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November 25, 2020

The Honorable Stephen M. Hahn, MD
Commissioner
Food and Drug Administration
Dockets Management Staff (HFA-305)
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: FDA-2020-N-0907 for Medical Device User Fee Amendments for Fiscal Years 2023 Through 2027; Public Meeting; Request for Comments.

Dear Commissioner Hahn:

FasterCures appreciates the opportunity to provide comments to the Food and Drug Adminstration's (FDA's) request for comments on the reauthorization of the Medical Device User Fee Act (MDUFA). We applaud the significant progress previous MDUFA commitments have supported, including advances in integrating patient perspectives into device development and review, advancing the use of real world evidence to enhance device development, and exploring innovative paradigms for regulating new tools for digital health. We look forward to contributing to the next round of action to ensure patients have access to new devices in a timely manner and we build a stronger, patient-centered medical device ecosystem for all.

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FasterCures, a center of the Milken Institute, is driven by a singular goal: to save lives by speeding scientific advancements to all patients. With an independent voice, FasterCures is working to build a system that is effective, efficient, and driven by a clear vision: working with our partners to build a patient-centric system where science is accelerated, unnecessary barriers are overcome, and lifesaving and life-enhancing treatments get to those who need them as rapidly as possible.

FasterCures' comments below focus on three priority areas:

(1) Increasing Diversity in Clinical Trials and Patient Engagement;

(2) Ensuring the Promise of Digital Health is Realized; and

(3) Enhancing Transparency and Continuing Progress Driven by COVID-19.

**Increasing Diversity in Clinical Trials and Patient Engagement**

Notwithstanding the attention paid to diversity in the last decade, a critical need still exists to increase enrollment of underrepresented populations, including racial and ethnic minorities, in clinical trials for high-risk medical devices. With meaningful subgroup analyses for both safety and effectiveness conducted and reported, patients can better understand whether a device is right for them, and can make better informed decisions for their care as specific information on relevant outcomes and risks are known.

But meaningful subgroup analyses require sufficient numbers of trial participants within racial and ethnic minority groups, as well as age and gender groups. And the value of this data only accrues to patients when these analyses are conducted and reported. A 2018 study looking at pivot trials for the 22 devices publicly reviewed at an FDA Advisory Committee meeting between 2014 and 2017 found that "[o]nly 3 (14%) of the devices provided subgroup analyses for both effectiveness and safety or both sensitivity and selectivity for gender, race, and age. However, 55% of the devices reported both of those subgroup analyses for at least 1 of the 3 subgroups. Whether analyses were reported or not, the number of patients in most subgroups was too small to draw meaningful conclusions. Subgroup analyses were more likely to be reported to the FDA's Advisory Committees than in the FDA's public reviews or labeling."[1]



We appreciate FDA's initiatives on clinical trial diversity including its guidances on "Collection of Race and Ethnicity Data in Clinical Trials"[2], and "Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies" which discussed considering relevant age, race,

[1] Fox-Rawlings et al. Diversity in Medical Device Clinical Trials: Do We Know What Works for Which Patients?, *Milbank Q* 2018 Sep; 96(3):499-529, available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6131322/ (last accessed Nov. 13, 2020).

[2] FDA Guidance, Collection of Race and Ethnicity Data in Clinical Trials, October 2016, available at: https://www.fda.gov/media/75453/download (last accessed Nov. 13, 2020).

ethnicity, and associated covariates when designing clinical trials, recommended analyses of study subgroup data, and outlined the Agency's expectations for reporting[3].

More can be done to increase diversity in device trials, and we recommend FDA build on these efforts and consider ways to further define agency expectations, share best practices and tools – both across the agency and externally -- , and drive the development of innovative approaches, including the use of mobile technologies, to increase racial and ethnic diversity in clinical trials, as appropriate. This may include:

- Public meetings and guidance specific to best practices, successful approaches to increasing racial and ethnic diversity, and lessons learned
- Pilots and/or grants, including to non-traditional grantees (e.g., community based organizations), for innovative approaches for outreach and education, enrollment, and retention for clinical trials for racial and ethnic minority populations
- Expected early consultation with the agency to discuss a sponsor's diversity plan (and patient engagement plan to inform the diversity plan)
- A repository of publicly available tools on FDA's website as a resource for stakeholders and/or other ways to share information learned from pilots and successful (and unsuccessful) approaches



This premise of increasing diversity applies equally to patient engagement, where it is essential to have as diverse and representative a voice as possible, defined by the aim of the engagement. In addition to hearing from a diverse set of patients – from different ages, racial and ethnic groups, genders, disease severity, or stage of disease – it is important for the agency to solicit and incorporate into its decision-making patient input from diverse sources and collection methods.

