on this, we estimate that over 71 million in user fee funding would be lost
1234 to the Agency, and this is an underestimate, not including drugs where we could
1235 not find Phase 1 trial location information or supplemental approvals.

1236 02:16:29 Again, the devil's in the details, and we also know that if something is not
1237 measured, it will not be managed. Notably, within the draft commitment letter,
1238 there are no performance goals related to public health priorities important to
1239 patients and clinicians who prescribe these drugs. Instead, nearly all are focused
1240 on speed of regulatory review and FDA interaction with regulated industry.

1241 02:16:47 We urge the FDA to consider inclusion of goals or commitments such as a pilot
1242 program with a report around the use of unvalidated or validated endpoints of
1243 regulatory approval; Advisory Committees to discuss new endpoints being
1244 considered, including through Rare Disease Endpoint Advancement program;
1245 frequency and rate of fulfillment of post-marketing requirements across drug
1246 products; and type of frequency of safety actions issued by the Agency across
1247 traditional and expedited review pathways.

1248 02:17:12 Inclusion of these goals would allow the Agency to truly evaluate the impact from
1249 a clinically meaningful and patient-centered perspective of other programs the
1250 Agency has and will adopt to speed regulatory review. And these are not new
1251 policies, but similar processes the Agency can adopt that help engender public
1252 trust in FDA's work. We welcome continued dialogue in the commitment letter
1253 and we'll be providing more extensive comments within the docket. Thank you so
1254 much.

1255 02:17:36 **Nana Adjeiwaa-Manu:** Thank you, Reshma. Next, we have Thomas Huang
1256 from Brigham and Women's Hospital and Harvard Medical School. Thomas, you
1257 may unmute and begin when you're ready.

1258 02:17:47 **Thomas Huang:** Thank you for the opportunity to provide public comment.
1259 My name is Thomas Huang. I'm a physician researcher and faculty at Harvard
1260 Medical School and the Brigham and Women's Hospital here in Boston. All views
1261 are my own. I'd like to present three key comments on FDA's proposed
1262 recommendations.

1263 02:18:01 The first one is the proposed fee structure should be modified to better reach early
1264 stage clinical research in the U.S. A discount that's applied only at submission of
1265 the application offers little relief to the small companies, nonprofits, and academic
1266 sponsors that originate much early-stage work. Instead, the FDA could consider a
1267 U.S.-anchored Phase 1 study run by an eligible small business, nonprofit, or
1268 academic sponsor to generate a fee credit that's transferable with the product and
1269 redeemable against application fee once submitted. And to prevent gaming, FDA

1270 should explicitly define U.S.-anchored as requiring at least both a U.S. IND and a
1271 minimum share of Phase 1 enrollment at U.S. trial sites.

1272 02:18:42 Second, the proposal raises fee fairness issues. Neither the draft commitment
1273 letter nor the Federal Register notice states whether the restaffing target or the
1274 capacity planning model accounts for expedited pilots that FDA has created
1275 outside PDUFA and statute, such as the Commissioner's National Priority
1276 Voucher Pilot, which would, in total, pull senior reviewers away from other fee-
1277 paying applications. FDA should clarify whether it's seeking congressional
1278 authorization for these pilots, count them in capacity planning, and ensure that
1279 they're not funded from the general fee pool.

1280 02:19:13 Third, the proposed personnel compensation and benefits set-aside would restaff
1281 PDUFA at a fiscal year 2025 level, adjusted for terminated and transferred staff.
1282 This undermines the set-aside's purpose by locking in reduced staffing and
1283 seemingly subtracting further. FDA should clarify this and instead define the
1284 baseline as fee-funded FTEs that were on board as of fiscal year 2024 and clarify
1285 that terminated or transferred positions reduced the baseline only when the
1286 associated PDUFA workload had been eliminated.

1287 02:19:43 To conclude, PDUFA's legitimacy requires predictable, adequately staffed review
1288 under transparent goals that Congress has approved. I urge the FDA to address
1289 these three recommendations before transmitting them to Congress, and I want to
1290 thank the FDA team for all the hard work on this negotiation and support efficient
1291 reauthorization by Congress next year. Thank you.

1292 02:20:04 **Nana Adjeiwaa-Manu:** Thank you, Thomas. Our final virtual speaker is
1293 Kara Berasi from Haystack Project. Kara, you may unmute and begin when you're
1294 ready.

1295 02:20:14 **Kara Berasi:** Thank you for the opportunity to provide comments today. I'm
1296 Kara Berasi, CEO of Haystack Project. We appreciate FDA's sustained dedication
1297 to rare diseases. However, the draft continues to use language and concepts
1298 grounded in the same assumptions.

1299 02:20:31 The Agency will be flexible when randomized controlled trials aren't feasible. In
1300 recent discussions, FDA leadership has made clear they understand the framing of
1301 flexible and feasible can diminish both science and the work of reviewers. For
1302 example, a novel study design, in some contexts, is a more rigorous choice than
1303 an RCT.

1304 02:20:53 FDA reviewers are capable of the scientific judgment required to design studies
1305 that produce interpretable evidence. Therefore, the central question for FDA is
1306 what study design and endpoints will yield adequate and well-controlled results in
1307 the context of a specific rare disease. It's not to ask if an RCT is feasible or if
1308 instead flexibility is needed.

1309 02:21:19 Nothing is lowered. The approval standard remains the same. Section 505(d)
1310 requires adequate and well-controlled investigations. The question is which
1311 control endpoints and statistical plan can answer the scientific question in the
1312 context of the disease. Rigor means using the right tool for the job. And perhaps
1313 FDA is reluctant to move forward because it's impossible to grasp the context of
1314 over 10,000 rare diseases.

1315 02:21:46 But reviewers don't have to. We hear from disease experts that they are eager to
1316 share their knowledge with FDA, and FDA doesn't have to defer to it, but the
1317 information received could inform study design and provide more reliable
1318 information for reviewers. It should also be documented and available to inform
1319 later review. This will improve transparency, consistency, accountability, and
1320 ultimately trust in FDA.

1321 02:22:12 FDA's efforts in rare must be paired with a durable disease-specific framework
1322 that is within FDA's existing statutory authority and does not depend on an
1323 additional fee revenue beyond what is required to train reviewers.

