U.S. FOOD & DRUG ADMINISTRATION

September 14, 2022

The Honorable Anna Eshoo
Chairwoman
Subcommittee on Health
Committee on Energy & Commerce
U.S. House of Representatives
Washington, D.C. 20515

Dear Chairwoman Eshoo:

Thank you for providing the Food and Drug Administration (FDA or the Agency) with the opportunity to testify at the March 30, 2022 hearing before the Subcommittee on Health, House Committee on Energy & Commerce entitled "FDA User Fee Reauthorization: Ensuring Safe and Effective Medical Devices." This letter is a response for the record to questions posed by the committee.

Sincerely,

Kimberlee R. Trzeciak -S
Digitally signed by Kimberlee R. Trzeciak -S
Date: 2022.09.15 17:40:15 -04'00'

Kimberlee Trzeciak
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**Questions for the Record**

**House Committee on Energy & Commerce**
**Subcommittee on Health Hearing**
**March 30, 2022**
**"FDA User Fee Reauthorization: Ensuring Safe and Effective Medical Devices"**

Jeffrey E. Shuren, M.D.,
Director, Center for Devices and Radiological Health, U.S. Food and Drug Administration

**The Honorable Nanette Diaz Barragán (D-CA)**

1. **In regards to MDUFA V, FDA held only one meeting with public stakeholders including patient groups. The agency, however, has met with industry stakeholders repeatedly during the MDUFA V negotiation process. Given the imbalance in the FDA's engagement with stakeholders, how will the FDA ensure that their recommendations will be addressed in MDUFA V?**

Consistent with the statutory directives in section 738A of the FD&C Act, FDA held one public meeting, and will hold a second on April 19, 2022.[1] FDA has also held monthly consultation meetings with non-industry stakeholders, including consumer and patient advocates, while negotiations with industry were ongoing.[2] In total, FDA will have hosted 15 meetings – one public meeting prior to the start of MDUFA V negotiations, one public meeting following the conclusion of such negotiations, and 13 monthly consultation meetings from March 2021 – March 2022. This cadence of meetings is consistent with all FDA user fee programs and with prior MDUFA negotiations as well.

The input from stakeholders through the public meetings and monthly non-industry stakeholder meetings has been very important to FDA. It informed the formulation of our goals for MDUFA V, as well as the development and prioritization of various proposals throughout the negotiation process. Stakeholder input was particularly useful in developing our proposals and commitments related to patient engagement, digital health, real-world evidence, and the Total Product Lifecycle Advisory Program (TAP) pilot. At the April 2022 public meeting, stakeholders from the four industry trade associations that participated in the negotiations; representatives from patient, consumer, scientific, academic, and healthcare professional groups; and other speakers will have an opportunity to make comments during the public comment period and provide feedback on the MDUFA V agreement. This feedback is critical and will inform potential updates to the commitment letter that is transmitted to Congress. A summary of the public

[1] https://www.fda.gov/industry/medical-device-user-fee-amendments-mdufa/medical-device-user-fee-amendments-2023-mdufa-v
[2] https://www.fda.gov/industry/medical-device-user-fee-amendments-mdufa/stakeholder-consultation-meetings-medical-device-user-fee-amendments-2023-mdufa-v

comments and explanation of the changes to the MDUFA agreement will be available on FDA's MDUFA V website.[3]

**2. Specifically, how does the FDA seek to incorporate patient groups suggestions to ensure appropriate and adequate post-market studies in light of an increasing number of medical devices receiving expedited review pathway designations that allow for faster review and less premarket evidence of safety and efficacy for FDA approval? How will the FDA do so, if user fees decrease whenever FDA fails to meet increased benchmarks for approvals?**

As noted, input from stakeholders received through the public meeting and monthly non-industry stakeholder meetings informed FDA's development and prioritization of proposals during negotiations. FDA will also receive valuable feedback during the second public meeting on April 19, 2022.

FDA also notes that the Agency has a robust Patient Science and Engagement Program that is committed to engaging with patients, understanding their experiences, and proactively integrating patient perspectives into medical device decisions and regulatory activities where appropriate. The Agency has created forward-leaning mechanisms to facilitate patient involvement in regulatory activities as well as fostered innovative approaches to supporting the science of patient input. By collaborating with patients, healthcare providers, the research community, and industry, FDA has fostered the creation of well-defined outcome measures and structured assessments of patient preferences that directly impact medical device decisions and assure that these devices include the evidence patients and providers depend upon.

