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FDA USER FEE AGREEMENTS: ADVANCING MEDICAL PRODUCT REGULATION AND INNOVATION FOR THE BENEFIT OF PATIENTS

HEARING

OF THE

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS

UNITED STATES SENATE

ONE HUNDRED SEVENTEENTH CONGRESS

SECOND SESSION

ON

EXAMINING FOOD AND DRUG ADMINISTRATION USER FEE AGREEMENTS, FOCUSING ON ADVANCING MEDICAL PRODUCT REGULATION AND INNOVATION FOR THE BENEFIT OF PATIENTS

APRIL 5, 2022

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C O N T E N T S

STATEMENTS

TUESDAY, APRIL 5, 2022

FDA USER FEE AGREEMENTS: ADVANCING MEDICAL PRODUCT REGULATION AND INNOVATION FOR THE BENEFIT OF PATIENTS

Tuesday, April 5, 2022

U.S. SENATE,
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The Committee met, pursuant to notice, at 10:02 a.m., in room 106, Dirksen Senate Office Building, Hon. Patty Murray, Chair of the Committee, presiding.

Present: Senators Murray [presiding], Casey, Baldwin, Murphy, Kaine, Hassan, Smith, Rosen, Hickenlooper, Burr, Collins, Cassidy, Braun, Marshall, and Scott.

OPENING STATEMENT OF SENATOR MURRAY

The CHAIR. Good morning. The Committee will come to order. The Senate Health, Education, Labor, and Pensions Committee will come to order. And today we are having the first of two hearings on reauthorizing four Food and Drug Administration user fee programs. I will have an opening statement followed by Ranking Member Burr. We will then introduce our witnesses.

After they give their testimony, Senators will each have 5 minutes for a round of questions. Again, while we are unable yet to have the hearing fully opened to the public or media for in-person attendance, live video is available on our Committee website at *help.senate.gov*. And if you are in need of accommodations, including closed captioning, you can reach out to the Committee or the Office of Congressional Accessibility Services.

Every day, families in Washington State and across the country count on the Food and Drug Administration to keep them safe more times than they even realize. Whether we are getting a meal or a prescription or an ultrasound, or almost anything in between, we have the FDA to thank for reviewing the data, inspecting the supply chain, holding companies accountable, and taking unsafe products off the market.

It is no small task ensuring the safety of nearly 80 percent of our Nation's food supply, inspecting thousands of food, drug, and device manufacturing sites each year, and of course, quickly and carefully reviewing the data on new and potentially lifesaving medical products. As we have seen throughout this pandemic, this work is incredibly important, which is why it is also important we reauthorize the user fee programs, which ensure as FDA gets new drugs or devices to consider for approval.

As it gets more potentially lifesaving work to do, it also gets more resources to support that work. Congress has regularly reauthorized the user fee programs in a bipartisan way, and I am glad to be working with Senator Burr and our colleagues on the Committee to get this done once again in a timely manner. Because it should be unthinkable that after 2 years when FDA's work has been more important than ever, we would fail to get this done and force the agency to send pink slips.

Just as it should be unthinkable that we would fail to learn the lessons of this pandemic, including lessons for FDA, like how we can get tests to families sooner, or how we can avoid political interferences like we saw during the Trump administration, including the reckless push for unproven treatments like hydroxychloroquine, or how we can improve transparency and communication to prevent some of the confusion and frustration we have seen around the timelines for booster shots and vaccines for younger children.

Beyond pandemic response, it is clear we can't simply settle for business as usual, because when you look at issues like the exorbitant cost of prescription drugs, the lack of diversity in clinical trials, the scourge of opioids and especially fentanyl, the lack of oversight for dietary supplements and cosmetics, and how long it took to get contaminated baby formula off the market, it is clear to me and to people back in Washington State that business as usual is not good enough.

We have to make sure the approval process works for families, not just pharmaceutical companies' bottom lines. That means better steps to ensure drugs work for everyone, such as increased diversity in clinical trials and pediatric drug research. It means ensuring the accelerated approval pathway benefits patients. And it absolutely means lower costs, because even a miracle cure is no help if it is too expensive for people who need it.

We need to fight skyrocketing health care costs with every tool in our arsenal from stopping pharmaceutical companies who game the FDA system to block competition and keep cheaper drugs off the shelves, to bringing down barriers that block cheaper generics and biosimilars from getting to market, to finally making good on legislation Congress passed to let hearing aids to be sold over-the-counter and at lower cost for millions of people.

I worked with many of my colleagues on this Committee to pass that into law a half a decade ago, and I am incredibly frustrated FDA has not been focused on helping so many Americans. There is just no good reason we are still waiting for FDA to implement that step and save millions of people thousands of dollars. We also need to do more to protect families from dangerous products that have gone for too long with too little scrutiny.

When it comes to cosmetics, products people put on their face, rub into their skin, and more, we have discovered known carcinogens like asbestos and formaldehyde in baby powder, children's makeup kits, and hair products. And when it comes to dietary supplements, people across the country who are looking to make healthy choices are faced with a shelf full of products that make health claims but lack rigorous oversight.

Yet FDA does not have the authority to collect basic information about those products or even to know what is on the market. That

makes no sense. People in Washington State and across the country buy, use, and entrust their health to these items every day. They deserve to know these products are safe, vetted, and subject to the same type of careful FDA oversight people rely on when it comes to food, drugs, and medical devices. So I hope we will make progress on all of those issues and more as we rework—as we work to reauthorize the user fee programs.

All of us on this Committee are grateful for the tireless work of FDA scientists during this pandemic to review and authorize safe and effective tests, treatments, and of course, vaccines for COVID–19. And we are grateful for the constant work they do to ensure the safety of our food supply, provide people with the information they need to make healthy choices, and uphold the gold standard of safety and effectiveness for drugs and medical devices. But the FDA does not run on gratitude.

I look forward to today's conversation on the user fee programs, and to working with my colleagues on bipartisan legislation that supports and strengthens FDA's ongoing work by reauthorizing these programs and taking additional steps to lower drug costs, increase diversity in clinical trials, ensure the safety of cosmetics and dietary supplements, and more.

With that, I will turn it over to Ranking Member Burr for his opening remarks.

OPENING STATEMENT OF SENATOR BURR

Senator BURR. Thank you, Madam Chair. And welcome to our witnesses here today. I look forward to our discussion. Every 5 years, this Committee is charged with evaluating FDA's user fee programs and the agency's performance in meeting its existing commitments. At their core, these programs are about bringing new hope to Americans.

The faster, more predictable, and more accountable the programs are, the more patients stand to benefit from lifesaving, innovative drugs and devices. When FDA does not live up to its commitments, patients are the ones that suffer. I have served in Congress since 1995, so I have been here for all but the first user fee process.

Each time, I have gradually added provisions to improve FDA's accountability to the commitments that FDA makes. Every 5 years, industry agrees to provide more funding under the duress of negotiating with the regulator. So it is Congress's job to make sure that those negotiations were not a hostage situation, and that these arrangements are a good deal for patients and the industry that brings that hope.

The user fee programs are intended to supplement FDA's congressionally appropriated resources to speed the review of medical products and get treatments to patients as quickly as possible. The user fee agreements negotiated between FDA and industry partners lay out the process for bringing new products to market that will treat, prevent, and cure disease. In 1992, under the first Prescription Drug User Fee Agreement or PDUFA, the drug application fee was about $100,000.

Today, the drug application fee is $1.3 million. The medical device user fee agreements were first signed into law in 2002. In

2007, a 510(k) submission was just over $4,000. Today, this application costs more than $12,700. When Members of Congress complain about the cost of prescription drugs or medical devices, we should evaluate all aspects of the pipeline, including the cost of development and regulatory review, to make sure costly and burdensome regulations are not part of the cost problem.

The enormous growth in the oldest of the user fee programs underscores my longstanding concerns. In 1993, FDA collected just over $35 million in annual fees from the Prescription Drug User Fee Program. Today, FDA collects over $1 billion in PDUFA user fees annually. Even accounting for inflation, that is an increase of more than 1,500 percent since the start of the program.

Yet FDA continues to request more and more resources from industry, even when they don't meet agreed upon performance goals. For example, in Fiscal Year 2019 and 2020, FDA missed 12 out of the 14 goals related to scheduled meetings, delaying needed conversations for innovators to move forward with their products. As part of the proposed new prescription drug program commitments, FDA is requesting an additional $324 million over the 5-year cycle. Let me say that again, $324 million.

The proposed agreement includes $111 million for hiring an additional 352 people. That is 122 more new hires than the agency committed to in the last cycle. In fact, across all four programs, FDA is committing to more than 880 new hires when the agency has more than 700 vacancies outstanding. Let me say that again. In fact, across all four programs, FDA is committing to more than 884 new hires when the agency has more than 700 vacancies outstanding today.

Generic and biosimilar drugs are our best tool at driving down the cost of prescription drugs and should be a top priority of the agency. The biosimilar agreement should help boost the number of biosimilars in the market, including biosimilars in insulin production. FDA, again, has struggled to meet some important program goals.

During Fiscal Year 2020, FDA missed its goal to review 90 percent of biosimilar applications within 10 months, only reviewing 50 percent within that time, and missed 7 out of 15 goals related to product development meetings. Under the proposed biosimilar agreement, FDA is requesting an additional $5 million over the 5-year cycle and 15 new hires.

The generic drug program collects more than $494 million in annual fees and supports more than 2,100 staff positions. Under the proposed generic drug agreement, FDA is requesting additional funding of more than $40 million and 128 new hires. While FDA appears to be on track to meet the majority of its commitments under the current generic agreement, its performance has been impacted by COVID–19 in terms of delayed facility inspections.

As of last August, these inspections challenges had delayed more than 29 generic drug applications, with many more applications likely delayed since then. Turning our attention to the medical device agreement, I have watched this very carefully and I am concerned. This Committee only recently received the draft medical device commitment letter.

The final medical device arrangements were due by law to Congress by January 15th. By the time we receive these final agreements, the device commitment letter was more than 3 months late. Under this proposal, FDA is requesting up to $1.9 billion over the 5-year cycle, nearly $1 billion increase.

This proposed increase is roughly doubling fee collections. Yet again, the FDA did not meet deliverables under this user fee program. The FDA missed goals for 510(k) reviews, resulting in longer review times, failed to explain its reasoning to sponsors each time it sent a deficiency letter about their product, and it failed to issue an important digital health guidance on time. Let me remind my colleagues, these are not optional actions.

These were requirements, requirements under the last deal for categories of submissions. For the first 2 years, review times for premarket approval applications would hold steady at 290 calendar days, and in the last 3 years, review times would reduce to 285 calendar days. Wow.

However, FDA is significantly walking back its current commitment to reviewing 510(k) submissions within 180 days. Instead, FDA is proposing longer review times of 108 days. FDA Safety and Innovation Act, which we passed in 2012, requires FDA to review 95 percent of these applications within 90 days. This agreement almost doubles the user fees and includes longer review times for some categories of products.

Pay more, get less is not exactly a selling point. MDUFA V also includes a new pilot program called TAP. This aimed to initiate early and frequent engagement between FDA and sponsors of innovative devices. I might say, something already negotiated in the agreement. As the author of the breakthrough device pathway, I still can't figure out whether this new program will offer anything different from FDA's current activities for breakthrough devices.

The new pilot program is set to grow over the 5-year cycle, without clear accountability, metrics, or deliverables to help measure the success of the program. No metrics. The pilot has the ability to grow to 325 devices, which would cost at least $477,000 per device. Congress deserves a full accounting of how FDA plans to spend these resources and operate this new nebulous program.

I will tell you right now, Congress is going to require accountability in the new program. With each reauthorization, FDA receives huge increases in resources despite not fulfilling or delivering what has previously been promised. And with a declining percentage of congressional appropriations for the overall program, FDA is increasingly removing itself from Congress's reach.

My colleagues should be concerned with this. I question whether the agreements both passed and proposed reflect a good deal for patients they are designed to serve. In 2017, during the user fee hearings in this Committee, I asked each industry representative testifying about the importance of the user fee agreements and whether they would support a mechanism to hold FDA more accountable.

The response was clear, FDA should be held accountable to its commitments. I look forward to hearing from each of you and about why you have agreed to these commitments, and how they would

accelerate innovation and lifesaving products for the American people. I thank the Chair.

The CHAIR. Thank you, Senator Burr. I would like to ask unanimous consent to introduce into the record a statement from the National Organization for Rare Disorders.

Senator BURR. Madam Chair, I would also like to ask unanimous consent to enter into the record letters that I sent to then Acting Commissioner Woodcock, requesting information about the user fee programs and the negotiations for these proposed new agreements, and the responses I received from the FDA. One of these letters I sent to the FDA in November last year, and I am still awaiting a response. I hope to receive that response soon.

The CHAIR. So ordered on both.

[The information referred to by Senator Murray was not submitted:]

[The information referred by Senator Burr can be found on page 59 in Additional Material:]

The CHAIR. With that, I want to welcome all of our witnesses today. Thank you for joining us. Our first witness will be Liz Richardson, who is the Director of the Health Care Products Project at the Pew Charitable Trusts. Ms. Richardson, thank you for sharing your time and expertise with us today.

I look forward to your testimony. Our next witness is Dr. Cartier Esham, the Chief Scientific Officer and Executive Vice President of Emerging Companies at the Biotechnology Innovation Organization. Thank you for joining us today, Dr. Esham. We look forward to your testimony. I am also pleased to welcome David Gaugh, who is the Senior Vice President for Sciences and Regulatory Affairs at the Association for Accessible Medicines.

Mr. Gaugh, I appreciate your being here today to share your perspectives. Finally, we have Mark Leahey, President and Chief Executive Officer of the Medical Device Manufacturers Association. Mr. Leahey, thank you for taking the time to be with all of us today. Ms. Richardson, you may begin your opening statement.

STATEMENT OF LIZ RICHARDSON, DIRECTOR, HEALTH CARE PRODUCTS PROJECT, THE PEW CHARITABLE TRUSTS, WASHINGTON, DC

Ms. RICHARDSON. Chair Murray, Ranking Member Burr, and Members of this Committee, thank you for the opportunity to testify today about how the reauthorization of the FDA user fee agreements can support patients and public health. The Pew Charitable Trust is a global non-governmental organization that seeks to improve public policy, invigorate civic life, and inform the public.

We believe that evidence based policies and investments can both spur the development of new drugs and medical devices and ensure effective oversight of these products. Today, I would like to focus my remarks on the role that the user fee agreements can play in promoting innovation and supporting a broad range of public health priorities, ultimately leading to improvements in patient care and outcomes.

Since 1992, user fees have provided FDA with significant and sustained resources that have allowed the agency to both facilitate

the development of urgently needed medical products and to review those products quickly so they can get to the patients who need them.

This issue is particularly important to Pew's Antibiotic Resistance Project, which is working to advance policies that would spur the creation of new antimicrobial products and establish stewardship programs that would ensure these products are prescribed only when necessary. Since 2014, FDA has approved 14 antibiotics, three of which represent a novel drug class or novel mechanism of action.

These advances are critical as the world faces a dangerous shortage of antimicrobial products to address both current and future patient needs. In 2002, Congress also established a user fee program for medical devices. The fees that FDA collects under these agreements provide the agency with resources to review applications and deliver a more efficient oversight process, one that can adapt to a rapidly evolving device market where emerging technologies like AI enabled digital health tools and 3D printing are posing challenges to traditional FDA oversight.

Pew is currently conducting research to inform how the agency can better facilitate ongoing innovation while still providing adequate public health safeguards for these rapidly changing products. But no matter how the agency decides to adapt its regulatory approaches, it needs adequate resources to fund its core activities, and this includes user fees.

A second key aspect of the user fee agreement process is how each successive reauthorization has provided an opportunity to advance other priorities that can advance patient health. For example, in its 2012 PDUFA Reauthorization Bill, Congress acknowledged the vital need for new antibiotics by enacting the GAIN Act as part of that package.

The GAIN Act represented an important first step in launching innovator companies devoted to antimicrobial research and development, but more work is needed to ensure that these companies can earn a fair return on investment and continue to innovate. But to that end, the PASTEUR Act proposes a unique, only pay for success pull incentive that will strengthen U.S. preparedness for future pandemics.

We urge Congress to include that measure in its current PDUFA reauthorization. Pew also believes that reforming oversight for diagnostic tests, an issue currently addressed in bipartisan legislation known as the VALID Act, is of critical importance. As the COVID–19 pandemic has shown, the Nation's public health depends on rapid access to accurate and reliable tests that can diagnose disease or identify past infection. But faulty diagnostic tests can compromise both patient care and the Nation's response to infectious diseases.

Current gaps in oversight have allowed tests that are developed and used within the same laboratories, called lab developed tests, to come to market without FDA approval, even if those tests are otherwise high risk. Pew believes strongly that tests should be regulated according to their risk to patients if they are inaccurate, not according to where they are developed and used.

By including VALID as part of the MDUFA reauthorization package, Congress can strengthen and update FDA's oversight of these critical products to make it more flexible and more risk-based.

Finally, I want to note that while review times are important insofar as they speed patient access to potentially important products, it is critical to remember that true innovation is not just about getting products to market faster, it is about developing products that are safer and more effective than what is already available.

While user fees are important to the efficient function of FDA, they cannot and should not be a substitute for adequate appropriations. User fees do not cover all of FDA's essential functions, such as conducting most post-market oversight activities or regulating non-drug products, including the large and ever-growing market of dietary supplements. FDA needs resources beyond user fees to sustain these core activities.

Because FDA is a public health agency that works to promote the health of all Americans, the agency should receive public funds and be accountable to the public, not just to the industries that it regulates. That being said, I want to conclude by underscoring again the importance of user fees to the basic functioning of the FDA.

Given the critical role that the agency plays in protecting and promoting public health, we urge Congress to reauthorize these agreements and ensure adequate funding for FDA to carry out its mission. Thank you for your time and I look forward to answering any questions.

[The prepared statement of Ms. Richardson follows:]

PREPARED STATEMENT OF LIZ RICHARDSON

Chair Murray, Ranking Member Burr, and Members of this Committee, thank you for the opportunity to testify about the proposed FDA user fee agreements and how legislation reauthorizing these agreements can support patients and public health.

Established in 1948, The Pew Charitable Trusts is a global nongovernmental organization that seeks to improve public policy, inform the public, and invigorate civic life. Through research and analysis, Pew's projects work to improve Americans' health and well-being. We believe that evidence-based policies and investments can help expand access to life-saving treatments, spur the development of innovative drugs and medical devices, and provide effective oversight of the benefits and risks associated with these products.

Today, I would like to talk about how the user fee agreements can promote innovation and help to ensure the safety and effectiveness of medical products, ultimately leading to improvements in health.

The User fee Agreements Promote Innovation of Drugs and Medical Devices

Since 1992, user fees paid by the drug and device industry have provided FDA with significant and sustained resources that allow the agency to facilitate the development of urgently needed medical products, and to review those products quickly.

This issue is particularly important to Pew's antibiotic resistance project, which is working to advance policies that would spur the creation of new antibiotics and establish stewardship programs to ensure that antibiotics are prescribed only when necessary in human health care settings. Since 2014, FDA has approved 14 anti-

biotics [1]—three of which represent a novel drug class or mechanism of action—to treat a variety of life-threatening bacterial infections, including community-acquired pneumonia and certain abdominal infections. These advances are critical as the world faces a dangerous shortage of antibiotics to address current and future patient needs.

Overall, the user fee programs have substantially sped up the review of new drug applications. In the decade after the first user fee agreement was passed, the median review time fell by half, from nearly 28 months to less than 14 months. Review times for drugs given priority status have also fallen significantly. Indeed, a standard review today is faster than a priority review a decade ago (around 10 months). [2]

In 2002, Congress also established a user fee program for medical devices. The fees FDA collects under these agreements provide the agency with additional resources to review applications and better facilitate the introduction of a wide variety of new medical technologies. Under the proposed agreement, the total fees collected are expected to reach at least $1.78 billion, [3] and if certain specified goals are met, the agency could collect up to $1.9 billion by 2027, up from about $1 billion in fees authorized under the previous reauthorization. [4] These funds help FDA deliver a more efficient and comprehensive oversight process that is better resourced to protect consumer safety and adapt to a rapidly evolving device market, where emerging technologies are posing challenges to traditional FDA oversight.

Today, for example, health care organizations use AI-enabled digital health tools for a growing range of clinical, administrative, and research purposes. FDA has approved or cleared nearly 350 AI-enabled devices for a broad range of applications. [5] Nearly 140 of these approvals or clearances have been granted since the start of 2020, [6] and the pace of submissions that include an AI component is only expected to grow over the next 5 years. These tools offer unique opportunities to improve patient care and health outcomes, but the volume of applications and the pace at which these products evolve pose unique challenges to FDA's traditional approach to oversight. These products will not only need to be reviewed to ensure they are safe and effective at the time of approval, they also need to be adequately monitored over time to ensure that they continue to be safe and effective in the real world, and when used on diverse patient populations. FDA must have sufficient resources—both through robust user fee programs and annual appropriations—as well as the internal expertise and commitment to develop regulatory policies that can facilitate ongoing innovation while still providing adequate public health safeguards for these rapidly changing products.

Similarly, 3D printing is increasingly being used at the point of care to manufacture a range of products, including anatomical models used to guide surgery planning and medical devices like surgical cutting guides. This technology allows for the decentralized manufacturing of highly customized products—which could 1 day include implants, pharmaceuticals, and even biological products—that are manufactured directly within health care facilities. However, 3D-printed devices—like any medical product—also carry risks, and existing laws, regulations, and guidance meant to ensure the safety of devices and drugs do not clearly map to this emerging technology. FDA needs the resources to be able to adapt its regulatory approach to meet the demands of the changing field and regulate the increasing number of sites that utilize the technology in order to ensure that medical products printed at the point of care are safe and effective.

The User fee Process can Support a Broad Range of Public Health Priorities

Though the matter of FDA funding is central to the user fee negotiation process, each successive reauthorization of those agreements has provided an opportunity for Congress to pass additional reforms that advance public health. For example, past

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[1] K. Talkington. "Analysis Shows Continued Deficiencies in Antibiotic Development since 2014", The Pew Charitable Trusts, last modified March 9, 2021, *https://www.pewtrusts.org/en/research-and-analysis/data-visualizations/2019/five-year-analysis-shows-continued-deficiencies-in-antibiotic-development*.

[2] *https://www.fda.gov/media/102796/download'msclkid=381a13f5b03e11ec9429b69ceba87906*.

[3] U.S. Food and Drug Administration, "FDA Statement on Medical Device User Fee Amendments (MDUFA)," news release, March 22, 2022, *https://www.fda.gov/news-events/press-announcements/fda-statement-medical-device-user-fee-amendments-mdufa*.

[4] FIND.

[5] *https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices*.

[6] Ibid.

reauthorizations led to the establishment of the Sentinel Initiative, provided important incentives for the development of new antimicrobial drug products, strengthened FDA's ability to require postmarket trials or labeling changes in response to safety signals, and facilitated efforts to better incorporate the patient perspective within the agency's decision-making process, among many other consequential changes.[7] We urge Congress to consider other worthy opportunities to improve public health during the current reauthorization.

In particular, the issue of diagnostic test oversight, currently addressed in bipartisan legislation known as the Verifying Accurate Leading-edge IVCT Development (VALID) Act, is of critical importance. As the COVID–19 pandemic has shown, the Nation's public health depends on rapid access to accurate and reliable tests that can diagnose disease or identify past infection. But faulty diagnostic tests can compromise both patient care and the Nation's response to infectious diseases.

Current gaps in oversight have allowed tests that are developed and used within the same laboratories, called lab-developed tests, to come to market without FDA approval, even if those tests are otherwise high-risk. Once used to test for rare diseases for which commercially manufactured diagnostics were unavailable, these tests have now become widespread and increasingly complex. However, because there is no central registration or reporting requirements for these tests, the exact size of the market is unknown, leaving countless people exposed to potential harm from unreliable or misleading results.

As Committee Members discussed at a recent hearing, the current MDUFA reauthorization is an appropriate vehicle for the VALID Act. By including VALID in the user fees legislation, Congress can strengthen and update current medical device regulations and enable FDA to adopt a risk-based approach to diagnostics oversight that balances safety and innovation.

Congress also acknowledged in its 2012 PDUFA reauthorization bill the importance of addressing the growing public health threat of antibiotic-resistant superbugs and the vital need for new antibiotics by enacting the Generating Antibiotic Incentives Now (GAIN) Act as part of that package. The GAIN Act represented an important first step that supported the launch of small biotechnology innovator companies devoted to antimicrobial research and development.

But on this front, more work is needed. A robust, market-based subscription model is necessary to ensure that these companies can earn a fair return-on-investment and continue to innovate. The sustainability of the antibiotic drug pipeline is absolutely foundational to modern medicine. To that end, the Pioneering Antimicrobial Subscriptions to End Upsurging Resistance (PASTEUR) Act proposes a unique, 'only pay for success' pull incentive that will substantially strengthen U.S. preparedness for future pandemics. We urge Congress to include that measure in its current PDUFA reauthorization.

The User fee Process is no Substitute for Adequate Funding

Review times are important insofar as they speed patients' access to potentially important products. The user fee agreements make review times a performance metric. However, it is critical to remember that true innovation is not just about getting products to market faster; it is about developing products that are safer or more effective than existing drugs and devices. While more challenging to measure than review times, protecting and promoting health is the ultimate goal of the FDA.

As important as user fees are to the efficient function of FDA, they cannot be a substitute for adequate appropriations. User fee agreements do not cover a broad range of essential health functions, such as enforcing good manufacturing practices, conducting most post-market safety activities, and regulating non-drug products, including food and the large and ever-growing market of dietary supplements. FDA needs sufficient additional resources beyond user fees to sustain these critical activities.

Furthermore, FDA is a public health agency that works to promote the health of all Americans. Because of the public interest in a well-performing FDA, the agency should receive public funds and be accountable to the public, not just to the industries it regulates.

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[7] A. Mitchell et al. "The Prescription Drug User Fee Act", *Medical Care*, Volume 60—Issue 4: 287–293, April 2022, *https://journals.lww.com/lwwmedicalcare/Citation/2022/04000/The-Prescription-Drug-User-Fee-Act-Much-More-Than.4.aspx*.

Conclusion

In conclusion, I want to emphasize the importance of user fees to the basic functioning of the FDA. We urge Congress to ensure that FDA has continued, sustained funding to carry out its important public health mission.

Thank you for your time and I look forward to answering any questions.

[SUMMARY STATEMENT OF LIZ RICHARDSON]

The Pew Charitable Trusts believes that evidence-based policies and investments can both spur the development of new drugs and medical devices, and ensure effective oversight of these products. Since 1992, user fees have provided FDA with significant and sustained resources that have allowed the agency both to facilitate the development of urgently needed medical products, and to review those products quickly.

This issue is particularly important to Pew's antibiotic resistance project, which is working to advance policies that would spur the creation of new antimicrobial products and establish stewardship programs that would ensure these products are prescribed only when necessary. Since 2014, FDA has approved 14 antibiotics, three of which represent a novel drug class or new mechanism of action. These advances are critical, as the world faces a dangerous shortage of antimicrobial products to address both current and future patient needs.

In 2002, Congress also established a user fee program for medical devices. The fees that FDA collects under these agreements provide the agency with resources to review applications and deliver a more efficient oversight process, one that can adapt to a rapidly evolving device market, where emerging technologies like AI-enabled digital health tools and 3D printing are posing challenges to traditional FDA oversight.

A second key aspect of the user fee agreement process is how each successive reauthorization has provided an opportunity to advance other public health priorities. For example, in its 2012 reauthorization of user fees, Congress acknowledged the vital need for new antibiotics by enacting the GAIN Act as part of that package. The GAIN Act represented an important first step, but more work is needed to ensure that drug developers can earn a fair return-on-investment and continue to innovate. To that end, the PASTEUR Act proposes a unique, 'only pay for success' pull incentive that will strengthen U.S. preparedness for future pandemics. Pew urges Congress to include that measure in its current user fee reauthorization.

Similarly, Pew also believes that reforming oversight for *in vitro* diagnostic tests, an issue currently addressed in bipartisan legislation known as the VALID Act, is of critical importance. The Nation's public health depends on rapid access to accurate and reliable diagnostic tests. But current gaps in oversight have allowed tests that are developed and used within the same laboratories, called lab-developed tests, to come to market without FDA approval, even if those tests are otherwise high-risk. Pew believes strongly that tests should be regulated according to their risk, not where they are developed and used. By including VALID as part of the MDUFA reauthorization package, Congress can strengthen and update FDA oversight of these critical products to make it more flexible and risk-based.

Finally, while user fees are important to the efficient function of FDA, they cannot be a substitute for adequate appropriations. User fees do not cover all of FDA's essential functions, such as conducting most post-market safety activities, or regulating non-drug products, including food and the large and ever-growing market of dietary supplements. FDA needs resources beyond user fees to sustain these core activities. And because FDA is a public health agency that works to promote the health of all Americans, the agency should receive public funds and be accountable to the public, not just to the industries it regulates.

The CHAIR. Ms. Richardson, thank you for your testimony. I am going to turn it over to Dr. Esham for testimony next. And then I am going to turn the Committee over to Senator Burr. I will go vote. There are two votes that are being called and I will be back shortly. Thank you, Senator Burr.

Dr. Esham.

STATEMENT OF CARTIER ESHAM, PH.D., CHIEF SCIENTIFIC OFFICER AND EXECUTIVE VICE PRESIDENT OF EMERGING COMPANIES, BIOTECHNOLOGY INNOVATION ORGANIZATION, WASHINGTON, DC

Dr. ESHAM. Thank you. Good morning, Chair Murray, Ranking Member Burr, Members of the Committee. My name is Cartier Esham, and I am the Chief Scientific Officer at the Biotechnology Innovation Organization, or BIO. BIO is the world's largest trade association, representing biotech companies, academic institutions, and related organizations across the United States and in more than 30 other nations.

While our membership includes most of the large pharmaceutical companies, the majority of our members are small, pre-revenue companies working on cutting edge biomedical innovations. We appreciate the opportunity to speak with you today, and we are committed to and working toward modernizing the clinical development paradigm to one that is more efficient, more patient centric, more inclusive, and best able to provide timely availability of next generation medicines that will improve the lives of patients and their families.

We do urge timely reauthorization of the prescription drug and biosimilar user fee agreements as they are vital to advancing these goals and to ensuring the FDA is able to effectively carry out its vital mission to protect and promote the public health.

Congress has built a strong foundation over many years with the enactment of previous user fee agreements and other key laws that have collectively worked to ensure effective and timely reviews, improve drug and biologic safety monitoring, enable the agency to keep pace with medical and scientific process, and provided the support necessary to ensure that advanced medicines are provided to patients as quickly and safely as possible.

The PDUFA and MDUFA User Fee Agreements will build on these efforts and foster next generation scientific medical advances that will benefit patients. For example, the PDUFA VII agreement aligns meeting opportunities with the needs of complex and innovative clinical development programs that will support productive scientific dialog and foster early identification, and better enable timely resolution of those issues when possible.

This includes the advancement of best practices—best meeting practices, as it is a shared responsibility between the biopharmaceutical industry and the FDA to ensure productive and effective meetings. The commitments in PDUFA will work to continue to advance the systematic integration of patient centric perspectives into drug development and review, building on efforts that began in earnest under the PDUFA V agreement.

They will provide the resources, capacity, and expertise needed for CBER to manage the exciting and vastly growing pipeline of cell and gene therapies. They will provide resources to improve safety monitoring and ensure the FDA is able to meet the demands and opportunities of the data and digital age.

Advance evidence collection and analysis approaches—analytical approaches that are more patient centric, more informative about health outcomes for all patients. They will provide resources and drive actions that will work better to enable the use of advanced

manufacturing technologies and ensure that processes relating to the safe manufacturing of complex medicines is done in a manner that does not unduly delay availability of these medicines.

The PDUFA commitments will also include provisions that will further strengthen the accelerated approval pathway and the orphan drug designation processes, both of which have been foundational in enabling the timely availability of medicines for patients suffering from devastating and life threatening diseases.

These include provisions that will advance regulatory understandings about what is necessary to support the utilization of a surrogate endpoint as a basis for approval and approve processes to ensure timely or post-market requirement assessments are made and better enable effective study designs, as well as improve the ability to engage with the FDA post-approval to resolve study challenges when they arise and better support timely determinations of continued scientific validity.

Like PDUFA, BsUFA agreement also works to ensure timely and productive scientific dialog, and advances regulatory science in key areas, including supporting the more efficient and better understood processes for the approval of interchangeable biosimilars. And they both work to ensure that FDA is best able—better able to recruit and retain world-class personnel and effectively manage resources.

Before I close, I would like to take this opportunity to convey BIO's commitment to improving clinical trial diversity. In addition to important commitments in the PDUFA VII agreement, BIO has provided Members of this Committee with proposals we believe are essential to advancing regulatory understandings that will drive change and support a clinical development ecosystem that is more inclusive and representative of the patients we serve.

Thank you again, and we look forward to working with you on these reauthorizations and toward advancing a new clinical development paradigm that is more expansive, more inclusive, more patient centric, and better enables the timely delivery of safe and effective next generation medicines that will improve the lives of patients and their families. Thank you.

[The prepared statement of Dr. Esham follows:]

PREPARED STATEMENT OF CARTIER ESHAM

Introduction

Good morning, Chair Murray, Ranking Member Burr, and Members of the Committee. My name is Cartier Esham, and I am the Chief Scientific Officer at the Biotechnology Innovation Organization, or BIO. BIO appreciates the opportunity to speak with you today about key priorities we believe will improve regulatory oversight and transparency, as well as enable biopharmaceutical companies to modernize the clinical development paradigm to one that is more patient-centric, efficient, and inclusive. Congress has built a strong foundation over many years that has served to expedite patients' access to safe and effective therapies, and helped innovators develop next-generation medicines that have improved the lives of patients and their families. We look forward to working with this Committee to continue to building on these efforts and urge that the Committee proceed with the timely reauthorization of the Prescription Drug User Fee Act and Biosimilar User Fee Act to ensure FDA can continue to meet its mission to protect and promote public health.

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and more than 30 other nations. While our membership includes

most of the large, international biopharmaceutical companies, the majority of our members are small biotechnology companies working on cutting-edge biomedical innovations. These companies are pre-revenue and take enormous risks every day to develop the next generation of biomedical breakthroughs for the millions of patients suffering from diseases for which there are no effective cures or treatments today. BIO is proud of their innovative spirit and dedication to improving the lives of patients and their families.

Since the initial enactment of the Prescription Drug User Fee Act (PDUFA) in 1992, user fees have played a key role in ensuring that effective and efficient regulatory processes keep pace with the continual advancement of scientific and medical innovation. As a result, more innovative treatments and therapies are first approved in the United States, providing our citizens with faster access to innovative medicines. Additionally, the PDUFA program ensures that FDA has the resources, capabilities, and processes in place to establish a clear and direct pathway from initial scientific discovery to widespread availability of cutting-edge medicines. This benefits not only regulators, patients, and the biopharmaceutical industry, but also the entrepreneurial community that makes significant investments in high-risk, early stage, innovative medicine development. Today, it can take anywhere from 10 to 15 years at an average cost of approximately $1 billion or more to advance a single drug or biological product from a promising idea to an approved product that benefits patients.[1,2] A well-run and comprehensible pathway to approval is critical to maintaining U.S. leadership in investment, development, and availability of next-generation medicines.

The Prescription Drug and Biosimilar User Fee Acts (PDUFA and BsUFA) have collectively worked to ensure effective and timely reviews, improve drug and biologics safety monitoring, enable the Agency to keep pace with medical and scientific advancements, allow for earlier and more frequent FDA-sponsor engagement to identify and resolve drug and biologic development challenges, and provide the support necessary to ensure that advanced medicines are available to patients as efficiently and safely as possible. These user fee programs, which are reauthorized by Congress every 5 years, provide FDA with the authority to collect fees from companies that produce certain human drugs, biologics, medical devices, and generics. These user fees, in addition to the resources provided through direct appropriations from Congress, have ensured that FDA is a global leader in regulatory advancement and oversight. Last year, 76 percent of novel drugs approved by FDA's Center for Drug Evaluation and Research (CDER) were approved in the U.S. before any other country.[3]

User fee programs are not fee-for-service programs, and fees paid by a company for a medical product application are not tied to the review of that particular application. Instead, these fees support a wide range of regulatory programs and ensure FDA has the resources, capabilities, and processes in place to maintain clear regulatory pathways and keep pace with medical and scientific innovation. The PDUFA and BsUFA agreements currently under consideration continue to advance those goals and activities and include additional commitments that will strengthen review fundamentals, enhance accountability and transparency, ensure stable growth of successful existing regulatory programs, and foster innovative scientific advancements.

Highlighting a few key topics that are most important to BIO, our member companies, and, most importantly, the patients we serve, we would like to emphasize the importance of promoting effective scientific dialog between FDA and sponsors of medical product development programs, enabling the utilization of regulatory tools that are more effective and support broader and more meaningful understandings of clinical outcomes for all patients, the incorporation of patient perspectives in clinical trials and post-approval data collection, and the necessity to provide the resources and capacity needed to meet the demands and opportunities of the digital age. The COVID–19 pandemic has shown us that decentralized clinical trials, digital health technology tools, and other innovations utilized during the pandemic have the potential to improve how we develop medicines that meet the needs of patients and greatly reduce the burden on clinical trial participants, especially for those who belong to historically underserved populations and for those who suffer from rare

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[1] Olivier J. Wouters, Ph.D; Martin McKee, MD, DSc; Jeroen Luyten, Ph.D. Estimated Research and Development Investment Needed to Bring a New Medicine to Market JAMA. 2020, 323(9).

[2] Joseph A. DiMasi; Henry G. Grabowskibi; Ronald W. Hansen. Innovation in the pharmaceutical industry: New estimates of R&D costs. 2016. Journal of Health Economics. 2016, Vol. 47.

[3] *https://www.fda.gov/media/155227/download*.

diseases, where clinical trial populations are small and geographically dispersed. We urge an on-time reauthorization of FDA's user fee programs to allow the enactment of the PDUFA VII and BsUFA III Commitment Letters that will continue to advance meaningful integration of the patient voice and experience into drug and biosimilar biological product development and review processes, build upon important lessons learned from the pandemic, and pave a path forward to a clinical development paradigm that is more effective, more informative, and more inclusive.

Overall Goals for PDUFA VII

Each user-fee Commitment Letter has continued to build upon the efforts of previous agreements. The following testimony will describe the content and benefit of critical provisions addressed in seven primary themes included in the PDUVA VII Commitment Letter:

1. Strengthen scientific dialog and advance innovation
2. Support the next wave of advanced biological therapeutics
3. Enhance patient-centric drug development, review, and protections
4. Modernize regulatory evidence generation and drug development tools
5. Enhance innovation in manufacturing and product quality reviews
6. Advance digital technologies and information technology (IT) infrastructure
7. Enhance FDA hiring, retention, and financial management

Strengthen Scientific Dialog and Advance Innovation

A goal of PDUFA VII most critical to advancing innovation involves enhancing and strengthening scientific dialog between sponsors of applications and FDA. To that end, FDA, for the first time, will provide consistent timelines for Initial Targeted Engagement for Regulatory Advice on CBER Products (INTERACT) meetings and expand the scope of these meetings to include products regulated by the Center for Drug Evaluation and Research (CDER). INTERACT meetings have been critical for sponsors of innovative biological products who face unique challenges that could otherwise delay entry into clinical development. FDA will also establish a new Type D meeting that enables FDA and sponsors to engage in more rapid and focused conversations about innovative approaches or unique challenges that will allow for earlier resolution of discrete issues. The Commitment Letter also formalizes a process where sponsors can submit clarifying questions to FDA following a meeting to ensure alignment on expectations and requirements. We collectively recognized that establishing and following best practices for productive meetings is a shared responsibility between biopharmaceutical companies and FDA.

There are at least 7,000 known rare diseases collectively impacting over 25 million Americans with new rare diseases identified each year. Because rare diseases have limited or no treatment options and lack well-established regulatory precedents, the development and review of these medicines introduces additional challenges that must be overcome to deliver new therapies to patients who need them. Key among these challenges is reaching agreement with regulators about determining the appropriate efficacy endpoints to support approval of innovative medicines for rare diseases. The current mechanisms for companies with rare disease treatments in their pipeline to collaborate with FDA has not consistently provided avenues for much needed discussions about these unique issues, which can cause delays in the development and availability of medicines to these patients who often lack options. The Rare Disease Endpoint Advancement (RDEA) pilot program in PDUFA VII will provide avenues for focused engagement opportunities that will serve to advance and share learnings and enable more efficient drug development and review process for all rare disease medicines.

