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Today. I'm going to talk about the important role of our prescription drug user feed program and our other user feed programs, discuss some of the new program enhancements we have as part of those user feed programs.

Okay, about breaking everything, talk about our prescription drug user feed program, our PDUFA, some of our other medical product user feed programs, some of the new program enhancements we have coming as part of those, and describe some of the, we heard briefly about our work of legislation, describe some of the important new legislative authorities we received at the end of last year and talk about what those, some of our work at FDA.

So 1st to focus a little bit on the Prescription Drug User Feed program or PDUFA as we call it there. You'll see there's a lot of strange acronyms in the work that we do at FDA, and especially when we talk about our user feed programs.

Newton helps FDA fulfill its mission of protecting the public health while facilitating the timely availability of innovative FDA regulated products, all without compromising the agency's commitment to scientific integrity, regulatory standards, patient safety and importantly, transparency.

The program was enacted more than 30 years ago in 1992. Before that, FDA lacked sufficient resources to do necessary product reviews that we were finding. At the time, those reviews could stretch out for more than two years. And with the advent of PDUFA, we've seen that shrink down to less than a year. So it's been a real game pager in terms of FDA to work in prescription drug product review.

The lack of stack previously meant that industry meetings between FDA and in the industry, we're considered a, right? This wasn't necessarily something that always happened, even required meetings and staff didn't have time available to develop the procedures and the standards they needed to ensure a consistent and predictable review process. As a result, access to innovative new medicines often lag behind in the United States compared to other countries. And then you will talk a lot today about the relationship between FDA, US and FDA in the world. I love the graphic of the bridge linking PQU and FDA. And we saw that there was a real cost there of the lack of resources, both for the US and globally.

In response to those obstacles, industry with support from patient advocates agreed to pay user fees to supplement the FDA budget in exchange for commitments to reduce review times. In implementing the system, FDA took steps to ensure its integrity, make sure that the program would not be perceived as a pay to play program under the sway of the regulated. We knew that this would only work if it was clear that the agency's decision making was still independent and was still always rooted in silence.

Thus, even though FDA moved into this era of collecting user fees, the outcomes of its decisions, such as whether to approve a product continue to be based on science, continue to be based on the agency's legal and regulatory standards. And we're in no way subject to sort of different influences relative to what it had been before we had those user feed programs. That in effect included in this approach was establishing a culture of transparency and a system of internal oversight, giving the staff ability to speak their minds, challenge decisions all the way to the commissioner. That's a really important I'm central ethos for us as agency. And the means for stakeholders, whether that was industry or consumer groups to challenge the agency, including in the courts.

Since 1992, the FDA and industry had negotiated agreements on user fees every five years. So we get into a room with our key experts from FDA, key representatives of industry, and we work through what user fees will be paid and what the program enhancements will be in exchange for those user fees. So as part of that process, the industry agrees to pay those fees in exchange for those commitments from the agency. And those can be things like timelines for making decisions on appropriate on applications, providing access to FDA experts via meetings, specifically around guidance or workshops that industry might be seeking for the agency to engage in.

And Congress then passes legislation every five years to reauthorize the agreements and enable the FDA to continue to collect fees. So it's a bit of an unusual system where we have this negotiation directly between the agency and our industry, and then we go to Congress with an agreement and we seek Congress's consent to move forward with that agreement.

Other user fee programs have been adopted since then. The 1st following PDUFA was MDUFA, the Medical Device User fee amendments. That was in 2002. You and was really important to improving the predictability and the transparency of regulatory processes for medical devices instead of rising innovation and getting more products to market faster.

Following up was GDUFA, the generic drug user fee amendments. That was in 2012. It helped ease a really challenging backlog of marketing applications that occurred as we saw the generic industry really blossoming. Following that was the 4th of our human medical product user fee programs or biBsUFA by a similar User Fee act. This was enacted in the same year and authorized FDA to collect user fees to expedite the review process for biosimilar biological product applications, including post market safety activities.

So we see a commonality across all four of these where we have entered into these user fee agreements, industry engages with the agency around those fees, but also what will be really meaningful in terms of the agency providing commitments around due timelines and other sort of programmatic enhancements.

