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Senate HELP Hearing on FDA User Fee Agreements: Advancing Medical Product Regulation and Innovation for the Benefit of Patients, FDA Center Directors

On Tuesday (April 26), the Senate Health, Education, Labor & Pensions (HELP) Committee held a hearing entitled, "FDA User Fee Agreements: Advancing Medical Product Regulation and Innovation for the Benefit of Patients, FDA Center Directors." The hearing was the second of two the committee has held on Food and Drug Administration (FDA) user fee agreements, which authorize the FDA to collect user fees from drug and device manufacturers and requires congressional reauthorization every five years.

During the hearing, committee members discussed a range of topics related to the Prescription Drug User Fee Amendments (PDUFA VII), Generic Drug User Fee Amendments (GDUFA III), Biosimilar User Fee Amendments (BsUFA III), and the Medical Device User Fee Amendments (MDUFA V), which would authorize new user fees for their respective industries for fiscal years 2023-2027. Witnesses at Tuesday's hearings included representatives from the FDA who answered questions on ways the latest agreements would improve FDA's ability to provide access to safe and effective drugs and medical devices, as well as related topics.

- *For more information*: https://www.help.senate.gov/hearings/fda-user-fee-agreements-advancing-medical-product-regulation-and-innovation-for-the-benefit-of-patients-fda-center-directors

Opening statements

Committee Chair Patty Murray (D-WA): "[T]he user fee programs have an important role to play when it comes to FDA's work ensuring the safety and effectiveness of medical products families rely on to stay healthy. These programs make sure that as FDA gets more new drugs or devices to consider for approval—as it gets more critical work to do—it also gets more resources to support that work. But it should also be unthinkable that we would let this moment slip by without looking carefully at what is, and what isn't, working at FDA," including pandemic response and preparedness, approval processes, diversity in clinical trials, and lowering the cost of prescription drugs. "And while there is clearly more we can do to strengthen FDA's oversight of drugs and devices, there are also an alarming number of products that currently get no meaningful oversight," including cosmetics and dietary supplements. "So I hope we'll be able to make progress on all of these issues, and more, as we work to reauthorize the user fee programs." Full Statement

Committee Ranking Member Richard Burr (R-NC): "If today's hearing had a theme, it would be accountability. … The agency needs to apply practices it used during the COVID response to its every day operations to help speed not only the review of products, but their development as well. … I want to work on updating FDA's regulation of diagnostic tests, and I am working with the Chair to update the regulation of other products like cosmetics and dietary supplements, too. … The FDA has a responsibility to meet the terms of the commitments it has made for the user fee programs. Based on my evaluation, you have not fully delivered. … Each of the new agreements this Committee is evaluating reflect major new commitments. More money, more staff, more government. But what are we to do about previous commitments that went, or remain, unfulfilled? … American patients deserve user fee programs that bring medicines to them on time, that keep pace with technology, that reduce the time and cost of

development of treatments, and that do not grow just to put more government between patients and cures." Full Statement

Witness Testimony

Patrizia Cavazzoni, M.D., Director, Center for Drug Evaluation and Research (CDER), FDA: "I will focus my opening remarks on the generic drug user fee program, or GDUFA, and the biosimilar user fee program, or BsUFA. These programs have allowed FDA to provide access to affordable high-quality medicines to millions of Americans. … We intend to build on this by approving more drugs in a single round of review, including complex generics with little or no competition. … GDUFA III will introduce new measures that allow for earlier approvals and will ensure that the agency has the appropriate staff expertise to deliver on our goals. … Since the enactment of BsUFA II five years ago, the number of approved biosimilar products has gone from five to 35 today, including an interchangeable insulin product. BsUFA III proposed to retain the majority of existing performance goals, with changes to some of the meetings between FDA and developers to improve communications. … The proposal seeks to expedite the review of new indications or other changes after the initial approval. Finally, BsUFA III doubles down on efforts to advance the development of interchangeable products that may be switched at the pharmacies. I cannot emphasize enough the importance of reauthorizing these user fee programs." Full Testimony