The Commitment Letter will establish a Split Real Time Application Review (STAR) pilot program for certain applications that are intended to treat a serious condition with an unmet need. The pilot builds on the concepts that have proven successful for FDA's Real Time Oncology Review (RTOR) program and expands them to other disease areas to enable more timely reviews and availability of these medicines to vulnerable patient populations. The STAR pilot will improve both the stakeholders and industry's workload management by allowing sponsors of applications to submit their applications in two parts rather than one, allowing for earlier review of key components such as proposed labeling, clinical protocols, and topline efficacy and safety results prior to the final application submission.

Biopharmaceutical companies and FDA recognize the importance of post-marketing requirements (PMRs) to ensure timely availability of information on the safety and efficacy of certain therapies to patients when further post-approval studies are warranted. PDUFA VII includes commitments to ensure necessary PMRs are identified and communicated earlier in the review process and enable the development and implementation of more thoughtful study designs. This will better ensure that these PMRs are completed on time and avoids delays in confirmatory trials. PDUFA VII will also establish stronger processes for the continued evaluation of PMRs post-approval to ensure requirements are being met, issues can be resolved, and the studies remain scientifically valid.

Support the Next Wave of Advanced Biological Therapeutics

Advancing the new wave of biological therapies is a top priority for BIO member companies. A 2020 analysis by BIO found that there were 231 gene therapy products under development compared to only 93 products in 2015, a trend that is expected to continue in the coming years. To ensure that new and innovative cell and gene therapy products are developed and available to patients in a timely manner, the Commitment Letter will provide FDA with the resources and capacity needed to address the growing workload of the Cell and Gene Therapy Program. This will enable FDA to maintain the level of highly trained and experienced Cell and Gene Therapy staff needed to address CBER's workload caused by increased regulatory submission volume as projected over the next 5 years as well as keep pace with scientific and technological advancements. As part of the commitment, FDA will facilitate a better understanding of patient perspectives on gene therapy products, including cell-mediated gene therapy, and provide greater clarity on expedited pathways for regenerative medicines. FDA will streamline and harmonize processes, procedures, and interactions by enhancing, improving, and issuing guidance describing best practices for communication related to aspects of Cell and Gene Therapy product development, including the use of novel trial designs.

Enhance Patient-Centric Drug Development, Review, and Protections

One of the most important goals of PDUFA VII involves continuing to advance the systematic integration of patient perspective data into drug development and review processes. This work began in earnest under PDUFA V with the establishment of the Voice of the Patient Program that supported public meetings where patients provided insights about their conditions and how they themselves evaluated benefits, risks, and needs. PDUFA VI advanced this work by holding a series of public meetings and publishing guidance that provided information about how to determine the most important impacts to patients, how to measure disease impact, and how to incorporate Clinical Outcome Assessments (COAs) into clinical development and review processes.

During PDUFA VII, FDA will continue this critical work by continuing to strengthen capacity and knowledge through the expansion of training opportunities for FDA staff and ability to better engage external methodological experts. FDA will seek public input on methodologies and approaches for the submission of high-quality patient perspective data designed to inform benefit-risk assessments and inclusion of information in the label. PDUFA VII will provide supplementary support to FDA's development of a publicly available virtual catalog of Standard Core Sets of COAs and related endpoints that will help make possible the broader utilization of patient perspective data in clinical product development. FDA will also seek public input on which diseases areas have the greatest need for Standard COA development. Additionally, FDA will work to increase shared understandings about how patient preference studies can inform meaningful benefit-risk assessments in therapeutic areas, which is of very high value to the patient community.

Modernize Regulatory Evidence Generation and Drug Development Tools

Advancing innovative, patient centric drug development tools, and modernizing the regulatory evidence generation paradigm is a top priority for BIO member companies. Advancements in science and technology offer real opportunities to reduce patient burden, improve ability to recruit and conduct effective clinical trials and provide more informative analyses of benefit and risk pre and post approval. PDUFA VII will continue to build on several key initiatives that were launched under PDUFA VI. Under this Commitment Letter, FDA will advance the use of real-world evidence (RWE) to support approval of labeling claims, approval of new indications and to satisfy post approval study requirements. The agreement establishes an Advance RWE pilot program that will provide shared learnings with the

public and inform the publication of guidance increasing broad knowledge about how and when RWE can be utilized in future applications.

Complex innovative trial designs can be more efficient, improve patient outcomes, and produce high-quality information faster compared to traditional trial designs. PDUFA VII will continue both the Complex Innovative Trial Design and Model-Informed Drug Development (MIDD) pilot programs which enable the utilization of these tools and approaches more broadly. Additionally, the Agreement will enhance the drug development tool (DDT) qualification pathway for biomarkers by retaining and enhancing staff capacity and piloting processes that enhance the review of biomarker qualification submissions. High quality biomarkers can accelerate and enable drug development in areas of unmet need, improve clinical trial feasibility and efficiency thus continued improvement of the qualification pathway is beneficial to regulators, the research and development community, and patient communities.

To enhance FDA's drug safety system, PDUFA VII provides resources and processes that will enable the adoption of new scientific approaches designed to improve the utility of existing tools for the detection, evaluation, prevention, and mitigation of adverse events. PDUFA VII will modernize and improve Risk Evaluation and Mitigation Strategies (REMS) approaches and processes through new guidance documents and timelines for feedback to companies on REMS methodologies. Newly allocated resources will expand and optimize FDA's electronic safety data base (the Sentinel program) including supporting the integration of Sentinel and BEST (Biologics Effectiveness and Safety) systems, and FDA will advance knowledge about how Sentinel data can be used for regulatory purposes (*e.g.*, PMRs, PMCs and labeling) and how real-world evidence (RWE) may be used for evaluating the effectiveness of medicines. Collectively, these improvements and advancements in FDA's drug safety system will improve patient protections and utilization of this vast data resource to gain deeper insights about the benefits and risks of medicines for all patients.

Enhance Innovation in Manufacturing and Product Quality Reviews

One of the critical needs for PDUFA VII was to advance innovation in manufacturing and inspection review processes and improve the ability to get medicines to patients in a timely manner. A rate-limiting step for the past several years has been discussions and resolution of chemical manufacturing and control (CMC) issues, especially for innovative biologic therapies and treatments. FDA will improve the timeliness and effectiveness of CMC communications through training and updating CDER and CBER guidance designed to enable more consistent review of high-quality information requests from sponsors. FDA will also engage a third party to assess, seek public comment, and provide recommendations about how these processes can be optimized to support modernization of CMC-related processes.

To address the outsized hindrance of timely availability of innovative treatments for serious and life-threatening diseases undergoing expedited reviews due to CMC issues, FDA will publish new internal documents to better align CMC communications and processes to meet the desired timelines for approval decisions more consistently. The FDA will also establish a CMC Development and Readiness Pilot (CDRP) in both CDER and CBER to provide additional opportunities for engagement between FDA and sponsors that will help companies meet critical CMC milestones. Learnings from this pilot and an associated public workshop will inform a strategy document describing the Agency's plans to revise processes and information about submission strategies to accelerate CMC development.

Over the past several years there have been significant scientific advancements about how to effectively and efficiently manufacture high-quality complex medicines. PDUFA VII will work to identify and remove current barriers to the utilization and adoption of advanced manufacturing technologies. FDA will conduct a workshop where best practices, case studies, and regulatory strategies will be shared and discussed, including how to assess innovative technologies across platform products and sites. We are pleased that this Committee included a focus on manufacturing in the PREVENT Pandemics Act, and BIO supports the pathways for reviews of technologies established under Sections 506 and 518 of that bill which will enhance these PDUFA goals and facilitate the adoption of advanced manufacturing.

During the COVID–19 pandemic, regulators, biopharmaceutical companies, and other key stakeholders from around the world held discussions about how best to ensure the continued availability of medicines and meet the needs of providing COVID vaccines and treatments to all in need. Among the results of those discussions were the increased utilization, when appropriate, of alternative tools such as use of information shared by trusted foreign regulatory partners and record requests

for assessing manufacturing facilities. PDUFA VII will continue the advancement of those lessons learned by issuing draft guidance about when and how these types of alternative approaches may be utilized beyond the pandemic.

Advance Digital Technologies and Information Technology (IT) Infrastructure

It is of vital importance that support be provided to FDA to increase its capacity and ability to meet the demands and opportunities of the data and digital age. Increasing utilization of cloud technologies is necessary for FDA to meet the growing needs, demands, and advantages of modern-day development and review of innovative medicines. Today's medical product applications have large and/or complex data sets that require high-quality repository and analytical capabilities. PDUFA VII activities and resources, collectively, will enable FDA to make the necessary changes to meet these needs. These advancements will serve to improve the quality of applications submitted to FDA and improve our ability to better understand the benefits and risks of medicines to all patients before and after they are approved.

First, FDA will continue to meaningfully advance its Data and Technology Modernization Strategy to improve both FDA's enterprise needs and to advance key PDUFA objectives such as completing transition to a cloud-based system. FDA also committed to regular engagement with the biopharmaceutical industry to provide progress updates, share learnings, and discuss challenges in meeting PDUFA VII goals and advancing objectives outlined in the Data and Technology Modernization Strategy.

Second, FDA will launch a series of demonstration projects in collaboration with external partners to improve the core capabilities necessary for reviewing data captured via digital technology tools. We expect continued growth in the utilization of digital technologies as they offer the ability to reduce burdens on patients in clinical trials, better assess clinical outcomes for all patients, and more efficiently collect high-quality data and evidence to support approvals and inform life-cycle management of medicines. Findings and planned next steps from these demonstration projects will be shared with biopharmaceutical companies and made available to the public on FDA's website.

Third, critical IT modernization and capacity needs for the review of Biologic License Agreements will be provided to CBER to meet the demands of current and future applications that are projected to increase significantly over the next 5 years. In coordination with the Data Technology Modernization Strategy described above, CBER will develop a specific multi-year modernization roadmap to chart specific steps necessary for CBER to meet current and projected needs necessary to continue to successfully carryout its mission.

Enhance FDA Hiring, Retention, and Financial Management

PDUFA VII continues to build upon the resource management and fiscal accountability provisions included in PDUFA VI. For example, the time reporting system initiated under the previous Agreement will be optimized to allow for time and associated costs to be reported and examined on a more continual basis. Additionally, to strengthen fiscal and staff resource management, accountability, and transparency, PDUFA VII will continue to mature the resource capacity planning system that includes a publication of an updated implementation plan describing how resource capacity planning and time reporting will be improved and implemented over the coming 5-year PDUFA cycle. A third-party assessment of the capacity planning system will be conducted and inform the 5-year fiscal planning activities. Recommendations and findings of this assessment will be included in the annual financial reports. Additionally, FDA will maintain a stronger operating reserve to ensure they are better able to mitigate against disruptions to funding resources and continue to carry out mission critical activities.

Ensuring FDA can recruit and retain world-class personnel is the bedrock for maintaining U.S. regulatory leadership around the world. PDUFA VII continues to provide resources and tools to better enable FDA to attract and retain leading medical and scientific professionals. Specifically, PDUFA VII provides FDA with resources to conduct a third-party assessment of hiring and retention to identify challenges and provide recommendations for the Agency. These recommendations will be made available to the public where FDA will also share its plans to address issues raised.

BSUFA III Highlights

The Biosimilar User Fee Agreement (BsUFA) contains several commitments that have the same goals and objectives as those included in PDUFA VII, including: maintaining and improving performance goals for the effective and timely review of biosimilars, improving scientific dialog and meeting best practices, modernizing IT capabilities, advancing utilization of RWE to assess safety and support regulatory decision-making, and strengthening the ability to recruit and retain world-class personnel. Below I will highlight a few key beneficial provisions included in the BsUFA III Commitment Letter most important to our member companies and the patients we serve.

Improving Scientific Dialogue

Ensuring timely scientific dialog throughout the review process is a top priority for BIO member companies. BsUFA will improve the ability to engage in timely and focused discussions through the creation of new and improved meeting opportunities. Specifically, FDA will now provide a new meeting structure that enables FDA and sponsors of applications to engage in focused conversations on a narrow set of issues. BsUFA III also reforms the biosimilar initial advisory (BIA)[4] advisory meeting process to better manage FDA workload and ensure productive discussions about whether licensure of a biosimilar is feasible, and if so, plans and expectations for the development of that biosimilar.

Improving Review Processes of Biosimilar Supplemental Applications

The BsUFA III agreement will bring more predictability and efficiency to the review of supplements. Specifically, there will be timelines and goals established for 6 different types of supplement categories. These commitments will increase efficiency, consistency, and predictability of biosimilar supplemental applications and provide patients with timelier access to these medicines.

Advancing the Development and Review of Interchangeable Biosimilars

BsUFA III will continue to support more efficient and better understood processes for the approval of interchangeable biosimilars. FDA will hold a scientific workshop to discuss shared learnings and remaining challenges to the development of interchangeable biosimilars that will help FDA determine what additional steps need be taken to support the development and availability of these medicines (*e.g.*, additional guidance or research). Following the workshop, FDA will publish a strategy document describing the specific actions FDA will implement to facilitate development of interchangeable biosimilars.

To advance regulatory science in this field, FDA will pilot a regulatory science program that is designed to advance the development of interchangeable products and improve the efficiency of their development. Specifically, this pilot program will work to improve knowledge about how data (including RWE) can be utilized to meet safety standards for determining interchangeability and what methodologies can be utilized to assess the potential impact of differences between proposed interchangeable biosimilars and their reference products. The findings and shared learnings from this pilot program will greatly advance the development, review, and availability of interchangeable biosimilar medicines.

Interchangeable Biosimilar Labeling and Manufacturing Guidance

Under BsUFA III, FDA will publish guidance that will serve to improve communication of important biosimilar labeling information to patients and their caregivers and better facilitate resolution of manufacturing issues. Specifically, FDA will publish a guidance on labeling for interchangeable biosimilars, a guidance on promotional labeling and advertising considerations for interchangeable biosimilar products, and a guidance on what information is needed to support post-approval manufacturing changes to approved biosimilar and interchangeable biosimilar products. Collectively, these will serve to provide a greater understanding of what is required for efficient review and approval of changes to labels and manufacturing processes.

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[4] A BIA meeting is an initial assessment limited to a general discussion regarding whether licensure under section 351(k) of the PHS Act may be feasible for a particular product, and if so, general advice on the expected content of the development program.

Priorities for Advancing Medical Product Regulation and Innovation for the Benefit of Patients

BIO strongly supports the objectives and activities outlined in the PDUFA VII and BsUFA III commitment letters. These commitments, in addition to other key pieces of legislation and initiatives from Congress and the pharmaceutical industry, will facilitate innovation that benefits all patients served by our member companies. The testimony below outlines additional priorities that we believe will support this objective.

Building a New Clinical Development Paradigm: More Inclusive, More Patient Centric and More Informative About Clinical Outcomes for All Patients

BIO is committed to enhancing clinical trial diversity, and we included this commitment as part of our BIOEquality Agenda launched in 2020. The COVID–19 pandemic highlighted the urgent need to remove barriers and advance solutions that enable clinical trials to be more representative of the patients being treated. Scientific advancements are providing opportunities to establish clinical development and post-approval data collection approaches that can improve our understanding of clinical outcomes for all patients. The PDUFA VII Commitment letter will provide resources, capacity, and the development of guidance that will significantly advance regulatory certainty and promote the acceptance of real-world data/evidence (RWD/RWE) and digital health tools (DHTs) like remote monitoring devices, cell phones, and smart watches that are essential in more broadly enabling the utilization of decentralized or non-traditional clinical trial locations.

BIO stands ready to work with Congress, the Administration, and stakeholders to create a more expansive, inclusive, and sustainable clinical development ecosystem. We need to modernize the regulatory system to accept innovative tools and approaches that enable increased participation in clinical trials from underrepresented communities and the ability to collect data that improve our understanding of clinical outcomes for all patients. In addition to important legislation addressing these issues that will be discussed today, BIO has provided this Committee with legislative proposals we believe are essential to removing barriers and establishing a regulatory framework that is more inclusive and representative of the patients we serve.

The lack of reliable data sources capturing U.S. demographics is a challenge that must be resolved. Incomplete or outright missing demographic data for many disease areas leads to poorly or inaccurately informed enrollment targets and action plans during drug development. While FDA regulations require sponsors to present a summary of safety and effectiveness data by demographic subgroups within their trials, it is difficult to compare this data to epidemiological data to understand whether enrollment targets are representative of the disease population. Sponsors also lack certainty regarding innovative clinical trial designs that could improve trial diversity. Traditional clinical trial designs are typically geographically centralized around academic medical centers and associated with significant burden for patients, such as multiple mandatory visits to the clinic. This creates significant challenges when recruiting individuals who are geographically dispersed, unable to travel, or unable to take leave from work. By contrast, modern trial designs that embrace innovative tools and methods, like digital health technologies, decentralized clinical trials, and RWD/RWE, have demonstrated success in facilitating trials and driving diverse enrollment throughout the COVID–19 pandemic,[5] but companies currently lack a regulatory framework to fully leverage such techniques and tools.

We need to re-examine and update approaches to and criteria for the establishment of inclusion and exclusion criteria and advance approaches to data collection for approved medicines that enhance our understanding of benefits and risks for all patients and enable that information to be more transparent and available to patients and their care givers. Our proposal requires public meetings with comment periods and the publication of guidance on each of these topics that together will work to remove present-day barriers and establish a regulatory framework that promotes inclusive and representative clinical development and review processes.

To help build a more expansive, inclusive, and sustainable clinical trial network infrastructure, BIO also recommends that HHS conducts a series of public roundtable discussions that converge stakeholders from FDA, NIH, CDC, community organizations, industry, and clinical research organizations (CROs) to discuss, develop,

[5] *https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2789002.*

and implement recommendations that will serve to create a more expansive and inclusive clinical development infrastructure. Roundtable discussion topics could include establishing a publicly available data base of well-indexed active clinical trialists, establishing clinical trialist training programs and mentoring networks for investigators/trialists serving underrepresented communities, and establishing a publicly available data base of community engagement organizations supported by NIH. HHS should also establish new or leverage existing programs for a federally funded clinical trial investigator fellowship pilot program for women, members of the LGBTQIA+ community, and racial and ethnic minorities to help increase participation of underrepresented populations in clinical trials.

To promote diversity and inclusion for workforce development in the STEM community, BIO also recommends requirements for FDA and NIH to improve transparency around hiring, retention, and promotion practices within their organizational leadership and scientific workforces. Requirements should outline clear objectives for staff and leadership diversification and include a regular reporting cadence to Congress on metrics related to progress on these objectives. Such provisions would work synergistically with human resources (HR) authorities established by the 21st Century Cures Act of 2016 that enable FDA to build and maintain a talented workforce that keeps pace with rapid scientific and technical advancements in the biopharmaceutical industry. These H.R. authorities grant FDA increased flexibility to streamline the hiring process for recruits with specific scientific, technical, and professional occupations. They also established a new pay authority enabling FDA to compete with the private sector and academia when recruiting and retaining highly qualified candidates for these key positions. Together, these activities would strengthen the Federal public health workforce in terms of talent, expertise, and diversity.

We acknowledge that removing regulatory barriers and enhancing and developing data sources and infrastructure will not address all existing barriers to inclusive clinical trial participation, including language and health literacy disparities and historical mistrust of certain clinical research tactics and ethics. We have established a website, The Power of Participation (*www.ctpop.org*), for patients, designed to help assess and locate clinical trial opportunities and identify patient and community organizations they may find helpful. We remain committed to working with stakeholders across the public health spectrum to provide meaningful educational materials for all patients.

Accelerated Approval Brings Life Changing Treatments to Patients who Urgently Need Them

BIO continues to strongly support the Accelerated Approval Pathway (AAP) for reviewing safe and effective therapies that address critical unmet patient needs in serious and life-threatening disease states. This pathway has proven to be very effective in addressing some of the most pressing public health needs and has been foundational to extending and saving countless lives since its enactment. As of June 2021, 269 new drugs or biologics to treat serious or life-threatening diseases or conditions with high unmet medical needs have been approved through this pathway, extending, and in certain cases, saving patients' lives by providing novel therapies earlier than would have been possible using the traditional pathway.[6] Medicines approved through this pathway meet FDA's well-established approval standard of safety and effectiveness. The AAP is essential to providing timely access to treatments where there is an unmet need and for patients who lack therapeutic options.

Since the AAP was established in 1992,[7] the pathway has led to the approval of treatments that have significantly improved the care of patients suffering from many different diseases, including rare cancers, Human Immunodeficiency Virus (HIV), bacterial infections, multiple sclerosis, sickle cell disease, and other serious and life-threatening conditions. The AAP encourages scientific and medical advancement by allowing the use of surrogate or intermediate clinical endpoints that are reasonably likely to predict clinical benefit to support approval. Prior to the establishment of the AAP, patients with HIV recognized the need for a new pathway as the development of treatments using traditional endpoints of disease progression and death were prohibitory to providing access to much needed treatments for patients suffering from this deadly disease. The AAP enabled the approval of the first

[6] *https://www.fda.gov/drugs/nda-and-bla-approvals/accelerated-approvals*.

[7] In 1992, and partially codified in 1997, FDA instituted the Accelerated Approval regulations (21 CFR 314 Subpart H and 601 Subpart E) to formalize the process for approving drugs to treat serious conditions that filled an unmet medical need based on a study of surrogate endpoints.

HIV/AIDS treatment based on the use of surrogate endpoints (viral load and CDR count) which served to prolong and save the lives of millions of patients. The PDUFA VII agreement includes commitments that will strengthen the AAP, such as advancing surrogate endpoint development through the RDEA Pilot Program and providing avenues for earlier and more timely discussions on the design of post-market requirements to avoid delays in confirmatory trials. (PMRs), which are critical to confirming the clinical benefits of products receiving accelerated approval.[8] The Commitment Letter will also serve to advance regulatory understandings about when and how RWE may be used to support PMRs that may significantly improve the ability to complete PMRs in a more effective and efficient manner, modernizing the conduct of confirmatory trials required by the AAP.

Patients have consistently voiced their support for the use of AAP over the last 30 years. We have all seen how this pathway has led to more timely access to treatments that improve, extend, and save lives and has been foundational to continued advancements in the treatment of serious and life-threatening diseases. BIO looks forward to working with the Committee to ensure that the Accelerated Approval Pathway is working efficiently, effectively, and as intended.

Closing Comments

BIO member companies are committed to advancing innovation on behalf of all patients, especially in areas of unmet medical need. Our members constantly adapt to keep pace with technological and scientific advancements that create opportunities to develop new therapies for patients without any other options. The regulatory framework established and refined over multiple reauthorization cycles by Congress, including Members of this Committee, enables our member companies to collaborate with the academic, advocacy, and patient communities to develop innovative solutions to health challenges that have historically left patients with little to no hope.

In 2021 alone, FDA approved 60 new therapeutic products between CDER and CBER, including treatments to prevent and mitigate the impact of COVID–19. 27 of these new drugs were first-in-class, up from 21 first-in-class approvals in the previous year. There were 26 approvals for rare disease treatments that received orphan drug designations.[9],[10] FDA staff adapted to unforeseen challenges to fulfill their mission to protect and promote public health, and industry continues to adapt as well. In addition to efforts from regulators, these life-changing and life-saving approvals would not have been possible without unwavering commitment by our member companies to create innovative treatments and ensure that they reach the patients who urgently need them. The biopharmaceutical industry supports and shares FDA's mission to protect and promote public health by ensuring access to safe and effective drugs and biological products for patients, and this shared commitment enabled continued progress toward this mission despite unprecedented obstacles posed by the pandemic. This reauthorization is an opportunity to build on lessons learned from responding to the COVID–19 public health emergency and incorporate these innovations into the regulatory paradigm.

Companies continue to invest in and develop advanced manufacturing technologies that offer the promise of increased capacity and efficiency to help expedite production, enhance product quality, and address shortages of essential medications. Innovation in new drug and biologic development has been robustly incentivized by the modern drug/biologic regulatory framework at FDA, and BIO continues to work with Members of Congress to tackle unprecedented technical and regulatory challenges like those associated with investment in advanced manufacturing technologies and tools to modernize medical product development and distribution.

Drug development for patient populations with unique needs, such as the pediatric community, remains a priority for BIO and our members, and we celebrate the many successes that benefit our youngest patients stemming from these efforts. Today, we have numerous therapies with pediatric indications, including for neonates, that are making a measurable difference for these patients and their families. We have seen advancements across a range of conditions, including recent drug approvals in sickle cell, cystic fibrosis, pediatric rheumatologic conditions, and even Ebola, and we are optimistic about the breakthroughs to come. BIO is committed

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[8] Sponsors planning to use surrogate endpoints as primary efficacy endpoints also gained an opportunity to consult with FDA earlier in the drug development process through Type C Surrogate Endpoint meetings established during PDUFA VI.

[9] *https://www.fda.gov/media/155227/download*.

[10] *https://www.raps.org/news-and-articles/news-articles/2022/1/fda-approved-more-first-in-class-drugs-more-with-a#:~:text-Other%20drugs%20approved%20by%20CDER,treatment%20options%20for%20rare%20diseases*.

to building on this progress by delivering more innovative medicines to pediatric patients.

PDUFA VII and BsUFA III include provisions to enhance drug development with the goal of advancing novel therapies for patients, including in disease areas with an unmet medical need and which have proven to be more challenging areas for developing therapies, like rare diseases and pediatrics. Leveraging advances in science, enhancing the application of drug development tools, and modernizing clinical trials are critical to continuing to improve the drug development paradigm and regulatory processes for these medicines so we can better serve these patients and their families.

These commitments will build on the numerous provisions Congress has enacted over the years to help foster the development of promising therapies for children, including the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA). The most recent PDUFA reauthorization bill (The FDA Reauthorization Act of 2017) included new requirements for pediatric studies of certain cancer drugs that FDA is in the process of implementing. The initial impact of that legislation is beginning to work through the development cycle and BIO and its member companies will continue to work with FDA to ensure effective implementation of these programs.

The Orphan Drug Act (ODA) is a critical tool used to incentivize the expensive and heavily uncertain investment necessary to bring therapeutics for rare and orphan diseases to market. It is difficult to identify a more successful and consequential regulatory incentive than the ODA. Before it passed, there were merely a handful of treatments for rare disease patients. Today, we have hundreds of life changing treatments for these patients with countless more in the pipeline. We celebrate scientific progress that has led to innovative medical product development alongside patients, parents, and caregivers who have new treatment options, and sometimes even cures, that were previously unthinkable. While there is now immense hope for even the rarest diseases, many more are still waiting. There are thousands of identified rare diseases afflicting patients across the globe, many of which still have no alternative or meaningful treatments on the market. Given the tremendous risk, capital, and time it takes to discover and develop such medicines, the rare disease development paradigm should be handled with the utmost care and with significant consideration for potentiality of unintended consequences.

BIO strongly supports timely enactment of the PDUFA VII and BsUFA III Commitment Letters. The resources provided will serve to maintain FDA's global leadership and enable the Agency to keep pace with the medical and scientific advances of today and tomorrow. We look forward to working with Congress to advance proposals that support a new clinical development paradigm that is more expansive, inclusive, and patient-centric and continues to incentivize the development and timely delivery of next-generation medicines that save and improve the lives of patients and their families.

[SUMMARY STATEMENT OF CARTIER ESHAM]

My name is Cartier Esham, and I am the Chief Scientific Officer at the Biotechnology Innovation Organization, or BIO. BIO appreciates the opportunity to speak with you today about key priorities we believe will improve regulatory oversight and transparency and enable biopharmaceutical companies to modernize the clinical development paradigm to one that is more patient-centric, efficient, and inclusive. We look forward to working with this Committee to build on the strong foundation forged by Congress over many years that has expedited patients' access to safe and effective therapies and helped innovators develop next-generation medicines that have improved the lives of patients and their families. We urge that the Committee proceed with the timely reauthorization of the Prescription Drug User Fee Act (PDUFA) and Biosimilar User Fee Act (BsUFA) to ensure FDA can continue to meet its mission to protect and promote public health.

We emphasize the importance of promoting effective scientific dialog between the FDA and sponsors of medical product development programs, enabling the utilization of regulatory tools that are more effective and support broader and more meaningful understandings of clinical outcomes for all patients, the incorporation of patient perspectives in clinical trials and post-approval data collection, and the necessity to provide the resources and capacity needed to meet the demands and opportunities of the digital age and the next wave of advanced biologic therapies. The COVID–19 pandemic has shown us that decentralized clinical trials, digital health technology tools, utilization of real-world data and evidence, and other innovations

have the potential to improve how we develop innovative medicines. Incorporating these lessons learned into the regulatory framework enables the biopharmaceutical industry to better meet the needs of patients, improve care, and greatly reduce burden on clinical trial participants, especially those who belong to historically underrepresented populations and those who suffer from rare diseases, where clinical trial populations are small and geographically dispersed.

BIO is committed to enhancing clinical trial diversity, and we included this commitment as part of our BIOEquality Agenda launched in 2020. We stand ready to work with Congress, the Administration, and all stakeholders to create a more expansive, inclusive, and sustainable clinical development ecosystem. In addition to important legislation addressing these issues that will be discussed today, BIO has provided this Committee with legislative proposals we believe are essential to removing barriers and establishing a regulatory framework that is more inclusive and representative of the patients we serve by building reliable demographic and epidemiological data, modernizing inclusion/exclusion criteria, utilizing clinical trial modernization efforts as a tool to improve diversity, formalizing scientific workforce diversification, and other key actions.

Further, we strongly support the Accelerated Approval Pathway (AAP) for reviewing safe and effective therapies that address critical unmet patient needs in serious and life-threatening disease states. The AAP has proven essential in addressing some of our most pressing public health needs and has been foundational to extending and saving countless lives since its enactment. We emphasize the role it plays in providing timely access to treatments when there is an unmet medical need and patients lack therapeutic options.

We urge an on-time reauthorization of FDA's user fee programs to allow the enactment of the PDUFA VII and BsUFA III Commitment Letters that will continue to advance meaningful integration of the patient voice and experience into drug and biosimilar biological product development and review processes, build upon important lessons learned from the pandemic, and pave a path forward to a clinical development paradigm that is more efficient, more effective, more informative, and more representative of the patients we serve.

Senator BURR. Cartier, thank you. David, the floor is yours.

STATEMENT OF DAVID GAUGH, SENIOR VICE PRESIDENT, SCIENCES AND REGULATORY AFFAIRS, ASSOCIATION FOR ACCESSIBLE MEDICINES, ALEXANDRIA, VA

Mr. GAUGH. Chair Murray, Ranking Member Burr, and Members of the Committee, thank you for the opportunity to testify about the critical role of GDUFA and BsUFA, and which they hold in increasing patient access to more affordable generic and biosimilar medicines. My name is David Gaugh, Senior Vice President for Sciences and Regulatory Affairs at the Association for Accessible Medicines.

I am a licensed pharmacist with many years of experience with a generic and biosimilar industries. I represent the industry in the initial development and in both subsequent renewals of generic and biosimilar user fee agreements. AAM's biosimilar council strongly support congressional reauthorization of GDUFA and BsUFA as negotiated and without changes.

Timely approval of the FDA user fee agreements ensure patients will continue to benefit from new, more affordable generic and biosimilar medicines. Over the last 10 years, GDUFA and BsUFA significantly increased the resources available to FDA for the review of applications. The benefits of this is clear.

A record number of generic drugs were approved in 2017, 2018, and 2019, and a total of 34 biosimilars have been licensed to date. A direct result of this increased competition is lower prescription drug costs for the American patients. Since 2012, patients in the

U.S. health care system have saved more than $2 trillion, including $469 billion from new generics and more than $12 billion from biosimilars.

GDUFA III and BsUFA III build upon the successes of the last decade. The user fee agreements incorporate lessons learned, include enhancements to ensure the timely review of applications, and will provide FDA with sufficient resources over the next 5 years. GDUFA III and BsUFA III are the culmination of months of negotiations, have been subject to public review and comment, and represent a careful balance between stakeholders.

My written statement details many improvements negotiated in GDUFA III and BsUFA III but let me highlight a couple. First, complex generics are generic versions of brand name drugs that have complex active ingredients or drug device combinations, for example. These drugs are more difficult to develop due to the part—due in part to the lack of FDA product specific guidance.

GDUFA III includes commitments to facilitate the development and publication of product specific guidance for complex generics. These commitments will increase transparency and developers' understanding of FDA's expectations to allow for a more predictable review process. Inspections.

Generic and biosimilar developers support FDA's inspection program. One of the original purposes of GDUFA was to provide resources for FDA to conduct risk based facility inspections. GDUFA III enhances the efficiencies of the inspection process by helping ensure re-inspections occur within a specified timeframe. In addition, under BsUFA III, FDA commits to increasing guidance on its use of alternative tools to request records for documentation.

BLA supplements. Biosimilar developers can submit supplements to modify an approved BLA. For example, updating labeling with new study information or changes to indications.

Under pursue BsURA III, FDA commits to accelerating supplemental reviews for safety labeling, for extrapolation, for label carve in, carve out, and also for new data. Interchangeability. As of March 2022, FDA has licensed two interchangeable biosimilars. BsUFA III will help manufacturers to develop more interchangeable biosimilars through the newly negotiated regulatory science demonstration projects.

These demonstration projects will also evaluate mechanisms to streamline overall biosimilar development. In closing, we strongly support the timely reauthorization of GDUFA and BsUFA.

We look forward to working with Members of both parties to accomplish this goal. Thank you for the opportunity to testify, and I look forward to answering any questions you might have.

[The prepared statement of Mr. Gaugh follows:]

PREPARED STATEMENT OF DAVID GAUGH

Chair Murray, Ranking Member Burr and Members of the Committee:

Thank you for holding today's hearing on the reauthorization of the Food and Drug Administration's (FDA) user fee programs and for the opportunity to testify about the critical role the Generic Drug User Fee Amendments (GDUFA) and the Biosimilar User Fee Act (BsUFA) hold in increasing patient access to more affordable generic and biosimilar medicines. My name is David Gaugh, Senior Vice President for Sciences and Regulatory Affairs at the Association for Accessible Medicines (AAM). I am a licensed pharmacist with more than two decades of experience working in and around the generic and biosimilar medicines industry, and I represented

the industry in the initial development and in both subsequent renewals of the generic and biosimilars user fee agreements.

AAM and its Biosimilars Council are the Nation's leading trade association for the manufacturers and distributors of FDA-approved generic and biosimilar prescription medicines. Today, generic and biosimilar medicines comprise 90 percent of prescriptions in the United States at only 18 percent of total drug spending.[1] AAM's members provide more than 52,000 jobs at nearly 150 facilities and manufacture more than 60 billion doses of generic medicines in the United States every year.[2] Our core mission is to improve lives by advancing timely access to high-quality, more affordable safe and effective generic and biosimilar medicines.

In today's testimony, I will highlight the success of the FDA's generic and biosimilars programs in significantly increasing patient access to lower-cost medicines and, in turn, dramatically lowering the cost of prescription drugs for America's patients and our health care system over the last 10 years; outline the improvements made to the public-private partnership embodied in GDUFA III and BsUFA III; and discuss how congressional approval of the FDA user fee programs for the next 5 years (FY2023–2027) will benefit patients and increase their access to more affordable treatments.

AAM and its Biosimilars Council strongly support congressional reauthorization of GDUFA and BsUFA as negotiated and without changes. Timely approval of the FDA user fee agreements ensures patients will continue to benefit from new, more affordable generic and biosimilar medicines. The GDUFA III and BsUFA III commitment letters were carefully negotiated to balance program enhancements and resource requirements provided to FDA. The agreements include a year-over-year capacity planning adjuster (CPA) that allows FDA to automatically add additional full-time equivalent (FTE) resources when increased workload criteria exceed expectations. Therefore, AAM would have concerns about adding policies into the reauthorization package that require additional FTEs to implement if the package does not also include corresponding appropriations. Adding such policies would increase industry's year-over-year costs beyond what was negotiated and agreed to with FDA.

GDUFA and BsUFA at 10 Years

Ten years ago, Congress created the FDA's user fee programs for generic and biosimilar medicines when it enacted GDUFA and BsUFA as part of the FDA Safety and Innovation Act of 2012. For generic drugs, the number of applications submitted to the FDA had increased substantially since enactment of the Hatch-Waxman Act. Prior to GDUFA, FDA's review of abbreviated new drug applications (ANDA) was often slow and unpredictable. For biosimilar medicines, FDA's licensure pathway for these new treatments had been created in 2010 as part of the Biologics Price Competition and Innovation Act (BPCIA). With passage of the first GDUFA and BsUFA iterations in 2012, Congress helped ensure FDA would have sufficient resources to carry out its mission.

Congressional authorization of the FDA's generic and biosimilars user fee programs in 2012 and reauthorization in 2017 substantially increased the resources available to the Agency to review applications. More than $4 billion in supplemental user fees from generic and biosimilars developers was and will be provided as a result.[3]

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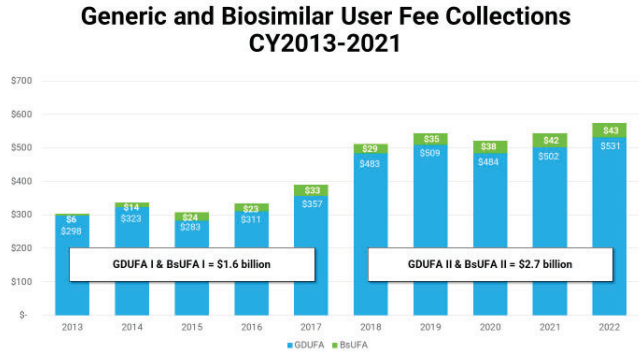
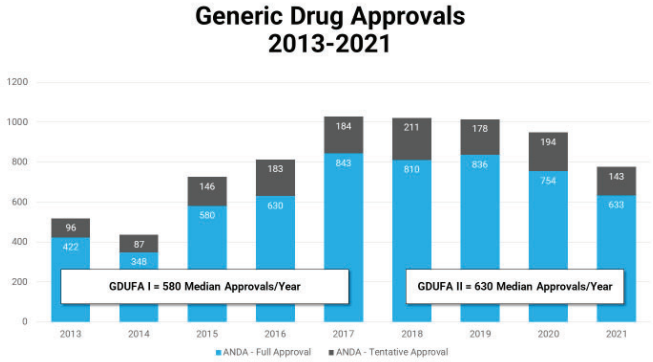
[1] AAM, "The U.S. Generic & Biosimilar Medicines Savings Report," October 2021 (*link*).

[2] "A Blueprint for Enhancing the Security of the U.S. Pharmaceutical Supply Chain," October 2021 (*link*).

[3] AAM Analysis of FDA's fiscal year 2014—fiscal year 2020 GDUFA and BsUFA Financial Reports and Five-Year Financial Plans (2021 Update). FDA's reports are available at *https://www.fda.gov/about-fda/user-fee-reports/user-fee-financial-reports*.



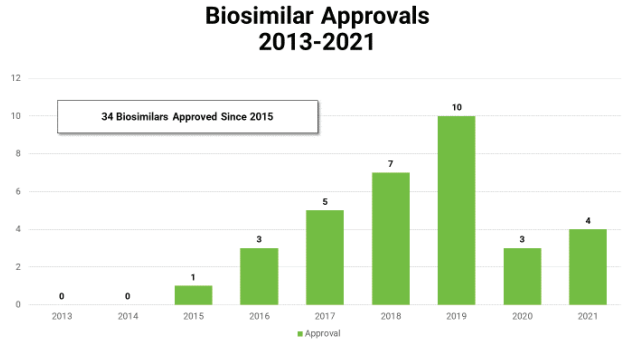
With the additional resources, FDA was able to increase efficiencies and approval of generic drugs increased significantly, with full and tentative approvals exceeding 1,000 in fiscal years 2017, 2018 and 2019. The median number of ANDA approvals has increased over time as a result of GDUFA I and GDUFA II.[4] The partnership between FDA and the generic industry has enhanced the overall stability and predictability of the GDUFA program and accelerated the timely review of ANDAs, increasing access to quality affordable generic medicines.



Following the creation of the biosimilars pathway and subsequent development of the biosimilars program, FDA licensed the first biosimilar in 2015 and has now licensed 34 biosimilars in the U.S.[5] Biosimilar medicines are safe, effective and more affordable treatments for patients and, with 21 products launched and available to patients, biosimilars are already delivering on their promise of lower costs and expanded patient access to care.