We applaud FDA's significant work on advancing the development and use of patient preference information, including holding a September 2020 public meeting on Using Patient Preference Information in Medical Device Regulatory Decisions: Benefit-Risk and Beyond[4], and patient reported

[3] FDA Guidance, Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies, September 2017, available at: https://www.fda.gov/media/98686/download (last accessed Nov. 13, 2020).

[4] FDA Website, Public Meeting – Using Patient Preference Information in Medical Device Regulatory Decisions: Benefit-Risk and Beyond, September 29, 2020, available at: https://www.fda.gov/medical-devices/workshops-

outcomes, including issuing a recent draft guidance on Principles for Selecting, Developing, Modifying, and Adapting Patient-Reported Outcome Instruments for Use in Medical Device Evaluation[5]. We encourage the agency to continue to (and encourage sponsors to) proactively look to sources of patient input beyond these tools. Patient input comes in many forms, including discussions held in focus groups or public hearings, health data generated by patient use of digital apps and remote tools, patient registries, natural history studies, and others. Patient input from these and other sources and methods can allow a more robust and full-rounded understanding of patients' experiences, preferences, desires, and needs, and can capture input from a more diverse set of patients.

We also ask FDA to consider how the agency can ensure patients, industry, and the broader public understand the impact of patient engagement and the use of patient input in device development and regulatory decision-making. It is important to patients and patient organizations to understand the impact of their efforts, so that limited resources can be directed to impactful initiatives and funneled away from work that cannot or does not get used. Whether this information makes it into a product label or into a product approval review summary, FDA should consider creating a publicly available set of examples as a resource for patients, manufacturers, and other stakeholders, and other ways to share information on what and how different types of patient input was used in device development and regulatory decision-making.



**Ensuring the Promise of Digital Health Tools is Realized**

The explosion of digital health tools is revolutionizing the healthcare industry. In order to harness the collective power of these tools, stay ahead of trends and innovation, and ensure the promise of digital health is safely realized for patients, FDA must lead the way. As such, we support additional resources for the agency to achieve this goal and continue to build its expertise and capacity to understand and review these tools.

conferences-medical-devices/public-meeting-using-patient-preference-information-medical-device-regulatory-decisions-benefit-risk?utm_campaign=2020-02-19%20CDRH%20New&utm_medium=email&utm_source=Eloqua (last accessed Nov. 18, 2020).

[5] FDA Draft Guidance, Principles for Selecting, Developing, Modifying, and Adapting Patient-Reported Outcome Instruments for Use in Medical Device Evaluation, August 2020, available at: https://www.fda.gov/media/141565/download (last accessed Nov. 18, 2020).

FasterCures is encouraged by the creation of the FDA's Digital Health Center of Excellence as a way to coordinate and streamline the understanding of, use, and review of digital health tools, and we greatly appreciate the agency offering numerous opportunities for external stakeholders to hear about, discuss, and comment on the development of the Center. Below we touch on a few of the Center's current areas of focus[6].

First, with respect to artificial intelligence and machine learning, we encourage the agency to take a proactive approach to understanding and minimizing bias in these tools. We applaud the agency for bringing this topic to the Patient Engagement Advisory Committee recently[7], and discussing the issue of training and validation data representing a sufficiently diverse set of patients, including demographic considerations, race and ethnicity, and age. We encourage FDA to continue to advance this work and meaningfully engage patients throughout its development so that all of regulated AI/machine learning innovations can perform their best in all populations for which the intervention is intended.