1324 02:22:27 It feels like trying to change the internal narrative is a little like turning a tanker in
1325 the ocean. Ripples at the surface, at the leadership level, are very positive, but the
1326 deeper current is continually pulling FDA back to conventions that don't work for
1327 rare. Thank you, and we look forward to working together toward change.

1328 02:22:48 **Nana Adjeiwaa-Manu:** Thank you, Kara. The remainder of our public
1329 comment speakers are joining us in person. Our next speaker is Diana Zuckerman
1330 from National Center for Health Research. Diana, please approach the
1331 microphone.

1332 02:23:05 **Diana Zuckerman:** Is this a good distance?

1333 02:23:07 **Nana Adjeiwaa-Manu:** Yes.

1334 02:23:08 **Diana Zuckerman:** Thank you. I'm Dr. Diana Zuckerman, President of the
1335 National Center for Health Research. Our nonprofit think tank has always
1336 supported the idea of user fees, but we've become increasingly concerned about

1337 how CDER is agreeing to so many labor-intensive tasks on industry's wish lists
1338 every five years.

1339 02:23:30 Like many of my colleagues, I spent hours attending the stakeholder meetings. As
1340 patient groups, medical professionals, and public health experts, we represented a
1341 variety of viewpoints, but we all agreed that user fees should support the
1342 important mission of the FDA, which is ensuring safe and effective treatments.
1343 Some of us were more concerned about speed and flexibility than others, but
1344 nobody, nobody urged the FDA to prioritize speed of approval over the quality of
1345 the reviews or of FDA approval standards.

1346 02:24:10 During the hours of meetings with the FDA, many of us repeatedly requested that
1347 PDUFA performance goals include metrics to evaluate the quality of evidence for
1348 approved drugs and not just speed. After all our efforts, we read a commitment
1349 letter that did not contain anything we asked for and included many things that we
1350 did not want. We also read about programs that we hadn't been told about and
1351 would've wanted to comment on.

1352 02:24:43 Even when the commitment letter aims to improve transparency, it's for industry,
1353 not for the public. For example, if there are biannual updates for drug sponsors
1354 about Sentinel or any other program, why aren't other stakeholders invited? Why
1355 aren't these meetings public? We may not pay user fees, but as taxpayers, we pay
1356 FDA salaries and we pay for those drugs and for health insurance policies that
1357 cover those drugs.

1358 02:25:19 We wonder if the FDA is still the gold standard for quality, not just speed, and
1359 how that will be tarnished by so many new time-consuming requirements for

1360 FDA staff at a time when there are fewer staff and when CDER has lost so many
1361 experienced scientists. The public deserves better and stakeholders deserve more
1362 than two and a half minutes. Thank you.

1363 02:25:45 **Nana Adjeiwaa-Manu:** Thank you, Diana. Next, we have Jon McCord from
1364 Physicians Committee for Responsible Medicine. Jon, please approach the
1365 microphone.

1366 02:25:54 **Jon McCord:** Thank you. Thank you so much for the opportunity to comment.
1367 Dr. Jon McCord speaking on behalf of the Physicians Committee for Responsible
1368 Medicine. We are a nonprofit organization and we are supported by one million
1369 supporters working to advance more effective, efficient, and ethical medical
1370 research and product testing.

1371 02:26:11 We thank the FDA for its collaboration with public stakeholders in developing the
1372 PDUFA VIII Commitment Letter. [We] strongly support FDA's proposed
1373 commitments to advance regulatory science tools, including model-informed drug
1374 development program, drug development tool qualification pathways, reviewer
1375 training, communication on the use of regulatory science tools, and computational
1376 biology capabilities.

1377 02:26:32 This PDUFA VIII is being negotiated amid broader modernization of U.S.
1378 biomedical research. The largest national primate research center has passed a
1379 resolution to transition to a NAM center and the second-largest breeding facility
1380 for dog testing was just closed. These reflect major institutional shifts away from
1381 animal use and towards new approach methodologies. PDUFA VIII should meet
1382 this moment in four areas.

1383 02:26:53 First, we support INTERACT meetings to address questions on NAMs ahead of
1384 IND submissions. Early discussions can identify existing data needs and enable
1385 sponsors using novel methods. We urge FDA to ensure staff with NAMs expertise
1386 participate in all of these meetings.

1387 02:27:08 Second, we strongly support reviewer training and regulatory science tools. That
1388 training should explicitly include NAMs and address how NAMs-generated data
1389 can be evaluated and incorporated into regulatory decisions. PCRM, we are ready
1390 to assist FDA with its efforts through our NAM Use for Regulatory Application,
1391 or NURA, training program, which provides regulators and other stakeholders
1392 with practical training and case studies.

1393 02:27:32 Third, we encourage FDA to use its proposed public meeting on regulatory
1394 science tools to improve transparency around NAMs. Sponsors need greater
1395 certainty about how NAMs data can contribute to regulatory decisions. FDA
1396 should share anonymized case studies showing when NAMs data have facilitated
1397 a regulatory decision, context of use, and the evidence weight. This kind of shared
1398 learning increases confidence in NAMs.

1399 02:27:54 Fourth, I STAND has already demonstrated its value for organ-on-a-chip and in
1400 silico tools, and we urge the FDA to expand PDUFA VIII's commitment on DDT
1401 qualification to support I STAND so that NAMs can receive the appropriate
1402 support.

1403 02:28:08 In summary, we encourage FDA to use PDUFA VIII to move beyond recognizing
1404 NAMs as regulatory science tools and towards systematically enabling their use.
1405 We're also supportive of comments from the Humane World for Animals, and we

1406 stand ready at the Physicians Committee to assist the Agency with NAMs-focused
1407 training and implementation efforts. Thank you guys again so much.

1408 02:28:25 **Nana Adjeiwaa-Manu:** Thank you, Jon. Next, we have Jeff Allen from
1409 Friends of Cancer Research. Jeff, please approach the microphone.