I'll know just very quickly, we're focusing today mostly on human medical products, but our animal drug programs are also based in user fees. So we have both a animal drug user feed ad in a generic animal drug user fiat. Those are both up for reauthorization this year. And so right now we're engaging with the Congress around those so that agreements have already been reached between industry and the agency. And we're engaging with Congress around reauthorization of those by the end of the fiscal year in September.

And also while we're talking about this sort of view across agency of user fiat are tobacco User Fee program funds, the agency's tobacco work to support public health driven regulation in that space as well. That's a little bit different. We don't negotiate the industry on our tobacco user fees, but nonetheless, it is a user fee supported program really central to the way that we do our work.

Originally, prescription drug user fees could only be used to support free market review of new drug applications or NDAs and biologic license applications, or BLAs. But there's been an evolution over time, other activities that relate specifically to prescription drug development, such as pre clinical drug development, certain post marketing activities and enhancements to technology systems have also been allowed to be funded by user feeds.

And in addition, really importantly, user fees now help pay for certain FDA inspections. This includes those that help ensure the right safety and welfare of participants and clinical trials, as well as reapproval inspections of manufacturing establishments to assess a manufacturer's ability to design and manufacture products in accordance with our current good manufacturing practices.

Every five year reauthorization cycle supports continuous program innovation, evaluation and improvement. So as you talked about, when industry and the agency come to the table every five years, it's really with an eye to where are we going and what program enhancements might we need in these next five years that, that weren't as that weren't the focus in the previous cycles.

As a result, through successive to do for reauthorizations, program enhancements have evolved and expanded to include extensive communication and consultation between drug sponsors and FDA. Really over the course of the drug development process, these interactions have given FDA the opportunity to provide more guidance to sponsors, including setting clear expectations of what data are necessary, properly review and evaluate the drug, get safe and effective drugs to patients sooner, which is at the end of the day what this is all about. It enables sponsors to incorporate advances in regulatory science into their development programs that in turn expedite drug development.

The Ledger line is that our user fee programs have been a win for the agency. They've been a win for industry, and as a result, they've been a win for patients. And they have addressed the reality that agency's review work was previously under resource. The user fee regime enabled the agency to speed up that application review process without compromising FDA's high standards for new drug safety, advocacy and quality accomplished even as FDA experienced a really unprecedented influx of submissions during the Covid 19 pandemic. These enhancements have met have meant rather that it's improved with our ability to approve products on the 1st cycle, but again, means that these safe and effective products are reaching patient sooner.

Moreover, user fees have been a bargain. Researchers at the department of health and Human Services, which is FDA’s parent agency were one of the independent agencies under the previous department of health and Human Services, developed an analytical model of medical product development between 2000 and 2018 that provided an estimate of the cost of medical product development at each stage of the process from the non clinical stage all the way to post marketing. And in this model, the cost of the FDA review stage was estimated using user fees paid by industry and the average time it takes for FDA to review a marketing application.

The results show that FDA user fees make up approximately 1% of the total capitalized cost of development for drugs, 2% for vaccines, and just half a percent for the development for complex medical devices. In other words, user fees are making up a tiny fraction of the total cost industry of bringing products to market successfully.

Last year, I saw the latest update to these user fee programs, PDUFA 7, MDUFA 5, GDUFA 3, and BsUFA 3, each named for the number of cycles into those programs that we are. And the Congress reauthorized all four of these in September for five years. So that began in 2023 and that will go through October FY27, Fiscal Year 27.

I want to spend a little bit of time talking about some of the important program enhancements in these programs, beginning with PDUFA Seven's impact on cellular and gene therapy development.

And we'll get to this a little bit later, but it's important to realize there's sort of two pieces of this. So one is these program enhancements that are negotiated between the agency and industry and then presented to Congress. We'll talk about that 1st. And then typically when this goes to Congress, Congress has an opportunity to think okay, we are doing we're passing this legislation for the next five years. What else do we think is important in terms of advancing FDA related policy? And we see it as a real opportunity to advance legislation as well. So we'll talk about that a little bit later.

Well, but on cellular and gene therapy development, this is a space where FDA has experienced exponential growth over the past 7 years. And we now have nearly 2000 active development programs. It would have been hard to imagine that really just a few years ago to address the continued influences solutions, our center for Biologic Evaluation and research or receiver has committed to higher additional staff, develop multiple guidance, conducts numerous public meetings to examine new technologies and new approaches and establish a patient focused effort to better understand patient perspectives on gene therapy products.