FDA is in fact at the forefront of describing ways that structured collection of patient preference information can be used as scientific evidence in the evaluation of medical products. Since issuing the guidance on patient preference information in 2016, industry is increasingly including this information in medical device submissions, growing from initially none to 26 studies that are completed or in the pipeline. In addition, patient-reported outcomes are being collected consistently in more than 50 percent of medical device submissions with clinical studies.[4] To help better work hand-in-hand with patients to incorporate their values and perspectives into all aspects of the medical device total product life cycle, FDA established the first advisory committee comprised solely of patients, caregivers and representatives of patient organizations called the Patient Engagement Advisory Committee (PEAC). The PEAC provides formal recommendations to FDA on general scientific matters related to medical devices such as patient involvement in the design and conduct of clinical trials, communicating cybersecurity vulnerabilities and medical device recalls, as well as the ways in which patient-generated health data can provide insights on medical device performance in real-world use. FDA integrates the

[3] https://www.fda.gov/industry/medical-device-user-fee-amendments-mdufa/medical-device-user-fee-amendments-2023-mdufa-v
[4] https://jpro.springeropen.com/articles/10.1186/s41687-022-00444-z

PEAC recommendations into regulatory actions like the recently issued final guidance[5] on the ways patients can engage as advisors in the design and conduct of clinical studies.

Moreover, as part of the MDUFA V agreement, the Agency will take many actions to continue engaging patients and incorporating their perspectives in the regulatory process. Where appropriate, the Agency will leverage collaborations and partnerships with patients, healthcare providers, industry, and others, as well as collaborations across FDA Centers, to:

- expand clinical, statistical, and other scientific expertise and staff capacity to respond to submissions containing voluntary, applicant-proposed use of patient preference information (PPI), patient-reported outcomes (PROs), and/or patient-generated health data (PGHD);
- issue a draft guidance providing best practices on incorporating into premarket studies clinical outcome assessments including their use as primary or co-primary endpoints;
- support the use of innovative technologies to capture patient input and reduce patient burden to inform clinical study design and conduct, with a goal of reducing barriers to patient participation and facilitating recruitment and retention; and
- hold a public meeting by the end of FY 2024 to explore ways to use patient-generated health data to help advance remote clinical trial data collection and support clinical outcome assessments.

It is also important to note that FDA has seen the size of medical device submissions steadily and significantly increase over time[6] – indicating that the Agency is receiving more evidence, rather than less, for medical device submissions. The average size of a 510(k), for instance, has steadily and significantly increased, nearly doubling to an average of 2,000 pages per submission in 2021. Average submission size has also increased for IDEs – which grew by 1,300 pages (from around 1,700 pages per submission in 2018 to more than 3,000 pages in 2021) – and for PMA Supplements, where the number of pages submitted has doubled (from around 650 pages per submission in 2018 to more than 1,300 pages in 2021).

Moreover, the MDUFA V user fee negotiation process did not involve negotiation of specific policy changes, such as policy that would impact the level of evidence required for marketing authorization. Nor does MDUFA include benchmarks or performance goals for approvals or other positive decisions on marketing submissions. Rather, the MDUFA commitments focus on enhanced performance goals for timeliness and level of interaction between review teams and companies submitting MDUFA-covered submissions, to determine if devices meet FDA's standards for safety and effectiveness, such that patients can depend upon them. The agreement aims to assure patients have timely access to new devices that they need to improve and extend their lives, while upholding FDA's standards for assuring safety and effectiveness of devices before they enter the market.

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[5] https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/webinar-patient-engagement-design-and-conduct-medical-device-clinical-studies-final-guidance .

[6] Witness Testimony_Shuren_HE_2022.03.30.pdf (house.gov)

Moreover, the MDUFA program helps support CDRH's overall total product lifecycle approach, which allows the Center to operate with a more holistic, team-based approach to premarket review, postmarket surveillance, and compliance that strengthens the Center's focus on safety and effectiveness throughout the entire lifecycle of medical devices. For some devices, even with robust premarket standards, safety signals may emerge only in postmarket use. For this reason, FDA has continued to work on a variety of fronts to enhance medical device safety across the total product lifecycle, including continued implementation of our comprehensive medical device safety action plan, to more quickly identify, assess and communicate emerging safety concerns, as well as actions patients and providers can take to mitigate them. This work includes a steadily increased focus on sources of real-world evidence, as well as partnerships with healthcare facilities, and provider and patient organizations. FDA's work on real-world evidence and patient engagement will receive increased resources under the proposed MDUFA V agreement.

3. **User fee statute requires FDA to hold patient stakeholder meetings monthly to receive feedback, however it remains unclear how this feedback is used during negotiations. FDA is required to publicly post meeting minutes on negotiations, yet these have not been produced prior to the publication of the proposed MDUFA V commitment letter. Please provide a detailed list of all negotiation meetings between FDA and the medical device industry and specify how patient and consumer stakeholder feedback was incorporated.**

As noted, FDA convened non-industry stakeholder meetings each month during the MDUFA V negotiation process. These meetings were used to inform interested stakeholders of the progress of the negotiations, as well as to solicit their input on the prioritization of various proposals advanced by FDA and our industry counterparts. The input from stakeholders informed FDA's proposals during negotiations, and we also presented the stakeholder perspective to industry in conjunction with FDA's proposals.

As noted, FDA incorporated stakeholder input in developing our proposals, particularly those related to patient science and engagement, digital health, real-world evidence and the TAP pilot. Further, FDA will hold its second public meeting in April 2022 where stakeholders including patient advocacy organizations and industry will have the opportunity to submit comments to the public docket; this feedback is critical and will inform potential changes FDA may make to the final commitment letter submitted to Congress. Prior to the transmittal of the final MDUFA V recommendations to Congress, FDA will post meeting minutes of all negotiation meetings online.[7] We apologize for the delay in posting the minutes as we know they are an important measure of transparency around the negotiations.