1410 02:28:34 **Jeff Allen:** Good morning. I'd like to commend the leadership and working
1411 groups from the FDA and industry for their efforts to produce the agreement letter
1412 that was recently made public. This occurred during a time in which FDA was
1413 experiencing unprecedented adversity, which speaks to the importance,
1414 predictability, and stability the PDUFA program provides. This agreement will
1415 chart the course for FDA and the broader research community to continue to
1416 develop life-improving medicines.

1417 02:28:59 As in years past, the proposed PDUFA agreement letter directs user fee-generated
1418 resources to support key processes and programs to ensure the safety and efficacy
1419 of medical products. It also supports a growing number of important regulatory
1420 programs shaping the next generation of treatments. For example, in Section I.L.,
1421 it describes the resource support for the Breakthrough Therapy program, Patient-
1422 Focused Drug Development, rare disease drug development, and the use of real-
1423 world evidence. The negotiators recognize the importance of several regulatory
1424 science programs and pilots, and have taken steps to make modifications and
1425 incorporate them into development and review processes.

1426 02:29:35 However, one program left unmodified is the Drug Development Tools
1427 Qualification Pathway for Biomarkers. Page 33 of the agreement describes: "To
1428 facilitate the continued use of Drug Development Tools Qualification Pathway for

1429 Biomarkers, FDA will utilize staff capacity to facilitate biomarker qualification
1430 review.” In a decade since the program was established, FDA has accepted over
1431 60 projects into it. Only eight have completed qualification, and only four have
1432 been withdrawn. That means over 80% of projects remain stuck in the
1433 qualification program for years.

1434 02:30:12 Part of this is a resource problem that could have been addressed through this
1435 agreement letter. But hopefully it can be addressed in the implementation of
1436 PDUFA VIII, because simply continuing as is not the solution to make this
1437 program work.

1438 02:30:24 To be clear, this is an important program for advancing tools that provide key
1439 measures used to evaluate drug safety and efficacy. FDA has made important
1440 efforts recently to improve the program, including a recent qualification. But as
1441 the PDUFA process advances, I would urge the FDA, industry, advocacy
1442 organizations, and Congress to thoroughly examine how this critical program can
1443 be supported and modernized to better achieve the goals of implementing new
1444 technologies for patient benefit. Thank you.

1445 02:30:54 **Nana Adjeiwaa-Manu:** Thank you, Jeff. Next, we have Tim Scott from
1446 Biocom. Tim, please approach the microphone.

1447 02:31:03 **Tim Scott:** Good morning. Thank you to the FDA for the opportunity to share
1448 our perspectives on the PDUFA VIII Commitment Letter. My name's Tim Scott.
1449 I'm the President and CEO of Biocom, the largest trade association representing
1450 the life science ecosystem in California. Our membership includes biotech,
1451 pharmaceutical, medical device and diagnostic companies of all sizes, as well as

1452 research universities and institutes, investors, and service providers. Prior to
1453 taking this position, I was a biotech entrepreneur for 25 years.

1454 02:31:33 I want to recognize the FDA industry negotiators and stakeholder groups whose
1455 hard work and dedication made the PDUFA VIII Commitment Letter possible.
1456 We recognize that reaching agreement on these commitments requires significant
1457 effort and collaboration, and we thank you for that.

1458 02:31:48 Biocom wants to ensure that the Agency has the necessary resources and expertise
1459 to review and approve products in a timely manner on behalf of the more than
1460 12,000 life science organizations in our state. At the beginning of the PDUFA
1461 VIII process, Biocom proposed several recommendations to strengthen the
1462 program. We are pleased to see many of these priorities reflected in the
1463 commitment letter.

1464 02:32:09 First, we appreciate the Agency's commitment to improving consistency and
1465 review practices across FDA divisions by strengthening reviewer training. Greater
1466 consistency in scientific and regulatory approaches can help provide greater
1467 predictability for sponsors while continuing to support the development of
1468 lifesaving therapies.

1469 02:32:29 Second, Biocom is encouraged by the new and enhanced engagement
1470 mechanisms established in the CMC Facility Lifecycle Program. These represent
1471 an important step forward in supporting more timely and transparent
1472 communication on CMC and facility-related issues between FDA and sponsors.

1473 02:32:48 Lastly, we appreciate the commitments aimed at improving the efficiency and
1474 effectiveness of interactions between sponsors and the Agency. From earlier

1475 consultation on the use of new surrogate endpoints to enhancements in formal
1476 meeting practices, these commitments can foster more productive engagement
1477 and greater regulatory clarity.

1478 02:33:08 The United States is at a pivotal moment for global competitiveness. At a time
1479 when other nations are investing heavily in biomedical research, maintaining a
1480 modern, efficient, and science-based regulatory framework is critical to
1481 preserving America's leadership in the life sciences. PDUFA VIII helps provide
1482 the stable and predictable regulatory environment needed to support innovation,
1483 strengthen competitiveness, and accelerate the development of drugs and
1484 biologics.

1485 02:33:36 Thank you again for the opportunity to comment on behalf of Biocom and its
1486 members. Our detailed comments, including recommendations for the
1487 implementation of PDUFA VIII, will be submitted to the docket.

1488 02:33:46 **Nana Adjeiwaa-Manu:** Thank you, Tim. Next, we have Suzanne Robotti
1489 from MedShadow Foundation. Suzanne, please approach the microphone.

1490 02:33:55 **Suzanne Robotti:** Hi, I'm Suzanne Robotti, Founder and Board President of
1491 MedShadow Foundation and Executive Director of DES Action USA. I also
1492 served for seven years on FDA's Drug Safety and Risk Management Advisory
1493 Committee.

1494 02:34:09 PDUFA has spent decades developing increasingly detailed performance goals,
1495 governing the FDA's obligations to drug sponsors. There are deadlines measured
1496 in days and performance goals of 90% or better. PDUFA also supports important
1497 post-market safety activities, including Sentinel, REMS, and post-marketing

1498 requirements, but there is not a comparable PDUFA framework of measurable
1499 accountability for sponsors for meeting their post-market safety obligations.

1500 02:34:38 FDA's own data shows why that matters. In fiscal year 2024, approximately 30%
1501 of open post-marketing requirements were off schedule. About one quarter of
1502 open safety PMRs required under Section 505(o)(3) were off schedule. Only
1503 about 78% of required annual PMR and PMC status reports were submitted on
1504 time. And among PMRs established in 2018, 24% were still delayed six years
1505 later.