Second, FasterCures believes that clarity and transparency is critical for wearable and patient-generated data, and arguably for all digital health. Specifically, given the newness of these technologies and the overlap or similarities to wellness tools, patients and other stakeholders need to understand exactly what is "digital health", which wearables are regulated and which are not, what is the difference between a wellness tool and a medical device, how is their data protected and what data is actionable and/or used and for what purposes. Creating specific public-facing definitions and explanations to these questions and more can go a long way in building trust and reducing misunderstandings about these tools. Again, meaningful engagement with a diverse group of patients is critical to identifying needs and communicating effectively with patients, other stakeholders, and the public at large.

And finally, digital tools hold great promise to build a more nuanced and robust understanding of each patient's experience through their use in clinical studies and as real world evidence, as well as reduce the clinical trial burden that can allow harder-to-reach volunteers to participate and complete clinical trials. We support FDA's work to advance the understanding and use of fit-for-purpose real world

[6] FDA Presentation at October 19, 2020 Webinar – Digital Health Center of Excellence Listening Session #1, available at: https://www.fda.gov/media/143078/download (last accessed Nov. 18, 2020).
[7] FDA, Executive Summary for the Patient Engagement Advisory Committee Meeting, Artificial Intelligence (AI) and Machine Learning (ML) in Medical Devices, October 22, 2020, available at: https://www.fda.gov/media/142998/download (last accessed Nov. 18, 2020).

evidence in the regulatory context, and ensure that clinical studies minimize the burden to participants, allow for greater patient-generated data, and increase opportunities for a more diverse participant pool to join and complete clinical trials. In addition, we encourage the Agency to explore the potential of using mobile health technologies to return study progress information and study results.

**Enhancing Transparency and Continuing Progress Driven by COVID-19**

In our current landscape, transparency, trust, and understanding how medical products are approved is more critical than ever. We appreciate that FDA publicly releases some information on how they make their decisions, and we encourage the agency to consider ways to increase transparency through additional disclosures that release valuable information while protecting company confidential information and patient privacy. Enhanced transparency can benefit the medical device ecosystem and patients specifically by minimizing costly replication of effort, reducing regulatory uncertainty, and enhancing patient engagement and public trust.

We recommend FDA create a position/group in the Commissioner's Office that can initiate, lead, and oversee the agency's transparency initiatives. In addition to ensuring that disclosed information is in a useable and understandable format for each audience, including patients and researchers, this group would be responsible for a consistent process of:



(1) identifying potential transparency initiatives that may benefit the public and other stakeholders, including efforts to harmonize disclosures across regulatory markets;
(2) consulting with relevant stakeholders, including patients, to investigate the feasibility and impact of these initiatives;
(3) running pilots of chosen initiatives and assessing impact/benefit; and
(4) ending, modifying, or installing as permanent programs these pilots, and communicating these decisions to the public.

We also encourage FDA to consider additional transparency initiatives, such as ensuring decision summaries for all medical devices include a robust discussion of FDA's decision-making, disclosing to the public how patient input is used by FDA and what other (non-sponsor submitted) sources were used to understand the patient experience, and sharing with the public lessons learned and best practices, including related to approaches for patient engagement and increasing diversity in clinical trials.

Additionally, FasterCures recognizes that the devastating COVID-19 pandemic offers some lessons that we would like to see continued after the pandemic subsides. We have witnessed unprecedented collaboration between the agency and industry, including non-traditional manufacturers, between diverse industry players, and among many stakeholders and across sectors. The urgency of the pandemic has led to a focus on what is critically important, and we would like to see the agency work to ensure that, as appropriate, these workflows, procedures, and forward-thinking flexibilities continue past the pandemic so that patients using future devices can benefit. For example, reducing the time to draft and release guidance documents can lead to these materials having more real-time impact and align with the quick, iterative development processes of medical devices.

And finally, the increased awareness and use of remote healthcare and the tools to make that happen seen during the pandemic have given us more opportunity to learn about and collect more patient generated data. We would like to see this progress continued so that patient-generated data can help paint a clearer picture of patient experience and be incorporated into more healthcare decision-making.

**Conclusion**



We appreciate FDA's consideration of these suggestions, and look forward to working with the agency throughout this MDUFA reauthorization. We are happy to discuss any of these areas in greater detail at any time. To do so, please contact me at bhuneycutt@milkeninstitute.org or by phone at 202-406-0811.

Sincerely,

Brenda Huneycutt, PhD, JD, MPH
Director, FasterCures