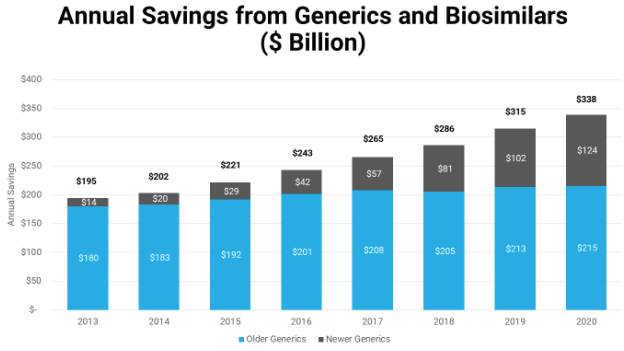
[4] AAM Analysis of the FDA Office of Generic Drug Annual Reports (2015–2020) and Activities Report of the Generic Drug Program (FY13-FY15, fiscal year 2021). FDA's reports are available at *https://www.fda.gov/drugs/generic-drugs/annual-reports*.

[5] Biosimilars Council, "FDA Biosimilars Approvals," March 2022 (*link*).



With FDA approval, the introduction of new generic and biosimilar medicines leads to competition in the pharmaceutical market—and the result is a significant reduction in the cost of prescription drugs for patients. Experience shows drug prices decline rapidly when generics enter the market. [6] According to FDA, prices fall as generics enter the market—by an average of 39 percent when there is only one generic and by nearly 80 percent when four or more generics enter the market. [7] Evidence with biosimilar medicines is similar with an average cost savings of nearly 50 percent. [8] Importantly, biosimilar competition also results in lower brand biologic costs—by more than 25 percent on average. [9]

Over the last 10 years, generics and biosimilars provided more than $2 trillion in savings—including $469 billion from new generics and more than $12 billion from biosimilars—to patients and the U.S. health care system. [10] In addition to the cost savings provided, patient access to life-saving treatments is broadened as the price of medicine falls. A recent analysis of Medicare Part D from the Congressional Budget Office noted "the number of standardized prescriptions dispensed for generic drugs more than doubled from 2009 through 2018." [11]



GDUFA and BsUFA aim to put FDA's generic and biosimilar drug programs on firm financial footing by enabling FDA to assess user fees to fund critical and measurable enhancements and, in turn, bringing greater predictability and timeliness to the review of applications. As a direct outcome, the generic and biosimilars drug

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[6] IMS Institute for Healthcare Informatics, "Price Declines after Branded Medicines Lose Exclusivity in the U.S.," January 2016 (*link*).
[7] FDA, "New Evidence Linking Greater Competition and Lower Generic Drug Prices," December 2019 (*link*).
[8] AAM Analysis of Average Sales Price Files, January 2022.
[9] Ibid.
[10] Ibid., AAM Generic & Biosimilar Savings Report.
[11] CBO, "Prescription Drugs: Spending, Use, and Prices," January 2022 (*link*).

programs have increased patient access to safe, effective and affordable quality medicines.

GDUFA III Enhancements

FDA plays a critically important role in making lower-cost, high-quality generic medicines available to patients. FDA reviews ANDAs submitted by generic drug manufacturers (ANDA sponsors). To receive FDA approval, data submitted in an ANDA must generally demonstrate that the generic drug is bioequivalent to the Reference Listed Drug (RLD), more commonly known as the innovator or brand product.

The GDUFA commitment letter specifies various fees the FDA sets and can collect from manufacturers, such as ANDA applications, Drug Master Files (DMF), and facility and program fees.[12] The fees paid by the generic drug industry aid FDA's ability to meet agreed-upon performance goals and commitments, such as timely reviews and other regulatory activities. FDA also provides annual reports to Congress on its performance.[13] The increases in transparency and communication are important to FDA's ability to meet the commitments, which enhance the overall stability and predictability of the GUDFA program.

The negotiated GDUFA III performance goals will further strengthen and build upon the progress made and lessons learned from GDUFA I and GDUFA II. Let me take a moment to highlight five areas—advancing approvals, complex generics, inspections, suitability petitions and sustainability—where we believe the FDA's generic drug program will be enhanced with congressional ratification of GDUFA III.

Advancing Approvals

GDUFA III includes important performance goals that will maintain FDA's rigorous ANDA review standards, building upon and improving the review process to increase timely patient access to high-quality, lower-cost generic medicines. For example, the newly negotiated provision known as "imminent action" will allow the FDA to extend a goal date by up to 60 days if, in FDA's judgment, an approval or tentative approval of the application is imminent. This commitment will mitigate the need to add additional review cycles unnecessarily and delay approvals over minor, easily resolvable issues.

Complex Generics

Complex generics are generic versions of brand-name drugs that have complex active ingredients, routes of administration, drug-device combinations or formulations. These drugs are more difficult to develop due in part to the lack of FDA product-specific guidance. Congress and FDA helped spur competition for complex products by including provisions in the previous user fee authorizations to increase product-specific guidance publication and meetings with FDA during the product development phase. GDUFA III builds on this success through performance goals to facilitate the development and publication of product-specific guidances for complex generic products—increasing transparency and understanding of FDA's expectations to allow for a more predictable review process.

Inspections

Generic and biosimilar developers support FDA's inspections program. One of the original purposes of GDUFA was to provide resources for FDA to conduct facility inspections. Under the inspections process, FDA typically inspects a facility and identifies deficiencies. The facility has a specified timeframe to address and correct the identified deficiencies and subsequently request a reinspection from FDA. In some cases, extended time passes from when a facility performs the corrective actions to resolve the deficiencies and the time period when FDA can reinspect. Delays in reinspection lead to significant delays in the review process. GDUFA III enhances the efficiencies of the inspection process by helping ensure reinspection occurs within a specified timeframe.

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[12] AAM, "The Generic Drug User Fee Amendments (GDUFA III)," October 2021 (*link*); FDA, "GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2023–2027," October 2021 (*link*).

[13] FDA, GDUFA Performance Reports, fiscal year 2015—fiscal year 2020 (*link*).

Suitability Petitions

Suitability petitions are required to be submitted to FDA when a generic drug manufacturer intends to seek approval of an ANDA for a drug that differs from the reference brand product in terms of the active ingredient (for a combination product), route of administration, strength and/or dosage form. Current law requires FDA to grant or deny suitability petitions within 90 days from petition submission. That deadline, however, is rarely met. This results in delays to generic market entry. GDUFA III includes performance goals and resources to facilitate the FDA's ability to conduct a timely review of suitability petitions. These new resources will help FDA meet these goals, including conducting completeness assessments within 21 days from petition submission and using agreed upon metrics to prioritize petition reviews.

Sustainability of Resources

Under GDUFA II, FDA committed to developing a Resource Capacity Planning (RCP) capability to optimize resources and better anticipate future resource needs. GDUFA III provides an additional tool to further enhance the utility of the RCP to allow FDA to better forecast resource needs via the Capacity Planning Adjustment (CPA). The CPA will help promote sustainability for both FDA and industry by allowing FDA to increase full-time employee needs as workload increases. In turn, the CPA will provide predictability for generic developers through a 3 percent cap to prevent significant fluctuation in fees and minimize the financial barriers for smaller generic manufacturers.

BsUFA III Enhancements

Similar to FDA's generic drug program, FDA helps ensure that America's patients can gain access to high-quality, more affordable biological products in the form of biosimilars. FDA reviews abbreviated biologics license applications (BLA) submitted by biosimilar developers. In order for a biosimilar to be licensed, data submitted in a BLA must demonstrate the biosimilar drug product is "highly similar" to the brand-name reference biologic and there are no clinically meaningful differences in safety, purity or potency.

BsUFA allowed FDA to assess and collect fees from developers and manufacturers that submit BLAs for FDA's review. The negotiated commitments enhance and improve the review process to facilitate timely access to biosimilar medicines and ensures the Agency has the necessary resources to fulfill the agreed upon commitments. FDA also provides annual reports to Congress on its performance. [14]

The negotiated BsUFA III performance goals will further strengthen and build upon the progress made and lessons learned from BsUFA I and BsUFA II. [15] Let me highlight several enhancements to FDA's biosimilars program: supplement reviews, meeting management, regulatory science and interchangeability, inspections, use of carryover funds and IT modernization. I will briefly describe each.

BLA Supplements

Biosimilar developers can submit supplements to modify an approved BLA, for example, updating labeling with new safety information or changes to indications. Under BsUFA III, FDA commits to accelerating supplement reviews for safety labels, extrapolation, label carve-in and carve-outs and new pharmacokinetic data.

Meeting Management

Biosimilar developers participate in meetings with FDA to gain insight into the agency's expectations and perspectives on different issues. These meetings help facilitate a predictable and efficient review process. BsUFA III includes commitments to: add a new type of meeting to get feedback on focused questions; make meetings more efficient; help provide FDA with sufficient information in advance of meetings; and obtain rapid clarification of meeting minutes.

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[14] FDA, BsUFA Performance Reports, fiscal year 2013—fiscal year 2020 (*link*).

[15] AAM, "Key Elements of BsUFA III," September 2021 (*link*); FDA, "Biosimilar Biological Product Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027," September 2021 (*link*).

Regulatory Science and Interchangeability

As of March 2022, FDA has licensed two interchangeable biosimilars. In order to achieve the interchangeable designation, a biosimilar must produce the same clinical result as the brand-name biologic. With the interchangeable designation and subject to state law, a pharmacist may dispense an interchangeable biosimilar when a brand-name biologic is prescribed without intervention from the provider. BsUFA III will help manufacturers to develop more interchangeable biosimilars through the new Regulatory Science Program's demonstration project. These demonstration projects will also evaluate mechanisms to streamline overall biosimilars development. Findings from the demonstration projects will inform a comprehensive strategy to advance interchangeability and the development of future guidance documents.

Remote Inspections

FDA uses alternate tools to conduct inspections and supplement its ability to assess manufacturing facilities remotely. Due to the COVID–19 pandemic, FDA used these alternate tools to request records and documentation from its regulatory partners. Under BsUFA III, FDA commits to issuing guidance on the use of alternative inspection tools.

Use of Carryover Funds

Any remaining user fees collected by FDA but not yet spent are carried over to the next year. Under BsUFA III, FDA commits to reducing the carryover balance from 39 weeks to 21 weeks over a 3-year period.

IT Modernization

FDA continues to modernize the Agency's IT capabilities. BsUFA III will further FDA's efforts. For example, FDA will modernize and move the Electronic Submissions Gateway to the cloud to help improve transparency and communication.

COVID–19 and FDA's Use of Remote Inspections

Given congressional interest about lessons learned from the COVID–19 pandemic and this Committee's leadership in driving forward solutions to prepare the country for future public health emergencies, I do want to take a moment to share the experience of AAM's members in regard to FDA inspections over the last 2 years. Manufacturing facility inspections are an essential part of evaluating applications to market all FDA-approved pharmaceuticals, including brand-name, generic, and biosimilar medicines. When FDA does not conduct inspections in a timely manner, approvals and patient access to new treatments, as well as more affordable options, can be delayed.

During the last 2 years, there have been significant disruptions to the inspections program. In March 2020, FDA announced that it was suspending domestic and foreign inspections due to the COVID–19 pandemic. The Agency focused only on "mission-critical" inspections, a narrow category that does not include inspections tied to most drug applications. As the pandemic subsided in mid–2021, FDA attempted to resume all domestic inspections. However, with the rise of the Omicron variant in December 2021, FDA reverted to performing only mission-critical inspections and did not resume a normal domestic inspection schedule until February 2022.

These inspection disruptions have had a significant effect on our members' ability to obtain timely approval of more affordable generics and biosimilars. By FDA's account, as of the end of fiscal year 2021—the most recent data available to AAM at the time of this hearing—52 human drug application decisions remain "delayed solely due to a pending inspection or facility assessment."[16] The tally of 52 likely underestimates the extent of the delays, as it excludes applications that might have had a minor issue unrelated to an inability to inspect. Inspections for biosimilar applicants are also impacted, including biosimilars for brand-name biologics like Humira®.[17] Prompt inspection of such facilities is urgently needed.

Under existing authorities FDA has several alternatives to physically inspecting facilities, including: (1) obtaining inspection records remotely; (2) requesting infor-

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[16] FDA, "An Update to the Resiliency Roadmap for FDA Inspectional Oversight," November 2021 (*link*).

[17] Center for Biosimilars, "FDA Delays Review of Alvotech's AVT02 Adalimumab Biosimilar Candidate," September 2021 (*link*).

mation and records from applicants, facilities, and other inspected entities; (3) conducting remote interactive evaluations (real-time video interactions with facilities that cover the same ground as inspections); and (4) relying on inspections conducted by trusted foreign regulatory authorities under the Mutual Recognition Agreements (MRA). FDA, however, infrequently uses these alternatives. For example, FDA informed AAM that, as of December 2021, it had conducted only five remote interactive evaluations.

AAM recognizes the important role inspections play in FDA's ability to assess the overall quality of applications. Our members also share the Agency's concerns about public health and preventing the spread of COVID–19 among FDA and manufacturing facility employees. The interruptions caused by COVID–19, however, delayed and denied patients prompt access to new therapies and generic and biosimilar choices that would lower drug costs. If new COVID–19 variants emerge, or if there is a future pandemic, FDA's inspections could be paused again.

AAM believes FDA should expand the use of remote interactive evaluations and use them more frequently in place of a physical inspection, in addition to using alternative tools in place of an in-person inspection to verify corrective actions for a site that had received a warning letter. Specifically, we recommend requiring FDA to evaluate alternatives when an in-person inspection is not possible. Should FDA determine that an alternative to an in-person inspection cannot be used, the Agency should be required to inform the applicant which alternatives were considered and the reasons why an in-person inspection was deemed necessary. We believe this additional transparency and accountability will encourage FDA to perform its critical mission without delay, while preserving the Agency's discretion and judgment to require in-person inspections when necessary.

Conclusion

Patient access to generic and biosimilar medicines has never been more critical. Over the last 10 years, GDUFA and BsUFA significantly increased the resources available to FDA for review of generic and biosimilars applications. The benefit of this partnership between FDA and industry is clear: record levels of generic drugs were approved in 2017–2019, and more than 30 biosimilar medicines were licensed. The end result is lower prescription drug costs for America's patients. Since the establishment of FDA's generic and biosimilars programs in 2012, patients and the U.S. health care system have saved more than $2 trillion—including $469 billion from new generics and more than $12 billion from biosimilars. Congressional passage of GDUFA and BsUFA, along with their reauthorization in 2017, made this possible.

GDUFA III and BsUFA III build on this success. The user fee agreements incorporate lessons learned, include enhancements to ensure the timely review of applications and provide FDA with sufficient resources over the next 5 years (FY23–27). GDUFA III and BsUFA III are the culmination of months of negotiations, have been subject to public review and comment, and represent a careful balance between stakeholders. AAM and its Biosimilars Council strongly support congressional reauthorization of GDUFA and BsUFA as negotiated and without changes. Timely approval of the FDA user fee agreements ensures patients will continue to benefit from new, high-quality and more affordable generic and biosimilar medicines. We look forward to working with Members of both parties to accomplish this goal.

Thank you again for the opportunity to testify on this important issue. I look forward to answering your questions.

[SUMMARY STATEMENT OF DAVID GAUGH]

The Association for Accessible Medicines (AAM) and its Biosimilars Council, represented by David Gaugh, Senior Vice President of Sciences and Regulatory Affairs, will provide testimony on the importance of timely reauthorization of GDUFA and BsUFA to continued patient access to high quality, more affordable generic and biosimilar medicines. Mr. Gaugh's testimony highlights the success of FDA's generic and biosimilar programs in significantly increasing patient access to lower-cost medicines and, in turn, dramatically lowering the cost of prescription drugs for patients over the last 10 years. Since 2012, more than $4 billion in funding has been provided under GDUFA (70 percent) and BsUFA (60 percent) to help ensure FDA has sufficient resources to review and approve applications. As a result, FDA approval of generic drugs increased significantly with full and tentative approvals exceeding 1,000 in fiscal years 2017, 2018 and 2019. The first biosimilar was approved in 2015 and now 34 biosimilars are approved in the U.S. These approvals increased

competition from generics and biosimilars and led to significant savings to patients and the health care system—more than $2 trillion in savings over the last 10 years. The GDUFA III and BsUFA III agreements includes enhancements with the goal of: advancing approvals; ensuring timely inspections; improving review of complex generics; streamlining suitability petitions; providing for BLA supplement reviews; addressing interchangeability; and ensuring the efficient of resources.

Senator BURR. David, thank you very much. Mark, the floor is yours.

STATEMENT OF MARK LEAHEY, PRESIDENT AND CHIEF EXECUTIVE OFFICER, MEDICAL DEVICE MANUFACTURERS ASSOCIATION, WASHINGTON, DC

Mr. LEAHEY. Thank you, Ranking Member Burr. Thanks again to Chair Murray and Members of the Committee for the invitation to testify today. My name is Mark Leahey, and I am the President and CEO of the Medical Device Manufacturers Association, a national trade association representing hundreds of medical technology companies.

MDMA was founded in 1992 to be the voice of the innovative and entrepreneurial sector of our industry. According to the Department of Commerce, 98 percent of medical technology companies have fewer than 500 employees and 80 percent have fewer than 50 employees.

These small companies drive the majority of innovation in medtech. Our industry is dedicated to one mission, to alleviate human suffering and improve patient care. Perhaps no recent example is more profound than what innovators have done since the outset of the COVID–19 pandemic.

In addition to the extraordinary efforts of our industry and health care professionals, I would also like to take a moment to acknowledge the dedicated professionals at FDA who are 24–7 on COVID and non-COVID medical technologies to improve patient care during the pandemic, their efforts ensure that patients have timely access to safe and effective products. The MDUFA V draft agreement that we are discussing today and the historic increase in user fee funding that it contains demonstrates our commitment to provide additional capacity and expertise to further advance FDA's mission.

MDUFA V provides over $2 million in investible funding to FDA. As a point of reference, MDUFA I totaled approximately $150 million. While each MDUFA typically provides the resources to fund approximately 200 new hires, under MDUFA V, FDA will be able to hire at a minimum 273 FTEs and up to 387 new FTEs.

This represents a historic increase in both overall funds and people, and it is our expectation that this will be the last major investment needed for the MDUFA program, and that moving forward, any necessary increases will be much more modest and targeted. MDUFA V also establishes more transparency around the use of funds, including ensuring that annual hiring targets are met.

FDA will also conduct an H.R. assessment during MDUFA V to identify how many MDUFA funded vacancies exist. Beyond the financial and accountability provisions that MDUFA V contains, performance goals associated with De Novos and PMA Total Time to Decision also improve over the course of the agreement.

One goal that was elusive under MDUFA IV was the total—510(k) total time to decision goal in Fiscal Year 2022 of 108 days. COVID did impact FDA capacity, including the ability to meet certain B MDUFA IV goals.

Under MDUFA V, the 510(k) total time to decision goal will improve each year, hopefully achieving 108 days by Fiscal Year 2026. Also for the first time the agreement incorporates add on payments that will provide the agency up to $150 million in additional funding above the baseline in the final year of the agreement if FDA meets modest but important performance goals in the first 2 years of the agreement.

The United States medical technology ecosystem is the envy of the world, and this is in no small part due to FDA's gold standard of reviewing the safety and efficacy of medical devices. The billions of dollars in user fees provided by industry under this agreement will enable FDA to hire hundreds of new reviewers and scientific experts, strengthening the agency's ability to maintain its strong track record.

This agreement also makes additional investments to enhance device safety. This includes increased funding to better incorporate the patient perspective in the product evaluation process, as well as funding to improve the use of real world evidence.

The agreement also contains resources to pilot the Total Product Lifecycle Advisory Program, also known as TAP, a top priority for FDA during these negotiations. Medical technologies that serve patients with unmet needs unfortunately can take longer to navigate the regulatory process.

This is often due to the complexity and novel approach that breakthrough devices encompass. Innovators participating in the Safer Technologies Program, or STeP, will also be eligible for the TAP pilot. TAP is designed to allow FDA and sponsors to share early feedback to improve the process.

Based upon the data and independent assessment of the pilot, industry and FDA will determine whether to continue, expand, or terminate the TAP pilot during the MDUFA V negotiations—VI negotiations, excuse me. In conclusion, this is a historic investment in the FDA and will be critical over the coming years to meet the goals and milestones within the user fee agreement to help ensure that the United States remains the global leader in medical technology development.

It is also critical that Congress continues its vital oversight role and provides the necessary appropriations to FDA to achieve its mission. MDMA and our members remain committed to working closely with you to reach our shared goal of providing safe and effective medical technologies to patients and providers in a timely manner.

Thank you once again, Chair Murray, Ranking Member Burr, and Members of the Committee, for the opportunity to testify, and I welcome your questions.

[The prepared statement of Mr. Leahey follows:]

PREPARED STATEMENT OF MARK LEAHEY

Thank you Chair Murray, Ranking Member Burr and Members of the Committee for this opportunity to testify today. My name is Mark Leahey and I am the President and CEO of the Medical Device Manufacturers Association ("MDMA"), a na-

tional trade association representing hundreds of medical technology companies. MDMA was founded in 1992 to be the voice of the innovative and entrepreneurial sector of our industry. While the industry is broadly represented throughout the United States, one of the unique components of this vibrant part of America's innovation ecosystem is that the majority of companies are small businesses. According to data from the Department of Commerce, over 98 percent of med tech companies have fewer than 500 employees, and more than 80 percent have less than 50 employees, yet they are the major source of innovation and America's competitive advantage in medical technology. Our industry is dedicated to one mission: to alleviate human suffering and improve patient care.

Our industry has a proud tradition of answering the needs of patients and providers, and perhaps no example is more profound than what innovators have done since the outset of the COVID–19 pandemic. Whether it was respiratory technologies, diagnostics, advanced patient monitoring, or personal protective equipment, the medical technology industry worked tirelessly to help the United States and the entire world to confront this challenge, and they continue to do so today. In addition to the extraordinary efforts of this industry and health care professionals, I would also like to take a moment to acknowledge the dedicated professionals at the FDA who worked 24/7 on COVID and non-COVID medical technologies to improve patient care during the pandemic. Their efforts ensured that patients had timely access to safe and effective medical technologies.

MDUFA V—A Historic Investment

The MDUFA V draft agreement that we are discussing today, and the historic increase in user fee funding that it contains, demonstrates our commitment to provide additional capacity and expertise to further advance FDA's mission.

MDUFA V provides over $2B in investable funding to FDA. As a point of reference, MDUFA I totaled approximately $150M over the 5-years of the program. While each MDUFA typically provides funding for an additional 200 new hires, under MDUFA V, FDA will be able to hire a minimum of 273 FTEs and up to 387 new FTEs to support the MDUFA program. This represents a historic increase in both overall funds and people, and it is our hope and expectation that this will be the last major investment needed for the MDUFA program and that moving forward, any necessary increases will be much more modest and targeted.

With these significant investments, MDUFA V also establishes more transparency around the use of the funds, including ensuring that annual hiring targets are met. FDA will also conduct a H.R. assessment during MDUFA V to identify how many MDUFA funded vacancies exist. Currently, CDRH is only able to track MDUFA IV and later FTEs. Public reports in 2016 indicated MDUFA funded vacancies exceeded 25 percent, and innovators want to ensure that the additional capacity we are funding through user fees is realized in the new additional hires and backfilling any vacancies that arise.

Beyond the financial accountability and transparency provisions that MDUFA V contains, performance goals associated with De Novos and PMA Total Time to Decision (TTD) also improve over the course of the agreement. One goal that was elusive under MDUFA IV was the 510(k) Total Time to Decision Goal in fiscal year 2022 of 108 days. As was mentioned earlier, COVID did impact FDA capacity, including the ability to meet certain MDUFA IV goals. Under MDUFA V, the 510(k) TTD goal will ramp down each year, hopefully achieving 108 days by fiscal year 2026. Also, for the first time, the agreement incorporates add on payments that will provide the agency up to $115 million in additional funding above the baseline in the final years of the agreement if FDA meets modest but important performance goals in the first 2 years of the agreement.

Maintaining FDA's Gold Standard

The United States medical technology ecosystem is the envy of the world, and this is in no small part due to the FDA's gold standard of reviewing the safety and efficacy of medical devices. The billions of dollars in user-fees provided by industry under this agreement will enable FDA to hire hundreds of new reviewers and scientific experts strengthening the agency's ability to maintain its strong track record. The agreement also makes targeted investments to enhance device safety. This includes increased funding for patient perspective and engagement in the product evaluation process to better incorporate their experiences, as well as new funding to improve the use of real-world evidence in the review process.

The agreement contains resources to start a pilot for the "Total Product Lifecycle Advisory Program," also known as "TAP." Medical technologies that serve patients with unmet needs unfortunately can take longer to navigate the regulatory process, despite the fact that these patient populations often have no other alternatives. This is often due to the complexity and novel approach that breakthrough devices encompass. Beyond breakthroughs, TAP will support devices developed to significantly improve the safety of currently available devices and diagnostics under the Safer Technologies Program (STeP). FDA was very vocal during negotiations about the importance of piloting the TAP concept. TAP is designed to allow FDA and innovators to share early feedback to improve this process. Based upon the data and assessment of the TAP pilot, industry and FDA will determine whether to continue, expand or terminate the TAP pilot during MDUFA VI negotiations.

Conclusion

As we all know, America's medical technology ecosystem was not built overnight. It took decades of work between countless stakeholders, including Congress, the FDA, innovators, physicians, patient groups and more to design the regulatory pathways that has resulted in the gold standard of safety and efficacy. At the same time, we all recognize that this is a delicate balance to ensure that the right policies are in place to support innovation, and to spur the next generation of cures, therapies and diagnostics that so many patients are relying on. As I noted, this is a historic investment in the FDA, and it will be critical over the coming years to meet the goals and milestones within this user fee agreement to help ensure that the United States remains the global leader in medical technology development. It is also critical that Congress continues its vital oversight role, and providing the necessary resources and investments to FDA for it to achieve its mission. MDMA and our members remain committed to working closely with you to reach our shared goal of providing safe and effective medical technologies to patients and providers in a timely manner. Thank you once again Chairwoman Murray and Ranking Member Burr for your passionate leadership on this important work, and I look forward to answering any questions that the Committee Members might have.

[SUMMARY STATEMENT OF MARK LEAHEY]

I am the President and CEO of the Medical Device Manufacturers Association ("MDMA"), a national trade association representing hundreds of medical technology companies. MDMA was founded in 1992 to be the voice of the innovative and entrepreneurial sector of our industry, including the small companies who make up the majority of the industry and drive medical innovation.

The device industry's singular mission—to alleviate human suffering and improve patient care—has been on display since the outset of the COVID–19 pandemic. Whether it was respiratory technologies, diagnostics, advanced patient monitoring, or personal protective equipment, medical technology innovators worked tirelessly—partnering with the dedicated professionals at the FDA—to help the U.S. and the world confront the pandemic.

MDUFA V—A Historic Investment—The MDUFA V draft agreement provides $2B in user fees enabling the FDA to hire a minimum of 273 FTEs and up to 387 new FTEs to support the MDUFA program. By comparison, MDUFA I totaled approximately $150M and subsequent MDUFA's typically provided funding for 200 new hires. It's our expectation that this will be the last major investment needed for the MDUFA program and that moving forward any necessary increases will be much more targeted.

MDUFA V also includes provisions to help ensure that annual hiring targets are met. Currently, CDRH is only able to track MDUFA IV and later FTEs. Public reports in 2016 indicated MDUFA industry-funded vacancies exceeded 25 percent, and it's essential that FDA hits the new hiring targets and backfills any vacancies.

Beyond the financial accountability and transparency provisions in MDUFA, performance goals associated with De Novos and PMA Total Time to Decision (TTD) also improve over the course of the agreement. One goal that was elusive under MDUFA IV was the 510(k) Total Time to Decision Goal in fiscal year 2022 of 108 days. COVID did impact FDA's ability to meet certain MDUFA IV goals. Under MDUFA V, the 510(k) TTD goal will ramp down each year, hopefully achieving108 days by fiscal year 2026. Also, for the first time, the agreement incorporates add on payments that will provide the agency up to $115 million in funding above the baseline in the final years of the agreement if FDA meets modest performance goals in the first 2 years of the agreement.

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Conclusion—It took decades of work between countless stakeholders, including Congress, the FDA, innovators, physicians, patient groups and more to design the regulatory pathways that has resulted in the gold standard of safety and efficacy. At the same time, we all recognize that this is a delicate balance to ensure that the right policies are in place to support innovation, and to spur the next generation of cures, therapies and diagnostics that so many patients are relying on. It is also critical that Congress continues its vital oversight role, and provides the necessary resources and investments to FDA for it to achieve its mission.

The CHAIR. Thank you very much. And thank you to all of our witnesses, and we do apologize having a vote, Members in and out, but we do have your written testimony and appreciate, again, all of you being here. We will now begin a round of 5-minute questions. I ask my colleagues to keep track of your clocks always and stay within the 5-minutes. Prescription drug prices in the United States continue to skyrocket. In 2020, our Nation spent over $535 billion on pharmaceuticals.

That number is rising. That is really outrageous. We have too many Americans who we know are choosing between paying their rent or mortgage and getting a lifesaving medicine. According to the Urban Institute, in 2018, nearly 13 million adults delayed getting or did not get needed medications because of the high cost, and Congress just really has to address this.

Families really need us to take some bold steps to get this problem under control like giving Medicare new power to negotiate and force drug companies to bring down prices and stopping the games pharmaceutical companies play to keep their prices high, for example, creating a tangle of patents that block competition.

I want you all to know I remain committed to working with all of my colleagues in Congress, on both sides of the aisle, to bring down prices and make sure prescription medication and lifesaving treatments are not just available, but accessible and affordable. Now, while FDA does not regulate drug prices, it does have a role in increasing access to lower cost generics and biosimilars, which can increase competition and drive down prices.

But for that to work, we have to build off the steps we took in the Lower Health Care Costs Act by doing more to stop pharmaceutical companies from gaming the system with sham petitions, exclusivity, parking, and other tactics that block cheaper generic drugs, and increase transparency and information sharing that can help bring more affordable generics and biosimilars to the market.

Mr. Gaugh, how do the generics and biosimilar user fee programs help increase competition and expand patient access to critical drugs without sacrificing safety, efficacy, or quality?

Mr. GAUGH. Thank you for the question. Yes, we have spent a significant amount of time in GDUFA III to get enhancements that we felt we had left on the table, if you will, in GDUFA II. So in that prospect, we have a 10 month time point within which the FDA is going to take an action on a product. We found that in that 10 month time point, at a certain point in time, we can get toward the end and run out of time, which means we get a complete response letter for that product.

In GDUFA III, we put forward an imminent action capability. So when the FDA knows that the product is about to be approved or could be approved with just a short period of time, they can take the imminent action route, which gives an additional 60 days for review. And while it is now a 12 month clock, it is also a first cycle approval.

If it went into a second cycle approval, that would be months down the road. So it would be at least 6 to 9 to 12 months delay. And this will help get access to the American public more quickly.

The CHAIR. What barriers exist for generic applicants in demonstrating their products have the same ingredients as more expensive brand name drugs, and how do we address those barriers?

Mr. GAUGH. Well, there is one area that we refer to is Q1, Q2. And in Q1, Q2, that is a qualitative and quantitative analysis of the product. So we know what the active ingredient is when we are reverse engineering the product, if you will. What we don't know is the inactive ingredients or the concentrations of those inactive ingredients.

Prior to 2017, when we had those issues come up, we would submit a control correspondence to the FDA, they would tell us what that product is, the inactive ingredient, and then we would look at ranges of what the concentration were and the FDA would say, usually high or low.

After 2017, that was changed. They no longer will tell us what the product is, nor give us a plus minus on the concentration. And when we put a control correspondence in to ask those questions, we can only have three products in that control correspondence.

If we don't guess right on the first time, it goes back for the next, and the next, and the next. So it is more of a guessing game and that delays even longer.

The CHAIR. Okay, thank you. Dr. Esham, we have seen pharmaceutical companies abuse the citizen petition process to delay cheaper drugs from competitors. In fact, the FTC and FDA have both called out that behavior, with FDA arguing that those shenanigans present obstacles to the availability of follow on drugs. Isn't it right that the citizen petition process should not be used to reduce choice for consumers?

Dr. ESHAM. Let me just start by saying that we do believe that the citizen petition process is an important mechanism not only for the public to express its views to the FDA, but also for the FDA to hear stakeholder perspectives on scientific, technical, and regulatory topics. We do understand that our colleagues at FDA have expressed concerns about situations where a company might try to

use this process to block generics or follow-on biologics from entering the market.

We also understand that they do conduct their own research. And while process requirement is associated with the 505(q), petitions have the potential to add some burdens to the generic drug review process. Citizen petitions have really delayed specific generic drug approvals.

That being said, if this is an issue that the Committee would like to explore, we stand committed to working with you and other stakeholders.

The CHAIR. Okay. Appreciate that.

Senator Cassidy.

Senator CASSIDY. Ms. Richardson, and Mr. Gaugh, I will probably hit you afterwards. Some go to the doctor, eye doctor, he gives me a prescription for something which is four times a day, eye drop for the pain, and it cost me like $50 bucks. Except they can't find it. The only thing I find is something which is taken twice daily.

Same active ingredient, which cost me $400. Now that clearly is not innovation. It is not a once monthly depo shot to prevent pregnancy or once daily shot for HIV. It is something which allows them to remove the generic so that instead of paying $50 bucks, the patient is now paying $400.

How do we differentiate true innovation from faux innovation, which frankly works to the detriment of the consumer?

Ms. RICHARDSON. Thank you very much for the question, Senator. I have to confess that the question of measuring innovation is not something that Pew has done any research on or is currently focused on, although certainly as a patient and as a consumer, it is on my mind all the time. Every time I go to the doctor——

Senator CASSIDY. Let me go to Mr. Gaugh. Mr. Gaugh, how do we measure innovation? It is something because I am a big believer that innovation needs to be rewarded and that we need to have that profit motive for people to innovate. But I am also recognizing that it is gamed at times so that, I call it faux innovation, is merely gaming the patient. How would you respond?

Mr. GAUGH. Thank you, Senator Cassidy. So you bring up a great point, and we have always believed and felt that the generic and biosimilar industry does promote innovation and moves the innovator companies to better products, different products. But there is still some gaming that goes on to your point.

Whether it is a single daily dose or it used to be three times a day goes to a single. That is not necessarily an innovation, but it is really hard to judge how you stop that gaming, if you will.

Senator CASSIDY. Okay. Ms. Esham—Dr. Esham, I am sorry. Clearly, we want to bring drugs to market more quickly, and there is this discussion of using the accelerated approval with this reliance upon post-market data. Now, tell me, just kind of from your perspective, what various sources of post-market data could be used to evaluate whether something is a true innovator value and improves patient outcomes to make sure that whatever we are using it for is bringing value to the patient.

Dr. ESHAM. Certainly. I would say that when we entered into the PDUFA agreements, we did recognize the need for improving how we design, have conversations pre-approval about post-market re-

quirements associated with—that are always required with accelerated approval, and improving processes post-approval to ensure that we are able to address challenges as they arise and not just let them hang there and, not know a path forward.

The processes improvements in the commitment letter we do think will be helpful. In addition, I think more specifically, probably to your question, is advancing the ability to utilize patient registries, real world evidence that we do believe have the potential to offer more efficiencies and realistic pathways toward completing those requirements.

Senator CASSIDY. These are patient registries that you are establishing, or will this be borrowed from some master registry of EHRs, etcetera?

Dr. ESHAM. I don't think it is an either, or, but happy to meet with you and your staff and discuss in more detail if that would be helpful.

Senator CASSIDY. Okay. Mr. Leahey, I am concerned—the cybersecurity. Now, there is a lot of stuff, a lot of medical devices that are going to be increasingly cyber, correct?

Mr. LEAHEY. Yes.

Senator CASSIDY. Senator Baldwin and I have a bill called the Patch Act, which requires a premarket demonstration of cybersecurity measures and post-market updates for any issue discovered. Can you tell me a little bit of how the manufacturers are thinking about cybersecurity in the context of hospital networks or individuals who may be affected?

Mr. LEAHEY. Thank you, Dr. Cassidy. As you noted, devices are becoming more interoperable each day. And MDMA as part of the HCC. It is a private, public partnership with HHS, FDA, hospitals, insurers working to address these issues. Fortunately, we haven't seen any issues directly related to compromising the devices themselves.

But as you noted with the ransomware and other issues, these have certainly become challenges. So in 2019, the HHSC published the Medical Cybersecurity Joint Security Plan to provide device makers with a playbook on how to develop best in class cyber management.

But clearly, much more work needs to be done, and we look forward to working with you and your colleagues to making sure that again, as technologies evolve, we make sure that the hospital system, the patients are ultimately protected within these cyber threats.

Senator CASSIDY. Thank you. I yield.

The CHAIR. Senator Kaine.

Senator KAINE. Thank you, Chair Murray. And thanks to our witnesses. Five years ago, when Congress last addressed user fee reauthorization, I asked Dr. Woodcock of the FDA a question on the availability of biosimilar drugs. This is something that Senator Collins and I have done some work on, together with the Biologic Patent Transparency Act.

Dr. Woodcock told me then that biosimilars were being analyzed and improved at that time, and that would set a standard for future biosimilars to come to market. She also shared that as of that time, 2017, the FDA had approved four biosimilars. I don't think

they were yet on the market. They had 13 pending applications and that there were 64 biosimilars in development.

Mr. Gaugh, in your testimony, you stated there are now 34 biosimilars approved by the FDA, 21 of which are on the market and available to patients, many others in development. Could you talk about how the advancements over the last 5 years have brought more biosimilars to market, have increased the number of available biosimilars to address the rising costs of prescription drugs, and how patients have benefited from the growth in this industry?

Mr. GAUGH. Thank you, Senator Kaine. Yes, your points are exactly right. So we started the biosimilar program in basically 2012, when legislation was put in place in 2010, but the guidance first came out in 2012 with the FDA, that gave us the pathway for biosimilars.

Since that time, we have approved 34—or the FDA has approved 34, as you just noted, and 21 on the market. But there has been a significant cost savings to the patients for that. So in the biosimilar realm, it is a cost savings of roughly 50 percent. Also, something that you don't see on the generic side is that the innovator price has come down about 25 percent on those products.

Having that access has provided cost savings for the patients. You noted 64 program development back in 2017. There is now 97 that we know of that are in development. So it is continuing to grow and expand, and BsUFA III is addressing several of the enhancements, if you will, from BsUFA II to BsUFA III that will improve that through meetings, through supplement review process and being more timely, and some things about inspections.

Senator KAINE. Excellent. Thank you. Dr. Esham, I have a question for you about treatment for rare diseases. It is clear that sponsor companies that want to address treatments for these diseases face a number of challenges, particularly the limited number of patients with these types of conditions. However, it is not a limited number of people who suffer from rare disease conditions.

There are about 7,000 known rare diseases, and they collectively affect over 25 million Americans. You also state in your written testimony that the current mechanisms for companies with rare disease treatments and their pipeline to collaborate with FDA have not consistently provided avenues for such needed discussions.

Could you talk a little bit about the provisions of PDUFA VII that would allow for better collaboration between the FDA and sponsor companies in the rare disease treatment area?

Dr. ESHAM. Yes. First, thank you for that question. And again, I think we are all very excited about the progress we have made, but there is just much more work to be done here in this—in terms of providing treatments for rare diseases. I think there are a number of provisions that collectively we believe will work to improve regulatory clarity and understanding for rare diseases.

That includes the Rare Disease Endpoint Advancement Pilot Program, which is really designed to pilot engagements with sponsors to increase our understanding about what is needed to develop and support utilization of an endpoint for the basis of approval for rare diseases.

Those learnings will be shared across industry, academics, researchers, and the entire research and development ecosystem. There are also provisions that I think will be particularly important for rare diseases, and that is the ability to have focused meetings on complex and unique challenges, both at preclinical as well as during development that I think will be—offer a chance to really address those unique challenges.

As well as some of the provisions designed to ensure that there is a better utilization of innovative clinical trial designs. And that is just to name a few. I don't want to run out of my time, but collectively again, we did try to work to make sure that there was the ability to engage at the right time and have those discussions in advanced innovation for these treatments.

Senator KAINE. Thank you. Mr. Gaugh, I am going to submit a question for the record about interchangeable biosimilars that I would direct to you, but I will put that in for the record. Chair Murray, I yield back.

The CHAIR. Thank you.

Senator Collins.

Senator COLLINS. Thank you, Madam Chair. Before I turn to my questions, let me thank the Chair and the vice Chair for their hard work on this issue and to express the hope that a bill that Senator Feinstein and I have worked on for some time, that has to do with personal care products, can also be considered.