We've also established the Operational Warp Speed Communications Pilot for Rare Diseases, which provides participating sponsors with initial FDA meetings, followed by ongoing informal FDA staff interactions via email or in a live meeting as an as an on an as needed basis, making sure that we really have that dynamic conversation happening between the agency and the folks who are developing these products.

PDUFA 7 also contains enhancements to the work of our center for Drug Evaluation and research, or Cedar. They'll enhance regulatory review, add more flexibility in the type of meetings we hold with industry.

And I see also it's agreed as part of this to establish some innovative new programs. I'll mention just a few of those. One, the Rare Disease Endpoint Advancement Pilot Program promotes innovation and evolving science by sharing learning on novel endpoint development through FDA presentations, guidance documents, public workshops and public facing websites.

These are tools that we use in many different areas to really make sure the industry has the information they need about how the agencies approaching its work. As a result of this program, Sieber and Cedar staff are expected to be able to enable and facilitate the development and use of novel endpoints to evaluate the efficacy of rare disease therapies.

Another example of the Advancing Real World Evidence program is designed to accomplish three things. 1St, it's designed to identify approaches for generating real world evidence that meet regulatory requirements in support of labeling, for effectiveness or for meeting post approval study requirements.

2Nd, there's a focus on developing agency processes that promote consistent decision making, shared learning regarding real world evidence.

And 3rd, to promote awareness of characteristics of real world evidence that can support regulatory decisions by allowing FDA to discuss study designs considered in the Advancing Real World Evidence program in a public forum. Meetings will be conducted with both Cedar and Seaber as well as FDA's Oncology Center of excellence throughout the five years of the PDUFA 7.

Finally, PDUFA 7 also puts a focus on digital health technologies. Again, you'll see a trend here. There's a real focus on areas where we're seeing an explosion, innovation, changes in technology. Look forward on medical product development. We know that digital health technologies offer a vast array of potential benefits in the development of medical products. As the world enters into a 4th industrial revolution. We know that rich and diverse sources of digital data are available at scale in real time, was potentially unlimited storage capacity. These data are becoming widely used as part of a clinical trial system.

And DHTs provide opportunities to foster more efficient conduct of clinical trials. As a result, for instance, we know that DHTs can facilitate the conduct of decentralized clinical trials where data can be remotely recorded and analyzed directly from participants as part of everyday tasks, wherever those participants may be, whether they're at home, at school, at work, even outdoors.

And the use of DHTs and the clinical investigation can help implementation, access to, and participation in clinical investigations by potentially reducing the burden of required visits to a research site. We know that this approach also means that we have the real ability to enhance diversity in our clinical research work, which is a really important part of how we think about decentralized clinical trials.

The 3rd reauthorization of GDUFA or the Generic Drug User Feed program seeks to address the fact that only 15% of submissions are approved in the 1st cycle by including new processes and new procedures designed to achieve earlier cycle approval, and by enhancing product development, pre submission and mid review cycle meetings prior to submitting an abbreviated New Drug application to market a generic drug.

In addition, FDA is setting new goals for the completion of product specific guidance that are important for the development of complex generic drugs. We know that industry really depends, depends on that guidance from the agency about how we're thinking about these important issues. I also need to do for FDA committed to making further enhancements to generic drug regulatory science programs. We have a number of priorities as we look forward to the next year in terms of science and research initiatives that involve generic drugs. And those include developing methods for generics to address impurities such as nitrosamenes and research on enhancing the efficiency of bioequivalence approaches for certain complex ingredients and certain complex products.

Finally, a few words about the BsUFA, the Biosimilar User Fee act. Like at the end we should have a little quiz where we put these acronyms up there and see who remembers which connect to which. That was enacted in 2012 and the 1st bio similar was approved by FDA in 2015. As of January 2022, there are more than 30 FDA approved biosimilars with dozens more in the cues. So again, a place where we've seen really significant changes in just a few years.

But BsUFA has enabled the FDA to implement a new review model and expand staff capacity to provide increased communication with companies, facilitating biosimilar product development. With BsUFA 3, the FDA will introduce new supplement types and expedited review timelines to speed the review of supplements. In addition, the FDA intends to enhance communication and feedback during the product development process and during application review, and also intends to introduce a new pilot program that will enhance regulatory decision making and facilitate science based recommendations.