4. **Meeting minutes from FDA and industry negotiations were not disclosed prior to the hybrid hearing held Subcommittee on Health of the Committee on Energy and Commerce. This has generated concern over the lack of transparency of the user fee**

[7] https://www.fda.gov/industry/medical-device-user-fee-amendments-mdufa/medical-device-user-fee-amendments-2023-mdufa-v

**process. Without this information, it is unknown how feedback and public comments are being used throughout the user fee reauthorization negotiations. Will this information be released before the close of the public comment period on April 21? How will FDA improve the speed at which patient and consumer organizations and Members of Congress access this information?**

We apologize for the delay in posting the minutes as we know they are an important measure of transparency around negotiations. FDA will post minutes[8] of all negotiation meetings prior to the transmittal of the final MDUFA V recommendations to Congress. FDA is committed to learning from each MDUFA reauthorization cycle and is committed to doing better in the timely posting of meeting minutes in the future.

5. **Do you believe there is a lack of patient stakeholder representation during negotiations between FDA and industry? If not, please clarify how the FDA is ensuring that patient and consumer organization perspectives are heard.**

As noted above, FDA has followed the process described by statute, including holding two public meetings with associated dockets for public comment, conducting negotiations with regulated industry, and hosting 13 monthly consultation meetings with public stakeholders (including patient and consumer advocates) while negotiations were ongoing. The process used to develop the recommendations for the MDUFA V reauthorization provided a significant opportunity for patient stakeholders and other members of the public to express their views and priorities. FDA thoughtfully considered this input (as noted in response to Question 1) in shaping and prioritizing its proposed recommendations for program enhancements. Contributions by patient, consumer, clinical, and other advocates and stakeholders were critical to informing FDA during the negotiations.

And, as noted, we incorporated stakeholder input in developing our proposals, particularly those for patient engagement, digital health, real-world evidence and the TAP pilot. Further, FDA will hold its second public meeting on April 19, 2022, and the comments received during that meeting and comments submitted to the public docket will help inform potential changes to the final commitment letter submitted to Congress.

**The Honorable Richard Hudson (R-NC)**

1. **Over the years, it has been the recognized stance of the Food and Drug Administration (FDA) that statutory change is unnecessary in the medical device servicing and remanufacturing space, and that FDA has consistently enforced requirements on entities engaged in remanufacturing.**

   **FDA's Report on the Quality, Safety, and Effectiveness of Servicing of Medical Devices, issued in May 2018, concluded that a majority of the comments, complaints, and adverse event reports received by the FDA alleging that inadequate "servicing" caused**

[8] https://www.fda.gov/industry/medical-device-user-fee-amendments-mdufa/medical-device-user-fee-amendments-2023-mdufa-v

**or contributed to clinical adverse events and deaths actually should be considered "remanufacturing," and not "servicing" at all. FDA's clear recommendation from this Report was to publicly clarify and distinguish between "servicing" and "remanufacturing," vis a vis a public issuance of guidance, as opposed to statutory changes. The Report states this guidance would "assist in differentiating these activities to allow more consistent interpretation and categorization," as well as "allow FDA to focus its regulatory oversight on those activities that have the greatest impact on the quality, safety, and effectiveness of medical devices."**

**In accordance with the 2018 Report, FDA released the draft guidance in June 2021, Remanufacturing of Medical Devices: Draft Guidance for Industry and Food and Drug Administration Staff. This guidance specifically states it is "not intended to adopt significant policy changes, but to clarify FDA's current thinking on applicable definitions, and clarify, not change, the regulatory requirements applicable to manufacturers."**

**The draft guidance provides explicit definitions of both remanufacturing and servicing, offers clear illustrations on how FDA defines activities that constitute remanufacturing, as well as relevant considerations, instructions, and flow charts for how entities performing activities on devices should determine whether each activity and the cumulative effects of such activities is considered remanufacturing. The guidance also includes recommendations for how and when entities should document the rationale for their decision.**

**It is my current understanding the FDA is now in support of legislation pertaining to remanufacturing. Has the FDA revised its thinking regarding the adequacy and appropriateness of the June 2021 remanufacturing guidance that was issued just less than one year ago? If the FDA has changed its position, please identify and explain the rationale behind this change, as well as the specific issues wherein FDA believes statutory change would be required that the guidance cannot or does not address already.**

As I testified before the Health Subcommittee in March, FDA believes that clarifying the definition of "remanufacturing" in statute could be helpful to stakeholders, if done correctly. The relevant definitions derive not from our June 2021 draft guidance but from our codified regulations, including 21 CFR 820.3. FDA has consistently enforced regulatory requirements on entities engaged in remanufacturing. Our draft guidance is intended to further clarify FDA's thinking on the matter, and to help entities determine whether their activities likely constitute remanufacturing.

While FDA maintains that it has the authority to regulate device servicing and remanufacturing, we support Congressional efforts to make these terms and concepts more explicit in statute.