1506 02:35:09 A drug is necessarily approved on limited information from a limited population
1507 over a limited time period. Millions of people take it. They take other drugs with
1508 it and they have conditions and characteristics that may not have been well
1509 represented in clinical trials. We learn much more about adverse events,
1510 interactions, and long-term effects. That makes the years after approval extremely
1511 important because patient harm is a major safety indicator.

1512 02:35:34 PDUFA VIII should create greater reciprocal accountability. Just as the FDA is
1513 held to measurable deadlines for reviewing applications and communicating
1514 PMRs and responding to protocols, sponsors should be held to measurable goals
1515 for initiating and completing required post-marketing studies, submitting required
1516 data on time and responding to identified safety signals. PDUFA should continue
1517 strengthening active surveillance through Sentinel and other systems that allow
1518 the FDA to find safety problems rather than waiting for enough individuals to
1519 report and reveal them.

1520 02:36:08 There's been a clearly expressed concern about staffing and expert knowledge
1521 today. At this meeting, I encourage renewed use of the Advisory Committee
1522 meetings, which are designed to add independent expertise and are part of the
1523 PDUFA program. We are not asking PDUFA to take on something outside its
1524 mission. Post-marketing drug safety is already part of PDUFA. We are asking that
1525 it be given the accountability and urgency it deserves. Drug approval is a moment
1526 in time. Drug safety is a lifetime responsibility.

1527 02:36:39 **Nana Adjeiwaa-Manu:** Thank you, Suzanne. Next, we have Jamie Sullivan
1528 from the RARE Foundation. Jamie, please approach the microphone.

1529 02:36:52 **Jamie Sullivan:** Hello and thank you for the opportunity to provide
1530 comments on behalf of the RARE Foundation, formerly known as the EveryLife
1531 Foundation for Rare Diseases. My name's Jamie Sullivan. I'm the Senior Vice
1532 President of Policy and Advocacy. Our comments today reflect the robust
1533 engagement of our Community Congress coalition members through a PDUFA
1534 working group we have convened over the last two years, our May scientific
1535 workshop, and our participation in the stakeholder consultation meetings.

1536 02:37:16 Many of the conversations that informed our comments focus on how greater
1537 transparency, consistency, coordination, and knowledge sharing across the FDA
1538 can ensure that scientific innovation, evolving regulatory tools, and policy
1539 progress translate into scalable outcomes for all rare disease communities. We are
1540 grateful for the FDA's continued commitment to the needs of the rare disease
1541 community and for including multiple policies of importance to the community in
1542 the commitment letter.

1543 02:37:41 While today's session and our comments are focused on the letter, we are also
1544 looking forward to working with Congress on legislative provisions that
1545 complement, reinforce, or build upon the letter, including by codifying the Rare
1546 Disease Innovation Hub and further strengthening the Agency's PFDD programs.

1547 02:37:55 The RARE Foundation is pleased that the letter contains several provisions of
1548 importance to rare disease, including, but not limited to, a focus on endpoint
1549 development, including opportunities to address surrogate endpoints earlier in the
1550 development programs and transitioning the Rare Disease Endpoint Advancement
1551 Pilot into practice; a commitment to advancing patient-focused drug development;
1552 setting a goal of 10 RISE workshops that address critical regulatory science
1553 topics; and renewed efforts to minimize potential delays associated with CMC
1554 issues.

1555 02:38:24 Beyond these provisions, we urge that the Agency commit to taking actions on the
1556 following: embracing a more rigorous commitment to systemic knowledge
1557 management by leveraging technology to make information about the Agency's
1558 approach to parallel scenarios easily accessible to reviewers; create a meeting
1559 mechanism to enhance opportunities for patient organizations that are driving pre-
1560 competitive therapy development work to engage with the Agency outside of
1561 sponsor-specific meetings; improving transparency into Agency staffing and rare
1562 disease expertise, including information about gaps in how FDA is planning to
1563 address them; and lastly, carefully monitoring and assessing the impact of any
1564 modifications to existing user fee waiver structures and the impacts they might

1565 have on rare disease therapy development in partnership with OOPD and external
1566 stakeholders.

1567 02:39:10 In closing, the RARE Foundation is encouraged by the provisions within the
1568 PDUFA VIII Commitment Letter and we look forward to working with the FDA
1569 and Congress to build upon these to advance the needs of the rare disease
1570 community. Thank you.

1571 02:39:21 **Nana Adjeiwaa-Manu:** Thank you, Jamie. Next, we have Andrew Coats
1572 from Telix Pharmaceuticals. Andrew, please approach the microphone.

1573 02:39:30 **Andrew Coats:** Good morning. I'm Andrew Coats speaking on behalf of
1574 Telix Pharmaceuticals. I want to thank the excellent team here at FDA for holding
1575 this final public hearing and very much appreciate all the hard work that's gone
1576 into this.

1577 02:39:43 Radiopharmaceuticals are an already changing medicine, but the proposed
1578 PDUFA VIII Commitment Letter does not mention them. Radiopharmaceuticals
1579 do not fit neatly into a regulatory system designed for conventional medicines.
1580 Radioactive decay creates a clock. Delays in manufacturing, inspection, or review
1581 can mean a patient dose cannot be delivered.

1582 02:40:08 Telix urges FDA to make three commitments in PDUFA VIII. First, establish a
1583 dedicated radiopharmaceutical development and review pathway. Second, invest
1584 user fee resources and specialized reviewers and inspectors who understand
1585 radiopharmaceutical science and manufacturing. And third, establish measurable
1586 commitments for timely, consistent cross-office review.

1587 02:40:32 This is not about lowering FDA standards. It's about applying standards with the
1588 expertise these medicines require. Regulatory capability must keep pace of the
1589 science and with the patients waiting for it. Thank you.

1590 02:40:46 **Nana Adjeiwaa-Manu:** Thank you, Andrew. Next, we have Ryan Fischer
1591 from Foundation for Angelman Syndrome Therapeutics. Ryan, please approach
1592 the microphone.

