AMA
AMERICAN MEDICAL ASSOCIATION

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August 20, 2020

The Honorable Stephen Hahn, MD
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20990

Re: Docket No. FDA-2010-N-0128, "Reauthorization of the Prescription Drug User Fee Act; Public Meeting; Request for Comments."

Dear Commissioner Hahn:

On behalf of the physician and medical student members of the American Medical Association (AMA), I appreciate the opportunity to provide comments in response to Reauthorization of the Prescription Drug User Fee Act (PDUFA); Public meeting; Request for Comments. I also thank the U.S. Food and Drug Administration (FDA) for the invitation to participate in the public hearing. Patrice A. Harris, MD, MA, AMA Immediate Past President, was pleased to present the AMA's perspective on this important issue. We commend the FDA for facilitating the dialogue among many stakeholders to improve the drug approval process and maintain the safety of drug products for our patients.

The AMA has long standing policy supporting adequate FDA funding and notes that "a strong and adequately funded FDA is essential to ensuring that safe and effective medical products are made available to the American public as efficiently as possible." The AMA has supported previous PDUFA authorizations based on a "primary purpose to make the drug approval process as efficient as possible without compromising standards for proof of efficacy and safety." The AMA has a strong interest in the future of PDUFA and we are pleased to comment on the questions from the Federal Register Meeting Announcement related to the assessment of the performance of PDUFA VI thus far and considerations for the next iteration of PDUFA for FDA to consider to enhance the efficiency and effectiveness of the human drug review process.

Assessment of the Performance of PDUFA VI Thus Far

The AMA has reviewed the FDA's FY 2018 and FY 2019 Performance Reports to Congress for the Prescription Drug User Fee Act, and we believe PDUFA VI has provided progress in several areas:

- It is clear that PDUFA VI has been highly successful in reducing application review times for drug and biological products.
- The extended range of activities for which FDA could use prescription drug user fee revenue, including post-market safety activities and adverse-event data collection systems, have also been useful.
- Advancements in FDA's regulatory science program, including the release of "Framework for FDA's Real-World Evidence Program" and continued efforts on FDA's Sentinel, are commendable.

Thus far, in FY 2020, FDA continues to make and report progress in performance goals despite the necessary shifting of Agency staff responsibilities due to COVID-19 and pandemic response activities. The current pandemic has exposed vulnerabilities in the global medicine supply chain leading to uncertainty, an increasing number of drug shortages, and potential quality issues. Inspections of foreign and domestic drug manufacturing facilities have been on hold, deficiencies in the drug supply chain have been amplified, and clinical trials have been disrupted. Following the pandemic, FDA will have residual challenges related to clinical trials to face and we urge flexibility and cooperation with clinical trial sponsors to find workable, customized solutions.

Considerations for the Next Iteration of PDUFA

Health Equity

In a recent article in *The Lancet*, AMA's Chief Health Equity Officer Aletha Maybank, MD, MPH, weighed in on the health inequities that exist in America.[1] In the article, she highlights that COVID-19 has exposed health inequities that have always existed and talked about how the U.S. Government's omission of data in Black, Hispanic, and Native American communities has impacted the need for positive change in these communities. **We urge the FDA to collect and share more accurate data related to race and ethnicity and to create and enforce strict requirements for clinical trials to accurately resemble patient populations.**

We understand that representation in clinical trials is not necessarily due to drug sponsors' unwillingness to diversify participants. Members of minority groups are often reluctant to participate, lack access to trials, and lack time and resources to participate. The AMA urges that resources be provided to community level agencies that work with those minorities who are not proportionately represented in clinical trials to address issues of lack of access, distrust, and lack of patient awareness of the benefits of trials in their health care.

Drug Supply Chain and Drug Shortages

Strengthening the supply chain to ensure an uninterrupted supply of essential medicines that are safe, meet standards for quality, and are beneficial to health should be a public health priority. Drug shortages remain an ongoing public health concern in the United States, and unprecedented demand for certain drugs due to large numbers of critically ill patients with COVID-19 is worsening the situation. An ideal situation for physicians is to use "first-line" medications—those that are considered more effective and have fewer side effects—at all times. Drug shortages force physicians to make adjustments and use second- or third-line medications, which causes additional time delays in treating patients to determine appropriate dose and routes of administration and increases risk for patients.

To maintain a strong and safe supply chain, regulators must know where medicines and their ingredients are manufactured and how they pass through the supply chain. The recently passed Coronavirus Aid, Relief, and Economic Security (CARES) Act took some steps to address supply chain issues, but more can be done, including expanding global reporting requirements for indicators of drug shortages, requiring drug manufacturers and ingredient suppliers to monitor and report on their capacity and

[1] Jaffe S. Aletha Maybank: AMA's Chief Health Equity Officer. Lancet. 2020;395(10242):1963. doi:10.1016/S0140-6736(20)31408-2.

ingredient quality, and providing incentives to manufacturers for manufacturing innovation and developing shortage mitigation plans.

The AMA urges:

- **Accelerating the development and adoption of pharmaceutical manufacturing innovations in manufacturing processes away from batch manufacturing to continuous manufacturing.**
- **Requiring drug manufacturers to establish a plan for continuity of supply, including resiliency and redundancy in manufacturing capability, of medications and vaccines to avoid production shortages.**
- **Requiring transparency from manufacturers regarding production locations of drugs and more detailed information regarding the causes and anticipated duration of drug shortages.**

Medication Quality and Drug Safety

The AMA is very concerned about medication quality and the safety of our patients and our Council on Science and Public Health currently has this topic under study. AMA policy supports the development and enforcement of standards that make the sources of pharmaceuticals and their chemical substrates used in the United States transparent. AMA policy also supports pharmaceutical tracking systems, punishment of pharmaceutical counterfeiters, and illegal activities in the pharmaceutical industry.

Current AMA policy also addresses the safety and quality of foreign manufactured pharmaceuticals and supports inspection of all products entering the United States, surveillance inspections of foreign manufacturers, and encourages Congress and the FDA to use their authorities to ensure safe imported drugs. The need for adequately conducted drug safety inspections abroad is paramount. The Government Accountability Office (GAO) outlined a number of deficiencies in the FDA's surveillance of foreign drug manufacturing, including the Agency alerting drug manufacturers in advance that it is planning an inspection.[2] GAO has been raised concerns and has identified FDA's issues with foreign drug inspections as a "high risk" issue for more than a decade.

The AMA urges:

- **The developing and enforcing of standards that make ingredients used to manufacture pharmaceuticals and ingredients used by patients in the United States transparent to prescribers and the general public.**
- **Conducting adequate and unannounced safety inspections abroad.**
- **Evaluating and facilitating of implementing effective tracking systems for pharmaceuticals.**
- **Continuing to modernize of the drug safety system and use of novel techniques, including real-world evidence, to maximize the usefulness of tools used for collecting adverse event information at various points during the product lifecycle.**

While COVID-19 has exposed weaknesses and opportunities for improvement, the AMA believes PDUFA reauthorization is critical to sustaining the improved performance of the FDA in expediting new drug and biological products to patients. **Because of its past success, the AMA strongly supports the**

[2] https://www.gao.gov/assets/710/703078.pdf

reauthorization of PDUFA in 2022. We look forward to continuing working collaboratively with FDA and other stakeholders.

Again, the AMA appreciates the opportunity to comment on this important subject. Should you have any questions or wish to discuss further, please do not hesitate to contact Shannon Curtis, Assistant Director, Federal Affairs, at Shannon.Curtis@ama-assn.org or 202-789-8510.

Sincerely,

James L. Madara, MD