Chair Murray brought that up in her opening statements, so I just wanted to mention it. Dr. Esham accelerated approval is a critical regulatory pathway that provides timely review of treatments for patients with serious and life threatening conditions for which there is an unmet need.

Sponsors must meet, as I understand it, the same substantial evidence standard as traditional approval, but they can rely on a surrogate endpoint that predicts a clinical benefit rather than measuring that clinical benefit directly. Obviously, clinical outcomes can take significantly more time to manifest. And an example is that tumor size is often used as a surrogate in oncology.

It can be measured much earlier than mortality and is reasonably likely to predict an effect on that devastating clinical outcome. Understanding that science does not move at the same pace across all disease areas, why hasn't this pathway been used to the same degree in fields like neurology or for rare diseases?

Dr. ESHAM. I really appreciate this question, and you are correct. We know that historically over 60 percent of accelerate approvals to date have been for oncology indications, and that is wonderful. There are multiple factors as to why this has been the case, including the maturity of an investment in oncology basic research.

There has also been incredible collaborations between doctors, academics, patient organizations, the pharmaceutical industry, and the regulatory leaders that have resulted in the identification of surrogate endpoints and other informative biomarkers and subsequent validations.

Again, we can't underscore—I can't undervalue the leadership that is really important in this, both within the industry research and the regulatory agency. And we have long advocated for broader utilization of this pathway across more therapeutic areas. We do

think that it would be helpful for the FDA to hold disease specific or disease or therapeutic area specific meetings or promote that multi-stakeholder dialog on appropriate biomarkers and clinical endpoints.

It is our hope that the Rare Disease Pilot Program that I have referred to earlier will also advance our learnings about how to approach—it is not just looking at an individual endpoint, it is thinking of the how, what is needed, how do you think about developing evidence, and how will that evidence be evaluated, that we think will hopefully drive more innovation and utilization of this pathway to, as you say, provide more timely access to these medicines that are—just really devastating.

Senator COLLINS. You have mentioned the Rare Disease Pilot Program, and I want to follow-up on that issue with you as well. More than half of the 400 million people in the world who are affected by rare diseases are children, and about one-third of those children will sadly die before the age of five.

Drug development is hamstrung by the fact that we simply do not have well characterized the endpoints for most rare diseases. The PDUFA agreement establishes the Rare Disease Endpoint Advancement Pilot Program, which would enable FDA and industry to collaborate to develop more meaningful, consistent, and relevant endpoints for clinical diseases.

I am thinking of diseases like Duchenne muscular dystrophy, for example. It is difficult to precisely measure progression of the neurological and neuromuscular effects associated with many of these diseases, and thus it can be difficult to determine a treatment's impact.

This pilot program that you referred to is limited to a few select applicants, but how can we share the lessons learned through this pilot to ensure that other rare disease drug applications can build on its findings?

Dr. ESHAM. Very important point to raise. And I will note that when we worked with the FDA to develop this pilot program, it was modeled after what we view as a successful pilot program for complex innovative clinical trials and modeled for drug development that used the same model of having only a limited number of applications that went through the pilot program, but that the learnings if you go through that program, the FDA has the ability to share those learnings to the entire stakeholder community.

It was very specifically modeled after that. We have seen that be successful and create opportunities for learnings across the academic, medical research, and biopharmaceutical industry.

It is our expectation that the minimum of the three public workshops will serve that. But we do expect more engagement and more shared learnings in other venues of scientific dialog that occur on a normal basis.

Senator COLLINS. Thank you.

The CHAIR. Senator Hassan.

Senator HASSAN. Well, thank you, Madam Chair. And I want to thank you and the Ranking Member for holding this hearing, and I want to thank all of our witnesses for being here today. Dr. Gaugh, let me start with a question to you. While Americans strug-

gle to afford lifesaving drugs, brand name manufacturers continued to increase prices.

Generic competition can help drive down drug prices now. So how do new generic drugs affect brand name prices? And how much do generic drugs save consumers each year?

Mr. GAUGH. Thank you for the question. So significant savings is brought forth by the generics. If you look at the numbers, over the last 10 years, we have saved $2 trillion, and $469 billion of that was in new generics that came to market.

It is a significant improvement in the increase for the patients. We find that when one generic drug is approved, the price comes down about 50 percent—the generic price comes down 50 percent, excuse me, not the brand. And with four or more, it is more like 80 to 85 percent. So it is a significant increase in savings to the American patient and U.S. health care systems.

Senator HASSAN. Thank you. Also another question to you, Mr. Gaugh. For some medications with serious safety concerns, FDA requires manufacturers to set up risk evaluation and mitigation strategies, otherwise known as REMS programs. REMS helps to minimize the risk associated with these medications and make them safer for the public and for patients.

For example, a REMS program may require prescribing clinicians to receive training on the risks of a drug and to perform monthly lab tests. Even though REMS programs are meant to protect patient safety, some brand name manufacturers have patented these programs to prevent generic competitors from entering the market.

Mr. Gaugh, how have brand-name manufacturers use REMS patents to delay the launch of generic drugs? And how have these delays affected drug prices?

Mr. GAUGH. Thank you. Thank you for the additional question. So REMS is a very important program. As you mentioned, it is about safety for patients, and it is a very restricted program in its set up. I would almost make it akin to new drug IRBs when they are doing the study process, so it has to be patient specific, signed off, and given.

REMS has really had two problems with, the first one was we as the generics, as we reverse engineer, need the product that we are reverse engineering to make that. The CREATES Act help solve that because we were being blocked from even getting the drug. We weren't a patient. We couldn't sign up for it. We wouldn't get it. So that has now been changed.

But what is new is what you just brought up, and that is the patenting of the REMS programs. And so if the REMS program is actually patented, then I, as a generic company, can't get on that REMS structure to be able to bring my product to market. So it is a further delay of not months, but years.

Senator HASSAN. And it is using the notion of patient safety to delay the development of additional drugs that could bring down the cost.

Mr. GAUGH. Absolutely.

Senator HASSAN. Yes. Okay, last question for you, sir. There is a long history of brand name manufacturers playing games with the law to delay and block the launch of generic drugs. As a result,

patients pay more at the pharmacy counter with some rationing life medications because they can't afford them.

I would expect that every single Senator on this Committee has heard stories from their constituents about their decisions to ration their drugs and the impact that has on their health. Mr. Gaugh, how are brand name manufacturers manipulating the system to limit generic competition?

Mr. GAUGH. We just talked about two of those methods. And Dr. Cassidy brought up the point about some quasi-innovation, if you will, moving a product from twice a day to one today, for example. And that in and of itself is not necessarily innovation. It is an improvement.

But in that particular case, the physicians and the pharmacists can overturn that by having the patient go ahead and take the twice daily at the lesser price than once daily at the higher price point level.

Senator HASSAN. Thank you. I yield my time.

The CHAIR. Senator Burr.

Senator BURR. Thank you, Madam Chair. Cartier, again, welcome. More than 278 therapies have been approved under the accelerated approval pathway over the 30 year history, saving and improving thousands of lives.

This pathway has been the subject of recent scrutiny. But it is a successful and important tool for the FDA to bring game changing innovation to patients faster. What promise does the accelerated approval pathway provide for companies investing in novel treatments and particularly treatments for rare diseases?

Dr. ESHAM. Thank you, Senator. The role of this program played in improving care for patients suffering from serious and life threatening diseases when their needs are not being met or where precedents are little or do not exist, or are not well known, cannot be overstated. And we have seen this be very successful in driving innovation and investment in oncology and infectious diseases.

It is our hope that we expand utilization of this pathway across more therapeutic areas, including for rare diseases. It is critical for continued innovation—continued investment and innovation in these disease areas that are complex and where there are little or evolving precedents, which is the case in many rare diseases.

It is also foundational to advancing scientific understandings that allow us to continue to innovate and continue to improve care for these complex and devastating diseases. And so if it did not exist or it is not able to function as intended, the path forward for timely access to improved care for these devastating diseases will be limited and delayed.

Senator BURR. May I ask you, how could we ensure the accelerated approval pathway is used to create new breakthroughs in more fields like neurology?

Dr. ESHAM. Great question. And there are provisions in the PDUFA VII commitment that we think will strengthen the pathway, such as the ability to engage with the FDA early to discuss what is needed to support the use of a novel surrogate endpoint. And as we have discussed previously, there is also the rare disease endpoint pilot program, which should lead to broader under-

standings about how to approach and develop support for the utilization of a surrogate endpoint to support approval.

There are also process provisions—process improvements to try to improve what the approach will be to accomplish post-approval requirements. Which again, in neurology, that is an assessment that you make before you endeavor into a clinical development program.

The more that we can improve those processes, enable utilization of things like real world evidence to enable them to be more realistically completed and in a more efficient timeline, will also be quite helpful, I think, in driving more investment and research and utilizing the accelerate approval more broadly.

Last, just one quick thing, can't underestimate the importance of multi-stakeholder engagement with regulators to really identify new surrogates and advance their utilization.

Senator BURR. Thank you. Mark, FDA is proposing longer review times for 510(k) devices. FDA committed to review 510(k)'s within 108 days in Fiscal Year 2022, and I understand that FDA is not currently meeting that goal. What does it mean for a small company when FDA misses these goals, and what does it mean to patients?

Mr. LEAHEY. Obviously meeting goals are critical to timely patient access and to small companies, the predictability. The small companies don't have a number of products to subsidize delays, so it is critically important. COVID was certainly an impact, but we need FDA to get back on track and meeting that shared outcome goal of 108 days as quickly as possible.

Senator BURR. Why did FDA agree, and why did the industry agree to longer review times of 128 days on 510(k)'s and provide the agency with so much more money?

Mr. LEAHEY. There is no doubt this is a significant increase in funding. And as I said in my opening testimony, this doubling of fees is certainly not sustainable. As MDMA is representing small companies, it is of great concern.

But we do recognize the challenges that FDA went through during COVID, and this investment is obviously put forward to get them back on track, and there are additional accountability measures to make sure that these metrics are met going forward.

Senator BURR. Just so I and my colleagues understand better, I went through a litany in my opening statements of the deficiencies in what FDA committed to and what they missed. And they missed resoundingly in things like meeting with applicants, explanations and deficiencies letters. Is this really a difficult thing, or is this just a choice by FDA to stiff somebody on meeting them, even though there is a requirement to do it?

Mr. LEAHEY. I can just say from our Members' perspective, the quality of the journey is so much more important than the time. If you have high quality inputs and timely interaction, you get there.

Obviously, it has been disappointing that simply providing the rationale for a deficiency is something that we have to bake into a commitment. And it is not just part of the basic offering. But we are where we are, and we hope that we have a productive and effective meeting for V.

Senator BURR. I thank all of you. Thank you, Madam Chair.

The CHAIR. Senator Smith.

Senator SMITH. Thank you, Madam Chair and Ranking Member Burr, and I really appreciate this Committee and all of your testimony. Madam Chair, I would like to request unanimous consent to submit into the record a letter from the biosimilars forum expressing support for the biosimilar user fee agreement and urging additional action to address the impact of the pandemic on approvals of low cost biosimilar products like biosimilar insulin.

The CHAIR. Without objection.

[The information referred to can be found on page 130 of Additional Material:]

Senator SMITH. Thank you. I think we all agree that these FDA user fee agreements are critical for supporting the FDA's work, and I want to just note that I worked with Senator Cassidy to move forward legislation to streamline the process for bringing biosimilar products to the market.

I want to thank Senator Hassan for her questions about how that streamline process and bringing biosimilars, bringing generic drugs to market helps to contribute to our goals of lowering costs for Americans, which is very much on the minds of my constituents. Mr. Gaugh, I want to ask you about something specific to the therapeutic equivalence ratings.

According to the FDA, complex generic products, I mean, there are so called because they have complex active ingredients, routes of administration, drug device combinations, or formulations. So in short, these drugs are more difficult for generic manufacturers to develop. Examples might include inhalers, or topical ointments.

These complex generic products face regulatory challenges compared to other generics. It is harder for them to be assigned a therapeutic equivalence or TE rating from the FDA. In fact, it can take years to get a rating if they ever get a rating at all.

This TE rating is important because it lets pharmaceuticals—pharmacists, excuse me, automatically substitute a lower cost generic product for a brand name product at the pharmacy counter so patients can get cheaper medicines.

Mr. Gaugh, could you please describe for us why it is harder for certain complex generic manufacturers to receive this TE rating, what medicines are impacted by this issue, and what we can do to make this process more efficient?

Mr. GAUGH. Thank you for the question. And there are different categories of generics, including and most often complex generics that have to use a 505(b)(2) pathway for approval. So it is not the normal generic pathway, if you will. That approval pathway does not give 100 percent therapeutic equivalence.

The FDA does not grant 100 percent therapeutic equivalence when the product is approved. Therefore, we have to go back to the FDA, as you mentioned, through a citizen's petition process to get the FDA to grant that. That can take years for that to happen. And to your point, if it is not granted, it is not therapeutically equivalent and therefore the pharmacist cannot automatically substitute it.

That is an area that we hope to work with Congress on, with this Committee on to get that changed and get the citizens petitions moving in a more quick process.

Senator SMITH. And is the solution to that to get those citizens petitions moving more quickly? Is that what you see?

Mr. GAUGH. Well, there is also some other rule, regulation processes that the FDA can put in place for that as well.

Senator SMITH. Thank you. So I am working with Senator Cassidy on legislation that would require the FDA to provide a TE rating at the request of an applicant on a much quicker timetable. And I look forward to working with the Chair and Ranking Member as we move forward with these user agreements.

Ms. Richardson, I have a question for you. I appreciate how your written testimony highlights that these user fee agreements are important for streamlining the review of medical products. But the FDA's role is not just about bringing products to market faster.

As you note, the FDA is a public health agency that works to promote health of all Americans. So could you just expand upon the recommendations that you have made that the FDA should be receiving public funds and be accountable to the public through these user free processes?

Ms. RICHARDSON. Thank you very much for that question, Senator. As I noted in my remarks and really just want to reemphasize, user fees are essential to the functioning of the FDA, but they are dedicated to specific functions like expedited review.

That is very useful, but it is limited because there are so many other areas that FDA's mission—of FDA's mission that don't enjoy that kind of support. They don't cover food, they don't cover supplement oversight, they don't cover a lot of the agency's post-market oversight activities like inspections.

Appropriations really are essential to fully support FDA's public health mission in the years ahead. So thank you again for the question. I welcome the opportunity to underscore how important it is to ensure adequate appropriations for the agency.

Senator SMITH. Thank you. And do you have any specific recommendations for how we should improve the use of free agreement process to better engage Americans in that process?

Ms. RICHARDSON. That is not an area that Pew works on, although I do know there have been suggestions about increasing transparency, right. I know that there were some issues with posting of meeting minutes, things like that. So I am sure that there are some solutions that FDA would be more than happy to consider, but I don't have any more specific recommendations.

Senator SMITH. Thank you very much. Thank you, Madam Chair.

The CHAIR. Thank you.

Senator Marshall.

Senator MARSHALL. Thank you, Madam Chair. If I could have a moment of privilege first and just start by congratulating my University of Kansas Jayhawks on their fourth national championship, and I would be remiss for not congratulating my friends from North Carolina on a great game, one of the greatest games in NCAA history, and just Kansas so much as a special connection to North Carolina, going back to Dean Smith being a player for KU

in the early 1960's. So congratulations to our amateur sports and my Jayhawks. Thank you.

Madam Chair, I want to start off by talking about the importance of innovation. I have always said that innovation would do more to drive the cost of health care down than any legislation that we can write. And I was so excited when biosimilars came on the market and I thought that competition would drive the cost of insulin down.

Unfortunately, brand name manufacturers have found out ways to prevent this competition, these new biosimilars to come to market. And it is so frustrating. We have a saying back in Kansas that pigs get fat and hogs get slaughtered. And my point is that these middlemen and big pharma is getting hogwash. That they are—they can't have it both ways. You can't want protection from price fixes or price costs, but you can't—but you don't allow innovation.

You can't allow it to work both ways. And my first question is going to be for Mr. Gaugh. Right now, we are seeing with these brand name manufacturers using inactive ingredients now to keep biosimilars to come to market. And I think of Humira using the size of a needle to keep something from coming to market.

I would ask both sides of the aisle, the staff to start looking into if we get rid of the rebates, that is what is going to solve this problem. If we get rid of the middlemen rebates, that is what is going to drive the price of insulin down. And if we put a price fixed at $35, a price cap, all that is going to do is drive up the cost of health care for everybody else in the plan.

It is just basically given the middleman a license to charge whatever they want to, even though the person that is getting the insulin is going to be capped with an out-of-pocket expense. It is going to drive the cost of prescriptions up for everybody else in the plan. So I am all about promoting competition.

Mr. Gaugh, what—in the review of this reauthorization, what can we do to make it better for patients to have faster access to generics and biosimilars without compromising innovation?

Mr. GAUGH. Thank you for the question. And so we did build in several enhancements in both GDUFA and BsUFA to help move that along more quickly. I talked earlier about the imminent approval in the GDUFA realm.

In the BsUFA realm, in the biosimilars—which we now have two interchangeable insulins that are in or one insulin that is in the market, so that is out there for competition and hopefully that will help bring——

Senator MARSHALL. Have we done everything we can, or do we need to do more?

Mr. GAUGH. There is always more that we can do. Absolutely, yes. So we built that in with meeting management and supplement reviews.

Senator MARSHALL. Thank you. Dr. Esham, my next question for you. It takes 10 years and $1 billion to get a new product to market and often maybe a 1 or 2 percent chance it ever actually reaches the market. The reauthorization process of these new drugs, authorizing these new medications, we talk about that process, but I want to back up in the research going on here. So often we are

using animal models, which are like night and day to the real world when it comes to human biology.

What we see in the animals, consequently, typically, not uncommonly, doesn't apply to humans. There is something now called where we can use human cells with bioprinting.

For instance, if we know a medication that is going to be metabolized through the liver, we would test it with human liver cells. Do you see any way that we can start implementing that technology in helping the process of approval for new medications?

Dr. ESHAM. Thank you, Senator. And first, let me say again, congratulations. As a University of Kentucky fan, I really hope that I believe that at some point. I will get there. But to your point, in all seriousness, we actually have a very active group of scientists in what we call our bio-safe working group that has been publishing papers on advancing non-human primate ability to use utilize alternative tools to primates for preclinical work.

We certainly see a lot of innovation in this space that you have mentioned, and we would be happy to bring our scientists to meet with you and discuss in detail their potential. But the bottom line is, yes, we do think we can continue to innovate here and be much more—less dependent on primates——

Senator MARSHALL. Speed up the process and hopefully make it safer. Both.

Dr. ESHAM. Yes——

Senator MARSHALL. That is a win, win.

Dr. ESHAM [continuing]. However they have—the goal is to fail earlier or fail better and then advance most optimistically.

Senator MARSHALL. Quickly to Mr. Leahy. I am a big fan of using real world evidence. And how does the FDA currently lack—does the FDA currently lacks the expertise and infrastructure to interpret real world data? And what can we do to make that situation better?

Mr. LEAHEY. Well, absolutely. This is critically important to leverage that, as you noted, information out there in the world to help accelerate additional patient access. Under MDUFA IV, we invested tens of millions of dollars to help build the real world evidence capacity in a private public, partnership.

We are continuing that investment in MDUFA V to help both private, public partnerships enhance their capabilities and also make sure that FDA have the personnel to take that information and leverage that for the purposes of application.

Senator MARSHALL. Thank you so much, Madam Chair. I yield back.

The CHAIR. Thank you. I will turn it over to Senator Casey. I am going to go vote and I will be back.

Senator CASEY. Chair Murray, thanks very much. I have a question for Dr. Esham and Ms. Richardson. Doctor, I want to start with you. Patients with rare diseases and conditions often face their diagnosis with either a limited or no treatment options.

I was glad to see PDUFA VII, the commitment letter, have dedicated pages to advancing the development of drugs for rare diseases, including a commitment for FDA's rare disease team staff to be more closely involved in training, outreach, and application review. With their expertise, what—I should say, while their exper-

tise is very valuable, I am not—I am sure you will agree that they are the voice and the unique experience of patients with rare diseases must be heard within FDA.

In your written testimony, you discuss the Rare Disease Endpoint Advancement Pilot Program in PDUFA VII. I know Senator Collins made reference to this on. Page five of your testimony, you say, and I am quoting, "key among these challenges is reaching agreement with regulators about determining the appropriate efficacy endpoints to support approval of innovative medicines for rare diseases."

How can we ensure that firsthand knowledge and expertise of this small group of patients, for whom the drugs are ultimately intended, are considered in developing endpoints that are meaningful for these patients?

Dr. ESHAM. Thank you for that question, and it is quite important. And, when—back in PDUFA V, when we, the commitment sort of started that voice of the patient meetings, I think that is where we learned really what mattered to patients, and more importantly, learned that we were often wrong about how to interpret their needs.

In addition to that pilot program, when you think about what is needed to support, what evidence is needed to support the utilization of surrogate endpoint, it is our hope that there will be—that the utilization of patient perspective data will be incorporated into that assessment, either for the assessment—the evaluation of the benefit, risk evaluation or as support as an endpoint.

Again, it is our hope, desire, and we will certainly be advocating for inclusion of those perspectives into the learnings of that pilot program.

Senator CASEY. Thanks, doctor. Ms. Richardson, I want to thank you for raising the issue of antimicrobial resistance. The Committee has taken steps in previous user fees reauthorizations to encourage the development of new antimicrobial drugs to mitigate the serious impact of antimicrobial resistance.

In 2012, we had the GAIN Act, for example. Yet the realities here, the financial realities of developing these new agents remain very challenging. And investment, as well as research, as well as drug development are not keeping pace with the need.

I know that the Pew Charitable Trust has been an important partner in a proposal that I have been working on with Senator Cassidy, the Disarm Act, which would use reimbursement tools through CMS to help stabilize the market for novel antimicrobial agents. Can you talk about why these multiple approaches are necessary?

Ms. RICHARDSON. Yes, Senator, and thank you for that question. I absolutely agree with you that antimicrobial resistance is a public health crisis, and no single solution is going to fix the problem. We need creative ideas that can realign current market incentives to encourage drug developers to stay in this business, right.

Large companies are exiting the market. Small companies are going bankrupt. It is just a tough business model. And so we need to provide new types of incentives to antibiotic drug developers so that this absolutely crucial antibiotics pipeline doesn't dry up completely. So your legislation, the DISARM Act, is certainly part of

that solution, as well as the PASTEUR Act, which is authored by Senators Bennet and Young.

We support both DISARM and PASTEUR, and we believe the solution to the broken antibiotic pipeline, it will require multiple creative solutions on both the legislative and the regulatory fronts.

We hope Congress will remain open to considering additional options like DISARM, and we support the PASTEUR Act as an immediate opportunity for policymakers to make progress in fixing the market.

The PASTEUR Act has an innovative only pay for success subscription approach that will stimulate the antibiotic drug pipeline and help ensure that patients will have access to these lifesaving drugs when they need them. Thank you, again, for that question.

Senator CASEY. Thank you. Thanks very much, Mr. Chairman.

Senator BURR. Senator Murphy.

Senator MURPHY. Thank you very much, Mr. Chairman. Thank you all for your testimony. I have been in and out of the hearing today, but I look forward to reviewing the record. I wanted to talk a little bit about the issue of mental health drug discovery. And I will maybe sort of ask this question to you, Dr. Esham, but others I am glad to hear from.

It is interesting, when you look at some of the data about recent drug discovery, it just doesn't seem that the development of new drugs in the mental health space is keeping up with the need.

I was taking a look at recent records from the FDA on novel drug approvals from 2015 to 2022, and there is about 333 approvals during that 8 year time span. And let me just sort of give a—my best attempt at an apples to apples comparison. Of those 333, 90 were cancer drugs.

About 40 percent of Americans over the course of their lifetime will be diagnosed with cancer. And so I am glad that there were 90. But 46 percent of Americans at some point over their life will have a diagnosable mental illness. And yet of those 333 drugs, only 12 of them were mental health drugs.

You hear this pretty routinely from the medical community that we just aren't keeping pace with the need when it comes to drug discovery in the mental illness space. So let me just sort of ask the sort of broad question here, how do we get your members, how do we get the private sector more interested in developing novel pharmaceuticals for mental health conditions? What are the barriers and are there public policies you would recommend to this Committee?

Dr. ESHAM. Thank you for that question. I think it is fair to state that none of us are—believe that we are anywhere near the level of innovation in mental health, providing innovative treatments for those suffering from mental health, anywhere near where we want to be.

There are—I will point you and your staff, your office and your staff to some reports that we did over the course of years, kind of looking at the challenges of highly prevalent chronic diseases. And we did one specifically in 2018 on depression, sort of as an example on the mental health space, to try to understand what was going on and sort of what looks like an inverse investment in public health need trend lines.

I think that there are some challenges in understanding the underlying causes of these diseases. There are challenges in developing and implementing clinical—effective clinical trial designs. And there are also challenges on the access coverage side. And so, it is a, unfortunately in the space I think it is all of the above more often than not.

But we would be happy to bring in some scientists and researchers from our companies working in this space to really kind of dove into the details here. But I think that clearly some pretty collaborative multi-stakeholder dialog is really needed here.

Senator MURPHY. Well, I will be glad to do that. And I will just note for the Committee, one part of your answer, you referenced an uncertainty about reimbursement, which is true generally in the mental health space.

We have been working very hard on this Committee over the years to make sure that there is parity between reimbursement for mental health and for physical health. I am interested to know whether that exists on the drug reimbursement side. I doubt it is as dire as it is on the sort of in-person treatment side, but I look forward to follow-up with you on that. Mr. Leahey, I wanted to ask you a question with my remaining time about the state of clinical trials and clinical research.

I heard Senator Murray references in her opening statements. But there, as you know, is a concern that trials and research often don't represent the democratic diversity of the populations that are going to ultimately benefit from these drugs and devices.

We have seen how COVID clearly had a disproportionate impact on racial ethnic minorities, and it has, I think, spurred a conversation about how we make sure that there is broader representation in those that are part of these trials.

Is that a question one that you are grappling with, that your members are grappling with? Why is it important that, and do you think it is important that we make sure that there is broad demographic representation amongst the populations who are part of the research and the trial process?

Mr. LEAHEY. Thanks, Senator, for that question. And absolutely, MDMA and our member companies support diversity in clinical trials and agree that the trial enrollment should accurately reflect the intended patient population. And we look forward to working with Congress and FDA to ensure that proposals are thoughtfully structured to achieve this objective.

Senator MURPHY. Just why is it important?

Mr. LEAHEY. Ultimately, it is because it is about the patient. We want to make sure that these drugs, devices all are tested in populations and age demographics, racial dynamics to ensure that, again, they meet the mark of having the safety and effectiveness for those who are intended to help.

Senator MURPHY. Right. Thank you. Thank you, Mr. Chairman.

Senator BURR. Thank you, Senator.

Senator Braun.

Senator BRAUN. Thank you. The FDA user fee program was established to provide a predictable and accountable regulatory framework that supports expedited FDA review and approval of

safe and effective treatments for patients. The user fee process has given lip service to the patient's voice in the conversation.

PDUFA commitment letter includes a number of provisions to address unmet medical needs and advance rare disease endpoint development. The purpose of today's hearing is to discuss advancing medical product regulation and innovation for the benefit of the patient.

There should be a witness here, I think, that would be from the patient's perspective. There is not. There should also be a representative from the rare disease community, which I have wrestled with since I have been here on for families that have issues, where the diagnosis is bleak, and time is the most important thing. They are not represented, either.

In fact, there is not one hearing scheduled for this that brings in that patient voice. I would like to submit to the record a letter I sent to the HELP Committee yesterday requesting a patient focused user fee hearing.

Senator BURR. Without objection.

[The information referred to can be found on page 131 in Additional Material:]

Senator BRAUN. In general, the Members of this Committee are given 5 minutes to talk about whatever they want to. Today, I had planned to show a video. There is really nothing in the rules that says I can't do that. We use video aids often here. But it hasn't been done before. A lot of things I have tried to do over 3 years I have been here is to fix the things that haven't been done before to give the patient, to give the constituent a better outcome.

In this case, it is Ala, a happy go lucky girl who dreams of 1 day becoming a scientist. Without the necessary FDA reforms, timely access to promising therapies, that is not going to happen. Won't be able to achieve that goal. Her parents share a similar grief knowing that they won't see their daughter graduate from college or walk down the aisle. The average survival time for this particular ailment is only a year.

Imagine from the patient, the family, are they interested in the cumbersome process that we always want to keep as a gold standard, but that doesn't necessarily mean you don't change it to adapt, keeping those standards in place to the particularities of this and many other ailments. The video highlighted the patient perspective and the need for the FDA to reform its process there.

As a U.S. Senator, I have been proud since I have been here to represent Main Street, to represent the voice that is not heard, to represent the patient and the family that wonders why. No rules have prevented it, yet we couldn't show it today.

I think it is kind of sad when you have got a hearing and that all kinds of different ways to make your point are generally available, and here, maybe because of the poignancy and the fact that it is coming from the patient who drives this process, maybe that is too much for us to bear when we keep giving it lip service and do nothing about it.

I have had the Promising Pathways Act out there, sponsored by many on this Committee, and it is just saying one thing, give some hope to these families that there is more than just what we have been doing for decades, which is a process we call the gold stand-

ard, but yet it lets so many individuals feel that they are not having their voice heard. I think as elected officials, we got to always point out something that we would rather see change in the process.

That is what I am doing here today. I think the Committee should have allowed it, but when that doesn't happen, you go to plan B. You can find that video on my Senate account, my Twitter profile at Senator Braun, and you will find that video is worth a thousand words, if not more, of what we will hear today, because it speaks to the frustration that people across the country feel when it comes to this particular issue. Thank you for listening.

Senator BURR. Thank you, Senator Braun. And before I move on, let me just say this Committee and many committees in Congress have held specific hearings over the years with rare disease individuals. That is not out of the ordinary.

One of the reasons that Pew is here, Pew represents the patients, the folks that don't have the opportunity to be here, the multiple categories. It is not one, it is hundreds of thousands of individuals.

We are grateful for Pew's participation in this. It is my hope that we will be able to satisfy your needs—I am not speaking for the Chair, but I will leave that up to her, because I think there is value to that.

But there is much more value outside of the user fee agreements. This is a small part of the access that they don't have today that they need in the future. And the No. 1 thing is innovating at what today's pace will allow us to do so that we would begin to bring those breakthroughs. So I thank you.

Senator Rosen.

Senator ROSEN. Well, thank you, Chair Burr, Ranking Member Burr, and of course, Chair Murray. Thank you all for being here, for the important work you do and participating today. I want to move on to something, of course, that is in everybody's thought every day is cybersecurity and getting hacked.

We have medical devices and I want to address medical device cyber security because cyber-attacks really remain a major threat to the health care sector, particularly as bad actors like Russia are beginning to target or threatening to target our domestic industries.

That is why I recently introduced bipartisan legislation with Senator Cassidy that improves collaboration among agencies to improve cybersecurity in the health care sector, sharing that threat information, and providing cybersecurity training to medical professionals. It is really important.

But however, as we work to increase the cybersecurity of our hospitals, our health care systems as a whole, we must also ensure there aren't cybersecurity gaps with our medical devices, our pacemakers, for example. As more and more medical devices become connected to networks, they are accessible online, they become more vulnerable to cyber-attacks. It impacts patient safety. It impacts their health, and the vulnerability of the entire health system to which the devices connect.

Mr. Leahey, the current FDA guidance for the medical device cybersecurity is from 2018. It is in the process of being updated. Can you speak about the importance of timely Federal cybersecurity

guidance, how nimble we have to be as technology just continues to outpace our ability to protect it?

Mr. LEAHEY. Absolutely. Thank you, Senator, for that question. And cyber is a top priority for our members. As we spoke with Dr. Cassidy earlier and you noted the interoperability of these technologies, how they interface with other technologies with hospital systems is of paramount importance.

I think that, fortunately, thus far there haven't been any devices that have been compromised that impact patients' safety. But as you noted, the ransomware, the security threats and how that impacts hospitals on the system is very important.

We have actually been active members of the HCC, the private public, partnership with FDA, HHS, hospital systems, insurers, innovators all together, sharing information in real time because this is something that is ever evolving. And in 2019, the HHSC published the MedTech Cybersecurity Joint Security Plan to provide device makers a playbook. As you noted, there is a guidance being updated.

This is something that we have to have real time conversations with all the stakeholders so that we are ahead of the curve. And we are committed to doing that and working with you and other Members of the Congress to ensure that we have the proper protocols in place.

Senator ROSEN. Thank you. I just introduced a bill for HHS and DHS to work with hospital systems just for what you are speaking about, ransomware, cyber-attacks, and really considering them critical infrastructure. But I would like to build a little bit upon what Senator Murphy was talking about, next clinical trial diversity, and more specifically, gender diversity, how it relates to women.

Because, Ms. Richardson, in 2015, FDA released a women's health research roadmap as a strategy for science and innovation to improve the health of women. And so among the topics included are improving clinical trial design and evaluating differences between men and women, how they respond to drugs and medical technologies.

Again, we are talking about roadmaps, we are talking about being nimble. Is it time for the FDA to update this roadmap so that women are included more broadly? And what actions do you recommend the FDA take to improve this?

Ms. RICHARDSON. Yes. Thank you so much for that question, Senator. As I noted in my testimony, one of the benefits of the user fee renegotiation process is that it provides FDA with an opportunity to think really clearly and concretely about where it wants to focus attention over the next 5 years.

Not just on reducing review timelines or meeting procedures, but where it really wants to focus its policies. And I think, of course, that could involve a renewal of the women's health roadmap, which I believe was housed within the Office of Women's Health. One of the core focus areas of the roadmap was to support studies to advance the understanding of how sex differences affect the safety and effectiveness of emerging technologies like AI enabled devices and 3D printing.

That has been a real area of focus for Pew and our research lately. I know that office has funded some important research in that

area. But I think that in addition to additional research funding, it would be helpful for the agency to focus on how that research gets translated into policy at the level of the centers, which is where the rubber meets the road policy wise. That is where it really happens.

CDRH, for example, recently announced strategic priorities that would focus on over the next 3 years, and health equity was a core focus area. As a part of their process, I think it will be important for them to focus on women's health in addition to other populations that may be underrepresented in clinical trials or in real world datasets, which includes not just women, of course, but also minority populations.

Thank you very much for that question.

Senator ROSEN. Thank you. Mr. Chairman, I see I am out of time, but I would have asked Dr. Esham about health equity and how the use of telemedicine, satellite sites, health centers, rural health clinics, we can improve diversity in clinical trials for urban and rural, for women and people of color. All of that really matters. Will ask for your response——

Dr. ESHAM. Will be happy to engage with you in detail following the hearing. Thank you.

The CHAIR. Thank you very much. And I was out of the room for the discussion before, but I really do understand the desire to bring in the voices of patients. And both Ranking Member Burr and I are very focused on keeping patients at the center of this conversation. I actually think every Member of this Committee believes what is best for patients and their families absolutely needs to be at the center of any discussion on medical advancements and innovation.

Like everybody, I have heard from patients across my state who are forced to choose between paying for medicines or paying for rent. I am sure we have all heard those. And it really is imperative that patient's voice be heard at every step of medical product development, from new research to pricing, user fee reauthorization, and I hope we can all work together to make sure that as this process goes forward, we can ensure that their voices are heard.

With that, I will turn it over to Senator Baldwin for her questions.

Senator BALDWIN. Thank you, Madam Chair. As Chair of the Appropriations subcommittee that provides funding for the Food and Drug Administration, I am well aware of the resource constraints that the agency is under. We recently worked on a bipartisan basis to increase FDA funding for Fiscal Year 2022, including for food safety activities, medical product safety, infrastructure and cross-cutting initiatives.

Still, I know that with current budget constraints, the increase will not be enough. Ms. Richardson, can you describe some of the agency's obstacles when it comes to critical operations and hiring necessary additional staff?

Ms. RICHARDSON. Yes, happy to. I will say that this is not an area that Pew has spent a lot of time focused on. And when it comes to hiring, I do know that, as I think Senator Burr pointed out, the agency has a lot of open positions.

They have a lot of trouble hiring. I do know that one proposal that FDA has supported in the past and continues to support is di-

rect hiring authority Pew doesn't take a position on that, but I think it is certainly worth considering, personally.

Senator BALDWIN. Thank you. Over the past week, NPR has been sharing stories of individuals diagnosed with cancer attributed to asbestos exposure. One possible source of that exposure is baby powder, which is a personal care product regulated by the FDA. The stories of these cancer patients are harrowing, but they also point to the fact that when it comes to personal care products, as widespread as make-up, deodorant, and lotion, we have really failed to protect consumers. Mr. Leahey, how many employees does FDA have assigned to work on medical devices?

Mr. LEAHEY. That is a question we asked during the negotiations. I know in the Congressional report, the 2021 Financial Report to Congress, I think there are about 1,800 or so FTEs related to the device review process. I think there are a few hundred more—hundreds more, but that is about 1,800 I would say.

Senator BALDWIN. Okay. Mr. Gaugh, how about the number for generics and biosimilars?

Mr. GAUGH. There are about 1,600 for generic and biosimilars that are paid for by the user fee dollars. 1,550 for the generic side and about 50 for the biosimilar side.

Senator BALDWIN. Dr. Esham, how many FDA employees work on drugs and biologics?

Dr. ESHAM. When—at the end of December 2021, I believe the CDER had around over 5,300 employees and CBER had around 1,200, a little over 1,200 employees. I would say the majority of those, probably in some way, work on the review of drugs and biologics.

Senator BALDWIN. Thank you. In contrast, the FDA has only 30 full time employees that work on personal care products, 30. And I don't believe that is acceptable. FDA needs more resources and more authorities to ensure that personal care products are safe, and cosmetics reforms—reform needs to be a part of this package. I yield back.

The CHAIR. Thank you very much. That concludes our hearing today, and I want to thank all of our colleagues for their very thoughtful questions. I want to thank all of our witnesses, Dr. Esham, Mr. Gaugh, Mr. Leahey, and Ms. Richardson for sharing your time and your expertise.

I am looking forward to continuing our work to reauthorize the FDA's user fee programs in the coming weeks to ensure the agency has the resources to support its vital work. With that, the Committee stands adjourned.

ADDITIONAL MATERIAL

United States Senate
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS
WASHINGTON, DC 20510–6300

January 24, 2022

Delivered via Email

Janet Woodcock, M.D.
Acting Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Acting Commissioner Woodcock:

I write to request additional information regarding the Food and Drug Administration's (FDA's) efforts to recruit, hire, and retain the qualified workforce it needs to complete its mission. The COVID-19 pandemic imposed extraordinary demands on your Agency, and I commend you and your staff for the long hours put in under difficult and unprecedented circumstances. However, FDA has long faced systemic hiring challenges, which the COVID-19 pandemic has only exacerbated.

The hiring challenges that plague the Agency pose significant hurdles to FDA's ability to meet its mission and keep pace with the latest science and innovation. FDA acts as a gatekeeper for novel medicines and other medical products for life-altering diseases and conditions. A qualified workforce is critical to ensuring the Agency has the scientific expertise needed to review such products as quickly as possible to make them available to the American people. As Congress begins to consider reauthorizing the medical product user fee programs that fund thousands of positions at the Agency, it is important to have updated and complete information regarding the status of FDA's current workforce and hiring efforts agency-wide.

I respectfully request written answers to the following questions regarding FDA's agency-wide workforce status and hiring practices by February 18, 2022.

1. In aggregate, and broken down by FDA's major components, including each center, and each user fee program, as applicable, please provide the following information separately for each of fiscal years 2018 through 2022:

a. Total employees (i.e., individual persons);
b. Total Full-Time Equivalents (FTEs);
c. Total vacancies, delineating between vacancies funded by user fees or Congressional appropriations;
d. Turnover rate;
e. Total number of new FTEs hired per year;
f. Total number of FTEs lost to attrition per year;
g. Total number of senior leadership employees;
    i. For this answer, please provide an explanation of how FDA is defining "senior leadership."

2. In a 2018 report, FDA estimated that 13% of its work force was eligible for retirement in 2017, and that half of the agency's senior leadership would be eligible for retirement by 2020. Broken down by FDA center and user fee program, as applicable, please provide the following:
    a. Total number and percentage of employees currently eligible for retirement;
    b. Total number and percentage of senior leadership eligible for retirement.
    c. An estimate for the number and percentage of employees and senior leadership who will be eligible by the end of the next user fee cycle.

3. As a part of the proposed user fee agreements, FDA is committing to hire at least 495 FTEs (not including the still-outstanding MDUFA proposal). For purposes of the commitments made as part of the user fee agreements, what is the definition of an "FTE"? How is "FTE" defined with respect to the number of hours worked per week or per year?