1593 02:40:57 **Ryan Fischer:** Thank you for the opportunity to comment on the proposed
1594 PDUFA VIII commitments related to patient-focused drug development and
1595 patient experience data.

1596 02:41:05 I want to start with something very simple. PFDD has worked. It has changed
1597 drug development and fundamentally changed the role of patient communities in
1598 that process. We are no longer just bringing stories to the FDA. Many of us
1599 generate rigorous evidence on disease burden, symptoms and outcomes that
1600 matter most, what meaningful benefit looks like, and a benefit-risk trade-off
1601 patients and caregivers are willing to accept. That is especially important in rare
1602 diseases where knowledge can be limited.

1603 02:41:33 The recent Booz Allen assessment reinforces that this work matters. FDA
1604 reviewers reported that patient experience data can inform endpoint selection, trial
1605 design, clinical outcome assessments, and benefit-risk considerations, but the
1606 report also points out a need for greater clarity around how PED is used in review,
1607 how it's evaluated across disciplines, and how that use is reflected in public-facing
1608 documents.

1609 02:41:59 The question is no longer whether patient experience data belongs in drug
1610 development. The question is how we make its use more systematic, more
1611 durable, and more visible. PDUFA VIII does take meaningful steps in that
1612 direction through reviewer training, public discussion, and case studies, but I
1613 would encourage us to view those commitments as a foundation, not the finish
1614 line.

1615 02:42:21 Patient communities are generating evidence across diseases and development
1616 programs. We need these commitments to help FDA consistently learn from that
1617 evidence and carry those learnings forward across the Agency. For patients and
1618 families, greater transparency means understanding in plain language not only
1619 that PED was reviewed, but whether it shaped the decision, how it shaped it, and
1620 when it did not.

1621 02:42:45 Patient organizations will continue investing in rigorous PED because we believe
1622 it will lead to better drug development and treatments that reflect what patients
1623 value. We need to understand which types of PED are informing decisions and
1624 how they advance regulatory science at FDA.

1625 02:43:02 So, in closing, PFDD taught us how to systematically bring the voice of the
1626 patient into drug development. The next chapter is making sure that voice
1627 meaningfully informs regulatory decision and drives real progress for patients.
1628 Thank you.

1629 02:43:16 **Nana Adjeiwaa-Manu:** Thank you, Ryan. Next, we have Mary Hilley from
1630 Humane World for Animals. Mary, please approach the microphone.

1631 02:43:25 **Mary Hilley:** Good afternoon. My name is Mary Hilley and I'm a specialist for
1632 animal research issues at Humane World for Animals, also speaking on behalf of
1633 Humane World Action Fund. In addition, we support the comments made by the
1634 Physicians Committee for Responsible Medicine.

1635 02:43:40 PDUFA VIII provides an opportunity for FDA to make commitments consistent
1636 with the overarching goal of its 2025 roadmap to reducing animal testing in
1637 preclinical safety studies. We will be submitting more substantial written
1638 comments that make several recommendations, but I will highlight three key
1639 points today.

1640 02:43:58 First, new approach methodology should be explicitly included in PDUFA VIII's
1641 regulatory science commitments. While the commitment letter does include a
1642 statement to enhance use of regulatory science tools to support drug development
1643 and regulatory review, it does not specifically identify human-based NAMs such
1644 as organ-on-chip technologies and computational approaches. NAMs should be
1645 incorporated throughout PDUFA VIII and their inclusion should be clearly
1646 stated.

1647 02:44:22 Next, NAMs should be incorporated earlier and more efficiently into all
1648 communications between FDA and drug development sponsors. Specifically,
1649 FDA should encourage sponsors to seek advice on the use of NAMs during pre-
1650 IND, INTERACT, Type C, Type D, special protocol assessment, and pivotal
1651 protocol interactions. Having NAMs as a standard agenda item during early
1652 discussions will help identify opportunities to use NAMs before development
1653 programs become committed to conventional approaches, and could reduce

1654 unnecessary animal testing. FDA must also ensure that reviewers have the
1655 expertise needed to evaluate NAMs.

1656 02:44:59 Third, FDA should demonstrate how these commitments are changing regulatory
1657 practice. The proposed third-party review is an opportunity to better understand
1658 and demonstrate how NAMs are being used in regulatory decision making for
1659 pharmaceuticals. The assessment could include specific questions about use of
1660 NAMs with responses tracked to demonstrate when NAMs are discussed,
1661 proposed, evaluated, and used in regulatory decision making, as well as to
1662 identify barriers to their uptake.

1663 02:45:26 Collecting metrics on NAMs use should become standard practice for FDA and
1664 should be included in annual PDUFA performance reports to promote
1665 transparency of how and when NAMs are being incorporated into the drug
1666 development process. Importantly, FDA should use this information not simply to
1667 track activity, but to demonstrate how these commitments are changing regulatory
1668 practices and identify opportunities where NAMs can generate data relevant to
1669 improving human safety while reducing unnecessary animal testing.

1670 02:45:54 We hope that PDUFA VIII is used by FDA as an opportunity to improve
1671 regulatory decision making in drug development by increasing consideration of
1672 how human-based approaches can lead to better outcomes for patients. Thank
1673 you.

1674 02:46:07 **Nana Adjeiwaa-Manu:** Thank you, Mary. Next, we have Patricia Kelmar
1675 from U.S. PIRG. Patricia, please approach the microphone.

1676 02:46:16 **Patricia Kelmar:** Good morning. I'm Patricia Kelmar with U.S. PIRG, the
1677 public interest research group. We're a nonprofit consumer organization
1678 unaffiliated with any health industry.

1679 02:46:26 As a participant in the public stakeholder process, we urge FDA to prioritize its
1680 public health mission by including measurable goals that don't merely speed up
1681 approvals, but rather ensure only safe and effective medicines are approved and
1682 that critical confirmatory trials are completed.