So as I mentioned, Congress typically uses the user fee reauthorization as a vehicle for attaching proposed reforms to the FDA regulatory framework. Last year, a lawmakers were unable to reach agreement on those provisions and time he told his result. The FDA related provisions were included in a separate appropriations vehicle.

So we saw that the user be programmed for reauthorized in September. It's extremely important to the agency that those happen on time. But Congress didn't want to and we didn't want them to give away their opportunity to sort of think about where the agency needed enhanced authorities. So they came back to the table in December and said we're going to sort of finish the job when it comes to these legislative authorities that typically would have been attached to that reauthorization.

So these were included in a legislative vehicle that signed into law at the very end of last year, December 29th of last year. You may know the Congress likes to push things to the very last minute and last year was no exception. And those reforms can be found in two laws that were sort of included in that package.

First, the food and Drug Omnibus Reform Act or FDORA, and the 2nd is known as the Prevent Pandemics Act there was a really a significant number of legislative forms in those packages. But I want to just spend a minute highlighting a few of those that I think might be a, a particular interest to people in this room. So among the most significant was those having to do with FDA's accelerated approval process for drugs and biologics.

FDA's accelerated approval pathway was established in 1992. This was largely in response to the hibas epidemic and the particular needs that we were seeing at that time to help get products to market that treat serious or life threatening conditions and importantly, fulfilling medical need. The pathway is accelerated in that it allows sponsors to seek approval with data that demonstrate efficacy based on an effect on the surrogate or immediate endpoint.

It's believed to predict clinical benefit for the disease or condition rather than on the primary clinical endpoint itself. For Hivas, the circuit endpoint has been viral load. That pathway has been used primarily for drugs aimed at diseases that progress slowly and as a result, waiting for trials to demonstrate primary clinical endpoints within a years long delay that the study before the study drug could be eligible for approval.

Under a traditional pathway. As a condition of receiving accelerated approval, sponsors have been required to conduct post approval studies to confirm the clinical benefit of the drug. Once that's satisfied, the conditions of accelerated approval are removed. But the agency experienced over time that while we have this really important authority under accelerated approval, there was a real need for enhancement, both to improve oversight and to really make sure that we were driving those post approval confirmatory studies in a manner that made sure the patients were really getting the full benefit. So we worked very closely with the Congress on that enhanced authority.

And as a result, FDORA clarifies FDA's authority to specify the conditions for any post approval studies. The agency has really significant flexibility in setting forth such conditions. So these can include things like enrollment targets, study protocols and milestones, including the target date of study completion. It also gives FDA the explicit authority to require that confirmatory studies be underway prior to approval. That's a really important part of this, as well as streamlined procedures to remove drugs from the market when necessary. That is as the confirmatory study is not completed or it fails to show benefit for patients, that the agency has the ability to more rapidly remove those products from our market and make sure that we are fully develop, fully delivering on the promise of the accelerated approval program.

We're working right now to implement these reforms. This just became law in December. So this is a brand new law for us and we're really excited about it. And we know that industry will continue to seek additional guidance for us outlining the changes and how we're thinking about accelerated approval and sort of this new era with these enhanced authorities. I mentioned very briefly earlier the idea of diversity in clinical trials. This is another issue that's a real priority for the FDA. And there's a number of FDORA provisions that encourage changes that will lead to greater diversity in the populations participating Local Studies.

1St sponsors are now required to submit to FDA diversity action plans for certain late stage trials for drugs and as well for devices. Unless otherwise waived or accepted, the default will be that the agency needs that information.

Befty's tasked with updating guidance on diversity action plans for clinical studies and hosting public stakeholder workshops focused on enhancing clinical trial diversity. So it says higher expectations for industry as well as for the agency to really drive this work forward.

We were also tasked with issuing or revising guidances on the appropriate usage decentralized clinical studies, which again we spoke very briefly about earlier in the development of drugs and devices, how digital health technologies can best be used in clinical trials and how seamless, concurrent and other innovative clinical trial designs can support expedited drug application development and review. Congress likes to give FDA deadlines for these things and so they've asked us to do that work in a year. So that is very much underway.