4. When FDA commits to hiring a certain number of FTEs as a part of the agreements, what is FDA committing to – hiring a certain number of *individual employees*, or a number of individuals who *in aggregat*e will work hours that are equivalent to a full-time employee?

5. When FDA reports that it has "met" a hiring goal pursuant to a user fee commitment, does FDA account for attrition and turnover in the applicable user fee program? Does this reporting include FTEs lost to attrition or otherwise? For example, if FDA had a commitment to hire 15 new FTEs, and it hired the equivalent of 15 new FTEs, but at the same time lost 25 FTEs to create a net loss of 10 FTEs, would FDA still consider its hiring goal to be met?

6. How does FDA account for funds that have "funded" a vacancy within a user fee program? Are such funds accounted for, or obligated within the program's carryover balance?

7. What is the average total cost of an FTE in each of the medical product user fee programs?

8. Please describe the functions of the offices at FDA with hiring-related responsibilities, including the Office of Talent Solutions and Office of Human Capital Management. Please describe the relationship and differences between those two offices in terms of their roles, responsibilities, and interactions; and the relationship between those two offices and the centers at FDA.

9. In the recent GAO report on FDA's hiring practices, *FDA Workforce: Agency-Wide Workforce Planning Needed to Ensure Medical Product Staff Meet Current and Future Needs*, GAO found that FDA lacks an agency-wide strategic workforce plan.

    a. Why does FDA not have an agency-wide strategic workforce plan?
    b. Is FDA planning to implement an agency-wide strategic workforce plan, consistent with GAO's recommendations? If not, why?
    c. Recognizing FDA may have center-specific strategic workforce or hiring plans, if that is the case, why hasn't FDA compiled those plans into an agency-wide strategic plan?
    d. Please describe any center-specific strategic workforce or hiring plans.

10. The GAO report referenced above provides a breakdown of FDA employees by the authority used to hire them, noting that approximately 80 percent of FDA employees were hired using hiring authorities under Title 5 of the U.S. Code. Could you please provide a further breakdown of how (i.e. for which center or specific areas of expertise) and when FDA has used its Title 5 authorities between general Title 5 authorities and direct-hire authorities under 5 U.S.C. § 3304(a)(3) for the last 5 years?

11. What is FDA's plan to address the risk of high turnover or attrition in the coming months as a result of pandemic-related work conditions?

12. In April 2021, the Office of Personnel Management released a detailed summary of the government-wide results of the 2020 Federal Employee Viewpoint Survey (FEVS) across all federal agencies.

    a. Can you please provide a summary of the FEVS results for FDA employees (i.e., a summary similar to the government-wide report published by OPM, but specific to FDA)?
    b. Understanding that the 2021 FEVS is currently being administered, please provide the date by which you will provide the same FDA-specific summary for the 2021 survey.

13. In April 2020, Booz Allen Hamilton published an Interim Hiring and Retention Assessment conducted pursuant to the PDUFA and BsUFA agreements.

a. What is the status of FDA's consideration and implementation of the conclusions and recommendations made in the April 2020 report?
b. When does FDA plan to publish its final assessment?

14. Numerous assessments and reports published by FDA and third-party contractors describe different steps that FDA has taken to help attract and retain talent, such as developing an alternative pay structure for certain positions, using hiring bonuses for hard-to-fill positions, recruiting through academic institutions, and others.

    a. Has FDA conducted an analysis to assess the comparative effectiveness of different hiring approaches and tools? If so, please describe. For example, does FDA look at time-to-hire metrics, or a yield rate comparing the success of different approaches in identifying candidates who are later hired?

15. Please describe efforts at FDA to streamline frequently used hiring processes, including processes within each center, and the metrics used to assess the success of such efforts.

16. Please describe any non-traditional efforts by FDA to hire qualified scientists and other experts, such as partnerships with academic institutions and/or industry, hiring bonuses for hard-to-fill positions, and other similar efforts.

17. Please provide an overview of the use of teleworking and alternative work schedules by FDA employees, including related results from the FEVS and any other relevant information. Where possible, please provide a breakdown of this information by center.

18. Please explain how FDA uses hiring authorities under Section 714 (related to the review of medical device and generic drug applications) and authorities under Section 714A (for "scientific, technical, or professional positions"), and compare and contrast its use of those authorities.

19. Related to the flexible hiring authorities that Congress granted FDA in the 21st Century Cures Act:

    a. What is the average time between posting of a position eligible to be hired under the 21st Century Cures Act authorities and the selected candidate starting work? How does this compare to the average time between public posting and start date for individuals hired under FDA's general hiring authorities?
    b. What percentage of individuals hired using the 21st Century Cures Act authorities are internal (i.e., already employed at FDA, or at other federal agencies) versus external?

c. In a 2018 report on the implementation of the 21st Century Cures Act, FDA noted that it had classified 38 occupations as eligible for those authorities. Has FDA updated this list? Could you please provide the list of occupations eligible for these authorities?

20. FDA operates a number of fellowship and other training programs, including those authorized under Section 746(b) of the FDCA. Please list and describe the fellowship programs that FDA operates today, including the status of the Commissioner's Fellowship, and the statutory authorities under which such programs are operated. Please also describe any assessments FDA has conducted regarding the effectiveness or utility of such programs.

21. Please describe the training that FDA medical product reviewers receive, including with respect to the review of products for rare diseases and regarding application review best practices.

I appreciate FDA's prompt attention to these questions and your continued actions to ensure patients have timely access to safe and effective medical products, and look forward to working with your Agency to ensure that you have the authorities and resources you need to meet the challenges FDA will continue to face.

Thank you for your attention to this matter.

Sincerely,

Richard Burr
Ranking Member

United States Senate

COMMITTEE ON HEALTH, EDUCATION,
LABOR, AND PENSIONS

WASHINGTON, DC 20510–6300

Delivered via E-Mail

Janet Woodcock, M.D.
Acting Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Acting Commissioner Woodcock:

I write seeking additional information regarding the status of the Food and Drug Administration's (FDA) medical product inspections, and the agency's plan for addressing the backlog of inspections it has not conducted during the COVID-19 pandemic. FDA inspections are a critical tool for ensuring that the drugs, biologics, and medical devices that patients rely on are safe and effective. The importance of a strong and consistent FDA inspections program is heightened by the global nature of medical product supply chains, and the need to ensure that all drug and device establishments that manufacture U.S. medical products, including foreign facilities, comply with FDA's stringent requirements. Since March 2020, FDA has allowed a substantial number of inspections to become overdue. These outstanding inspections, coupled with the inspections that FDA is otherwise responsible for conducting in 2021, will continue to jeopardize on-time product approvals. It is vital that FDA use every tool at its disposal, including its existing authorities and the significant funds Congress has allocated to help address the growing number of inspections to ensure life-saving treatments and therapies are available to patients in as timely a manner as possible.

The COVID-19 pandemic has hampered FDA's ability to conduct in-person inspections of medical product establishments. In March 2020, FDA postponed all domestic and foreign routine inspections. In July 2020, FDA resumed certain on-site domestic inspections subject to a risk-based prioritization system to identify the categories of regulatory activity that could occur in a given geographic area, in light of pandemic-related risks. On a case-by-case basis, FDA continued to conduct what it deemed "mission critical" inspections.

These changes resulted in FDA conducting far fewer inspections than it would have otherwise been responsible for conducting absent the pandemic. According to the GAO,[1] the total number of FDA foreign and domestic establishment inspections was 56 percent lower in fiscal year 2020 than during each of the previous two fiscal years.[2] From March 2020, when FDA postponed non-mission critical inspections, through the end of the fiscal year, FDA conducted only three foreign mission critical inspections—one each in Canada, Germany, and India.[3] In contrast, during the same time in each of the prior two years, FDA conducted more than 600 foreign inspections.[4] Similarly, from March to October 1, 2020, FDA conducted 52 domestic inspections, compared to conducting about 400 inspections during this period in the two previous years.[5]

I am particularly concerned about the impact of the lack of pre-approval inspections on FDA's ability to meet its review commitments under the applicable user fee agreements and the effect related delays may have on patients and providers. There have been a number of public reports that underscore that FDA's lack of inspections over the last year has delayed its ability to review and potentially approve new product applications.[6] As the GAO noted, while FDA has reported that it was operating above its 90 percent on-time performance goal as of November 2020, a continued pause in pre-approval inspections may delay future approvals.[7]

FDA has existing authorities, and in certain instances has used such authorities, to leverage alternatives to in-person inspections, such as remote interactive evaluations, records requests, and reviewing documentation from trusted regulatory partners. However, the agency's use of these tools is in its infancy and its assessment of these alternatives remains ongoing. These are promising tools from authorities that Congress provided to help FDA more efficiently and effectively conduct necessary

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[1] Statement of Mary Denigan-Macauley, Director, Healthcare, GAO, FDA's Future Inspection Plans Need to Address Issues Presented by COVID-19 Backlog. Testimony before the Subcommittee on Agriculture, Rural Development, Food and Drug Administration, and Related Agencies, Committee on Appropriations, House of Representatives (Written testimony for hearing held on March 9, 2021).

[2] GAO, *COVID-19: Critical Vaccine Distribution, Supply Chain, Program Integrity, and Other Challenges Require Federal Attention*, GAO-21-265 at 149 (Jan. 2021).

[3] *Id.* at 150 – 151.

[4] *Id.* at 150.

[5] *Id.* at 151.

[6] *See, e.g., Fierce Pharma, Mallinckrodt faces regulatory delay as COVID-19 restrictions continue to upend FDA's inspection schedule* (Feb. 12, 2021); Revance Therapeutics, *FDA Defers Approval of DaxibotulinumtoxinA for Injection in Glabellar Lines Due to COVID-19 Related Travel Restrictions Impacting Manufacturing Site Inspection* (Nov. 25, 2020).

[7] *Supra* note 2 at 155.

inspections to ensure timely regulatory action for the benefit of patients, and understanding how FDA intends to put such authorities into practice is critical.

To better understand the magnitude of FDA's task to normalize its inspections program, and FDA's plan to address its outstanding inspections and ensure that patients have access to needed medical products, I respectfully request that FDA provide written responses to the following questions:

1. How many new or supplement product applications did FDA defer action on due to a lack of inspection during the COVID-19 public health emergency? How many Complete Response Letters did FDA issue in the absence of a pre-approval inspection during that time period?
    a. Please break these figures down by application type (*i.e.*, NDA, ANDA, BLA, PMA).
2. How many total pending applications does FDA estimate could be impacted by the lack of normalized pre-approval inspection activity?
3. What steps will FDA take to ensure that a lack of pre-approval inspection will not unduly delay the agency's review of new and supplement product applications moving forward, including mission critical and non-mission critical applications?
4. What is the current status of FDA's inspections program (including both international and domestic inspections) for pre-approval, surveillance, and for-cause inspections?
    a. Approximately how many in-person inspections is FDA conducting on a weekly and/or monthly basis, and how does this compare to FDA's activity level in 2019, 2018, and 2017 prior to the pandemic?
        i. Please break these figures down by application type, as applicable.
    b. What are FDA's criteria for prioritizing in-person inspections? How is FDA prioritizing the conduct of inspections that are required for products pre-market compared to inspections related to post-market requirements or activities (*e.g.*, pre-approval inspections, inspections at facilities on "Official Action Indicated" status, or that otherwise need an FDA inspection to address identified quality issues, etc.)?
5. What is the status of FDA's assessment of alternatives to in-person inspections? When does FDA anticipate that this assessment will be complete? Please specify by each type of alternative (*e.g.*, real-time video streams, records reviews, reliance on trusted regulatory partners, etc.).
    a. With respect to the guidance document FDA issued on April 14, 2021 regarding remote interactive evaluations, how will remote interactive evaluations be used in lieu of in-person inspections to resolve warning letters or other enforcement actions?
6. How frequently is FDA currently implementing in-person inspection alternatives and for which types of applications (*i.e.*, how frequently are these alternatives being used as *complements* to versus *substitutes* for in-person inspections)?

Dr. Janet Woodcock, M.D.
April 30, 2021

7. How is FDA currently using its statutory and regulatory authorities and processes to use in-person inspection alternatives to address outstanding inspections? For how many applications will FDA utilize such alternatives to more efficiently conduct inspections?

8. What statutory or resource obstacles, if any, does FDA face in using these alternatives?

9. How will the agency apply lessons learned using alternatives to in-person inspections during the COVID-19 pandemic to ensure an efficient and flexible inspections program in the future?

10. How is FDA using the funds that it has received from Congress intended to support activities related to the pandemic response to resume its normal inspection activities? Please include specific dollar amounts and the agency offices and programs to which those funds have been or will be directed.

I appreciate FDA's prompt attention to these critical issues, and your continued efforts to ensure that patients have unimpeded, timely access to safe and effective medical products.

Sincerely,

Richard Burr
Ranking Member
Committee on Health, Education, Labor and Pensions

United States Senate

COMMITTEE ON HEALTH, EDUCATION,
LABOR, AND PENSIONS

WASHINGTON, DC 20510–6300

September 22, 2021

Delivered via E-Mail

Janet Woodcock, M.D.
Acting Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Acting Commissioner Woodcock:

I write regarding the medical device user fee program and the ongoing negotiations for the next Medical Device Use Fee Agreement (MDUFA) for fiscal years 2022 through 2027. We are at a critical moment in the advancement of biomedical innovation, particularly for medical devices and associated biotechnology. The COVID-19 pandemic created previously unimaginable challenges for the medical device industry, and for the Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH). For this reason, it is of the utmost importance that the medical device user fee program incorporate the best practices gained during such a difficult time, and that the next agreement have a foundation that prepares the agency and industry for the next generation of scientific advancements.

Unfortunately, there are concerning reports about meeting the deliverables in the current MDUFA IV agreement and the slow progress toward MDUFA V that must be addressed in order to ensure the medical device user fee program is designed in the best interest of patients today and in the future.

On May 5, I sent a letter requesting regular updates from FDA and industry partners to ensure that the committee and Congress remain informed of the progress towards a user fee agreement. Complying with that request, on June 24, FDA and industry provided an overview to HELP Committee bipartisan staff regarding the medical device review program under MDUFA IV, and a status update of negotiations over the commitment letter for MDUFA V. It is my understanding that discussions and progress towards agreeing on the MDUFA V commitments are delayed due to disagreements regarding previous commitments under MDUFA IV and potential new commitments under consideration for the next cycle.

Dr. Janet Woodcock, M.D.
September 22, 2021

First, I am concerned that there are such disagreements regarding the MDUFA IV commitments, a four year old agreement that should otherwise be almost completely fulfilled by this time. Reports indicate that there are questions as to whether such commitments have been or will be met, and the activities on which the current and significant carryover balance should be spent.

Second, it is concerning that there is a sizeable gulf between FDA and industry partners with respect to proposed new commitments under consideration for the next user fee agreement, including programs that could expand FDA's mission and reach beyond that envisioned and authorized by Congress when it created the MDUFA program.

Third, I have continually expressed concern regarding user fee goal letters containing policy negotiated and agreed to by FDA and industry that require Congress to authorize new statutory programs or authorities without debate.

The user fee programs are intended to supplement FDA's congressionally appropriated resources to support the review of new medical products and ensure that patients have access to safe and effective medical products as soon as possible. In fiscal year 2020, user fees account for 43 percent of the medical device review budget – it is important that the FDA remain accountable to Congress with respect to its operation of the medical device review program. These programs help FDA keep pace with cutting-edge science to bring novel medical technologies to patients who need them. The MDUFA program plays a critical role in ensuring that innovative medical devices meet FDA's gold standard and are available to patients in a timely manner.

As noted in my letter on May 5, and in a letter I sent in August of 2019 prior to the beginning of negotiations, I have long held concerns that the agreements between FDA and industry allow resources to be expended on administrative agency priorities, programs and activities unrelated to product development and review. This is not the intent of the user fee programs. Moreover, to request additional support and resources for new commitments when underlying commitments remain unfulfilled, jeopardizes the integrity of the user fee program.

In light of these concerns and the outstanding status of negotiations, I respectfully request that the FDA and industry partners provide the committee with an update on the progress towards agreement on the MDUFA V commitments. Please work with my staff to identify a date and time to provide such briefing before October 15.

Dr. Janet Woodcock, M.D.
September 22, 2021

Additionally, I respectfully request written responses by October 5 to the below questions regarding the medial device user fee program:

1. How many Full Time Equivalents (FTEs) are funded under the MDUFA program?

2. On average, how many FTEs are needed to review PMA submissions, De Novo submissions, 510(k) submissions? Please provide the number of FTEs per submission type.

3. What is the average cost of a MDUFA FTE? Please provide a breakdown of costs associated with a MDUFA FTE.

4. How many user fee dollars go towards a MDUFA FTE?

5. The August 3, 2021 quarterly performance report includes data that FDA has received and accepted more than 2,100 510(k) submissions in FY21 and has reviewed 88.45% of such submissions within 90 days. According to the MDUFA IV commitment letter, FDA has a goal of reviewing 95% of such submissions within 90 days.
    a. Does FDA plan to meet this commitment by the end of this MDUFA cycle?
    b. How does FDA plan to meet the 95% review goal by the end of this MDUFA cycle?
    c. If FDA does not meet this commitment, will the agency provide a refund or otherwise factor in this unmet commitment as part of MDUFA V?

6. The MDUFA IV goal letter included a commitment to publish final guidance related to submissions for software modifications.
    a. When does FDA expect to publish this final guidance?
    b. If FDA is not able to meet this commitment before the end of FY22, will the agency provide a refund or otherwise factor in this unmet commitment as part of MDUFA V?

7. The MDUFA IV goal letter included a commitment that "all deficiency letters will include a statement of the basis for the deficiencies." According to the March 17 meeting minutes, FDA provided statements on the basis of the deficiency for 25% of the deficiency letters issued in FY19, and 50% of letters issued in FY20.
    a. For deficiency letters issued in FY21, how many has FDA provided a statement of the basis for deficiency?
    b. The March 17 meeting minutes also note there is a disagreement on whether the MDUFA IV commitment was to provide a statement of the basis for deficiencies for "all deficiency letters" meant 100% of letters – will FDA and industry clarify this commitment and the metrics by which this commitment will be met as part of MDUFA V?

8. MDUFA IV provided funding for FTE positions at the FDA.
    a. How many FTE positions funded under MDUFA IV are currently filled?
    b. How many FTE positions funded under MDUFA IV are currently vacant?
    c. Are any FTE positions funded by MDUFA I, II, or III currently vacant? If so, how many?

9. For any commitments that FDA is not able to meet before the end of FY22, will the agency provide a refund or otherwise factor in such unmet commitments as part of MDUFA V?

10. Will FDA and industry revise any unclear commitments included in MDUFA IV or otherwise ensure that MDUFA V includes clear, concise commitments in order to avoid confusion and future disagreements over whether commitments have been met for the next review cycle?

11. According to meeting minutes, FDA has proposed a new program for MDUFA V, the Total Product Life Cycle Advisory Program.
    a. What statutory authorities provide FDA the authority to create and implement this proposed new program? Please provide the specific sections of the Federal Food, Drug, and Cosmetic Act providing this authority.
    b. How many resources does FDA estimates this proposed new program will cost? Please provide both dollars and number of FTEs.
    c. What percentage of the proposed new program will include activities directly related to FDA product review? What percentage is aimed at activities following product review and approval?
    d. Did FDA include this program in its FY22 budget request? How many resources did FDA request for this new program as part of FDA's budget request?
    e. Will the proposed new program directly result in decreased review times? If so, by how many days per submission?
    f. Will the commitment letter reflect decreased review times as a result of this proposed new program?

12. In the MDUFA IV commitment letter, FDA and industry removed the commitment related to activities on which to spend any carryover balance; however, the commitment letter notes that, "*If the collections are in excess of the resources needed to meet performance goals given the workload, or in excess of inflation adjusted statutory revenue targets, FDA and industry will work together to assess how best to utilize those resources to improve performance on submission types with performance goals and/or quality management programs, using, as input for the discussion: workload information, performance objectives and ongoing reported performance.*"
    a. How much is the FY21 carryover balance?

b. On what activities or programs has FDA and industry agreed to spend the available carryover balance? Please provide amounts per activity or program.
c. Please provide the statutory authority or specific commitment that allows the carryover balance to be spent on such activities or programs.

I appreciate FDA and industry's prompt attention to these critical issues, and your continued efforts to update Congress on the progress toward negotiating the MDUFA for fiscal years 2022-2027.

Sincerely,

Richard Burr
Ranking Member

CC: Scott Whitaker, President and CEO, Advanced Medical Technology Association
Mark Leahey, President and CEO, Medical Device Manufacturers Association
Patrick Hope, Executive Chairman, Medical Imaging & Technology Alliance

United States Senate
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS
WASHINGTON, DC 20510–6300

November 18, 2021

Delivered via E-Mail

Janet Woodcock, M.D.
Acting Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Acting Commissioner Woodcock:

I write regarding the medical device user fee program and the still ongoing negotiations for the next Medical Device Use Fee Agreement (MDUFA) for fiscal years 2023 through 2027. I appreciated the briefing on October 20 regarding the status of the ongoing negotiations. I remain concerned about the lack of public transparency of this process. The U.S. Food and Drug Administration (FDA) has failed to publish meeting minutes from negotiations dating back to May of this year. The public and Congress have been in the dark for seven months on the future of a program that affects the lives of millions of Americans.

The limited information I have learned thus far about the negotiations creates additional concerns. First, FDA is asking for more dollars and new programs without having fulfilled its commitments under the MDUFA IV agreement. In particular, FDA is delinquent in publishing a final digital health guidance, FDA has failed to provide justifications in all deficiency letters, and FDA is in jeopardy of missing time-to-decision goals for 510(k) device submissions. In addition to unmet commitments, FDA has an enormous carryover balance in this program, and it is concerning that these funds could be directed to activities unrelated to product review, the foundational mission of the user fee program.

Second, FDA is proposing new commitments with no insight into accountability metrics, particularly the new Total Product Lifecycle Advisory Program (TAP). Little detail has been publicly released about this contemplated program, such as the proposed resources and FTEs required to stand it up, or whether external stakeholders, such as non-FDA employees, physician societies, or payors, would be involved and held accountable. Moreover, I question whether FDA even has the statutory authority to create such a program. It is critical that rigorous performance metrics are included for all FDA commitments included within the letters. I am willing to consider the merits of new authorities or programs that could benefit American patients. However, the FDA and industry commitment letters should not contain new programs that

require Congress to rubber stamp new statutory programs or new authorities without Congressional debate.

Third, FDA continues to ask for more funding for FTEs as part of new or updated commitments while it still cannot fill existing MDUFA hiring targets and maintains vacancies funded by other user fee programs. According to information provided by FDA, there are approximately 238 total vacancies within the human medical product user fee programs, including 34 vacancies within the MDUFA program. It remains unclear how FDA plans to meet new hiring commitments across all user fee programs. Funding for *more* MDUFA FTEs in light of systemic, agency-wide hiring challenges, on top of existing vacancies, and without meaningful deliverables is irresponsible. American patients bear the cost of new and unused resources collected under each user fee program. User fee dollars should be used to expedite the availability of new medical products to patients or returned to innovators, not sit in an FDA account to be spent later at the agency's discretion.

The COVID-19 pandemic response has required FDA to prioritize its workload and has challenged the agency in an unprecedented manner. The agency and industry are *still* learning lessons from the pandemic response that should be considered within the next cycle's commitments to enable a better agreement for both parties, but especially one that benefits patients.

In light of the concerns I have outlined, I respectfully request your timely response to the below questions by December 3.

1. FDA officials shared in public comments that the agency may struggle to meet MDUFA IV performance goals for FY21 and FY22. Which goals may the agency have trouble meeting, by how much does FDA anticipate missing the goals, and why? Given the potential of missing some of the performance targets in FY21, does FDA expect to maintain the same performance targets for these goals for MDUFA V?

2. Please provide an update on the following MDUFA IV commitments.

    a. The MDUFA IV agreement included a commitment to review 95% of 510(k) submissions within 90 days. The most recent performance report notes FDA has reviewed 88.38% of 510(k) submissions within 90 days for FY21. What is the current percent reviewed within 90 days? How many 510(k) submissions will FDA take greater than 90 days to review?

    b. What is the timeline for issuing the final digital health guidance on the Content of Premarket Submissions Contained in Medical Devices?

    c. How many deficiency letters did FDA issue in FY2021? How many deficiency letters included a statement on the basis for deficiencies in FY2021??

3. MDUFA IV included a commitment to hire 217 new FTEs, and has hired for 183 of those FTE positions. Is CDRH on track to hire the 34 outstanding MDUFA IV FTEs before September 30, 2022? If so, what is the timeline for these outstanding hires? If not, what is the amount of fees collected for these FTE slots and what is the FDA's plan for these funds?

4. In light of the agency's longstanding hiring challenges and the current vacancies, both within the MDUFA program and other user fee programs, what is FDA's plan to fulfill any new hiring commitments included in MDUFA V? How many FTEs does the agency plan to hire each year of the MDUFA V cycle?

5. During the October 20 briefing, FDA mentioned potential accountability and performance metrics for the TAP program.

    a. Has the agency shared draft accountability and performance metrics with MDUFA industry negotiators?

    b. What specific accountability and performance metrics will a proposed TAP program include?

6. Will the TAP program cover both pre-market device review activities and post-market activities (such as coverage, reimbursement, and physician uptake)? If so, what are the proposed CDRH performance metrics or commitments for both pre-market and post-market activities?

    a. The April 7, 2021 meeting minutes note that payers and physician societies may participate in the TAP program. What commitments, if any, would such external stakeholders be responsible for fulfilling or helping FDA to fulfill?

    b. What are the proposed performance metrics for external stakeholders? Who will hold them accountable for their performance?

7. What are the projected annual resource needs for the TAP proposal with regard to dollar amounts and FTEs?

8. The MDUFA program had a $299 million carryover balance in FY20, the equivalent of at least a year of fee collections. What activities is CDRH spending or planning to spend these dollars on?

    a. How will those activities improve performance for product review?

    b. What are the commitments or performance metrics associated with those activities?

Dr. Janet Woodcock, M.D.
November 18, 2021

9. The FY20 MDUFA Financial Report notes that of the $299 million carryover balance, $90 million is "otherwise obligated." What are those existing obligations? Please provide a detailed summary.

10. FDA and industry have disagreed upon whether certain MDUFA IV commitments were met, because the commitment was either unclear or aspirational. How are you ensuring that *all* commitments are clear and concrete to all parties for MDUFA V?

11. The last meeting minutes publicly posted are from April 28, more than 6 months ago. When does the agency expect to publish all outstanding meeting minutes? What is the reason for the delay in publication?

I appreciate your commitment to ensuring medical devices reach Americans in as timely a manner as possible. Thank you for your timely attention to these important matters, and your continued efforts to update Congress on the progress toward negotiating the MDUFA commitments for fiscal years 2023-2027.

Sincerely,

Richard Burr
Ranking Member

CC: Scott Whitaker, President and CEO, Advanced Medical Technology Association
Mark Leahey, President and CEO, Medical Device Manufacturers Association
Patrick Hope, Executive Chairman, Medical Imaging & Technology Alliance

U.S. FOOD & DRUG ADMINISTRATION

June 25, 2021

The Honorable Richard Burr
United States Senate
Washington, DC 20510

Dear Senator Burr:

Thank you for your letter regarding the impact of COVID-19 on the Food and Drug Administration's (FDA) inspections programs for the regulation of medical products. We recognize that the COVID-19 pandemic is impacting many aspects of public health, including drug development programs, ongoing manufacturing operations, and our ability to conduct inspections.

In the spirit of transparency, we issued the *Resiliency Roadmap for FDA Inspectional Oversight* (Resiliency Roadmap) report[1] on May 5, 2021, detailing the effect of the pandemic on inspections and describing scenarios that would inform our return to a more consistent state of operations. Fortunately, while keeping the safety of our staff participating in inspections and staff at facilities we inspect foremost in mind, we are able to announce our plan to transition to standard operations for domestic inspections beginning July 1, 2021. This will mean that we will assign, schedule, and gradually return to conducting all domestic inspections, including those that were delayed during the COVID-19 pandemic. Due to continuing restrictions on global travel, we will continue to prioritize only mission-critical work for foreign inspections. As we carry out this plan, I assure you that we are committed to working as quickly as possible to help get medical products to market and to ensure that these products are safe, effective, and of high quality.

I am grateful for the continued support from Congress and look forward to working with you to fulfill our mission to protect and promote public health. We offer the following responses to your specific questions:

1. **How many new or supplement product applications did FDA defer action on due to a lack of inspection during the COVID-19 public health emergency? How many Complete Response Letters did FDA issue in the absence of a pre-approval inspection during that time period?**

    a. **Please break these figures down by application type (*i.e.*, NDA, ANDA, BLA, PMA).**

    Inspections to inform decisions on applications submitted for medical product approval or authorization are not always required; instead, these inspections are conducted when we determine an inspection is needed to support the application decision. We consider

[1] *https://www.fda.gov/media/148197/download.*

U.S. Food & Drug Administration
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risk factors, such as the novelty of the product, complexity of the manufacturing process, and the firm's history of compliance with quality management requirements at the facility where the product will be made, in deciding whether a facility inspection is needed. We received over 13,500 applications for medical product approval or authorization between March 2020 and the end of March 2021, and by applying risk factors like those described above, determined that approximately 600 applications needed a facility inspection, review of records, or oversight of some type before action.

By the end of March 2021, an estimated 68 applications had been delayed solely due to our inability to conduct pre-approval, pre-market, or pre-license inspections because of travel restrictions from the COVID-19 public health emergency. Most of the delayed applications—61 of the 68—are not considered mission-critical. With our return to standard operations for domestic inspections beginning July 1, 2021, we expect these inspections to be completed in fiscal year (FY) 2021 (i.e., by September 30, 2021). Please see the following table detailing this information:

Commodity	**Delayed Application Decisions Solely Due to a Pending Inspection or Facility Assessment (March 2020 through March 2021)**	
	Total	Mission-Critical
Human Drugs	48	6
Animal Drugs	9	0
Medical Devices and Radiological Health	7	0
Biologics	1	0
Bioresearch Monitoring	3	1
Total Applications Delayed Pending Inspection	68	7

We issued the guidance for industry on May 17, 2021, *Manufacturing, Supply Chain, and Drug and Biological Product Inspections During COVID-19 Public Health Emergency Questions and Answers* (Inspections During COVID-19 guidance),[2] which outlines how we intend to address issuing complete response (CR) letters[3] during the COVID-19 pandemic. In the guidance, we clarified that CR letters will not be automatically issued if we cannot conduct an inspection due to travel restrictions resulting from the public health emergency. (Since June 2020, we have not issued any CR letters solely due to a lack of pre-approval inspection.) We also clarified that all decisions regarding applications will

[2] *https://www.fda.gov/media/141312/download.*

[3] A CR letter is a written communication to an applicant from us describing deficiencies identified during our review of the application that must be satisfactorily addressed before the application can be approved.

be based on the totality of the information available to us, including information obtained from the use of alternative tools.[4]

2. How many total pending applications does FDA estimate could be impacted by the lack of normalized pre-approval inspection activity?

We recently performed an analysis of user fee metrics across our prescription drug and generic drug programs that demonstrate that we have been able to take on-time actions to evaluate and close out these drug applications more than 90 percent of the time, meeting our mandated review program performance levels.

As noted in response to Question 1, from March 2020 through March 2021, decisions on 68 of the 13,500 applications submitted during the time period were pending because an inspection or facility assessment was needed and could not be conducted due to the COVID-19 pandemic. Only seven of the remaining inspections are considered mission-critical under our established criteria and with our return to standard operations for domestic inspections beginning July 1, 2021, we expect all delayed domestic inspections and any delayed foreign inspections considered to be mission-critical to be completed before the end of FY 2021.

3. What steps will FDA take to ensure that a lack of pre-approval inspections will not unduly delay the agency's review of new and supplement product applications moving forward, including mission critical and non-mission critical applications?

To help achieve our oversight goals, we constructed a systematic method for tackling postponed inspectional activities, which included reviewing data showing the impact of the COVID-19 pandemic on inspections, establishing prioritization plans by commodity, and developing an overall prioritization approach for inspectional operations for all regulated commodities. We applied this prioritization approach during the COVID-19 public health emergency and expect to continue to apply it until the end of the pandemic and after travel restrictions and other impediments to inspections are eased or lifted. Details of these prioritization plans can be found in the recently published Resiliency Roadmap.

As mentioned, on July 1, 2021, we will be returning to standard operations for domestic inspections. Drug inspections are conducted based on risk, and we will continue to prioritize mission-critical inspections, which are identified by applying established criteria, on a case-by-case basis, as described in the Resiliency Roadmap. These criteria include whether (1) the product that is the subject of the application received breakthrough therapy or regenerative medicine advanced therapy designation, (2) the product is used to treat a serious disease or medical condition that has no other treatment option, (3) there is a public health need for follow-up (e.g., due to a recall, evidence of serious adverse events, or outbreaks of a foodborne illness), or (4) the product is related to the nation's COVID-19 response. With our return to standard operations for domestic inspections, we will be conducting mission-critical inspections for applications as well as those that do not meet these criteria (i.e., for non-mission-critical applications). At this time, global conditions and travel restrictions remain in

[4] See *https://www.fda.gov/drugs/coronavirus-covid-19-drugs/manufacturing-supply-chain-and-drug-inspections-covid-19.*

place for foreign drug facility inspections and FDA will be limited to conducting foreign inspections considered to be mission-critical.

We also recently published a guidance for industry *Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities During the COVID-19 Public Health Emergency*,[5] describing our current thinking on using voluntary remote interactive evaluations (for example, livestreaming video of drug manufacturing facilities) during the COVID-19 public health emergency to support our regulatory decisions and oversight of facilities.

4. What is the current status of FDA's inspections program (including both international and domestic inspections) for pre-approval, surveillance, and for-cause inspections?

Throughout the COVID-19 pandemic, our inspection program continued to conduct mission-critical inspections across all commodities, regardless of the location of the site to be inspected. With our return to standard operations for domestic inspections, FDA investigators will be assigned and travel to domestic establishments to conduct inspections. Drug inspections needed at a foreign establishment will continue to be subject to a case-by-case mission-critical determination as described above. The current status for pre-approval, surveillance, and for-cause inspections is as follows:

Pre-Approval Inspections: We apply several risk factors—such as the novelty of the product, the complexity of the manufacturing process, and the history of compliance with quality management requirements at the facility where the product will be made—in deciding whether a facility inspection is needed. Between March 2020 through March 2021, we applied these risk factors and determined that approximately 600 applications needed an inspection or oversight of some type before action. From March 2020 through March 2021, FDA completed approximately 440 application-based inspections, including both mission-critical and prioritized[6] inspections. By March 2021, an estimated 68 applications had been delayed due to the inability to conduct pre-approval, pre-market, or pre-license inspections due to travel restrictions associated with the public health emergency. The majority of these delayed applications—61 of the 68—are not considered mission-critical. Inspections in support of the seven delayed applications that are considered mission-critical are scheduled to be completed by September 30, 2021.

For-Cause Inspections: In FY 2020, we planned to conduct 79 domestic Official Action Indicated (OAI)/compliance follow-up activities to meet our performance target, and we

[5] *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/remote-interactive-evaluations-drug-manufacturing-and-bioresearch-monitoring-facilities-during-covid.*

[6] As described in the Resiliency Roadmap, prioritized domestic inspections include surveillance and certain for-cause inspections that were not determined to be mission-critical. These are prioritized according to factors such as whether the inspection: (1) is intended to follow up on a previous violative inspection, (2) is needed to support a product approval decision when no other application deficiencies are known that would preclude approval, (3) is considered high risk under statutory inspection frequency mandates, or (4) otherwise maximizes the use of limited inspectional resources to achieve the greatest public health impact during the COVID-19 pandemic.

were able to complete 90 percent of them, delaying only eight of these activities. In FY 2021, we planned to conduct 164 domestic OAI/compliance follow-up activities to meet our performance target, which includes the eight postponed in FY 2020. By March 2021, we had conducted 49 of the 164 planned, leaving 115 OAI/compliance follow-up activities to be conducted in FY 2021 to meet our performance target. However, for-cause inspections can arise on an ad hoc basis (for example, when there are consumer complaints or reports of adverse events) based on information received from state or foreign regulatory partners or due to unforeseen emergency situations. We prioritize these inspections and, depending on the circumstance in each case, for-cause inspections may be considered mission-critical.

Surveillance Inspections: During the COVID-19 pandemic, routine surveillance inspections have not been considered mission-critical. When establishing priorities during the pandemic, most routine surveillance inspections were postponed, constituting the majority of our foreign and domestic inspections not completed due to the pandemic. However, with our return to standard operations starting July 1, 2021, we will return to scheduling domestic surveillance inspections using our usual risk-based approach.

a. Approximately how many in-person inspections is FDA conducting on a weekly and/or monthly basis, and how does this compare to FDA's activity level in 2019, 2018, and 2017 prior to the pandemic?

i. Please break these figures down by application type, as applicable.

Please see the enclosed table that shows the number of domestic and foreign on-site inspections conducted per month, per medical product inspection program, for FY 2017 through FY 2021.

b. What are FDA's criteria for prioritizing in-person inspections? How is FDA prioritizing the conduct of inspections that are required for products pre-market compared to inspections related to post-market requirements or activities (*e.g.*, pre-approval inspections, inspections at facilities on "Official Action Indicated" status, or that otherwise need an FDA inspection to address identified quality issues, etc.)?

As described in response to Question 3 above, we have established criteria and are using a risk-based approach, including information from remote assessments, sample collections, import alerts, and other compliance requirements to prioritize inspections to ensure the quality and safety of our regulated products. Our highest priority will continue to be those inspections that are determined to be mission-critical. Starting in July 2020, prioritized domestic surveillance inspections resumed using a rating system that we had developed to assist in determining when and where it is safest to conduct prioritized domestic inspections. The COVID-19 Advisory Rating system (COVID-19 Advisory Level)[7] used real-time data to qualitatively assess the number of COVID-19 cases in a local area based on state and national data. We plan to suspend use of the

[7] *https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-prepares-resumption-domestic-inspections-new-risk-assessment-system.*

– The Honorable Richard Burr

COVID-19 Advisory Level starting July 1, 2021, as we return to standard operations for domestic inspections.

To help achieve our oversight goals, we constructed a systematic method for tackling the oversight activities that were not considered mission-critical and had to be postponed; this method involved reviewing data showing the impact of the COVID-19 pandemic on inspections, establishing prioritization plans by commodity, and developing an overall prioritization approach for inspectional operations for all regulated commodities.

The following table shows the elements of these prioritization plans, which consider public health risks related to conducting an inspection or sampling assignment, such as the impact of the product's availability on public health, as well as investigator safety and travel restrictions/advisories.

COMMODITY	TIER 1: MISSION CRITICAL	TIER 2: HIGHER PRIORITY	TIER 3: LOWER PRIORITY
Human and Animal Drugs	Agency crisis or emergency response activities	For-cause but not considered mission critical	Post-approval inspection
	For-cause public health emergency work		
	Essential medicine assignment	Application-approval inspection not considered mission critical	
	Application-approval for high-priority products		Routine-surveillance, including inspection and sampling assignment
	Mission-critical violation follow-up	Compounding inspection not considered mission critical	
Medical Devices and Radiological Health	Essential product assignment	Application-approval inspection not considered mission critical	Post-approval inspection
	Agency crisis or emergency response For-cause work	For-cause but not considered mission critical	
	Application-approval for high-priority product	Overdue MQSA inspection*	Routine-surveillance, including inspection and sampling assignment
	Mission-critical violation follow-up	High-risk assignment based on Risk Based Work Plan	
Biologics	Emergency-use authorization product	Application-approval inspection not considered mission critical	Routine-surveillance inspection
	Agency crisis or emergency response For-cause work	For-cause but not considered mission critical	
	Application-approval for high-priority product		
Bioresearch Monitoring	Agency crisis or emergency response For-cause work	Application-approval inspection not considered mission critical	Routine-surveillance inspection
	Application-approval for high-priority product	For-cause but not considered mission critical	

– The Honorable Richard Burr

5. **What is the status of FDA's assessment of alternatives to in-person inspections? When does FDA anticipate that this assessment will be complete? Please specify by each type of alternative (*e.g.*, real-time video streams, records reviews, reliance on trusted regulatory partners, etc.).**

    a. **With respect to the guidance document FDA issued on April 14, 2021 regarding remote interactive evaluations, how will remote interactive evaluations be used in lieu of in-person inspections to resolve warning letters or other enforcement actions?**

    Remote interactive evaluations are valuable to our surveillance and oversight of drug manufacturers as an alternative tool to inspections, especially during this public health crisis and in other situations when inspections are not feasible (e.g., State Department travel advisories). However, inspections remain the most valuable tool to evaluate the overall compliance status of a manufacturing facility because an inspection provides an opportunity for investigators to use all their senses, interview personnel and observe body language, and move into and freely observe all manufacturing areas. Although a remote interactive evaluation is useful, it is not a replacement for an inspection.