1683 02:46:47 Despite repeated requests for greater transparency of FDA approval decisions and
1684 facility inspections, the agreement's only section entitled "Transparency" is
1685 limited to quarterly industry meetings focused on IT or processes, with no focus
1686 on quality metrics that show achievement toward public health goals and no
1687 inclusion of public stakeholders. Furthermore, the annual reporting of Sentinel's
1688 use and the biannual update meetings will only be with the regulated industry
1689 rather than being made public. This is not the patient-centered focus that a
1690 responsible PDUFA agreement should take.

1691 02:47:30 We also expressly ask that more user fee resources be dedicated to the
1692 enforcement of post-market surveillance for safety and efficacy to ensure that
1693 patients are using medicines with proven clinical endpoints. Because this
1694 agreement expands alternative clinical designs and use of surrogate markers, it's
1695 more important than ever that FDA has dedicated resources to demand and
1696 enforce post-market requirements to prove that the drug is truly effective. Instead,
1697 the agreement actually goes on to emphasize that post-approval PMRs are not
1698 PDUFA-tracked metrics nor subject to performance goals.

1699 02:48:14 Despite FDA self-reported staffing shortages, PDUFA VIII maintains swift
1700 timelines and initiates new programs, but how is this possible when there are far
1701 fewer staff? We've heard that discussed a lot. What is not captured in the
1702 agreement is an evaluation of which FDA functions will be eliminated or slowed
1703 down to achieve the demanded performance goals in PDUFA VIII. There's been
1704 no discussion of what those cuts mean for public health and that should be
1705 considered.

1706 02:48:44 This agreement fails to prioritize FDA's resources for its most pressing work to
1707 answer the public's question: despite speedy approvals based on limited clinical
1708 evidence, is my drug safe? Is it effective? Combining limited staffing with time-
1709 boxed approvals could be a deadly combination. We'll continue to press for
1710 greater transparency and smart resource allocation to allow patients and the public
1711 to keep FDA committed to its public health mission. We'll be submitting more
1712 expansive comments to the public docket. Thank you very much.

1713 02:49:20 **Nana Adjeiwaa-Manu:** Thank you, Patricia. Next, we have Taylor Livelli
1714 from 1Day Sooner. Taylor, please approach the microphone.

1715 02:49:30 **Taylor Livelli:** Good morning. I'm Taylor Livelli. I'm the U.S. Advocacy
1716 Director at 1Day Sooner. We are a nonprofit that works to lower the cost of
1717 generating health evidence and get more value from the evidence we already
1718 have.

1719 02:49:42 Thank you so much for the opportunity to comment on the draft PDUFA VIII
1720 Commitment Letter. Today, I'm going to focus on three priorities, and I should

1721 also say we expect Congress to do the customary and legislate to expand upon and
1722 enhance the performance goals and commitments embodied in the agreement.

1723 02:49:59 So, first I will touch on Sentinel. We support Section M's commitments to
1724 maintain Sentinel, implement the 3.0 model, and strengthen ARIA. We ask for
1725 two enhancements. Sentinel relies largely on claims data and electronic health
1726 records fill its known gaps. PDUFA VIII should name integration of Veterans
1727 Affairs health data as a modernization priority. Congress called for this in 2007
1728 and FDA has already piloted this, but what's missing is a commitment to act.

1729 02:50:30 We also ask that PDUFA VIII direct FDA to build predictable access pathways
1730 for qualified non-FDA users, starting within HHS, and to share Sentinel 3.0
1731 details with independent researchers, patients, and clinicians alongside industry.

1732 02:50:47 Second, global reciprocity. FDA's inspection agreements with the UK, the EU,
1733 and Switzerland show that reliance on peer regulators works while FDA standards
1734 stay intact. PDUFA VIII should support a review of those agreements and pilot
1735 expansions across the product lifecycle limited to peer regulators with the FDA
1736 keeping final authority. FDA should also work with EMA and Health Canada,
1737 which already released clinical portions of approved applications, towards
1738 common disclosure standards.

1739 02:51:20 And then third, transparency. FDA should formally commit to continue
1740 publishing complete response letters with a public dashboard summarizing the
1741 primary reasons behind them. PDUFA VIII should also fund an expansion of Elsa
1742 to support AI-assisted redaction. Reliable redaction makes routine CRL release
1743 feasible without major new staffing, and it also opens the door to releasing longer

1744 documents, like common technical documents, which could speed drug
1745 development and drug repurposing.

1746 02:51:49 Our written comments cover these points in more detail along with
1747 recommendation on AI-assisted predictive analytics in FDA review. Thank you so
1748 much.

1749 02:52:00 **Nana Adjeiwaa-Manu:** Thank you, Taylor. Next, we have Alexander Naum
1750 from Generation Patient. Alexander, please approach the microphone.

1751 02:52:09 **Alexander Naum:** Hello, my name is Alexander Naum. I'm a rare disease
1752 patient and the Policy Manager at Generation Patient. Generation Patient
1753 represents the over 25 million young adults living with chronic and rare
1754 conditions in the United States. We do not accept funding from the
1755 pharmaceutical industry or any other healthcare industry sources.

1756 02:52:26 Generation Patient has been actively engaged in the PDUFA VIII reauthorization
1757 process, including attending every public stakeholder meeting and providing
1758 written comments. Unfortunately, the needs of young adult patients are not
1759 appropriately represented in the PDUFA VIII draft commitment letter. This is
1760 especially true in the lack of reporting for young adults in clinical trials and in the
1761 surveillance of adverse events.

1762 02:52:47 For example, in FDA's clinical trial snapshots for Mounjaro, data for young adults
1763 and other adult age groups are reported in a broad 18 to 64 category, and FDA's
1764 Adverse Event Monitoring System, also known as AEMS, reports drug- and
1765 biologic-related adverse events in a broad 18-to-64 age bracket. These large data
1766 groupings obscure differences in the therapeutic disposition that occur in young

1767 adulthood, impacted by hormone maturation, metabolic changes, and brain
 1768 development.

1769 02:53:17 This is why it's crucial that FDA disaggregate adult data by developmentally
 1770 appropriate 10-year brackets in both pre-market reviews and post-market
 1771 surveillance activities: to ensure safety and efficacy signals specific to young
 1772 adults are appropriately identified and properly accessible to patients.