Peter Marks, M.D., Ph.D, Director, Center for Biologics Evaluation and Research (CBER), FDA: "For my portion of the testimony, I'll focus on the prescription drug user fee program or PDUFA. The PDUFA VII commitment letter includes the following categories: enhance CBER support for the development, review, and approval of cell and gene therapy products and new allergenic extract products; advance scientific research to expedite drug development; it will continue the enhancement and modernization of the drug safety system; advance utilization of innovative manufacturing technologies; and improve FDA's hiring and retention. … The proposal will support development of multiple guidance's, numerous public meetings to examine new technologies and approaches, a patient-focused drug development meeting to better understand patient perspectives on gene therapy products, and public outreach to facilitate product development and approval." Full Testimony

Jeffrey Shuren, M.D., J.D., Director, Center for Devices and Radiological Health (CDRH), FDA: Shuren's testimony focused on MDUFA V. He said, "I personally regret that we missed the statutory deadline to bring recommendations to Congress. … CDRH continued to meet and exceed most performance goals through the first half of MDUFA IV." However, Shuren noted that CDRH "missed some goals later on" in part due to "a rise in our workload for which we were not fully funded" and the COVID-19 pandemic. He said, "The MDUFA V proposal takes important steps to address resource gaps that began to show before COVID-19 and to support improved performance. It also features many new accountability measures, one of which is for add-on payments under which FDA would receive additional user fees if it meets specified goals. … The agreement includes a new voluntary pilot, [The Total Product Lifecycle Advisory Program Pilot] TAP, to provide earlier, more frequent, and more strategic engagement with sponsors of breakthrough designated devices and those included in the safer technologies program to speed device development. … The MDUFA V proposal would also support advancing the patient perspective in regulatory decisions." Full Testimony

Q&A

Committee Chair Murray asked about the delay in authorizing a COVID-19 vaccine for children under 5 to which Dr. Marks implied the agency is still waiting for completed applications, saying, "The agency will take action to

begin reviews once completed applications are submitted." Sen. Murray also asked what FDA is doing to address the growing number of drug overdoses and fentanyl use in the United States. Dr. Cavazzoni said CDER is redoubling its efforts to address the opioid epidemic, including issuing a request for comment on a proposal to provide mail-back envelopes to facilitate the safe disposal of opioids, as well as looking for ways to expand access to over-the-counter naloxone. In addition, Sen. Murray in her opening statement called on FDA to address gaps in food safety and nutrition efforts and accelerate the agency's response to public health threats, such as recent containments in baby foods and infant formula.

Ranking Member Burr asked about staff vacancies at CDER, noting that it currently has 260 vacancies despite being on track to meet its PDUFA IV requirement to hire 230 new employees. Dr. Cavazzoni noted that when staffing is viewed as a whole the center's vacancies are in line with other organizations. Sen. Burr also noted that he is working on the VALID Act to reform diagnostic test regulations. When asked if he agrees there is need for reform, Dr. Shuren said yes, but added that any legislation must encompass all diagnostic tests. Sen. Burr also asked about the delay in publicly posting meeting minutes from the latest MDUFA negotiations to which Dr. Shuren said all meeting minutes will be posted by the end of the week. In addition, Sen. Burr questioned whether the TAP pilot program included in MDUFA V is needed and urged Dr. Marks to develop recommendations on how to measure the program's success.

Sen. Maggie Hassan (D-NH) asked Dr. Cavazzoni about the apparent conflicts of interest surrounding the consulting firm McKinsey, citing a *New York Times* article that highlighted the firm worked for the agency while also simultaneously working for opioid manufacturers. Dr. Cavazzoni said the FDA follows U.S. government contracting rules and requires contractors to disclose any potential conflicts of interest. When pressed by Sen. Hassan on actions FDA is taking in light of the claims, Dr. Cavazzoni said CDER does not currently have a contract with McKinsey and broader action will be determined pending investigations. Sen. Hassan expressed an interest in examining government contracting rules to determine if self-reporting of conflicts of interest is sufficient.