FDORA also addresses bio research monitoring inspections. The new law clarified that is permitted to inspect facilities involved in the development, the conduct of the analysis of clinical and non clinical studies submitted to FDA as well as other persons holding study records or involved in the study process. Congress there asked FDA to draft guidance on this. That will happen within a year and a half of the announcement of that new log.

And then finally, to Prevent Pandemics Act states that foreign drug and device manufacturing establishments are subject to registration listing requirements, even if a drug or device undergoes further manufacture, preparation, propagation, compounding or processing at a separate establishment outside the US prior to being imported into the States. The law required FDA to update its registration regulations there as well, and that will happen within two years to reflect that provision.

When we think about FDORA and this package that happened at the end of the year, I want to give a little bit of a sense of just the scope of what this legislation for the agency. I focused here on some of the provisions that are most meaningful when we think about our medical product development and that relate most closely to some of those program enhancements with our negotiations with industry and the user fees themselves.

But we also for the 1st time got enhanced cosmetics authorities. We've been essentially been operating with the same legislative framework for cosmetics in 1738. So really a historic change there when it comes to the agencies oversight of cosmetics. We got very important new hiring authorities that make sure that when we think about our fuse program, they have the same ability to get the best and brightest folks into those jobs as we do on the medical product side already. And many other provisions as well.

But just to give a sense of that, this really is a once every five years we have this real opportunity to engage in advancing legislation for the FDA. And I think we really saw Congress deliver on that last year. Nonetheless, I would note that not all of FDA's legislative priorities were adopted in that package at the end of last year. So the agency will continue to work with Congress on those priorities that weren't enacted. This includes things like the oversight of diagnostic testing, very important priority for the agency and one where the Covid 19 pandemic really shown the light on.

Some places for improved authorities, dietary supplement product listing. As with cosmetics, our dietary supplement oversight regime really could benefit from significant updates to make sure that the agency can really deliver on its mission to protect public health. That's something we'll continue to work with the Congress on, as well as the application of orphaned drug exclusivity.

We also believe that there are several places where the Congress could build on our current authorities with respect to the supply chains, thinking about I'm a strong and a resilient supply chain is something that has been a focus for many years. But again, where the pandemic really reminded us of how critically important this work is, many of these are in the drug space. So these are things like the ability to require drug manufacturers to notify the FDA of an increase in demand or disruptions in the supply chain, lengthening aspiration dates where it's appropriate to mitigate critical drug shortages, requiring drug labeling to include the original manufacturer and supply chain information.

These are kind of basic, almost obvious things to make sure that the agency and the consumers have the visibility that we need, and providing for enhanced reporting by drug manufacturers, suppliers and reliance on such supplies. So we're thinking not just about the final product, but everything all along the supply chain to get there.

We've also been very focused on medical device supply chain. During the pandemic, the agency got new authority to have improved visibility into the medical device supply chain and make sure that we were hearing from industry where there were threats of short bridges. But that authority was tied specifically to there being a public health emergency either happening or imminent. So we're focused on removing those sort of temporal restrictions because we know that medical device shortages can happen completely regardless of whether there's a public health emergency either happening or right around the corner.

So I've covered a lot today. I know that's really a reflection on everything I have come to learn from my team about the really important work happening here at the King University. And I hope that this has provided a bit of a grounding around FC's user feed programs across our medical products, some of the significant new reforms that we have from Congress from this package last year, as well as some of our legislative priorities going forward.

There are two important takeaways from my remarks that I'd like to quickly emphasize before finishing. The 1st is that FDA collects these fees for medical product manufacturers, but the outcome are our decision when it comes to approving or disapproving a product is based solely on our commitment to science, to regulatory standards, to patient safety, and to transparency. That's never going to change. That's core to how the FDA does our work.

The 2nd is that this system works. The user fee system allows my agency to meet certain performance, performance goals, such as making decisions on drug applications within a predictable timeline. It improves the potential for those 1st cycle approvals so that we're getting products to patients faster. And as a result, the US continues to be a global leader in drug innovation. And that's meaningful, again, not just for patients in the US, but for patients around the world. So thank you for the time today. Look forward to the rest of the morning. And again, thank you so much for the invitation to be here.