1773 02:53:37 A written comment will address this topic further and discuss other deficiencies in
 1774 the draft commitment letter, including, but not limited to, concerns with surrogate
 1775 and other endpoint expansion into common diseases; concerns with increased
 1776 real-world evidence use in pre-market reviews and holistically satisfying post-
 1777 market requirements; and concerns with new avenues for sponsors to be released
 1778 from post-market requirements.

1779 02:54:00 We have consistently shared these points with FDA and we expect a greater
 1780 recognition from both FDA and sponsors. We look forward to seeing greater
 1781 representation of the current and next generation of patients in the commitment
 1782 letter. Thank you for your time.

1783 02:54:14 **Nana Adjeiwaa-Manu:** Thank you, Alexander. Next, we have Erin O'Quinn
 1784 from Parkinson's Foundation. Erin, please approach the microphone.

1785 02:54:26 **Erin O'Quinn:** Morning. I'm Erin O'Quinn with the Parkinson's
 1786 Foundation. The next five years of PDUFA are incredibly important for the 1.1
 1787 million people living with Parkinson's disease. There are currently no disease-
 1788 modifying therapies, and neurological drug development is particularly
 1789 challenging with a near 100% failure rate.

1790 02:54:44 For Parkinson's disease specifically, a lack of clinically useful biomarkers means
1791 that by the time someone is diagnosed, more than half their dopamine cells are
1792 already gone, making it hard to demonstrate neuroprotection benefits. But we're
1793 on the cusp of potential breakthroughs, and with a strong PDUFA and adequate
1794 FDA staffing and expertise, the landscape will look different in five years.

1795 02:55:07 Completing this draft commitment letter is an accomplishment. We welcome the
1796 expansion of Type C meetings. Early engagement matters, particularly on
1797 endpoints, and we're pleased to see the continued focus to advance the use of real-
1798 world evidence and patient experience data. Today I'm going to focus on three
1799 gaps.

1800 02:55:25 First, endpoints. The current Biomarker and Clinical Outcome Assessment
1801 Qualification Program does not work as intended. Continuing with the status quo
1802 does a disservice to patients. There needs to be a more practical and broadly
1803 applicable process to establish regulatory acceptance of endpoints. This is
1804 especially true for digital health technologies. The current standard to evaluate
1805 progression of Parkinson's disease is a 50-question point-in-time inventory.

1806 02:55:54 Wearable devices can detect subtle changes missed by this tool and provide
1807 insights into how Parkinson's symptoms like tremor, dyskinesia, and changes in
1808 gait change over time and in real-world settings. For a disease where symptoms
1809 fluctuate throughout the day, the potential for wearables to more accurately detect
1810 disease progression and treatment response is significant. No drug has been
1811 approved using a wearable device as a primary endpoint, and there have been no

1812 formally qualified sensor-derived endpoints. The drug development tool pathway
1813 is slow and complex, which is a deterrent.

1814 02:56:29 While it's not an FDA and PDUFA problem alone, excluding dedicated
1815 commitments is a missed opportunity. Clear guidance and a timeline for
1816 incorporating data from wearables as endpoints is needed.

1817 02:56:40 Second, we ask that you restore cell and gene therapy program commitments.
1818 Losing dedicated commitments is a step in the wrong direction for precision
1819 medicine. Future gene- and cell-based therapies hold promise for people living
1820 with Parkinson's, and a continued FDA focus is essential.

1821 02:56:55 Finally, our vision for the drug program includes a TAP for drugs modeled off
1822 devices, structured early engagement between industry and outside stakeholders,
1823 and a focus on collaboration with CMS to align on evidence requirements early.
1824 Thank you for your time today and consideration of these opportunities.

1825 02:57:14 **Nana Adjeiwaa-Manu:** Thank you, Erin. Next, we have Michael Abrams
1826 from Public Citizen. Michael, please approach the microphone.

1827 02:57:23 **Michael Abrams:** Hi there. I'm Michael Abrams, senior health researcher
1828 with Public Citizen, no financial conflicts to report.

1829 02:57:31 The draft commitment letter, unfortunately, like previous ones, we do not think
1830 address many patient and consumer concerns, and you've heard that from others.
1831 The absence of public health-oriented measures remains a critical deficiency, so
1832 that's what I'm going to focus on, especially in the pre-market space. Here's a
1833 short list of specific measures that we think could easily be added to the

1834 commitments. And I might add these would be commitments that would, instead
1835 of being made to industry, be made to consumers and patients.

1836 02:58:05 For each newly approved medication, including supplemental approvals, FDA
1837 performance measures should include direct consideration of the number of
1838 clinical trials reviewed and how many were positive and how many were not. This
1839 should include a timely posting and a recording of these in clinicaltrials.gov. It
1840 should also record the time to posting of review documents that are so important
1841 to transparency that record the review materials on drugs at FDA.

1842 02:58:40 There should be a flagging of whether or not trial participants were sufficiently
1843 representative in the approval packages of the U.S. population for things like age,
1844 race, and gender at a minimum. There should be flagging indicating whether
1845 approval decisions were unanimous or not among FDA scientists, FDA
1846 leadership, and external advisors, and we encourage those—as others have—to be
1847 used more frequently; FACA-compliant Advisory Committees.

1848 02:59:14 For medications approved in the most recent years and for medications from prior
1849 years, there should be information reported and recorded and regularly available
1850 as performance measures about things like whether there were withdrawals,
1851 recalls, warnings, missed post-marketing report deadlines, fraudulent marketing
1852 issues—something that's become hugely important in this age of social media—
1853 and other adverse events. The FDA should take this information to facilitate
1854 independent evaluation of all of these data and to use it as indeed a gauge of the
1855 Agency's performance vis-à-vis new drug approvals. Period.

1856 02:59:56 Although these are reasonable asks of the FDA's drug approval programs, such
1857 performance measures have mostly been ignored by this group and by the FDA in
1858 general, we believe. And certainly they are not mentioned at all in the latest
1859 commitment letter. Adjustments to the commitments may well help address
1860 ongoing concerns about industry capture and other FDA deficiencies that too
1861 often harm consumers and prescribers. Thank you.

1862 03:00:25 **Nana Adjeiwaa-Manu:** Thank you, Michael. Our final public comment
1863 speaker is Kathryn Lowell from NORD. Kathryn, please approach the
1864 microphone.