    The use of a remote interactive evaluation depends on the nature of the facility and the reason for the assignment, including, but not limited to, the inspection history and any data integrity concerns. Drug manufacturers with a history of noncompliance or lack of sustained compliance with current good manufacturing practice (CGMP) requirements are generally not considered to be good candidates for remote evaluations. Historical data show that when we re-inspect a facility that has previously received a warning letter, we often find that corrective actions have not been implemented and the facility continues to be in CGMP noncompliance. This is true even though we typically do not re-inspect the facility until the firm has advised us that they have finished implementing all necessary corrective actions.

    In light of these facts, and consistent with our risk-based approach to inspections, we will continue to assess alternatives to inspections and, as we gather more experiential data, use the most robust tools, including inspections, to assess compliance.

6. **How frequently is FDA currently implementing in-person inspection alternatives and for which types of applications (*i.e.*, how frequently are these alternatives being used as *complements* to versus *substitutes* for in-person inspections)?**

We have been using inspection alternatives that have been useful both in assessing certain applications for marketing approval and in evaluating the risk of facilities currently manufacturing drugs for the U.S. market. However, we do not intend to replace traditional inspections with inspection alternatives. Ideally, inspections supplemented by additional tools, including records requests and remote interactive evaluations, would provide us the greatest depth of information.

Between March 2020 and March 2021, we used a number of alternative methods, including requesting records under section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act

(FD&C Act) and relying on information from trusted foreign regulatory partners through Mutual Recognition Agreements, to support our oversight work. Use of these alternative tools have informed 150 ANDA, 84 NDA, and 11 BLA actions, including 41 ANDA, 59 NDA, and 11 BLA approvals.

Additionally, we have leveraged audits from the Medical Device Single Audit Program (MDSAP) in lieu of routine inspections. MDSAP is an internationally harmonized third-party audit program that allows recognized auditing organizations to conduct a single regulatory audit of a medical device manufacturer that satisfies the relevant requirements of the participating regulatory authorities (i.e., Therapeutic Goods Administration of Australia; Brazil's Agência Nacional de Vigilância Sanitária; Health Canada; Japan's Ministry of Health, Labour and Welfare, and the Japanese Pharmaceuticals and Medical Devices Agency; and us).

7. How is FDA currently using its statutory and regulatory authorities and processes to use in-person inspection alternatives to address outstanding inspections? For how many applications will FDA utilize such alternatives to more efficiently conduct inspections?

We have been increasing and refining our use of authority under section 704(a)(4) of the FD&C Act to request records and other information in advance of or in lieu of an inspection of a drug manufacturing facility. Use of this authority, the extent of which is described in the previous responses, has been critical in enabling us to increase our reach during the COVID-19 pandemic, to support approval decisions, to plan and prioritize future on-site inspections, to issue warning letters, and to carry out other regulatory responsibilities. This authority is available only for drug and biologics manufacturing facility inspections; we lack similar explicit authority to request records and information in advance of or in lieu of an inspection for other medical product commodity programs, including for medical devices and for our bioresearch monitoring program.

We are also using drug establishment inspection information from capable foreign regulatory authorities under the Pharmaceutical Annex to the United States and European Union Mutual Recognition Agreement (MRA) and the Pharmaceutical Annex to the United States and United Kingdom MRA, as well as through other confidentiality commitments. This approach has provided additional information regarding a facility's conformance with regulatory requirements, which helps inform decisions related to drug approvals and shortages and can be used in lieu of certain inspections. Even before COVID-19, we were using MRA work to receive more information on foreign drug firms and to incorporate in-country work conducted by member countries as part of our surveillance activities. MRA work became increasingly vital when non-mission-critical foreign travel was suspended in March 2020. In response to the global pandemic, we assessed expanding the use of MRAs beyond in-country inspections to include third-country inspections, and we have begun to accept, review, and classify third-party inspections conducted by countries deemed capable under section 809 of the FD&C Act.

As stated in our response to Question 6, between March 2020 and March 2021, use of these alternative tools has informed 150 ANDA, 84 NDA, and 11 BLA actions, including 41 ANDA, 59 NDA, and 11 BLA approvals.

– The Honorable Richard Burr

8. What statutory or resource obstacles, if any, does FDA face in using these alternatives?

Under section 704(a)(4) of the FD&C Act, we have the authority to request records in advance of or in lieu of an inspection of a drug manufacturing facility. We have found this authority to be extremely helpful and efficient. However, we do not similarly have this authority for devices, foods, tobacco, cosmetics, or bioresearch monitoring inspections.

We currently do not have explicit statutory authority to require firms to participate in remote interactive evaluations; therefore, we have conducted them on a voluntary basis during the pandemic. We have received some refusals for remote interactive evaluations, in which case the firm's inspection would remain a priority when we resume surveillance inspections.

9. How will the agency apply lessons learned using alternatives to in-person inspections during the COVID-19 pandemic to ensure an efficient and flexible inspections program in the future?

Although physical access to facilities provides a unique view into the components of a facility's operations, yielding insights that are important for regulatory oversight, inspections have not always been possible during the pandemic. We have adapted to this reality by using existing authorities to conduct remote oversight and by developing new tools to extend our reach in ensuring the safety and quality of regulated products.

To help achieve our oversight goals, we constructed a systematic method for tackling postponed oversight activities, which included reviewing data showing the impact of the COVID-19 pandemic on inspections, establishing prioritization plans by commodity, and developing an overall prioritization approach for inspectional operations for all regulated commodities.

COVID-19 has created an unprecedented public health emergency that has both challenged traditional oversight activities and afforded us an opportunity to consider other regulatory approaches that increase our efficiency, ensure product quality, and fulfill our public health mission. We continue to work to advance our regulatory convergence and to expand our mutual reliance with trusted regulatory partners. We are also working to leverage our internal collaborative approaches to foster alignment around modernization policies and practices and determine how they can best be deployed to meet our mission.

We will soon begin a multi-year modernization effort to further transform our data enterprise platforms and cross-program interoperability infrastructure to better support innovation related to our regulatory oversight role, including remote approaches. This modernization effort will include a review of approaches to regulatory oversight using next-generation assessment technologies and improvements.

We will also continue to work to enhance our coordinated approach to inspections, information sharing, and other processes to accelerate the evaluation and potential integration

– The Honorable Richard Burr

of new oversight methods and tools. This will allow the consistent use of tools and technologies and provide additional flexibility to enhance data-driven, risk-based oversight modeling for us and for the nation's public health system.

10. How is FDA using the funds that it has received from Congress intended to support activities related to the pandemic response to resume its normal inspection activities? Please include specific dollar amounts and the agency offices and programs to which those funds have been or will be directed.

The American Rescue Plan Act of 2021 (Public Law 117-2) appropriated to us $500 million to respond to emerging variants; to ensure that COVID-19 tests, therapeutics, and vaccines continue to be safe and effective; to conduct critical inspections; and to prepare for the next challenge by accelerating work in areas such as advanced manufacturing and supply chain monitoring. Of the $500 million appropriated, our spend plan reflects approximately $73.5 million to address inspections delayed due to the COVID-19 public health emergency. Of this total, $38.3 million will support our Center for Drug Evaluation and Research's plans outlined in "Pandemic Recovery: Medical Product Inspections"; and $35.1 million will support our Office of Regulatory Affairs' COVID-19 recovery activities, including inspectional modernization and the hiring of staff to conduct inspections delayed due to the COVID-19 public health emergency.

Thank you again for contacting us regarding this matter. If you have any questions, please let me know.

Sincerely,

Janet Woodcock, M.D.
Acting Commissioner of Food and Drugs

Enclosure

United States Senate

COMMITTEE ON HEALTH, EDUCATION,
LABOR, AND PENSIONS

WASHINGTON, DC 20510–6300

May 5, 2021

Dr. Janet Woodcock, M.D.
Acting Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Dear Acting Commissioner Woodcock:

I write regarding the medical product user fee programs and the Prescription Drug User Fee Agreement, the Medical Device User Fee Agreement, the Generic Drug User Fee Agreement, and the Biosimilar User Fee Agreement that the agency is currently negotiating with its industry partners. These agreements are under review during a unique and critical moment in the United States. The agency and each industry partner have the opportunity to assess the Food and Drug Administration's (FDA) medical product review programs to thoroughly evaluate the changes, successes, efficiencies, challenges, and failures of the FDA during the pandemic response to inform all aspects of these important negotiations. As ranking member of the Committee on Health, Education, Labor and Pensions, the committee responsible for congressional oversight of the FDA, I am requesting an update on the progress toward the renewal of these agreements and to better understand how each agreement may incorporate lessons learned during one of the greatest public health challenges ever faced by the FDA.

In August 2019, I wrote to many of the leading industry partners in advance of the medical product user fee negotiations regarding the importance of designing the agreements to be in the best interest of patients. In the COVID-19 era, the content of these agreements are even more critical. FDA's statutory authorities and responsibility to review medical product applications have been a key component of rescuing the United States and the world from a global pandemic.

The COVID-19 pandemic has demanded more of the FDA and industry in order to save as many lives as possible from this virus. The FDA has acted quickly and provided flexibility and regulatory certainty to manufacturers of tests, treatments, vaccines, and other countermeasures, allowing a swift response to this unprecedented public health threat. Throughout the response, FDA relied on the authorities and tools Congress provided over the last 20 years which were designed to strengthen the agency's regulatory readiness and preparedness and gave FDA the direction, authority, and flexibility needed to guide the response to the COVID-19 pandemic today.

Dr. Janet Woodcock, M.D.
May 5, 2021

The Project BioShield Act of 2004 gave FDA authority to authorize medical products for emergency use to protect against a public health threat. The FDA has effectively used this authority, granting more emergency use authorizations than at any other time in the agency's history – authorizing three vaccines, nine treatments, and more than 370 tests for emergency use aimed at fighting COVID-19.[1] Many of these countermeasures were developed and authorized for use in a matter of months or even weeks, without compromising the commitment to safety and efficacy – a testament to the agency's partnerships with commercial partners and dedication to its mission.

As part of FDA's pandemic response, the agency created the COVID Treatment Acceleration Program (CTAP) to help accelerate clinical studies, address complex manufacturing challenges, and prioritize rapid product review with the goal of speeding the development of treatments for COVID-19. As of April 29, FDA reported that through CTAP it has reviewed more than 440 investigational new drug (IND) applications and is engaged in reviewing over 600 drug development programs in the pre-IND phase.

It is my hope that the number of countermeasures authorized and available to combat COVID-19 will continue to grow, and that FDA and industry partners identify the regulatory policies that have enabled the rapid development and review of medical countermeasures in order to permanently implement such policies for patients battling other serious and life-threatening diseases and conditions. FDA's CTAP program has identified ways to accelerate development of medicines to treat COVID-19 – such development tools could be leveraged across the agency and product categories.

It is critical to strengthen the FDA's regulatory readiness and efficiency for the next generation of science and biomedical innovations across all medical product categories, and for the forthcoming user fee agreements to look ahead to the next five years of scientific advancements that industry will bring forward for the FDA's consideration. It is therefore equally as critical that the medical product user fee agreements between industry and FDA reflect the lessons learned from the response to the COVID-19 pandemic. The FDA should continue to encourage flexible clinical trial designs, modernize the way data is collected and evaluated, and support greater use of surrogate endpoints, real world evidence, and platform technologies to encourage swifter development of safe and effective medicines and medical technology.

Congress has provided the FDA with ample resources dedicated to COVID-19 and certain other agency priorities. In Fiscal Year 2021, FDA received more than $3 billion in overall budget authority, and more than $700 million in emergency funding over the last year to prepare for and respond to COVID-19. In light of these resources and on behalf of American patients and taxpayers, I encourage FDA and each industry partner to keep in mind the intended mission of the user fee programs and ensure funding is used for product review and speeding the

[1] https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#covidinvitrodev

development of life-saving medicines and medical technologies – not administrative agency priorities.

FDA is responsible for reviewing medical products that can save or improve lives, determining whether they meet the FDA's gold standard for safety and efficacy, and when patients can access them. The user fee programs supplement FDA's congressionally appropriated resources to bring new medical products to market as quickly as possible, support product review staff, and keep pace with science and technology to bring cutting-edge medical treatments and technologies to patients who need them.

I am concerned that the resources dedicated from and agreed to by industry partners under each user fee program do not fulfill the goal of bringing life-saving medicines to patients as swiftly as possible. Instead, the agreements between FDA and industry may allow resources to be expended on programs and activities unrelated to product review, straying from the Congressional intent in the authorization and anticipated renewal of these agreements. Performance and fiscal reporting from the FDA have shown that the agency has not fulfilled its commitments in their entirety. Yet, with each negotiation, the FDA requests additional support and resources from industry.

The collection of medical product user fees began in Fiscal Year 1993, pursuant to the authorities in the Prescription Drug User Fee Act. The fee for a drug application then was about $100,000.[2] Today, a drug application fee is more than $2.8 million.[3] In fiscal year 2019, user fees accounted for 71 percent of FDA's drug review budget, 30 percent of its medical device review budget, 72 percent of its generic drug review budget, and 64 percent of its biosimilar drug review budget.[4] I have concerns that the agency's growing reliance on industry user fees results in less accountability to Congress, and therefore, the American patients and families they represent.

Since 1990, FDA has steadily increased the number of medical products it approves each year. However, the time it takes to develop a novel treatment or therapy, including conducting clinical trials, has remained stagnant. According to a study published in the Journal of the American Medical Association in January 2020, the time between submitting an Investigational New Drug (IND) application and receiving approval from FDA has increased from an average of 7 years in 1997-2007 to more than 9 years in 2008-2017.[5,6] According to the National Institutes of Health, diagnostic device development can take up to 7 years.[7] These development times stand in stark contrast to the rapid development of vaccines, treatments, and tests this nation experienced in response to the COVID-19 pandemic over the last year. As a country, we should set the baseline

[2] https://www.crs.gov/Reports/RL33914?source=search&guid=cfab3e61f20944299b2d54ee36dc473c&index=1
[3] https://www.fda.gov/industry/fda-user-fee-programs/prescription-drug-user-fee-amendments
[4] https://www.crs.gov/Reports/R44750
[5] https://jamanetwork.com/journals/jama/article-abstract/2758605
[6] https://pharmaintelligence.informa.com/resources/product-content/sharfstein-us-fda-incentives-not-broke-but-fix-them
[7] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6113340/

expectation that the efficient performance by the FDA in authorizing COVID-related vaccines, treatments, and diagnostics becomes the norm.

As negotiations over the user fees and goals in exchange for such fees continue, I respectfully request that FDA and its industry partners provide the committee with regular updates to ensure Congress remains informed of the progress towards agreements that benefit American patients during this critical time for public health, and that the agency is prepared for the next decade of scientific advancements. Please work with my staff to identify dates to provide briefings on the progress toward the user fee agreements for fiscal years 2022 through 2027.

I appreciate the opportunity to work together to strengthen the agency, learn from the pandemic response, and better leverage scientific innovation to benefit all Americans.

Sincerely,

Richard Burr
Ranking Member
Committee on Health, Education, Labor and Pensions

Cc: Scott Whitaker, President and CEO, Advanced Medical Technology Association
Dan Leonard, President and CEO, Association for Accessible Medicines
Michelle McMurry-Heath, MD, MPH, President and CEO, Biotechnology Innovation Organization Mark Leahey, President and CEO, Medical Device Manufacturers Association
Patrick Hope, Executive Chairman, Medical Imagine & Technology Alliance
Stephen Ubl, President and CEO, Pharmaceutical Research and Manufacturers of America

U.S. FOOD & DRUG ADMINISTRATION

April 1, 2022

The Honorable Richard Burr
United States Senate
Washington, D.C. 20510

Dear Senator Burr:

Thank you for your letter of January 24, 2022, regarding the Food and Drug Administration's (FDA or the Agency) workforce and hiring practices. Hiring and retaining a world-class workforce is critical to executing FDA's mission.

We offer the following responses to your specific questions below:

1. **In aggregate, and broken down by FDA's major components, including each center, and each user fee program, as applicable, please provide the following information separately for each of fiscal years (FY) 2018 through 2022:**
   a. **Total employees (i.e., individual persons):** Please see Attachment A.
   b. **Total Full-Time Equivalents (FTEs):** Please see Attachment B.
   c. **Total vacancies, delineating between vacancies funded by user fees or Congressional appropriations:** Please see Attachment C.
   d. **Turnover rate:** Please see Attachment A.
   e. **Total number of new FTEs hired per FY:** Please see Attachment A.
   f. **Total number of FTEs lost to attrition per FY:** Please see Attachment A.
   g. **Total number of senior leadership employees:**

FY 2018	FY 2019	FY 2020	FY 2021	FY 2022
104	144	152	184	202

[1] Data as of February 16, 2022

   i. **For this answer, please provide an explanation of how FDA is defining "senior leadership."**

      Within FDA, there are several categories of senior leadership positions. These are classified above the GS-15 level or an equivalent position and are not required to be filled by Presidential appointment with Senate confirmation.

      - Members of the Senior Executive Service (SES), in which the incumbent directs the work of an organizational unit, are held accountable for the success of one or more specific programs or

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projects; monitor progress toward organizational goals and periodically evaluate and make appropriate adjustments to such goals; supervise the work of employees other than personal assistants; or otherwise exercise important policy making, policy determining, or other executive functions.

- Title 42(f) and Cures (Title 21) positions that perform duties involving one or more of the SES functional criteria listed above are considered SES Equivalent.

- Senior Level (SL) positions incorporate executive-level duties that are broad and complex enough to be classified above GS-15 but do not involve supervisory authority to an extent that meets the SES criteria.

2. **In a 2018 report, FDA estimated that 13% of its work force was eligible for retirement in 2017, and that half of the agency's senior leadership would be eligible for retirement by 2020. Broken down by FDA center and user fee program, as applicable, please provide the following:**

   a. **Total number and percentage of employees currently eligible for retirement:** Please see Attachment D.

   b. **Total number and percentage of senior leadership eligible for retirement:** Please see Attachment D.

   c. **An estimate for the number and percentage of employees and senior leadership who will be eligible [for retirement] by the end of the next user fee cycle.**

      Calculating retirement eligibility relies upon a number of variables that are likely to change by the end of the human medical products' next user fee cycle; thus any estimate FDA would provide now would be subject to significant variation by September 2027.

3. **As a part of the proposed user fee agreements, FDA is committing to hire at least 495 FTEs (not including the still-outstanding MDUFA proposal). For purposes of the commitments made as part of the user fee agreements, what is the definition of an "FTE"? How is "FTE" defined with respect to the number of hours worked per week or per year?**

   The new hires outlined in the proposed user fee agreements are for new positions. This means FDA will hire at least 705 new staff (individual persons) over the course of PDUFA VII, GDUFA III, BsUFA III, and MDUFA V. We note that the hiring table in section III.A.1 in the PDUFA VII commitment letter uses the term FTE, which may cause confusion since those numbers represent new hires and not full-time equivalents.

FDA follows the Office of Management and Budget's (OMB) definition of an FTE: "FTE employment" (often referred to as "staff year"), as defined by OMB Circular A-11 (OMB A-11), section 85, means the total number of regular straight-time hours—not including overtime or holiday hours—worked by employees, divided by the number of compensable hours applicable to each fiscal year. Annual leave, sick leave, compensatory time off, and other approved leave categories are considered "hours worked" for purposes of defining FTE employment.

4. **When FDA commits to hiring a certain number of FTEs as a part of the agreements, what is FDA committing to – hiring a certain number of *individual employees*, or a number of individuals who *in aggregate* will work hours that are equivalent to a full- time employee?**

   The user fee commitment letters outline commitments related to hiring individual employees.

5. **When FDA reports that it has "met" a hiring goal pursuant to a user fee commitment, does FDA account for attrition and turnover in the applicable user fee program? Does this reporting include FTEs lost to attrition or otherwise? For example, if FDA had a commitment to hire 15 new FTEs, and it hired the equivalent of 15 new FTEs, but at the same time lost 25 FTEs to create a net loss of 10 FTEs, would FDA still consider its hiring goal to be met?**

   FDA reports progress in filling the vacancies outlined in the commitment letters and does not factor data on attrition.

6. **How does FDA account for funds that have "funded" a vacancy within a user fee program? Are such funds accounted for, or obligated within the program's carryover balance?**

   In any given year, FDA uses a mix of current year user fees and prior year (carryover) user fees to implement the programs. We use this funding for both payroll and operating expenses and track it in our financial system of record, the United Financial Management System.

7. **What is the average total cost of an FTE in each of the medical product user fee programs?**

   The table below shows the average total cost of an FTE in each applicable human medical product user fee program. This number accounts for the fully loaded cost (inclusive of payroll costs, benefits, overhead, and operations) for an average FTE in the relevant medical product user fee programs, regardless of GS level. Average costs are used for estimation purposes only.

	CBER	CDRH	CDER
PDUFA	$307,567	$301,537	$312,185

GDUFA	$307,567	N/A	$312,185
BsUFA	$307,567	N/A	$312,185
MDUFA[2]	$295,393	$295,393	N/A

[2] Note: PDUFA, GDUFA, and BsUFA use center-specific cost-per-FTE estimates. MDUFA uses an average cost per FTE and excludes one-time operating costs from the calculation.

8. **Please describe the functions of the offices at FDA with hiring-related responsibilities, including the Office of Talent Solutions and Office of Human Capital Management. Please describe the relationship and differences between those two offices in terms of their roles, responsibilities, and interactions; and the relationship between those two offices and the centers at FDA.**

   In 2018, FDA reorganized its human resource (HR) function into two distinct organizations that partner together to deliver services to FDA. The Office of Talent Solutions (OTS) and the Office of Human Capital Management (OHCM) work together, yet each office operates independently and has its own mission, vision, and strategic plan. Both offices work collaboratively with staff from the centers.

   OTS is responsible for sourcing, recruiting, and hiring candidates. Additionally, OTS manages recruitment of and scientific outreach to prospective employees using our different hiring and pay authorities; determines classification, pay, and compensation; coordinates political appointees with the Department of Health and Human Services (HHS) and the White House; administers Public Health Service (Commissioned Corps) HR management; and develops FDA HR policy, accountability, and special placement programs.

   OHCM is responsible for managing employee lifecycle programs including new employee orientation, retirement and benefits, payroll, records management, workplace flexibilities, and performance awards; managing programs that support the efficiency of federal service; overseeing employee and labor relations; maintaining HR information systems; supporting human capital programs focused on retention, workforce planning, and succession planning; and managing agency-level training programs, including our anti-harassment program.

9. **In the recent GAO report on FDA's hiring practices, *FDA Workforce: Agency-Wide Workforce Planning Needed to Ensure Medical Product Staff Meet Current and Future Needs*, GAO found that FDA lacks an agency-wide strategic workforce plan.**

   a. **Why does FDA not have an agency-wide strategic workforce plan?**

      Workforce planning is done at the center level due to the various user fee and other funding authorities unique to FDA centers. OHCM facilitated a work group to develop an agency-wide Succession Management Strategic Plan and provides detailed agency-level and center-specific workforce profiles to inform workforce planning across the enterprise.

b. Is FDA planning to implement an agency-wide strategic workforce plan, consistent with GAO's recommendations? If not, why?

Yes. Recent studies, including the recent study by GAO, reveal efficiencies we could realize with a more integrated approach to human capital management. FDA has begun agency-wide strategic workforce planning through a phased approach that will incorporate several functional areas, among them outreach and recruitment, employee and leadership development, employee engagement and retention, rewards and recognition, and diversity, equity, inclusion, and accessibility.

c. Recognizing FDA may have center-specific strategic workforce or hiring plans, if that is the case, why hasn't FDA compiled those plans into an agency-wide strategic plan?

FDA's OHCM will collaborate with OTS to develop an agency-wide strategic plan that incorporates center-specific hiring plans.

d. Please describe any center-specific strategic workforce or hiring plans.

OTS collects annual talent acquisition plans from each center/office to plan and create hiring strategies and track progress towards the Agency's hiring goals. Below are plan details from the Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), and Center for Drug Evaluation and Research (CDER), to align with other data in this response.

CBER: CBER's Office of Management meets with senior leadership as well as all hiring managers to provide support and strategic direction in all activities of the hiring process.

Biweekly meetings with leadership from each office provide updates and identify the best hiring authorities and strategy for each vacancy. CBER ensures the program offices dealing with extremely high workloads have additional support to facilitate the hiring process by prescreening resumes, coordinating interviews, and developing summary charts to highlight skill sets and specialties, which hiring managers use to save time and ensure expedited recruitment actions.

CBER leadership promotes hiring initiatives during CBER all-hands meetings and updates hiring managers through email communications about the different hiring strategies and outreach events aimed at a diverse network using social media campaigns and targeted recruitments journal advertisements. CBER developed an outreach framework tailored to the needs of individual offices. The strategy prioritized three components: targeting outreach, diversifying candidate sourcing methods, and using OTS

material to engage candidates throughout the hiring process. Hiring methods included direct marketing campaigns aimed at appealing to universities and career centers and internal FDA resources to attract new talent while leveraging the networks of existing employees. Next, CBER developed a social media outreach strategy tailored to open positions, including senior- and executive-level roles. CBER also leveraged OTS resources to build new outreach material that informed candidates of the hiring process, keeping them engaged and making the overall process more transparent.

During FY 2021, CBER partnered with OTS on the CBER Hiring Surge initiative to expedite the recruitment to fill vacancies in critical and leadership positions. CBER launched five rounds of hiring surges (November 20, 2020; February 5, 2021; April 5, 2021; April 12, 2021; and July 23, 2021) using COVID-19 Direct Hire Authority to address the large need for FTEs in the center. CBER provided detailed instructions and recruitment materials to assist all hiring managers during the interview and selection processes. Through these hiring surge campaigns and outreach initiatives, CBER filled 188 vacancies by the end of FY 2021.

CDRH: CDRH's Office of Management meets with leadership across the programs to review current workforce data, determine future workforce needs, and identify skill sets and experience to fill knowledge/expertise gaps and vacant positions. The next step is to develop hiring strategies to support recruitments. Strategies include, but are not limited to, developing interdisciplinary position descriptions allowing for a more streamlined and efficient hiring of positions; reviewing the CDRH resume repository to assist with matching job seekers to our positions; using shared certificates derived from vacancy announcements posted by other HHS operating divisions and FDA centers; deploying strategic recruitment campaigns including the use of social media strategies; assessing the need for contractor support to fill gaps when the specialized expertise has not been found in the candidate pool; and using a variety of hiring authorities, such as direct hire, Cures (Title 21), the Pathways Program for students and recent graduates, and staff fellowships, to appoint new candidates with the requisite qualifications. The CDRH Office of Management works closely with hiring managers in the program offices throughout the life cycle of the recruitment process to ensure we develop positions; post and socialize job opportunities; and equip managers with the tools to review resumes, interview candidates, and make qualified selections.

CDER: CDER's Office of Management evaluates its hiring requirements on an annual basis to help identify the occupation-specific needs of each program office. CDER considers several factors such as workforce profile data, user fee hiring commitments, budget (affordability), critical vacancies that support programmatic goals of the mission and other data points that inform the center's decision making. This information is translated into an annual Talent Acquisition Plan, which CDER shares with OTS to plan and

create hiring strategies and track progress towards the Agency's hiring goals. CDER-specific strategies include, but are not limited to, maximizing the use of the Cures hiring and pay authority to recruit and retain staff, which allows for more streamlined and efficient hiring; using CDER's resume repository and the FDA special placement repository to assist with matching talent to vacant positions; and using the HHS (Hire Now) shared certificate process, Pathways, staff fellows, and direct hire, to appoint new candidates. The CDER Office of Management Recruitment and Outreach Team also formed an internal Recruiters Community of Practice. The Office of Personnel Management (OPM) trained this group of professionals on recruitment and outreach to help strengthen this skill set within the center. CDER leverages this group to support recruitment and outreach events (i.e., career event and associations) and host occupation-specific information sessions using subject matter experts. CDER also uses OPM's USA Staffing resume mining features, maximizes the use of professional network sites such as LinkedIn and professional job boards to build talent pools, and conducts outreach at local military installations and colleges and universities.

10. **The GAO report referenced above provides a breakdown of FDA employees by the authority used to hire them, noting that approximately 80 percent of FDA employees were hired using hiring authorities under Title 5 of the U.S. Code. Could you please provide a further breakdown of how (i.e. for which center or specific areas of expertise) and when FDA has used its Title 5 authorities between general Title 5 authorities and direct-hire authorities under 5 U.S.C. § 3304(a)(3) for the last 5 years?**

    As a point of clarification, the data FDA provided to GAO indicated that 80% of the current workforce is currently Title 5; however, this is not a direct correlation to the recruiting process. In FYs 2018-2021, FDA hired 1,724 new staff using the government-wide, COVID-19, and Vaping direct hire authorities provided to the Agency. Centers leveraged the direct hire authorities to onboard individuals with expertise in a variety of areas.

11. **What is FDA's plan to address the risk of high turnover or attrition in the coming months as a result of pandemic-related work conditions?**

    FDA will continue to offer workplace amenities to create work-life balance, incentives such as tuition reimbursement, and flexible workplaces opportunities.

12. **In April 2021, the Office of Personnel Management released a detailed summary of the government-wide results of the 2020 Federal Employee Viewpoint Survey (FEVS) across all federal agencies.**

    a. **Can you please provide a summary of the FEVS results for FDA employees (i.e., a summary similar to the government-wide report published by OPM, but specific to FDA)?**

b. Understanding that the 2021 FEVS is currently being administered, please provide the date by which you will provide the same FDA-specific summary for the 2021 survey.

In response to both questions 12a and 12b, please see Attachment E, which is a summary of FDA's 2021 FEVS results, including many comparisons to 2020 benchmarks.

13. In April 2020, Booz Allen Hamilton published an Interim Hiring and Retention Assessment conducted pursuant to the PDUFA and BsUFA agreements.

a. What is the status of FDA's consideration and implementation of the conclusions and recommendations made in the April 2020 report?

FDA launched several initiatives focused on strategic thinking, cross-agency collaborative activities, tangible outputs, and—in some cases—measurable impact to address fundamental HR challenges. We have also developed a roadmap for an integrated HR IT system and invested in enterprise-level data integrations and employee eSolutions.

b. When does FDA plan to publish its final assessment?

We posted the final assessment[1] on December 10, 2021, and the public meeting[2] occurred on March 15, 2022.

14. Numerous assessments and reports published by FDA and third-party contractors describe different steps that FDA has taken to help attract and retain talent, such as developing an alternative pay structure for certain positions, using hiring bonuses for hard-to-fill positions, recruiting through academic institutions, and others.

a. Has FDA conducted an analysis to assess the comparative effectiveness of different hiring approaches and tools? If so, please describe. For example, does FDA look at time-to-hire metrics, or a yield rate comparing the success of different approaches in identifying candidates who are later hired?

FDA commissioned studies on the effectiveness of different hiring approaches for various types of FDA positions. These studies identified improvement activities such as establishing strategic plans, collaborative

[1] *https://www.fda.gov/industry/prescription-drug-user-fee-amendments/completed-pdufa-vi-deliverables*
[2] *https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/fda-pdufa-hiring-and-retention-final-assessment-public-meeting-03152022*

working groups, key performance indicators, and mutually agreed-upon expectations of roles and responsibilities, plus a performance goal that demonstrates the success of the improvement activities. The studies also identified longer-term improvements, such as system integration for various HR functions.

FDA has also worked to address technological deficiencies. We have developed and implemented the Applicant Tracking and Lifecycle Analysis Solution (ATLAS), a robust HR workflow tracking system, to improve hiring processes, timeliness, and accountability. ATLAS is part of the FDA's Hiring Modernization Pilot and allows FDA to monitor time-to-hire metrics. FDA is pleased to report considerable progress since the inception of the pilot. One goal of the pilot was to decrease the average time-to-hire for general schedule new hires to the range of 80 to 140 days, and FDA has reduced the average time-to-hire below 70 days. Prior to the pilot, the average time to hire was approximately 150 to 550 days for general schedule new hires.

It is important to note the progress we have made over the past three fiscal years. FDA continues to exceed its hiring goals as shown in Attachment A.

Of the nine hiring authorities available to FDA, the Cures (Title 21) authority is by far the most flexible, competitive, and efficient. Cures authority currently improves FDA's ability to recruit and retain scientific, technical, and professional experts in certain occupational series that "support the development, review, and regulation of medical products." Through the Cures authority, FDA has been able to recruit high-caliber talent as illustrated by exceeding our hiring goals. In addition, FDA has been able to retain exceptional scientific and biomedical talent by converting existing staff to positions under Cures authority. Innovation is occurring in every product area FDA regulates. Cures authority is not available for use by the entire Agency, however, and many program areas outside the medical products portfolio could benefit from the efficiencies and competitiveness FDA has been able to realize with this hiring authority if it were extended to the entire agency.

15. **Please describe efforts at FDA to streamline frequently used hiring processes, including processes within each center, and the metrics used to assess the success of such efforts**.

Streamlining hiring processes to recruit and hire the best scientists and public health employees in the world is a top priority for FDA. To do this, FDA leverages its nine different hiring authorities available–each with its own policies, limitations, and pay caps, and implements new and innovative ideas for optimizing FDA's hiring practices and procedures to reduce the average time to hire.

FDA works in tandem with the centers to review candidates for special program

eligibility and qualifications. Each center has unique goals and missions and therefore different authorities are used to meet the needs of each center. OTS coordinates with centers on recruiting efforts and building a recruiting pipeline using both non-traditional and tried-and-true recruiting sources to identify candidates. For all hiring authorities, each center sets an overarching annual hiring goal metric. OTS assists each center to develop a recruitment strategy to set the annual goal. OTS then tracks and monitors the center's progress to measure success. OTS monitors the rate the centers submit recruitment packages for review and processing to ensure each center remains on track to meet its annual goal. Throughout the year OTS makes suggestions such as sharing certificates, extending posting deadlines, and leveraging streamlined applicant review processes.

Additionally, FDA uses the Senior Biomedical Research and Biomedical Product Assessment Service (SBRBPAS), an authority expanded under the Cures authority. The SBRBPAS allows FDA to recruit and retain the most outstanding research and review scientists. Prior to FY 2021, it took FDA almost a year to appoint or retain an individual seeking appointment/conversion to the SBRBPAS for varying reasons including biannual credentialing meetings. The FDA streamlined processes, including but not limited to, (1) issuing a charter with representation from each center and office; (2) issuing FDA-wide guidance on preparing packages; (3) lessening the administrative burden on required documentation; (4) implementing a shared SBRBPAS IT platform site; (5) establishing the SBRBPAS Review Board, and (6) reviewing, approving, and processing submissions within 45 days from date of receipt.

16. **Please describe any non-traditional efforts by FDA to hire qualified scientists and other experts, such as partnerships with academic institutions and/or industry, hiring bonuses for hard-to-fill positions, and other similar efforts**.

Since FY 2018, FDA established more than 275 partnerships with academic institutions, government entities, and professional associations to promote careers at FDA, which directly supported hiring STEM experts and others for FDA. In FY 2021, FDA increased focus on veteran associations and added four new veteran groups to our partnership list. With these new partnerships, FDA engaged with more than 500 veterans and military spouses on FDA's hiring process and open vacancies. This included Recruit Military, Texas Veterans Commission, U.S. Chamber of Commerce Foundation's Hiring our Heroes, and Military Spouse Fellowship Program.

In FY 2021, FDA strongly focused on underrepresented groups, specifically the Hispanic/Latino and Black/African-American communities. FDA added the Atlanta University Center Consortium to our partnerships list, which includes four Historically Black Colleges and Universities (HBCU) institutions, such as Morehouse University School of Medicine, and strengthened existing HBCU partnerships, such as with Meharry Medical College and Alabama A&M University. FDA also established partnerships with Hispanic Servicing Institutions, including

California State University, Florida International University, Marymount University, University of Arizona Global Campus, and University of Texas at San Antonio.

In FY 2020, FDA established a partnership with the American Association of Retired Persons (AARP). AARP is the nation's largest nonprofit, nonpartisan organization dedicated to empowering Americans 50 and older to choose how they live as they age. The partnership with AARP includes posting on their career boards to target more seasoned candidates for hard-to-fill positions and improve age diversity in our hiring practices.

Additionally, between FY 2018 and FY 2022, FDA's recruitment team established location-specific partnerships to target candidates for hard-to-fill positions with the National Center for Toxicological Research (NCTR) and Office of Regulatory Affairs (ORA).

In FY 2019, FDA began to actively use the platform Handshake, a career network website for students and recent graduates to connect with hiring managers and learn about career opportunities. In FY 2020, FDA added Symplicity to its list of recruitment platforms, which is a platform focused on early talent recruiting for students and recent graduates. FDA uses both platforms for collegiate events and job board posting.

17. **Please provide an overview of the use of teleworking and alternative work schedules by FDA employees, including related results from the FEVS and any other relevant information. Where possible, please provide a breakdown of this information by center.**

In accordance with the Telework Enhancement Act, FDA promotes and offers employees both telework and alternative work schedules in efforts to increase workplace flexibilities that help balance work-life and commuting costs. We encourage supervisors to work with employees to use flexible schedules to the greatest extent possible when establishing work schedules. Such work schedules include maximizing telework, Flexitime, Flexiplace, MaxiFlex, and Compressed Work Schedules. HHS recently implemented the Workplace Flexibilities policy, which gives each Operating Division the autonomy to develop and implement varying telework, remote and/or flexible work schedule opportunities for their employees.

18. **Please explain how FDA uses hiring authorities under Section 714 (related to the review of medical device and generic drug applications) and authorities under Section 714A (for "scientific, technical, or professional positions"), and compare and contrast its use of those authorities**.

FDA's hiring authority under Section 714 enabled the Agency to hire individuals who administered and supported activities related to processing and/or reviewing medical device applications and human generic drugs. Section 714 was granted to

FDA for three years, sunsetting in July 2015, and was intended to operate consistent with user fee goals. These appointments were in the excepted service and were limited to the GS-pay scale.

FDA's hiring authority under Section 714A is broader and permits the Agency to hire outstanding and qualified candidates to scientific, professional, and technical positions that support the development, review, and regulation of medical products. Section 714A allows the Agency to utilize recruitment efforts to target positions that are mission critical and hard to fill and retain while streamlining the recruitment process to reduce the time to hire. Section 714A provides greater flexibility for competitive salaries through an alternative pay system, and appointments are in the competitive service.

19. Related to the flexible hiring authorities that Congress granted FDA in the 21st Century Cures Act:

a. What is the average time between posting of a position eligible to be hired under the 21st Century Cures Act authorities and the selected candidate starting work? How does this compare to the average time between public posting and start date for individuals hired under FDA's general hiring authorities?

At this time, we do not have comprehensive data on the time between public posting and start date across all FDA hiring authorities. The Booz Allen Hamilton analysis from the 2021 Assessment of Hiring and Retention shows that hiring under Title 5 (including Direct Hire and Schedule A flexibilities) takes an average of 86 days, Cures (Title 21) takes an average of 47 days, and Title 42(g) takes an average of 29 days.

b. What percentage of individuals hired using the 21st Century Cures Act authorities are internal (i.e., already employed at FDA, or at other federal agencies) versus external?

This table shows Cures (Title 21) external hires and internal conversions, which FDA tracks collectively.

Total Cures Hires + Conversions			
Center	**FY 2019**	**FY 2020**	**FY 2021**
CBER	6	10	29
CDRH	16	81	217
CDER	43	137	731
Total	65	228	977

c. In a 2018 report on the implementation of the 21st Century Cures Act, FDA noted that it had classified 38 occupations as eligible for those

authorities. Has FDA updated this list? Could you please provide the list of occupations eligible for these authorities?

Please see Attachment F.

20. FDA operates a number of fellowship and other training programs, including those authorized under Section 746(b) of the FDCA. Please list and describe the fellowship programs that FDA operates today, including the status of the Commissioner's Fellowship, and the statutory authorities under which such programs are operated. Please also describe any assessments FDA has conducted regarding the effectiveness or utility of such programs.

FDA offers a wide range of training programs and fellowships.