Sen. Bill Cassidy (R-LA) noted that he and Sen. Tina Smith (D-MN) recently introduced the Modernizing Therapeutic Equivalence Rating Determination Act to integrate therapeutic equivalence ratings into the 505(b)(2) application process and asked what FDA needs to make that change. Dr. Cavazzoni expressed concern with the bill, noting that the 505(b)(2) pathway is not set up to generate the data needed to make a therapeutic equivalent determination, and suggested lawmakers instead look to address barriers in the generic drug review program, which is able to produce therapeutic equivalence ratings. Sen. Cassidy also asked about the impact of a recent court ruling that limits FDA's ability to award Orphan Drug Exclusivity to the entire condition. Dr. Marks said the decision is likely to have impacts for pediatric rare disease drugs and would welcome working with Congress to address the problem. In response to a separate question from Sen. Cassidy, Dr. Shuren said FDA would welcome congressional clarity around FDA's device export certification program and whether FDA can certify devices that are made in FDA-inspected facilities abroad and are exported to both the United States and other countries.

Sen. Jacky Rosen (D-NV) noted that she and Sen. Cassidy have introduced the Healthcare Cybersecurity Act and that she is working on additional legislation related to cybersecurity guidance for medical device manufacturers. She asked Dr. Shuren how Congress can ensure medical device cybersecurity guidance is up to date and nimble. Dr. Shuren said FDA works with multiple agencies, including Federal Bureau of Investigation, to address medical device cybersecurity and that the agency would benefit from Congress approving funding included in the fiscal year 2023 budget proposal and giving the agency full authority to ensure devices are cyber safe. Sen. Rosen also emphasized the importance of FDA supporting early career researchers at universities to which Dr. Cavazzoni agreed.

Sen. Tammy Baldwin (D-WI) also asked about the potential impacts of the court decision on Orphan Drug Exclusivity and asked whether FDA has mandatory recall authority over personal care products. Dr. Cavazzoni

echoed Dr. Shuren's concern about the ruling's impact on the development of drugs to fight rare diseases, particularly for pediatric patients and said the agency does not have mandatory recall authority for over-the-counter products that are regulated as drugs, with the exception of biologics.

Sen. Susan Collins (R-ME) expressed her desire to fill gaps in FDA's authority over personal care products via her Personal Care Products Safety Act. Sen. Collins focused the rest of her questions on the recent Aduhelm approval and coverage determination, expressing concern that that Centers for Medicare and Medicaid Services (CMS) "did not stay in their lane" when they commented on the drug's safety as part of the coverage determination. She also asked about CMS's decision's impact on the accelerated approval pathway pipeline. Dr. Cavazzoni said FDA stands by its decision regarding Aduhelm and noted she could not comment on CMS's role in the process. As for the potential impact on the future pipeline of accelerated approval drugs, Dr. Cavazzoni said she wouldn't speculate but noted the current pipeline is "robust."

Sen. Mike Braun (R-IN) noted that his bill the Promising Pathway Act would create a new treatment pathway for individuals with rare and serious illnesses and asked Dr. Marks if he is comfortable with the agility and framework in place to address issues for those with rare diseases. Dr. Marks said FDA through the Accelerated Approval Pathway has lots of flexibility to bring treatments to that patient population but acknowledged the agency could be more creative in how they leverage it. Sen. Braun also emphasized the need to turn to research and development from other countries and to get patients' perspectives on drug approval processes.

Sen. Roger Marshall (R-KS) focused his questions on FDA's decision to allow the abortion medication, Mifepristone, to be prescribed via telemedicine or over the phone. Sen. Marshall, who is an OB-GYN, expressed concern that prescribing the drug without confirming gestational age via an ultrasound increases risks for women. Dr. Cavazzoni said FDA conducted an exhaustive review of the drug and concluded that prescribers must confirm evaluation of gestational age before prescribing, but it left open to the prescriber how that is completed. Sen. Marshall also discussed the Ensuring Innovation Act, which targets the practice of brand name drugmakers making slight modifications to ingredients to get additional exclusivity, also known as "evergreening."

Sen. John Hickenlooper (D-CO) asked about ways to enhance transparency in FDA's accelerated approval pathway in instances such as the Aduhelm approval in which FDA's approval decisions diverge from independent advisory committee recommendations. Dr. Cavazzoni reiterated FDA's commitment to the Aduhelm decision and outlined two areas in which Congress could support the accelerated approval pathway: Granting FDA the authority to require post-market trials be underway or a detailed plan for the trials outlined by the time the drug is approved, and expediting the withdrawal of drugs when confirmatory trials do not confirm clinical benefit. Sen. Hickenlooper also asked witnesses about ways to prepare for the next pandemic.

If you have questions, please contact Heather Meade or Heather Bell.