1865 03:00:37 **Kathryn Lowell:** Hello. Thank you to the entire FDA team for engaging the
1866 patient community throughout the PDUFA reauthorization process. I'm Kathryn
1867 Lowell, Executive Vice President of Government Affairs and Policy for the
1868 National Organization for Rare Disorders.

1869 03:00:54 For our community, the question is not simply whether PDUFA VIII makes
1870 review more efficient. It is whether FDA has the tools and resources to evaluate
1871 therapies when traditional development approaches do not work. We support
1872 continued investment in rare disease expertise and approaches such as novel
1873 endpoints, biomarkers, innovative trial designs, modeling, and real-world
1874 evidence. The Rare Disease Innovation Hub plays an important role in bringing
1875 this work together across the Agency and should have the resources and support
1876 to do so.

1877 03:01:35 The science of rare disease and the therapies we can now develop have advanced
1878 enormously since the Orphan Drug Act. Our regulatory framework has not always
1879 kept pace. PDUFA VIII is the opportunity to help close that gap.

1880 03:01:52 Small populations, heterogeneous disease, limited natural history data, and rapidly
1881 evolving science are realities of rare disease. Addressing them does not mean
1882 lowering standards. It means rigorous regulatory approaches designed for rare
1883 disease, using the best available science, the right evidence for the questions being
1884 asked, and applying those approaches consistently across the FDA.

1885 03:02:25 Patient experience must also be a continuous part of drug development and
1886 regulatory decision making. We welcome greater transparency into how patient
1887 experience data informs FDA decisions, not simply whether it was submitted, but
1888 how it was used. And none of this succeeds without a strong FDA workforce with
1889 deep scientific and regulatory expertise.

1890 03:02:53 PDUFA is an opportunity to build FDA's capacity to keep pace with advances in
1891 science. For people living with rare diseases, the urgency is to get this right. It
1892 could not be greater. Thank you.

1893 03:03:09 Nana Adjeiwaa-Manu: Thank you, Kathryn, and thank you to all of our
1894 public comment speakers. That concludes our scheduled Public Stakeholder
1895 Perspectives. We would now like to invite any in-person attendees that have not
1896 already provided remarks to provide brief remarks. Please, keep your remarks to
1897 no longer than two minutes and keep in mind that FDA will not answer questions
1898 during this session. If you would like to provide remarks, please approach the mic
1899 stand. Please, begin your remarks by sharing your name and affiliation.

1900 03:04:11 **Shion Chang:** Good afternoon and thank you for the opportunity to comment
1901 during the meeting. I'm Shion Chang, Assistant Vice President of Policy and
1902 Regulatory Affairs at the National Health Council, whose membership includes
1903 some of the nation's leading patient organizations. We support timely
1904 reauthorization of PDUFA and appreciate the proposed agreement's emphasis on
1905 the stability, transparency, capacity, and predictability of the drug review
1906 program.

1907 03:04:38 The RARE Foundation and other patient organizations have emphasized the
1908 importance of consistency, institutional knowledge, and translating lessons from
1909 individual programs across review teams. The NHC shares that view, particularly
1910 as FDA implements its PFDD, rare disease, and endpoints commitments.

1911 03:05:04 We welcome the proposed PFDD case studies, public review, public meeting,
1912 reviewer training, and greater transparency in review documents. These activities
1913 can help patients, sponsors, and reviewers understand not only whether patient
1914 experience data were submitted, but how those data informed regulatory decision
1915 making and what considerations may have limited their use.

1916 03:05:33 We also support dedicated expertise and reporting for real-world evidence and
1917 continued investment in Sentinel. Several speakers have raised important
1918 questions about public transparency surrounding Sentinel 3.0. Patient and
1919 consumer stakeholders should have meaningful opportunities to understand and
1920 inform its implementation, including when post-market evidence generation
1921 approaches may affect patient burden or the outcomes evaluated.

1922 03:06:03 The assessments of the formal meetings and first-cycle reviews, together with
 1923 new CMC facility engagement mechanisms, could help resolve issues earlier and
 1924 reduce avoidable review cycle extensions and complete responses. That objective
 1925 should remain focused on preventable process and communication problems
 1926 without weakening FDA's evidentiary, safety, effectiveness, and manufacturing
 1927 standards.

1928 03:06:32 Finally, successful implementation will require sustained recruitment, retention,
 1929 training, and deployment of FDA's workforce along with reporting that
 1930 demonstrates whether the Agency has sufficient expertise and capacity across
 1931 CDER and CBER. The NHC will provide more detailed comments and look
 1932 forward to supporting implementation of PDUFA. Thank you.

1933 03:06:56 **Nana Adjeiwaa-Manu:** Thank you for your comments. Great. We have time
 1934 for about one or two more. Alright. Final call for comments. Alright. Well, thank
 1935 you very much for sharing your perspectives. That concludes our public comment
 1936 session. I'll now turn it over to Andy Kish to provide closing remarks.

1937 [Closing Remarks](#)

1938 03:07:41 **Andrew Kish:** Yeah, I know it's lunch and people are really hungry, so I'll
 1939 be quick. Again, [I] just really want to thank everyone for participating
 1940 throughout the process today and giving your feedback. We have taken lots of
 1941 notes. We'll also go through everything that got submitted to the docket. We'll
 1942 review it thoroughly like we always do. We'll post our assessment of that before
 1943 this transmits to Congress. We are very much looking forward to passing this on
 1944 to Congress so they can carry it forward to reauthorization.

1945 03:08:11 And I guess I really-- Also really want to thank everyone behind the scenes, I
1946 think it was mentioned earlier, for all their hard work. Many are not in the room
1947 today, but some of them are, like Nana and Emily, who did an incredible job
1948 throughout seven months of very intense meetings and negotiations, including all
1949 industry colleagues and people behind the scenes for the negotiators in the
1950 industry and everyone, the patient and advocacy groups and consumer groups
1951 who showed up and everyone supporting them. We really, really appreciate it. I
1952 think this is a very thoughtful agreement and thank you everyone.
1953 [End of recording.]