- *Pathways Program* offers federal internship and employment opportunities for current students, recent graduates, and those with an advanced degree. The Pathways Program offers three different paths: internship program, recent graduate program, and the Presidential Management Fellowship (PMF) program.
- The last cohort of the *Commissioner's Fellowship Program* was in 2017, with the program sunsetting in 2020.
- *Staff Fellowship Program* encourages and promotes research/regulatory review, studies, and investigations related to health. Related health areas include medical, physical, biological, mathematical, social (economic and others), biometric, epidemiological, behavioral, and computer sciences directly related to the mission of the Agency. Depending on the length and experience possessed by a candidate, he or she may be hired as a Staff Fellow or a Senior Staff Fellow.
- *Visiting Scientist Programs* provide opportunities for distinguished foreign scientists at all levels of their careers to work on problems of mutual interest. There are two categories of FDA's Visiting Scientist Program participants: Visiting Associates and Visiting Scientists.
- *Oak Ridge Institute for Science and Education (ORISE) fellowships* provide educational and training programs designed to engage students and recent graduates in the research performed at FDA. ORISE is administered by Oak Ridge Associated Universities through Oak Ridge Institute for Science and Education under an agreement between FDA and the U.S. Department of Energy.
- *FDA/National Cancer Institute Inter-Agency Oncology Task Force (IOTF) Joint Fellowship Program* trains scientists in research and research-related regulatory review, policies, and regulations to develop a skill set that bridges the two disparate processes.
- *FDA-National Center for Advancing Translational Sciences (NCATS) Translational Science Inter-Agency Fellowship* aims to provide training in both translational science and regulatory science.
- *Pharmacy Student Experiential Program* provides an opportunity to learn about

FDA's multidisciplinary processes for addressing public health issues involving drugs, biologics, and medical devices. This program falls under the student volunteer service program (SVSP).

- *Joint Institute for Food Safety and Applied Nutrition (JIFSAN) Student Internship Program* provides various volunteer scientific opportunities in partnership with the University of Maryland.
- *Regulatory Pharmaceutical Fellowship* trains selected candidates in one of three tracks focused on the medical and regulatory aspects of drug information dissemination, drug advertising and promotion, or medication safety.
- *Tobacco Regulatory Science Fellowship* is designed for mid-career professionals to gain experience and expertise to further define and develop the field of regulatory science as it relates to the regulation of tobacco products and FDA's authorities under the Family Smoking Prevention and Tobacco Control Act.
- *Veterinary Clerkship Program* is designed to give fourth-year veterinary students a real-world opportunity to see how policies guiding the approval of new animal drugs are developed and implemented by FDA's Center for Veterinary Medicine.
- *Federal Information Privacy Internship Program* gives students an opportunity to learn about federal programs and policies with a focus on the application of privacy laws, regulations, and policies.
- *Interdisciplinary Toxicology Program* is a partnership between FDA's National Center for Toxicological Research and University of Arkansas for Medical Sciences (UAMS) located in Little Rock, Arkansas, as part of the UAMS Pharmacology and Toxicology Graduate Program.
- *Student Volunteer Service Program (SVSP)* is for students who are currently enrolled in an accredited educational institution seeking unpaid work experience or education-related training opportunities.
- *Oncology Center of Excellence Summer Scholars Program* is designed to expose high school students and recent high school graduates to the entire spectrum of oncology drug development and introduce career opportunities in government, regulatory medicine, and cancer advocacy.
- *Visiting Pediatric Pharmacology Fellows Rotation Program* promotes regulatory opportunities for individuals engaged in clinical pediatric pharmacology training and establishes formal outreach links to academic training programs.
- *Regenerative Medicine Fellowship* under the CBER Service Fellowship Program in the Office of Tissues and Advanced Therapies aims to enhance FDA's ability to regulate regenerative medicine products and support the development of highly trained scientists and engineers with unique multicenter experience.

21. Please describe the training that FDA medical product reviewers receive, including with respect to the review of products for rare diseases and regarding application review best practices.

CBER: New medical product reviewers are required to complete a standard

curriculum covering relevant courses for their discipline and their review responsibilities. In addition, reviewers typically attend foundational training including Biologics Law and a multiday interactive New Reviewer Training course on the regulatory review process for CBER-regulated products. This latter course incorporates case studies and group exercises to simulate the reviewer experience in diverse areas (e.g., toxicology; clinical; chemistry, manufacturing and controls, statistics, labeling, and pharmacovigilance). CBER's training program also offers specialized multiday courses such as Risk Management for Biologics and Risk Communication for Biologics. In addition, CBER has several ongoing courses and training series such a Review Management Updates, which typically covers regulatory policy updates and other seminar series specific to a variety of disciplines. CBER's training program also offers professional development courses to strengthen reviewers' skills in writing reviews and related documents and in preparing and giving presentations, and provides opportunities for formal mentoring and coaching, and leadership training.

CDRH: CDRH's Reviewer Certification Program (RCP) is a two-month training program for new medical device reviewers that consists of 38.5 hours of classroom and independent learning. In addition to new reviewer training via the RCP, CDRH offers additional training opportunities on new and modified regulations, guidance documents, policies, and procedures. CDRH's RCP and additional training opportunities cover a wide variety of device review topics, including application review best practices and the Humanitarian Device Exemption pathway for Humanitarian Use Devices intended to benefit patients in the treatment or diagnosis of a rare disease or condition.

CDER: CDER's new medical product reviewers are required to complete a standard 18-month curriculum covering relevant topics for their discipline and their review responsibilities, including topics in the regulatory review process for CDER-regulated products. This course incorporates case studies and group exercises to simulate the reviewer experience in a wide range of clinical, scientific, and regulatory areas. CDER's training program also offers professional development courses to strengthen skills in review writing, public speaking, and collaboration, and provides opportunities for formal mentoring, coaching, and leadership training.

Rare Diseases: CBER, CDER, CDRH, and the Office of Orphan Products Development collaborate to develop an annual day-long training course for review staff on drug development for rare diseases as a PDUFA V and VI commitment toward advancing development of drugs for rare diseases. FDA held the course for the eleventh time in 2021. Each year a team of staff from across FDA (led by CDER's Rare Diseases Team) develops the curriculum to ensure that it covers timely regulatory topics relevant to rare disease medical product development. Presentations typically include a legislative update, case studies of recent rare disease product approvals for CBER and CDER, overviews of collaborative efforts with stakeholders, and presentations by external guest speakers about key efforts.

The Honorable Richard Burr –

Other venues that provide opportunities for FDA review staff from all centers to learn more about development of medical products for rare diseases include the CDER-coordinated quarterly Rare Disease Seminars, which host outside experts on topics such as CRISPR and gene editing and Bayesian designed trials; Patient Listening Sessions, coordinated by the Office of Patient Affairs; and FDA-led and externally led Patient Focused Drug Development meetings. FDA-held public workshops focused on specific challenges and disease areas are open to FDA staff and are also an excellent venue for staff to learn from outside experts about current challenges and progress in rare disease product development (e.g., CBER-held public workshop on Facilitating End-to-End Development of Individualized Therapeutics on March 3, 2020).

Thank you again for contacting us regarding this matter. If you have any questions, please let us know.

Sincerely,

Kimberlee R. Trzeciak -S

Digitally signed by Kimberlee R. Trzeciak -S
Date: 2022.04.01 13:24:42 -04'00'

Kimberlee Trzeciak
Associate Commissioner for
Legislative Affairs

Attachments:
A, B, C, D, E, F.

The Honorable Richard Burr – Attachment A

1. **In aggregate, and broken down by FDA's major components, including each center, and each user fee program, as applicable, please provide the following information separately for each of fiscal years (FY) 2018 through 2022:**

   This table responds to the following items from your request. All figures in the table below report individual persons, rather than FTE:

   a. **Total employees (i.e., individual persons)**

   d. **Turnover rate**

   e. **Total number of new FTEs hired per year**

   f. **Total number of FTEs lost to attrition per year**

FDA Hiring and Attrition History, FY 2018 through FY 2022 (Individual Persons)

	FY 2018 As of 9/30/2018				FY 2019 As of 9/30/2019			
Center	**Onboard**	**Gains**	**Losses**	**Attrition**	**Onboard**	**Gains**	**Losses**	**Attrition**
CBER	1,083	119	88	7.8%	1,116	137	108	9.3%
CDER	5,043	508	358	6.9%	5,089	438	375	7.0%
CDRH	1,679	199	205	11.5%	1,699	209	187	10.4%
Total[1]	**7,805**	**650**	**699**	**9.0%**	**7,904**	**637**	**613**	**7.8%**

	FY 2020 As of 9/30/2020				FY 2021 As of 9/30/2021			
Center	**Onboard**	**Gains**	**Losses**	**Attrition**	**Onboard**	**Gains**	**Losses**	**Attrition**
CBER	1,122	120	104	9.0%	1,208	168	79	6.5%
CDER	5,283	491	321	5.9%	5,359	460	389	7.0%
CDRH	1,919	386	157	8.3%	1,963	233	202	9.7%
Total[1]	**8,324**	**1,118**	**529**	**6.4%**	**8,530**	**955**	**605**	**7.1%**

	FY 2022 As of 3/28/2022			
Center	**Onboard**	**Gains**	**Losses**	**Attrition**
CBER	1,205	31	40	N/A
CDER	5,331	139	173	N/A
CDRH	1,949	72	83	N/A
Total[1]	**8,485**	**249**	**349**	**N/A**

[1] Note: For gains and losses, individual center totals do not sum to combined CBER-CDER-CDRH totals. Internal FDA personnel movements from center to center are included in center-row gains and losses but excluded from overall totals.

The Honorable Richard Burr – Attachment B

1. **In aggregate, and broken down by FDA's major components, including each center, and each user fee program, as applicable, please provide the following information separately for each of fiscal years (FY) 2018 through 2022:**

   This table contains information on the following items from your request:

   b. Total Full-Time Equivalents (FTEs)

FTE Report by Center by User Fee Program

FY 2018					
Center	**PDUFA**	**MDUFA**	**GDUFA**	**BsUFA**	**Total**
CBER	791	155	1	1	948
CDRH	25	1,386			1,411
CDER	3,110		1,660	186	4,956
Total	3,926	1,541	1,661	187	7,315

FY 2019					
Center	**PDUFA**	**MDUFA**	**GDUFA**	**BsUFA**	**Total**
CBER	857	153	2	2	1,014
CDRH	20	1,381			1,401
CDER	3,103		1,613	163	4,879
Total	3,980	1,534	1,615	165	7,294

FY 2020[1]					
Center	**PDUFA**	**MDUFA**	**GDUFA**	**BsUFA**	**Total**
CBER	835	137	2	1	975
CDRH	23	1,136			1,159
CDER	3,055		1,689	117	4,861
Total	3,913	1,273	1,691	118	6,995

FY 2021[1]					
Center	**PDUFA**	**MDUFA**	**GDUFA**	**BsUFA**	**Total**
CBER	893	124	2	1	1,020
CDRH	25	1,365			1,390
CDER	3,119		1,692	138	4,949
Total	4,037	1,489	1,694	139	7,359

Sources: FY 2021 PDUFA Financial Report, table 9; FY 2021 MDUFA Financial Report, table 9; FY 2021 GDUFA Financial Report, table 9; FY 2021 BsUFA Financial Report, table 9.

[1]Redirecting FDA's resources to respond to COVID-19 reduced resources available to support the user fee processes in FY 2020 and FY 2021.

The Honorable Richard Burr – Attachment C

1. **In aggregate, and broken down by FDA's major components, including each center, and each user fee program, as applicable, please provide the following information separately for each of fiscal years (FY) 2018 through 2022:**

   This table contains information on the following items from your request:

   c. Total vacancies, delineating between vacancies funded by user fees or Congressional appropriations

Vacancies by User Fee Program and Budget Authority					
Center	**FY 2018 Vacancies**	**FY 2019 Vacancies**	**FY 2020 Vacancies**	**FY 2021 Vacancies**	**FY 2022 Vacancies**
CBER[1]	**166**	**147**	**190**	**155**	**153**
Budget Authority	81	67	89	70	69
PDUFA	79	74	91	77	76
MDUFA	6	6	10	8	8
CDER[2]	**N/A**	**N/A**	**119**	**136**	**361**
Budget Authority			60	37	94
PDUFA			41	46	184
GDUFA			16	24	60
BsUFA			2	29	23
CDRH[3]	**295**	**352**	**235**	**193**	**221**

[1] CBER vacancies are as of the end of the fiscal year for FY 2018 through FY 2020, as of September 13, 2021, for FY 2021, and as of March 25, 2022, for FY 2022.

[2] FY 2018 and FY 2019 data are not available for CDER. FY 2020 through FY 2022 figures are funded vacancies minus actual hiring. Expected attrition is built into the FY 2022 vacancy count.

[3] CDRH vacancies are as of the end of the fiscal year for FY 2018 through FY 2021 and as of March 2022 for FY 2022. CDRH vacancies are a mix of funding types (budget authority, user fee programs) and are therefore reported as overall totals.

2. In a 2018 report, FDA estimated that 13% of its work force was eligible for retirement in 2017, and that half of the agency's senior leadership would be eligible for retirement by 2020. Broken down by FDA center and user fee program, as applicable, please provide the following:

a. Total number and percentage of employees currently eligible for retirement

Center	% Retirement Eligible (All Employees)	Count of Retirement Eligible (All Employees)
CBER	21.2%	256
CDER	14.3%	766
CDRH	13.5%	262
CFSAN	20.9%	230
CTP	6.2%	68
CVM	15.5%	105
NCTR	23.2%	67
OC	14.5%	117
OO	18.2%	281
ORA	15.4%	752
FDA-Total (All Employees)	**15.4%**	**2,904**

b. Total number and percentage of senior leadership eligible for retirement

Center	% Retirement Eligible (Senior Leadership)	Count of Retirement Eligible (Senior Leadership)
CBER	70.0%	7
CDER	31.5%	17
CDRH	23.5%	4
CFSAN	53.8%	7
CTP	28.6%	2
CVM	33.3%	2
NCTR	50.0%	1
OC	29.0%	9
OO	11.1%	2
ORA	42.3%	11
FDA-Total (Senior Leaders)	**33.5%**	**62**

12. In April 2021, the Office of Personnel Management released a detailed summary of the government-wide results of the 2020 Federal Employee Viewpoint Survey (FEVS) across all federal agencies.

a. Can you please provide a summary of the FEVS results for FDA employees (i.e., a summary similar to the government-wide report published by OPM, but specific to FDA)?

b. Understanding that the 2021 FEVS is currently being administered, please provide the date by which you will provide the same FDA-specific summary for the 2021 survey.

2021 FEVS FDA-wide Summary Results Report

Response Rate:

The 2021 Federal Employee Viewpoint Survey (FEVS) was administered between November 8 and December 10, 2021. FDA's response rate was **50.1%** and was slightly higher than the HHS-wide response rate of 48.9%. FDA's 2021 FEVS results are highly representative of the full FDA workforce with very low margin of error.

Belief in Action:

In the 2021 FEVS, just under two-thirds (**61%**) of respondents agreed with the statement "*I believe the results of this survey will be used to make my agency a better place to work.*" This result was the same for the 2020 FEVS.

Employee Engagement Index:

The Employee Engagement Index did not change from 2020 to 2021. This index remains at **80%** and three percentage points above HHS as a whole (77%).

Global Satisfaction Index:

The Global Satisfaction Index (GSI) decreased slightly from 77% in 2020 to **75%** in 2021. The GSI consists of three individual FEVS items: Considering everything, how satisfied are you with 1.) your job? 2.) your pay? 3.) Your organization? FDA's 2021 GSI is three percentage points above HHS as a whole (72%).

Performance Confidence Index:

For the 2021 FEVS, the Office of Personnel Management introduced a new index called the "Performance Confidence Index" (PCI). The PCI is a combination of five new items assessing employees' perception of their work unit's ability to achieve goals and produce work at a high level. The PCI is defined as "The extent to which employees believe their organization has an outstanding competitive future, based on innovative, high quality products and services that are highly regarded by the marketplace." FDA's 2021 PCI is **93%** and is three points above HHS as a whole. Although formally introduced in 2021, all PCI items appeared on the 2020 FEVS. No change occurred between the 2020 PCI and 2021 PCI.

The Honorable Richard Burr – Attachment E

2021 FEVS Top 5 Individual Items:

	% Positive
Q15 - Employees in my work unit contribute positively to my agency's performance.	95%
Q14 - Employees in my work unit meet the needs of our customers.	94%
Q19 - Employees in my work unit achieve our goals.	93%
Q16 - Employees in my work unit produce high-quality work.	93%
Q7 - I know how my work relates to the agency's goals.	92%

2021 FEVS Bottom 5 Individual Items:

	% Positive
Q10 - In my work unit, steps are taken to deal with a poor performer who cannot or will not improve.	52%
Q5 - My workload is reasonable.	59%
Q24 - I believe the results of this survey will be used to make my agency a better place to work.	61%
Q12 - In my work unit, differences in performance are recognized in a meaningful way.	61%
Q32 - In my organization, senior leaders generate high levels of motivation and commitment in the workforce.	64%

Largest positive shifts from 2020 to 2021:

	2021	2020	Change
Q8 - I can disclose a suspected violation of any law, rule or regulation without fear of reprisal.	75%	71%	+4%
Q33 - My organization's senior leaders maintain high standards of honesty and integrity.	73%	70%	+4%
Q10 - In my work unit, steps are taken to deal with a poor performer who cannot or will not improve.	52%	48%	+3%
Q22 - My agency is successful at accomplishing its mission.	91%	89%	+2%
Q14 - Employees in my work unit meet the needs of our customers.	94%	92%	+2%

Largest negative shifts from 2020 to 2021:

	2021	2020	Change
Q5 - My workload is reasonable.	59%	66%	-7%
Q17 - Employees in my work unit adapt to changing priorities.	89%	94%	-5%
Q18 - Employees in my work unit successfully collaborate.	87%	91%	-4%
Q43 - Considering everything, how satisfied are you with your pay?	65%	68%	-3%
Q38 - Senior leaders demonstrate support for Work-Life programs.	77%	80%	-3%

COVID Leadership 2020 to 2021 changes:

	2021	2020	Change
48 - My organization's senior leaders demonstrate commitment to employee health and safety.	88%	93%	-5%
49 - My organization's senior leaders support policies and procedures to protect employee health and safety.	88%	93%	-5%
50 - My organization's senior leaders provide effective communications about what to expect with the return to the physical worksite.	68%	N/A	N/A
51 - My supervisor shows concern for my health and safety.	92%	92%	0%
52 - My supervisor supports my efforts to stay healthy and safe while working.	91%	93%	-2%
53 - My supervisor creates an environment where I can voice my concerns about staying healthy and safe.	88%	89%	-1%
54 - Does the type of work you do require you to be physically present at a worksite (e.g., border patrol agent, TSA agent, meat inspector)?	11%	9%	+2%
55 - My agency's leadership updates employees about return to the worksite planning.	83%	NA	N/A
56 - In plans to return more employees to the worksite, my organization has made employee safety a top priority.	77%	87%	-10%
57 - Based on my organization's handling of the COVID-19 pandemic, I believe my organization will respond effectively to future emergenci	84%	86%	-2%

The Honorable Richard Burr – Attachment F

19. Related to the flexible hiring authorities that Congress granted FDA in the 21st Century Cures Act:

c. In a 2018 report on the implementation of the 21st Century Cures Act, FDA noted that it had classified 38 occupations as eligible for those authorities. Has FDA updated this list? Could you please provide the list of occupations eligible for these authorities?

As of September 3, 2021, FDA has 52 job series classified as eligible for Cures positions. The statement of duties must demonstrate that the position meets Cures eligibility criteria.

Professional Series			
0101	Social Science	0855	Electronics Engineering
0110	Economist	0858	Bioengineering and Biomedical Engineering
0131	International Relations	0893	Chemical Engineering
0301	Miscellaneous Administration and Program	0905	General Attorney
0340	Program Management	1001	General Arts and Information
0341	Administrative Officer	1515	Operations Research
0343	Management and Program Analyst	1520	Mathematics
0505	Financial Management	1529	Mathematical Statistics
0560	Budget Analysis	1530	Statistics
0685	Public Health Program Specialist	1550	Computer Science
0801	General Engineering	1701	General Education and Training
0806	Materials Engineering	1712	Training Instruction
0830	Mechanical Engineering	1811	Criminal Investigation
0850	Electrical Engineering	1910	Quality Assurance
0854	Computer Engineering	2210	Information Technology Management
Scientific Series			
0401	General Natural Resources Management and Biological Sciences	0660	Pharmacy
0403	Microbiology	0662	Optometry
0405	Pharmacology	0665	Speech/Language Pathology and Audiology
0413	Physiology	0668	Podiatry
0415	Toxicology	0680	Dentistry
0440	Genetics	0696	Consumer Safety
0487	Animal Science	0701	Veterinary Medical Science
0601	General Medical and Healthcare	1301	General Physical Science
0602	Physician	1306	Health Physics
0610	Nursing	1310	Physics
0644	Clinical Laboratory Science	1320	Chemistry

February 01, 2022

Ranking Member Richard Burr
Committee on Health, Education, Labor, and Pension
United States Senate
Washington, D.C. 20510

Dear Senator Burr:

Thank you for your letters of September 22, 2021, and November 18, 2021, and your continued engagement regarding the medical device user fee program and the ongoing negotiations for the next reauthorization of the Medical Device User Fee Amendments (MDUFA) for fiscal years (FY) 2023 through 2027. As discussed, when we briefed you and your staff on October 20, 2021, we share the goal of maintaining a strong user fee agreement that supports innovation and safety, both of which are necessary to assure patients in the United States have timely access to the safe and effective medical devices they depend upon to improve and extend their lives. The Food and Drug Administration's (FDA or the Agency) Center for Devices and Radiological Health (CDRH) remains committed to assuring that innovators continue to bring new advances to the United States and continues working to better position this nation to enable patients to have access to more innovative and better performing devices – and therefore more options – than at any other time in our history.

Reauthorization of the MDUFA program comes at a pivotal time for the device ecosystem. We seek to continually improve our effectiveness in fulfilling our public health mission, by planning strategically and regularly monitoring our progress, facilitated, in large, by strong MDFUA agreements.

- FDA approved, cleared, or authorized a record high of 132 novel medical devices in 2020, surpassing the 40-year high mark set in 2018.[1]
    - This is a marked increase from the 29 novel devices FDA authorized in 2010.
- Since the beginning of FY2018, FDA has granted over 500 breakthrough designation requests, and has approved, authorized, or cleared 23 breakthrough devices through the Premarket Approval (PMA), De Novo classification request ("De Novo"), or premarket notification (510(k)) pathways.[2]
- FDA reduced the median time it takes to approve an Investigational Device Exemption (IDE) application by more than one year, from 442 days in FY2011 to 30 days in FY2015 and remained at 30 days each subsequent year through FY2020.

[1] *Reflections on a Record Year for Novel Device Innovation Despite COVID-19 Challenges | FDA*
[2] *Reflections on a Record Year for Novel Device Innovation Despite COVID-19 Challenges | FDA*

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- The number of approved early feasibility studies in the United States, where devices are evaluated early in development, more than doubled – from 21 in FY2014 to 49 in FY2020.
- 62 percent of novel technology manufacturers intend to bring their devices to the United States first or in parallel with other major markets.[3]

The device ecosystem is experiencing some of its greatest challenges. The first emergency use authorizations (EUAs) issued for the COVID-19 public health emergency (PHE) were for medical devices. As innovators across the device ecosystem mounted a remarkable response, the volume of EUA requests quickly surpassed (by several orders of magnitude) that of any prior PHE or situation. FDA engaged in an unprecedented effort to engage with sponsors from the outset, to provide regulatory flexibility where appropriate, and to handle the influx of EUA submissions along with a simultaneously increasing volume MDUFA work. In doing so, FDA contended with a workload that far exceeded our capacity.

Through the progress we have made and the challenges we continue to face during the pandemic, it has become even more clear how important medical devices are to patients and our health care providers – and to our health care system as a whole. MDUFA supports both FDA's capacity to assess new medical device technologies and provide a predictable, transparent path to market, which will ultimately lead to patients having timely access to new devices. FDA set clear goals for our current MDUFA negotiations, focusing on enhancing operational success of the program, reducing device development times and accelerating patient access to safe and effective devices, optimizing FDA's infrastructure to provide stronger support for premarket activities, and improving medical device safety. We are committed to continuing to make progress in the ongoing negotiations.

Thank you again for the opportunity to continue discussion on this important program. We appreciate the chance to address your questions and have restated them in bold below, followed by our responses.

1. Q: How many Full Time Equivalents (FTEs) are funded under the MDUFA program?

As noted during the October 20th briefing with your staff, we believe this question is requesting information related to "FTE burn" or the number of "FTE utilized" as part of the MDUFA program. MDUFA Process FTEs represent a paid staff year devoted to the MDUFA program, not individual staff members, and this metric reflects the amount of MDUFA process work that is performed each year, excluding overtime hours worked. As reported in the FY2020 Financial Report, the number of FTE utilized by the MDUFA program during MDUFA IV is:

- FY2018, a total of 1,711 FTE.
- FY2019, a total of 1,692 FTE.
- FY2020, a total of 1,399 FTE.

[3] *Based on an 87% response rate from companies contacted about novel technology devices between 2018 and 2020, 62% of companies intended to bring their devices to the United States first or in parallel with other major markets by December 31, 2021:* CDRH 2016-2017 Strategic Priorities (fda.gov).

– The Honorable Richard Burr

Throughout the current negotiations with industry, we continue to work to better explain our process for calculating resource needs as a function of hours of time needed for MDUFA process work, which we convert into the equivalent of a paid staff year. To enhance transparency and industry's understanding, FDA has proposed that MDUFA V include funding for a qualified, independent contractor to assess FDA's hiring and retention of staff that conduct MDUFA process work, and related questions.

2. **Q: On average, how many FTEs are needed to review PMA submissions, De Novo submissions, 510(k) submissions? Please provide the number of FTEs per submission type.**

FDA provided the data requested below, with an explanation of how we calculated the numbers.

First, the figures in the table below represent three-year averages, and the number of hours spent reviewing these submissions varies depending on complexity. The number of hours CDRH spends reviewing a premarket submission for complex, novel technology, for instance, will likely vary from the number of hours spent reviewing a premarket submission for more well-established technology. Even within a category such as 510(k)s, where a device is evaluated in comparison to a predicate, the complexity of technology and other factors can impact the hours CDRH needs to review and determine if the submission meets the standard to be cleared, and we see variability.

Second, we calculated these averages using data from FY2019-2021, based on hours reported per submission decision in our time reporting data. We then converted the number of hours into our FTE model to create an approximate number of FTEs per submission.

We also note that these averages reflect device submission decisions by CDRH, not including CBER, given the comparatively small volume of CBER-reviewed device submissions and that FDA centers have different time reporting systems.

Lastly, this time reflects hours spent in substantive review of the devices, required to determine whether they meet the standard to be approved, cleared, or authorized. It does not include some of the steps required to complete review of a submission, such as management. Based on these calculations, the average number of FTEs per submission for each of the submission types listed is:

Submission Type	Average Hours Per Submission	FTE/submission
PMA Original and Panel Track Supplements	1,890 hours	1.18
De Novos	821 hours	0.51
510(k)s	104 hours	0.06

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3. Q: What is the average cost of a MDUFA FTE? Please provide a breakdown of costs associated with a MDUFA FTE.

A MDUFA FTE does not equate to an individual employee, but we have detailed data on FDA's methodology for the fully-loaded cost per FTE for MDUFA. For FY2023, we project the fully loaded costs to be $299,329. The methodology starts with FY2019 actuals as the base and relies on the standard inflation adjustment to project the costs in FY2023 dollars.

The MDUFA fully loaded cost for FY2023 reflects the following sub-components:

Category	Amount
Pay Costs	$180,000
Non-Pay Costs	$95,385
Rent	$23,944
Total	*$299,329*

This figure underestimates true FTE costs to FDA. Use of the 21st Century Cures Act (Cures Act) pay authority enabled FDA to be more competitive in hiring and maintaining qualified personnel and to compensate highly qualified employees at a rate more comparable to pay in the private sectors. Since the pay costs in the fully-loaded cost per FTE are based on actual pay costs in FY2019, they do not reflect CDRH's higher payroll costs due to the use of Cures pay authority, since CDRH's use of the Cures Act pay authority increased beginning in FY2020.

4. Q: How many user fee dollars go towards a MDUFA FTE?

The information in the table below – from the FY2020 MDUFA Financial Report – breaks down the amount of MDUFA user fee obligations for payroll and operating expenses, excluding costs associated with rent and shared services. These obligations provide for payroll and operating costs that support the allowable activities for which MDUFA fees may be expended, as set forth in the statute. Total payroll and operating expenses paid for from MDUFA user fees in FY2020 were $ 170,074,845, excluding rent and shared services. A further breakdown is reflected in Table 5 of the FY2020 Financial Report.[4]

	FY2019	FY2020
CDRH	$ 95,706,387	$ 149,591,477
CBER	$ 11,145,127	$ 11,006,994
ORA	$ 1,639,099	$ 2,124,606
HQ	$ 6,991,017	$ 7,351,768
Total	*$ 115,481,630*	*$ 170,074,845*

[4] *https://www.fda.gov/media/150381/download*

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5. Q: The August 3, 2021 quarterly performance report includes data that FDA has received and accepted more than 2,100 510(k) submissions in FY21 and has reviewed 88.45% of such submissions within 90 days. According to the MDUFA IV commitment letter, FDA has a goal of reviewing 95% of such submissions within 90 days.

Does FDA plan to meet this commitment by the end of this MDUFA cycle?

We assume "the end of this MDUFA cycle" to be inquiring whether FDA expects to achieve this review goal for FY2021. FDA has received 3,985 510(k) submission in FY2021. This is the highest number of submissions we have received in the past 15 years. Approximately, 95% of submissions ultimately get accepted. Each time a submission is not accepted, a firm has 180 days to provide the necessary information to become accepted. This time, along with FDA's 90 days of review time, as well as any industry hold time does not allow us to determine if we met the review goal until approximately two years from the beginning of the fiscal year. At this point it is not likely that FDA will achieve the FY 2021 review goal.

Meeting this commitment, like all MDUFA commitments, remains our goal and we are taking critical steps to improve performance relative to the FY2021 cohort. As you are aware, CDRH's workload was unexpectedly and dramatically impacted by COVID-19. For CDRH, this work began in January 2020 – two months before a global pandemic was declared – and the Center saw an unprecedented level of EUA submissions for devices, including tests, ventilators, personal protective equipment (PPE), and other devices. We prioritized that work, while still striving to meet our MDUFA goals. We are now transitioning to pre-pandemic review times, and expect to see improvements in MDUFA review performance as we transition beyond the pandemic. Additional information about CDRH's actions to address the large increase in work volume can be found in an FDA Voice Blog, A Year Into the Pandemic: How the FDA's Center for Devices and Radiological Health is Prioritizing its Workload and Looking Ahead (April 15, 2021).[5]

How does FDA plan to meet the 95% review goal by the end of this MDUFA cycle?

As described in the FDA Voice blog, we have been transparent about impacts of the unprecedented volume of COVID-19 work on CDRH, and quickly developed a plan for how to address the MDUFA submissions affected by the PHE. As of June 2021, the Center had all MDUFA marketing submissions under active review. We are now transitioning to pre-pandemic review times and expect to see improvements in our review performance overall.

If FDA does not meet this commitment, will the agency provide a refund or otherwise factor in this unmet commitment as part of MDUFA V?

As a threshold matter, the MDUFA IV commitment letter, like the commitment letters for the other medical product user fee programs, provides the basis for financial arrangements relating to user fees and does not contemplate refunds when a single commitment is not met, or in this instance, may not be met for a sub-portion of the MDUFA IV period. More fundamentally, even

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[5] *A Year Into the Pandemic: How the FDA's Center for Devices and Radiological Health is Prioritizing its Workload and Looking Ahead | FDA*

– The Honorable Richard Burr

if FDA does not achieve a particular premarket review goal, our staff are working diligently to review those submissions as efficiently as possible. Further, if FDA misses specific goals relative to review timelines, that it is likely a function of FDA being under-resourced relative to the workload, which would render refunds counterproductive. Finally, in the context of the COVID-19 pandemic, since reduced performance on certain review goals was a direct result of the agency prioritizing pandemic response work, FDA is concerned that considering a refund would be effectively penalizing CDRH's efforts to respond to COVID-19.

FDA does consider the performance of user fee commitments a key factor in the next reauthorization cycle. We are actively discussing with industry what level of performance can be achieved with potential MDUFA V resources, considering our experience in MDUFA IV.

6. The MDUFA IV goal letter included a commitment to publish final guidance related to submissions for software modifications.

When does FDA expect to publish this final guidance?

Please note that FDA met the commitment to publish final guidance related to submissions for software modifications in October 2017.[6]

The Agency assumes this question refers to the commitment regarding exploring the Software Pre-certification approach, and work on novel digital health technologies, including publishing a revised draft version of the "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" (referred to in short as the "Premarket Software guidance"). FDA published this draft guidance on November 4, 2021.

After finalizing the MDUFA IV Commitment Letter and through our work to operationalize the digital health program, FDA determined that issuance of the other guidances was a necessary prerequisite to issuing the Premarket Software guidance. In doing so, FDA needed time to solicit public input to inform our policy development, including providing time for public comment on the other guidances. Many of these actions were not specified in the commitment letter but were important for meeting the spirit of the commitment letter, to "streamline and align FDA review processes with software lifecycles for Software as a Medical Device (SaMD) and software inside of medical devices (SiMD)," and to "take into account real world evidence while incorporating principles established through international harmonization." As a result, FDA took many additional actions to fulfill this commitment,[7] including:

- Clarifying policy changes resulting from Section 3060 of the 21st Century Cures Act,[8]
- Piloting a Digital Health Software Pre-Certification Program,
- Actively engaging with stakeholders from industry, researchers, patient advocacy organizations, and others, including by posting four discussion papers on pre-certification

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[6] *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-software-change-existing-device*

[7] *FDA summarized these actions and provided links to relevant material online in the FY2019 MDUFA Performance Report to Congress (https://www.fda.gov/media/139848/download). See pages E-7 through E-10. In addition, FDA provides an overview of all its work related to the Pre-Cert program here: https://www.fda.gov/medical-devices/digital-health-center-excellence/digital-health-software-precertification-pre-cert-program.*

[8] *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/changes-existing-medical-software-policies-resulting-section-3060-21st-century-cures-act*

and artificial intelligence/machine learning (AI/ML) with open public comment periods, publishing two updated discussion papers which incorporated public input, holding numerous stakeholder calls, webinars, and participation in numerous conference presentations and panel discussions,
- Hosting a public workshop in 2018, and
- Publishing seven final and one draft guidance related to software and novel digital health technologies. [9]

FDA understands the importance of meeting these and other commitments. The Agency is also committed to assuring our nation's health care system recognizes the promise of digital health technologies and assuring that safe, new innovations are brought here to the U.S. and reach patients as quickly possible. FDA established the Digital Health Center of Excellence, to connect and build partnerships, share knowledge and best practices, and innovate regulatory approaches. Recent highlights include publishing an AI/ML-Based Software Action Plan,[10] posting a list of AI/ML-enabled medical devices marketed in the United States,[11] hosting a virtual public workshop on transparency of AI/ML-enabled devices,[12] and participating in four Collaborative Communities with digital health-related work.[13]

If FDA is not able to meet this commitment before the end of FY22, will the agency provide a refund or otherwise factor in this unmet commitment as part of MDUFA V?

FDA expects to fulfill this unmet commitment before the end of the MDUFA IV period. Regardless, FDA would not intend to issue refunds for our digital health commitments (as we discuss further in response to Question 5). CDRH's overall performance in this area exceeded what was contemplated by the Commitment Letter (as noted above).

7. **The MDUFA IV goal letter included a commitment that "all deficiency letters will include a statement of the basis for the deficiencies." According to the March 17 meeting minutes, FDA provided statements on the basis of the deficiency for 25% of the deficiency letters issued in FY19, and 50% of letters issued in FY20.**

   For deficiency letters issued in FY21, how many has FDA provided a statement of the basis for deficiency?

The data for FY2021 comes from the independent assessment conducted by an independent contractor (Booz Allen Hamilton), which assessed deficiencies in several ways. When assessing FDA's performance according to criteria most consistent with the commitment letter language, the independent contractor found that FDA's letters included a statement of the basis for the deficiency 93 percent of the time for both PMAs and De Novos. When using a more stringent

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[9] https://www.fda.gov/medical-devices/digital-health-center-excellence/guidances-digital-health-content
[10] https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-software-medical-device
[11] https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-aiml-enabled-medical-devices
[12] https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/virtual-public-workshop-transparency-artificial-intelligencemachine-learning-enabled-medical-devices
[13] Digital Health Measurement Collaborative Community http://datacc.dimesociety.org/, Ophthalmic Imaging Collaborative Community https://www.cc-oi.org/, Pathology Innovation Collaborative Community https://mdic.org/program/picc/, Xavier AI World Team https://www.xavierhealth.org/ai-overview

interpretation of FDA's deficiency policy, which FDA developed with a goal of driving continuous process improvements and which is stricter than the commitment letter language, the independent contractor found that FDA's letters met the criteria 69 percent of the time among the De Novos, and 48 percent of the time among the PMAs.[14]

The independent contractor's report further noted there are "challenges interpreting and/or applying the existing criteria". Among the MDUFA IV commitments, FDA agreed to incorporate findings and recommendations of the independent assessment, as appropriate, into our management of the premarket review process. We are in the process of evaluating how the assessment's findings related to deficiency letters should be incorporated into future process improvements, and are engaged in technical negotiations with industry about potential commitments on this topic as part of MDUFA V.

The March 17 meeting minutes also note there is a disagreement on whether the MDUFA IV commitment was to provide a statement of the basis for deficiencies for "all deficiency letters" meant 100% of letters – will FDA and industry clarify this commitment and the metrics by which this commitment will be met as part of MDUFA V?

FDA notes that the Independent Assessment concluded that the MDUFA IV commitment was to publish an update to FDA's guidance on deficiencies to reflect that deficiency letters should include a statement of basis and to undergo supervisory review, train staff and managers on the updated guidance, and complete one internal deficiency letter audit. The Independent Assessment concluded that FDA met these commitments (Section 4.5.6, page 43).[15]

However, we understand there has been ambiguity regarding commitments in the MDUFA IV Commitment Letter, and take any differences of interpretation as an opportunity to improve mutual understanding in MDUFA V.

We are also committed to assuring our evidentiary requirements are transparent so that sponsors will better understand the evidentiary requirements to meet FDA's review standards, to enhance the quality of medical device submissions to, ideally, have far fewer submissions subject to deficiency letters and denials over time.

8. MDUFA IV provided funding for FTE positions at the FDA.

How many FTE positions funded under MDUFA IV are currently filled?

As part of MDUFA IV, FDA received funding for 217 new FTEs. To enable CDRH to track the progress in hiring new staff, the Center implemented a new position tracking system and designated 217 positions as "MDUFA IV hires." CDRH filled all 217 new MDUFA IV positions as of the end of FY2021. As of the end of FY2021, 204 of these positions were encumbered, meaning the position was currently occupied by a CDRH employee, and 13 were vacant due to

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[14] *Please note that the assessment referred to in the March 17th meeting minutes was an internal CDRH audit of performance related to 510(k) submissions, so the assessment conducted by the independent contractor should not be used for a year-over-year comparison.*
[15] *https://www.fda.gov/media/152594/download*

attrition, meaning we had filled the position one or more times but that we were in the process of re-filling the position as of September 30th.

By way of context, please note that FDA does not use the term "FTE position," but rather "full time equivalent (FTE)" or "position." The term "FTE" means the equivalent of a paid staff year devoted to the MDUFA program. The term does not track individual people, but rather the number of labor hours expended on MDUFA activities. This mechanism is used to measure the amount of work performed on the MDUFA program each year, as reported in FDA's annual MDUFA Financial Reports, and it is used as part of MDUFA negotiations to estimate future staff resources that will be needed to perform MDUFA process work. Ultimately, individual salaries for CDRH employees (as well as those employees in the other parts of the Agency that perform MDUFA process work) are funded by a combination of non-user-fee appropriations and user fees.

How many FTE positions funded under MDUFA IV are currently vacant?'

As of the end of FY2021, 13 new MDUFA IV positions were vacant due to attrition, meaning one or more hires filled the position but that, at the September 30th snapshot, the position was not encumbered.

Are any FTE positions funded by MDUFA I, II, or III currently vacant? If so, how many?

Prior to MDUFA IV, CDRH did not tag positions as being related to new user fee funds, so we can't answer the precise question. When we updated your staff on June 24th, we provided the total number of vacancies CDRH-wide. Using that same methodology, as of the end of FY2021, CDRH had 193 total vacancies Center-wide. Not all of these vacancies are associated with submission review or in offices that perform such functions.

Please note these positions – and thus, vacancies – are not designated by one funding type (e.g., non-user fee appropriations, user fees). This is because we rely on the FTE system to attribute hours to the MDUFA program, as explained above. During negotiations for the MDUFA V reauthorization, industry has made clear that it is important for CDRH to have the ability to identify positions, and vacancies, as "MDUFA-funded." We understand the value of providing greater transparency about how user fees translate into staffing levels, so FDA has proposed that MDUFA V include funding for a qualified, independent contractor to assess our hiring and retention of staff that conduct MDUFA process work. The details of this proposal are still the subject of ongoing technical negotiations, but we believe such a mechanism would help address this concern and could further enhance FDA's tracking for the MDUFA program overall.

9. For any commitments that FDA is not able to meet before the end of FY22, will the agency provide a refund or otherwise factor in such unmet commitments as part of MDUFA V?

FDA is considering how to factor in any unmet commitments as part of MDUFA V, but is not contemplating refunds. We understand the importance of fulfilling our commitments and have a

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solid track record of meeting nearly all of them, including many cases where we have exceeded those commitments. We are also transparent about our progress towards meeting these goals, holding quarterly meetings with industry to update them and highlighting areas where we believe we may fall short, when we determine that is a possibility.

Section 904 of the FDA Reauthorization Act of 2017 (FDARA), codified at section 738A(a)(2) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), requires FDA to issue a corrective action report to the Senate Committee on Health, Education, Labor and Pensions (and others) that details FDA's progress in meeting the review and performance enhancement goals identified in MDUFA IV for the applicable fiscal year. If the Secretary determines, based on the analysis presented in the MDUFA annual report, that any review or performance enhancement goals for the applicable fiscal year were not met, the corrective action report must include a justification, including a summary of the circumstances and trends that contributed to missed review goal times. With respect to performance enhancement goals that were not met, FDA must provide a description of the efforts FDA has put in place to improve the ability of the Agency to meet each goal in the coming fiscal year. Though such a description of corrective efforts is not required by statute for review time goals, FDA nonetheless provides this information in an effort to be complete. We take these obligations seriously and as indicative of Congressional expectations that FDA will take actions to address missed commitments.

Please note there are some situations in which CDRH's workload is higher than anticipated in our resource projections. In such cases, to meet our commitments, the Center may need additional resources. As a general matter, the MDUFA V agreement builds off of the prior experience of program, particularly the previous user fee agreement. It is our experience that meeting our UFA commitments – both positive as well as potentially unmet commitments – factor prominently into the negotiations of the current agreement.

As previously discussed, FDA would not intend to issue refunds for unfulfilled commitments – if any – where such refunds were not contemplated by the agreement (including the statute), where FDA still performed all the work contemplated by the commitment, or where further reducing resources to the Agency would be counterproductive in terms of achieving the shared goals of industry and FDA.

10. Will FDA and industry revise any unclear commitments included in MDUFA IV or otherwise ensure that MDUFA V includes clear, concise commitments in order to avoid confusion and future disagreements over whether commitments have been met for the next review cycle?

Yes, FDA and industry are actively considering how to ensure that MDUFA V contains clear and concise commitments that are understood by both parties as well as all stakeholders. We note that the Independent Assessment was able to audit performance across all dimensions of the commitment letter and found no areas where it was unable to audit performance due to ambiguity. That said, we always learn lessons from prior agreements, and we are applying those as we continue our negotiations, in an effort to produce an even more clear and more concise commitment letter for MDUFA V.

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11. According to meeting minutes, FDA has proposed a new program for MDUFA V, the Total Product Life Cycle Advisory Program.

What statutory authorities provide FDA the authority to create and implement this proposed new program? Please provide the specific sections of the Federal Food, Drug, and Cosmetic Act providing this authority.

Please note that the Total Product Life Cycle Advisory Program (TAP) proposal is still subject to ongoing technical negotiations. Both industry and FDA have put forward funding proposals that are inclusive of resources for TAP to be implemented as a pilot program. Based on the current state of negotiations, we expect that implementation of a TAP pilot generally would fall within the current scope of MDUFA process activities, as defined in section 737 of the FD&C Act. More specifically, we expect that activities contemplated by the TAP pilot proposal would fall within the definition of "process for the review of device applications" as described in section 737(9) of the FD&C Act, particularly paragraphs A, E, F, H, I, J and K, and we are evaluating whether any changes to section 737(9) would be needed to use fees to support aspects of the TAP pilot. FDA's statutory authority for the breakthrough devices program, as well as FDA's premarket review authorities for devices, also support aspects of the pilot.

The underlying concepts for the TAP program are not new and aim to address issues that we know you are particularly concerned with – namely assuring that device developers have a clear, predictable path to market such that patients have timely access to new devices. Avoiding pitfalls in early product development can better ensure devices actually reach patients and that, ultimately, there is a clear, predictable path to market from development to bedside, to continue to foster the innovation pipeline.

The goal of TAP is to enable faster patient access to safe and effective devices by applying lessons learned from our experience with existing Center efforts — including:

- how we interacted with developers during the COVID-19 response,[16]
- our existing structure for "sprints" for breakthrough devices,[17]
- our model for providing rapid responses to inquiries related to digital health technologies,[18]
- our experience working with other stakeholders such as patients[19] and payers[20] to provide input to device developers, and
- our activities to support medical device innovators.[21]

We appreciate that the TAP program may not be the right approach for every device, but there is tremendous value in de-risking the development process for novel products—such as devices that are designated as breakthrough or qualify for our Safer Technologies program. Because we

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[16] *https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/center-devices-and-radiological-healths-response-coronavirus-covid-19-infographic*
[17] *https://www.fda.gov/medical-devices/how-study-and-market-your-device/breakthrough-devices-program*
[18] *See page 60: https://www.fda.gov/media/152594/download*
[19] *https://www.fda.gov/about-fda/center-devices-and-radiological-health/cdrh-patient-science-and-engagement-program*
[20] *https://www.fda.gov/about-fda/cdrh-innovation/payor-communication-task-force*
[21] *https://www.fda.gov/about-fda/cdrh-innovation/activities-support-medical-device-innovators*

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are still negotiating with industry about the contours of a potential, voluntary TAP pilot, we will continue to evaluate this question as we move forward.

How many resources does FDA estimate this proposed new program will cost? Please provide both dollars and number of FTEs.

This is a topic of the ongoing negotiations. Both FDA and industry have put forward proposals to resource the TPLC Advisory Program. FDA believes the pilot is scalable, and we have presented options to industry for how the pilot could be scaled and the resource estimates for those options.

What percentage of the proposed new program will include activities directly related to FDA product review? What percentage is aimed at activities following product review and approval?

As currently conceived, the TAP Pilot is focused on interactions beginning before FDA receives a marketing submission. It is an enhancement to existing programs, such as our pre-submission, breakthrough sprint interactions, and other programs, as noted above.

Did FDA include this program in its FY22 budget request? How many resources did FDA request for this new program as part of FDA's budget request?

No. The program is being formulated as part of the MDUFA V negotiations. For reference, FDA's FY 2022 budget request can be reviewed here: FDA Fiscal Year 2022 Justification of Estimates for Appropriations Committees.[22]

Will the proposed new program directly result in decreased review times? If so, by how many days per submission?

FDA's goal is to accelerate patient access to innovative, safe and effective devices by supporting more frequent interaction between sponsors, FDA, and other stakeholders as appropriate, beginning earlier in the device development process. Because the TAP Pilot is focused on interactions before a marketing submission is received, we do not expect to measure, during the time period of MDUFA V, whether TAP results in decreased review times. However, based on FDA's experience interacting with sponsors as part of the COVID-19 response, we expect that TAP will lead to a higher proportion of submissions that FDA can review in one cycle and fewer deficiencies. Over a longer time horizon, we believe that TAP will also lead to shorter reviews of qualifying products, quicker adoption by payers and other downstream entities, and ultimately more timely patient access to novel devices, including breakthrough technologies.

Will the commitment letter reflect decreased review times as a result of this proposed new program?

We are still negotiating the details of the pilot, including what would be measurable milestones to include in the commitment letter. At this point, because the focus of the program is on pre-

[22] *https://www.fda.gov/media/149616/download*

– The Honorable Richard Burr

review activities, we do not expect that this is something that can be measured during MDUFA V.

12. **In the MDUFA IV commitment letter, FDA and industry removed the commitment related to activities on which to spend any carryover balance; however, the commitment letter notes that, "*If the collections are in excess of the resources needed to meet performance goals given the workload, or in excess of inflation adjusted statutory revenue targets, FDA and industry will work together to assess how best to utilize those resources to improve performance on submission types with performance goals and/or quality management programs, using, as input for the discussion: workload information, performance objectives and ongoing reported performance.*"**

    How much is the FY21 carryover balance?

FDA has not completed the end-of-year accounting sufficient to answer this question for FY2021 but we can share information related to the carryover balance at the end of FY2020. The total MDUFA carryover balance at the end of FY2020 was $299M, of which $209M was available for use. The table below includes planned budgeted amounts for the available carryover balance. The $209M carryover balance available for use includes approximately $69M in excess earned collections from FY2020 (i.e., earned collections in excess of the FY2020 target revenue amount).

FY 20 EOY Carryover Balance	**$209 M** (inclu. $ 69 M excess earned collections)
Portion of Digital Transformation Expenses* • *FY 21 Budgeted* • *FY 22-24 Budgeted*	**($82 M)** *($23 M)* *($59 M)*
FY 22 Estimated CDRH Funding Need *Projected funding needed to address higher personnel costs*	**($46 M)^**
MDUFA IV Third Party Review Funds *Funds to be spent during MDUFA V*	**($6 M)**
Balance	**$75 M**
** Digital Transformation is being funded primarily through non-user-fee appropriated dollars, including new appropriations from Congress. The amount here reflects a portion of Digital Transformation expenses, including funds that accrued in the carryover balance in FY2017-2020 as a result of FDA using a higher proportion of non-user-fee appropriations to support the MDUFA program in those years. Digital Transformation will replace aging, legacy IT systems and their associated costs. The budgeted amounts presented here reflect FDA's best estimate based on current projections.* *^ This budgeted amount represents the estimated CDRH funding need for FY22 to maintain current staffing levels but it is subject to change, for instance depending on the details of FDA's FY 2022 budget. (Note: The Agency is currently operating under a*	

– The Honorable Richard Burr

continuing resolution.) This budgeted amount includes use of $4.5 M in user fees provided under MDUFA IV in FY 2018-2020 to support employee retention.

On what activities or programs has FDA and industry agreed to spend the available carryover balance? Please provide amounts per activity or program.

As part of MDUFA V negotiations, FDA and industry are discussing how to allocate the balance of funds that are available to be spent, such as for pre-hiring new staff to handle increases in MDUFA workload.

Please provide the statutory authority or specific commitment that allows the carryover balance to be spent on such activities or programs.

Carryover balance funds are being spent on qualifying MDUFA expenditures, including meeting the on-going MDUFA IV commitments, consistent with the qualifying categories of expenditures as defined under section 737 of the FD&C Act.

Thank you again for contacting us regarding this matter. If you have any questions, please let us know.

Sincerely,

Andrew Tantillo
Acting Associate Commissioner for
Legislative Affairs

Count of In-Person Medical Product Inspections by Month - FY17 to FY21 (to date)

Inspection Type	Fiscal Year	Month	Bioresearch Monitoring (BIMO)	Biological Products	Pharmaceutical Products	Medical Devices & Rad Health	TOTAL
Domestic Inspection		October	70	125	94	118	**407**
		November	85	148	95	195	**523**
		December	77	154	104	149	**484**
		January	88	143	87	147	**465**
		February	89	111	101	182	**483**
		March	117	186	123	247	**673**
	2017	April	113	138	104	206	**561**
		May	104	133	101	229	**567**
		June	106	155	94	279	**634**
		July	102	144	66	245	**557**
		August	93	182	81	298	**654**
		September	91	147	66	211	**515**
		TOTAL	**1,135**	**1,766**	**1,116**	**2,506**	**6,523**
		October	84	127	78	148	**437**
		November	93	159	91	172	**515**
		December	79	127	82	156	**444**
		January	92	92	78	187	**449**
		February	108	142	100	201	**551**
		March	115	136	98	232	**581**
	2018	April	90	148	83	160	**479**
		May	106	135	76	231	**548**
		June	113	170	53	204	**540**
		July	72	192	73	201	**538**
		August	106	189	87	248	**630**
		September	77	166	90	195	**528**
		TOTAL	**1,135**	**1,781**	**989**	**2,335**	**6,240**
		October	77	127	66	102	**372**
		November	96	123	89	191	**499**
		December	71	89	79	153	**392**
		January	77	72	74	53	**276**
		February	85	166	69	164	**484**
		March	98	184	94	210	**586**
	2019	April	75	135	93	221	**527**
		May	97	127	76	224	**524**
		June	87	163	72	196	**518**
		July	74	160	63	198	**495**
		August	93	134	95	243	**565**
		September	85	160	71	196	**512**
		TOTAL	**1,018**	**1,640**	**941**	**2,151**	**5,750**
		October	81	98	60	185	**424**
		November	80	120	70	131	**401**
		December	67	106	72	154	**399**
		January	84	127	89	166	**466**
		February	85	124	70	172	**451**
		March	51	74	56	114	**295**
	2020	April	6	1	4	2	**13**
		May	9		3		**12**
		June	28	4	2	1	**35**
		July	29	1	6	2	**38**
		August	35	5	20	7	**67**
		September	55	17	28	15	**115**
		TOTAL	**610**	**677**	**480**	**949**	**2,716**
		October	49	10	18	13	**90**
		November	44	3	10	3	**60**
		December	36	2	4	4	**46**
		January	44	1	5	3	**53**
	2021 (to-date)	February	34	11	8	14	**67**
		March	51	13	42	41	**147**
		April	48	17	21	35	**121**
		May	13	1	3	16	**33**
		TOTAL	**319**	**58**	**111**	**129**	**617**

Count of In-Person Medical Product Inspections by Month - FY17 to FY21 (to date)							
Foreign Inspection	2017	October	11	4	40	43	98
		November	27	2	66	52	147
		December	27		76	75	178
		January	26	7	63	59	155
		February	34	5	90	88	217
		March	53	2	85	71	221
		April	31	1	62	63	157
		May	38	13	85	113	249
		June	39	3	103	94	239
		July	29	1	88	47	165
		August	25	2	56	56	139
		September	34	7	211	25	277
		TOTAL	374	47	1,035	786	2,242
	2018	October	37	2	33	31	103
		November	24	4	65	67	160
		December	35		90	47	172
		January	34		41	19	94
		February	21	6	54	54	135
		March	32	6	105	46	189
		April	26	3	73	60	162
		May	30	14	120	77	241
		June	17	4	133	47	201
		July	16	5	88	59	168
		August	24	3	81	65	173
		September	24	8	85	51	168
		TOTAL	320	55	968	623	1,966
	2019	October	22		53	26	101
		November	19	6	77	57	159
		December	22	8	70	38	138
		January	14		60	43	117
		February	28	3	86	47	164
		March	37	13	80	19	149
		April	24	7	59	31	121
		May	27	6	82	81	196
		June	30	11	68	51	160
		July	22	1	106	39	168
		August	41	3	105	35	184
		September	29	2	158	43	232
		TOTAL	315	60	1,004	510	1,889
	2020	October	34	2	74	42	152
		November	25	6	96	43	170
		December	24	1	37	21	83
		January	28	1	69	37	135
		February	26	8	89	17	140
		March	17	3	20	6	46
		April			1		1
		May	1				1
		June	1				1
		July			1		1
		August	4				4
		TOTAL	160	21	387	166	734
	2021 (to-date)	October	1		1		2
		November	2		4		6
		December			4	1	5
		January			2		2
		February			3		3
		March			4	1	5
		April	2		2		4
		May	1				1
		TOTAL	6	0	20	2	28

Counts generated 5/24/2021

BIOSIMILARS FORUM,
WASHINGTON, DC 20006,
April 4, 2022.

Hon. PATTY MURRAY, Chair,
Hon. RICHARD BURR, Ranking Member,
U.S. Senate Committee on Health, Education, Labor, and Pensions,
428 Dirksen Senate Office Building,
Washington, DC 20510.

Re: **FDA User Fee Agreements: Advancing Medical Product Regulation and Innovation for the Benefit of Patients**.

DEAR CHAIR MURRAY AND RANKING MEMBER BURR AND MEMBERS OF THE COMMITTEE:

On behalf of the Forum members, I would like to thank you for considering this letter in advance of the hearing "FDA User Fee Agreements: Advancing Medical Product Regulation and Innovation for the Benefit of Patients."

The Biosimilars Forum is the non-profit trade association representing the companies with the most significant U.S. biosimilars development portfolios, including: Biogen, Boehringer Ingelheim, Coherus BioSciences, Organon Inc., Pfizer Inc., Samsung Bioepis, Sandoz, Teva, and Viatris. This letter represents the views of our members, all of whom manufacture or market biosimilar products in the US as well as other parts of the world.

Biosimilars have the potential to provide very significant health care savings in the U.S. Without robust competition, innovator biologics will continue to represent approximately 40 percent of total prescription drug spending while they represent only 4 percent of the medicines prescribed to patients. Biosimilars provide competition to allow Americans access to lower-cost biologic alternatives, and their timely licensure and launch is vital to ensuring patient access to lower cost biologic medicines.

The Biosimilars Forum is supportive of the negotiated BsUFA III agreement, and we believe it represents important progress in facilitating timely access to safe and effective biosimilar medicines for patients. We are pleased the commitment letter codifies review timelines for labeling supplements, provides meeting management enhancements, and promotes best practices of communication between FDA and sponsors.

The Forum is particularly pleased that the BsUFA III program will include a regulatory science program that can help bring more biosimilars to market faster. Since the BPCIA was enacted over a decade ago, there have been many advances in the science of developing biological drugs. The regulatory science program will provide FDA and industry the ability to incorporate the latest scientific innovations into biosimilar development and regulation.

Although we are very satisfied with the progress represented in the BsUFA III commitment letter, we want to stress that the pandemic has impacted biosimilars and patient access disproportionately hard for almost 2 years. COVID–19 has stalled onsite inspections for biosimilars delaying their approvals.

While biosimilar inspections have been delayed over the past 2 years, on-time actions for the GDUFA and PDUFA programs have averaged over 90 percent; and the BsUFA program, plunged to 75 percent during Quarter 4 of fiscal year 2020, and further dropped to 67 percent during Quarter 1 of fiscal year 2021 and it remains at 67 percent today. In addition, per the Agency's May 2021 Roadmap for FDA Inspection Oversight, biosimilar inspections are not, considered to be "mission critical" and thus are not prioritized. This has the ultimate outcome of slowing timely approvals of biosimilars. We would like to ask the FDA for clarity to sponsors and the public as to the estimated timelines the FDA believes it will take to address the backlog in inspections and reviews and why biosimilars are not prioritized or treated equitably.

For the BsUFA III Commitment Letter to be a success the inspection backlog for biosimilars must be addressed and remote inspections be implemented consistently across all programs, biosimilars cannot remain a low priority for the Agency.

The Forum is encouraged by FDA's commitment to hire and retain sufficient numbers and types of technical and scientific experts to efficiently conduct reviews and applauds the agency's efforts to improve its use of data and technology. Industry understands FDA staff works on numerous types of applications, a small cadre of

focused Biosimilar staff could help expedite the assessment and inspection process for Biosimilars. We will work with the FDA to determine how can we allocate reviewers specifically for BsUFA goals.

As we head into BsUFA III we look forward to working with the Agency to implement the commitment letter to the mutual benefit of biosimilar sponsors and FDA. We are committed to developing a robust biosimilar industry in the US, and to help the BsUFA program further develop over the next 5 years. We are at a critical inflection point for the biosimilars industry and we believe that enhancing the process for biosimilar development, review and educating the public of the importance of biosimilars is critically important to sustaining and cementing the biosimilar pathway for years to come, but as you all know, more needs to be done outside of BSUFA to help us all achieve our goal of lowering the costs of medicines and improving patient access to biosimilars.

To conclude, thank you for the opportunity to provide this letter. The Forum strongly supports efforts to advance the FDA's biosimilars program. We need to see the FDA prioritize biosimilar inspections and continue their work to streamline the development of biosimilars as well as advance the guidances we need. Policies that support timely approval of biosimilars will ensure that patients have more access to high quality, safe, effective, and affordable biological therapies.

Sincerely,

JULIANA M. REED,
Executive Director.

SENATOR MIKE BRAUN,
WASHINGTON, DC 20510,
April 4, 2022.

Hon. PATTY MURRAY, Chair,
Hon. RICHARD BURR, Ranking Member,
U.S. Senate Committee on Health, Education, Labor, and Pensions,
428 Dirksen Senate Office Building,
Washington, DC 20510.

DEAR CHAIR MURRAY AND RANKING MEMBER BURR:

As Senate hearings begin tomorrow on the U.S. Food and Drug Administration (FDA) user fee renewal, I write to urge you to have a patient-focused hearing that allows the rare disease community to testify at Senate Health, Education, Labor, and Pensions (HELP) Committee. Simply put, the user fee renewal process will not be successful if it ignores the end users of the medicines in the hearing process, or rubberstamps a proposal without patient input.

The overarching mission of the FDA user fee program is to provide a predictable and accountable regulatory framework that supports expedited FDA review and approval of pharmaceuticals and medical devices, ensuring Americans receive access to safe and effective products. Recognizing the importance of incorporating patient voices in the review and approval of medical products, the FDA, medical industries, and Congress have taken steps to encourage patient-focused drug and device development. Integrating patient perspectives with drug development is especially important for patients with rare, lesser known, progressive, and serious diseases and conditions, as well as for diseases with unmet clinical. It is therefore critical that the FDA user fee program incorporate patient experiences and perspectives, especially patients with rare diseases and unmet needs.

In September 1992, Congress passed the *Prescription Drug User Fee Act* into law, authorizing the FDA to collect fees from pharmaceutical companies to review their product applications for approval. Since its enactment, Congress has reauthorized the user fee program every 5 years, and is responsible for reauthorizing the program for the sixth time in September 2022. Over the last 30 years, the user fee program has expanded to include medical devices, generic drugs, and biosimilars. Importantly, the user fee program reauthorization process has evolved into an opportunity for Congress to direct FDA and medical industries to implement new policies for the benefit of patients, including 21st Century tools and techniques to address rare disease drug development.

While the FDA, medical industries, and Congress have made great improvements to include patients and patient perspectives in the user fee program, there is still more to be done to ensure that patients with rare diseases receive representation and consideration for the September 2022 user fee reauthorization. For example,

during the 2012 and 2017 user fee reauthorization process, the Senate HELP Committee invited a witness to provide the patient perspective and testimony, in addition to witnesses from the pharmaceutical and medical device trade associations, at user fee reauthorization hearings. I commend the Committee for its efforts to ensure patient representation in user fee reauthorization discussions and hearings. However, I am concerned about the lack of representation of patients with rare diseases at upcoming HELP hearings, especially given the considerable number of provisions related to rare disease drug and device development included in FDA and industry's final user fee agreements for 2022.

In general, rare and lesser known diseases present a unique set of challenges, particularly for drug and device development, clinical trial design, and patient access to therapies, that are not commonly experienced during traditional product development. For example, clinical trials for rare disease drugs often struggle to recruit and maintain a patient sample size large enough to generalize the data, as well as lack biomarkers and endpoints to adequately demonstrate efficacy. Despite increased efforts to address these issues and expedite approval of rare disease treatments, more than 90 percent of rare diseases have no treatment. [1] Unfortunately, the current regulatory framework for rare disease product development has failed to support efficient development, review, and approval of treatments for rare diseases, further preventing patients from access to therapies.

The FDA user fee program and reauthorization has helped modernize FDA regulatory requirements, establish new approval pathways, and improve the Agency and development process in tandem with medical and technological advancements to ensure expedited approval of products that benefit patients across the United States and globally. The FDA and industry fmal agreements reflect a shift in FDA and industry priorities to encourage and advance rare disease product development and accessibility. As a result, it is imperative that Senate ensures the rare disease community is represented by a witness in the on-going user fee reauthorization discussions held in the Senate HELP Committee to ensure the translational success of new policies incorporated into the final user fee agreement.

For these reasons, I request that the Senate HELP Committee provide a full patient representative hearing from the rare and life threatening disease community in order to advance medical product regulation and innovation for the benefit of patients, including those diagnosed with rare diseases. I appreciate your attention to this request, and my staff and I are willing to help you both organize this hearing.

Sincerely,

SENATOR MIKE BRAUN.

QUESTIONS FOR THE RECORD

RESPONSE BY CARTIER ESHAM TO QUESTIONS FROM SENATOR BRAUN, AND SENATOR ROMNEY

SENATOR BRAUN

The PDUFA commitment letter stresses the importance of new programs to allow earlier patient access to therapies that address unmet medical needs and advance rare disease endpoint development.

Question 1. What challenges exist in FDA's current framework for rare disease drug development? Does the PDUFA agreement go far enough to provide the necessary regulatory flexibilities to address these challenges?

Answer 1. Due to the smaller than average patient populations affected by rare diseases, study recruitment, retention, and other factors that can inhibit adequate endpoint measurement, thus limiting drug development in these spaces. BIO supports the PDUFA VII Rare Disease Endpoint Advancement (RDEA) Pilot Program and its goal to advance and facilitate the development and timely approval of drugs and biologics for rare diseases, including rare diseases in children. The RDEA pilot is modeled after the Complex Innovative Trial and Model Informed Drug Develop-

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[1] Nord, "New Report Finds Medical Treatments for Rare Diseases Account for Only 11 percent of U.S. Drug Spending; Nearly 80 percent of Orphan Drug Products Treat Rare Diseases Exclusively," Mar. 4, 2021, *https://rarediseases.org/new-report-finds-medical-treatments-for-rare-diseases-account-for-only 11-of-us-drug-spending-nearly-80-of-orphan-products-treat-rare-diseases-exclusively/#:-:text=Approximately%207%2C000%20known%20rare%20diseases,rare%20diseases%20have%20no%20treatment*.

ment programs initiated under PDUFA VI, which provide foundational experience for a potentially successful rare disease pilot.

The RDEA Pilot's aim to accept a proposal for a development program for a common disease that includes innovative or novel endpoint elements can allow for new rare disease treatments that utilize the most cutting-edge and patient-centric study designs to reach the right patients.

Given the FDA Pilot's small allotment of a maximum three participating sponsors per year, we look forward to engaging with the Agency regarding the best ways to glean useful and broadly applicable data to inform our members, and most importantly, yield faster and better results for our rare disease patient community.

Overall, we are optimistic that the RDEA pilot can provide learnings to the biotech and greater R&D community regarding surrogate endpoint use in rare disease drug development.

SENATOR ROMNEY

U.S.-China Competition—FDA approval of a new drug or device does not grant the U.S. exclusive access to that drug or device. Companies aren't prohibited from also applying for approval in other countries, where regulatory bodies may move comparatively faster to approve new products.

Question 1. Aside from the consumer health benefits, how does timely FDA approval promote American interests?

Answer 1. BIO agrees that the timely approval of safe and effective medical products by FDA can mean the difference between death, disability, relief, or potentially a cure for American patients with urgent medical needs who lack other treatment options. We agree that beyond consumer health benefits, timely FDA approval promotes American interests in areas outside of patient outcomes.

FDA approval is often considered the "gold standard" globally with respect to regulatory authority and rigor due to stringent safety and efficacy standards. This reputation of regulatory excellence and consistency has policy implications; for example, the US engages in Mutual Recognition Agreements (MRAs) with almost 30 other countries, allowing for a degree of reciprocity and data sharing between trusted health authorities if FDA deems those authorities capable of conducting inspections that meet US standards. In 2021 alone, almost half (27/60) of FDA's new drug approvals in the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) were first-in-class. That same year, 76 percent of novel drugs approved were approved in the US before any other country. [1], [2] Approval by FDA can indicate likelihood for approval by other health authorities. For example, a study indicated that FDA and the European Medicines Agency (EMA) had 91–98 percent concordance in decisions on marketing approvals between 2014 and 2016. [3] Approval in multiple markets translates into more revenue for US-based sponsors, increasing their ability to conduct research and development on new innovative treatments to help more patients.

In addition to economic and financial benefits, timely FDA approval yields earlier availability of US-generated real-world evidence and real-world data (RWE/RWD). As soon as patients have access to new treatments, American academic institutions, health systems, software/technology companies, and other stakeholders can begin to harness and apply clinical outcome data generated by the use of these novel products. In addition to supporting regulatory submissions and decision-making, increased availability of RWE/RWD improves health equity for Americans. Such data enable the utilization of decentralized and non-traditional clinical trial locations, allowing for increased diversity in clinical trials that can improve our understanding of clinical outcomes for all American patients.

Question 2. How does timely approval affect the rate and willingness of U.S.-based firms to invest in research and development?

Answer 2. Bringing a drug to market in the US is associated with significant time, effort, resource expenditure, and risk for American companies. It can take anywhere from 10 to 15 years at an average cost of approximately $1 billion or more

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[1] *https://www.fda.gov/media/155227/download.*

[2] *https://www.raps.org/news-and-articles/news-articles/2022/1/fda-approved-more-first-in-class-drugs-more-with-a#::text=Other%20drugs%20approved%20by%20CDER,treatment%20options.*

[3] Kashoki, M., Hanaizi, Z., Yordanova, S., Vesely, R., Bouygues, C., Llinares, J. and Kweder, S.L. (2020), A Comparison of EMA and FDA Decisions for New Drug Marketing Applications 2014–2016: Concordance, Discordance, and Why. Clin. Pharmacol. Ther., 107: 195–202. *https://doi.org/10.1002/cpt.1565.*

to advance a single drug or biological product from a promising idea to an approved product that benefits patients.[4,5] Timely review and approval helps mitigate risks and opportunity costs associated with regulatory submissions for American firms.

Every day that an approval is delayed translates into unrealized revenue for the sponsor of an application. Small companies with limited research and development budgets, or even new companies that are pre-revenue, are disproportionately impacted by such delays. These firms might only have the resources, staff, and facilities to manage a single product in their pipeline at a given time. Delayed approval results not only in financial impact but can also chill innovation efforts due solely to resource constraints. As approval timelines shorten, US-based firms are more likely and more able to invest in biopharmaceutical research and development.

Question 3. How does U.S.-based research and development investment in medical products (drugs and devices) compare to Chinese-based investment?

Answer 3. The biopharmaceutical industry is one of the largest economic sectors domestically and globally. A recent study indicated that total US medical and health research and development reached $245.1 billion in 2020. Specifically, US private industry accounts for 66 percent of these investment dollars at $161.8 billion.[6] During that same year, Chinese pharmaceutical research and development reached $187 billion.[7]

According to census data from *datacommons.org*, American and Chinese populations in 2020 were 329.5 million and 1.402 billion, respectively. Using private industry spending data, we can estimate per capita research and development spending at $49.1 in the US and $62.1 in China.

RESPONSE BY DAVID GAUGH TO QUESTIONS FROM SENATOR KAINE, AND SENATOR ROMNEY

SENATOR KAINE

Mr. Gaugh, in your testimony you shared that as of March 2022, the FDA has licensed two interchangeable biosimilar products. We know that interchangeable biosimilars must produce the same clinical result as the brand-name biologic and that a pharmacist may dispense an interchangeable biosimilar when a brand-name biologic is prescribed without intervention from a provider. As you shared in the hearing, the development of biosimilars, and interchangeable biosimilars, has worked to reduce the price that patients pay at the drug counter. We also know this is a relatively new space and that we are still learning more about the best science and oversight in the development of these products.

Question 1. Mr. Gaugh, which provisions of the BsUFA III agreement will help manufactures quickly develop additional interchangeable biosimilar products?

Answer 1. Following enactment of the BPCIA in 2010, the first biosimilar was licensed by FDA in 2015. Today, a total of 35 biosimilars including two interchangeable biosimilars—are now licensed in the United States. Biosimilar medicines are safe, effective and more affordable treatment options for patients than their brand-name counterparts. Biosimilars are already delivering on their promise of lower costs and expanded patient access to care with average prices of nearly 50 percent less than their reference biologics at time of the biosimilar's launch. Biosimilars represent much needed competition to the specialty medicines that now account for more than 55 percent of all drug spending.

The interchangeable designation permits a pharmacist to dispense, subject to state law, an interchangeable biosimilar when a brand-name biologic is prescribed without intervention from the provider. It requires a biosimilar developer to demonstrate the same clinical result for its medicine as the brand-name biologic. It is important to note that the interchangeable designation is unique to the Unites States and is not an indication of superior quality.

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[4] Olivier J. Wouters, Ph.D; Martin McKee, MD, DSc; Jeroen Luyten, Ph.D. Estimated Research and Development Investment Needed to Bring a New Medicine to Market JAMA. 2020, 323(9).

[5] Joseph A. DiMasi; Henry G. Grabowskibi; Ronald W. Hansen. Innovation in the pharmaceutical industry: New estimates of R&D costs. 2016. Journal of Health Economics. 2016, Vol. 47.

[6] U.S. *Investments in Medical and Health Research and Development 2016–2020*. Research! America. (n.d.). Retrieved April 29, 2022, from *https://issuu.com/researchamerica*.

[7] Zhang, W. (2022, January 27). *China: Pharmaceutical R&D spending 2023*. Statista. Retrieved April 29, 2022, from *https://www.statista.com/statistics/1202091/china-pharmaceutical-randd-spending/*.

As part of the industry's negotiations with FDA, enhancements were made to help facilitate more timely patient access to interchangeable biosimilars. BsUFA III will help manufacturers to develop more interchangeable biosimilars through the new Regulatory Science Program's demonstration project. These demonstration projects will also evaluate mechanisms to streamline overall biosimilars development. In our view, the findings from these demonstration projects will inform a comprehensive strategy to advance interchangeability and the development of future guidance documents.

We appreciate your interest and attention to the important role biosimilar medicines—and, in particular, interchangeable biosimilars—can play in lowering prescription drug costs. We would welcome the opportunity to further discuss how Congress could take steps to reduce the clinical burden on biosimilars and interchangeable manufacturers to ensure more timely patient access to low-cost medicines.

SENATOR ROMNEY

U.S.-China Competition—FDA approval of a new drug or device does not grant the U.S. exclusive access to that drug or device. Companies aren't prohibited from also applying for approval in other countries, where regulatory bodies may move comparatively faster to approve new products.

Question 1. Aside from the consumer health benefits, how does timely FDA approval promote American interests?

Answer 1. In addition to the consumer health benefits, timely FDA approval of generic and biosimilar medicines benefits America's interests through increased market-based competition and lower health care costs. Experience shows drug prices decline rapidly when generics enter the market. According to FDA, prices fall as generics enter the market—by an average of 39 percent when there is only one generic and by nearly 80 percent when four or more generics enter the market. Evidence with biosimilar medicines is similar with an average cost savings of nearly 50 percent. Importantly, biosimilar competition also results in lower brand biologic prices—by more than 25 percent on average for brands with biosimilar competition.

Over the last 10 years, generics and biosimilars provided more than $2 trillion in savings—including $469 billion from new generics and more than $12 billion from biosimilars—to patients and the U.S. health care system. In addition to the cost savings provided, patient access to life-saving treatments is broadened as the price of medicine falls. A recent analysis of Medicare Part D from the Congressional Budget Office noted "the number of standardized prescriptions dispensed for generic drugs more than doubled from 2009 through 2018." And biosimilars have already resulted in more than 10 million additional patient days of treatment.

GDUFA III and BsUFA III, as negotiated, will further these interests. Both GDUFA and BsUFA aim to put FDA's generic and biosimilar drug programs on firm financial footing by enabling FDA to assess user fees to fund critical and measurable enhancements and, in turn, bringing greater predictability and timeliness to the review of applications. As a direct outcome, the generic and biosimilars drug programs increase patient access to safe, effective and more affordable quality medicines.

Question 2. How does timely approval affect the rate and willingness of U.S.-based firms to invest in research and development?

Answer 2. Timely approval of generic and biosimilar medicines by FDA increases the likelihood generic and biosimilar developers will invest in bringing more affordable medicines to market going forward. AAM's member companies invest significant resources in building and operating U.S.-based facilities and in bringing generic and biosimilar medicines through FDA's approval process to market. Manufacturing sites can cost as much as $1 billion to build in the U.S. In addition, the development and approval of biosimilar medicines, for example, require 8–10 years at a cost of $100 to $250 million.

GDUFA III and BsUFA III ensure FDA has sufficient resources for review of generic and biosimilars applications, while building on the success and incorporating lessons learned over the last 10 years. As described in more detail in my written statement, GDUFA III and BsUFA III include a number of enhancements to ensure the timely review of applications over the next 5 years (FY23–27). Timely approval of the FDA user fee agreements ensures America's patients will continue to benefit.

Question 3. How does U.S.-based research and development investment in medical products (drugs and devices) compare to Chinese-based investment?

Answer 3. We do not have any data on how U.S.-based investment in the research and development of generic and biosimilar medicines compares to Chinese-based investment.

RESPONSE BY DAVID LEAHEY TO QUESTIONS FROM SENATOR BURR

SENATOR BURR

Question 1. Aside from the consumer health benefits, how does timely FDA approval promote American interests?

Answer 1. There is broad bipartisan agreement on the importance of American patients gaining first access to American medical technologies, a goal shared by innovators, FDA and most importantly, patients. In addition to the health benefits, a timely and efficient FDA review of medical technologies strengthens the entire medical device ecosystem. Physicians, surgeons and all healthcare professionals are able to work collaboratively with innovators to improve existing technologies, as well as develop the next generation of cures, therapies and diagnostics here in the United States. Unnecessary regulatory delays also drive capital to markets outside the United States and weaken our Nation's global leadership in device innovation. It's in our collective public health, economic and national security interests that the U.S. remains the most attractive country in the world for medical device development and manufacturing.

Question 2. How does timely approval affect the rate and willingness of U.S.-based firms to invest in research and development?

Answer 2. FDA has made significant progress since 2009. At that time, FDA's performance slipped and as a result venture investments fled the device markets. Thankfully, Congress intervened and passed key reforms to improve FDA's review programs. FDA, to their credit, has made improvements since then, and our expectation is that the $2B in new resources provided under the MDUFA V agreement—a doubling of fees from the current MDUFA—will build on this progress. Still, the harsh reality remains that every dollar spent on research and development carries risk, and many ventures fail. Ongoing improvements in transparency, consistency and accountability at FDA will help ensure that research and development investments in new medical technologies continue.

Question 3. How does U.S.-based research and development investment in medical products (drugs and devices) compare to Chinese-based investment?

Answer 3. While there has always been shifts in venture capital investments and others who support the medical technology ecosystem, there has been an alarming trend of the majority of investments being made in later stage companies. This is certainly necessary and beneficial to patient care, but it is critical that investments are also being made in early stage companies and startups. Reports show that there are ongoing increases in these types of investments in China with direct support from the Chinese government. In fact, the People's Republic of China identified medical technologies as a critical sector of investment as part of their Made in China 2025 industrial policy to grow indigenous industries. Keeping the Chinese market open to U.S. exports is critical to U.S. manufacturers, but improvements to the regulation and reimbursement of medical technologies in the United States will protect our Nation's leadership position in this vibrant industry.

Question 4. How confident are device manufacturers these adjustments will incentivize the FDA to meet its own commitment's?

Answer 4. The milestones and commitments contained in the MDUFA V draft agreement are designed to help ensure that the investments being made by industry will strengthen patient care and innovation. As the agency works to maintain its gold standard of providing safe and effective medical technologies to the public, we are confident that the structure of the agreement before Congress will achieve our shared goal of protecting the United States' leadership position in medical technology innovation. Ongoing congressional oversight will also play a central role to ensure that these important goals are met.

Question 5. How confident are device manufacturers that the FDA's methods for measuring and reporting on hiring goals will provide both accurate and reliable data?

Answer 5. During the MDUFA V negotiations, it was concerning to learn that FDA was unable to identify how many MDUFA I-IV funded positions were vacant. FDA did implement a tracking system for MDUFA IV hires and has committed to an independent assessment during MDUFA V to better assess workforce tracking and management. Given the significance increase in funding under MDUFA V, it is a reasonable expectation that FDA will do more to ensure timely hiring for new positions and existing vacancies during MDUFA V and beyond. The results of the independent assessment, coupled with FDA's annual financial report to Congress,

should provide more transparency into these workforce issues and any gaps that need to be filled.

[Whereupon, at 11:49 a.m., the hearing was adjourned.]

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