Attachment—Additional Questions for the Record

Subcommittee on Health
Hearing on
" FDA User Fee Reauthorization: Ensuring Safe and Effective Drugs and Biologics "
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The Honorable Gus Bilirakis (R-FL)

1. Dr. Vereshchagina, as Co-Chair of the Rare Disease Caucus I'm particularly interested in the work FDA and Congress can do to facilitate and improve regulatory pathways for rare disease R&D. Can you tell me more about the proposed pilot programs for Split Real Time Application Review in the PDUFA agreement and what that means for rare disease patients?

The Split Time Application Review (STAR) Pilot Program[i] allows sponsors to split submissions of certain efficacy supplements, and FDA to split review of required sections of marketing applications. One of its goals is to shorten the time from the date of complete submission to the action date in order to expedite earlier patient access to novel uses of existing therapies that address an unmet medical need. The STAR program will expedite patient access to novel uses for existing therapies by supporting initiation of review earlier than would otherwise occur and therefore allowing earlier approval for qualified efficacy supplements. This program, beginning in fiscal year (FY) 2023, will apply across all therapeutic areas and review disciplines for applications that meet specific criteria.

As many rare diseases represent areas of unmet medical need, PhRMA hopes that sponsors developing drugs and biologics for new rare disease indications will be utilizing this program and that rare disease patients will benefit from the expedited drug review process.

In order to increase transparency and opportunities for public engagement, the Food and Drug Administration (FDA or Agency) will develop a public-facing webpage outlining detailed criteria for potential acceptance and participation in the STAR program. FDA will also conduct an interim assessment that includes internal activities related to STAR by the end of FY 2025. A public workshop will be held to discuss the potential value and feasibility of expanding the pilot program to select New Drug Applications (NDAs) for New Molecular Entities (NMEs) and Biologics License Applications (BLAs) and solicit feedback on experiences with the pilot program from industry stakeholders. FDA also committed to training review staff on STAR processes and providing a publicly available report summarizing training activities conducted.

PhRMA would also like to highlight additional PDUFA VII provisions that will advance and facilitate the development and timely approval of drugs and biologics for rare diseases, including rare diseases in children. Importantly, FDA's Center for Biologics Evaluation and Research (CBER) and Center for Drug Evaluation and Research (CDER) have committed to continuing the integration of rare disease staff into review divisions to ensure rare disease expertise is optimized throughout the review process.

PDUFA VII also includes the Rare Disease Endpoint Advancement (RDEA) pilot program to develop novel endpoints for rare disease clinical trials. The lack of regulatory precedent, small trial populations, and/or limited understanding of disease natural history associated with rare diseases creates unique challenges when determining the appropriate efficacy endpoint(s) for clinical trials intended to evaluate the effectiveness of rare disease therapies. Though difficult to establish, well-developed efficacy endpoints, especially those that could apply to other rare diseases with similar manifestations, drive the general advancement of rare disease drug development. In addition to challenges associated with developing endpoints that appropriately capture key signs and symptoms of a rare disease and directly measure how patients feel, function, or survive, surrogate endpoint development is also challenging in diseases with slow progression, small patient populations, or other challenges commonly associated with drug development in rare diseases.

Current mechanisms for sponsors of rare disease drug development programs to collaborate with FDA are not structured to provide repeated, intensive interactions with the Agency. The Pilot will offer additional engagement opportunities between FDA and the sponsor to support the advancement of rare disease treatments. In addition, FDA will hold public workshops to discuss various topics relevant to endpoint development for rare diseases. To promote innovation and evolving science, novel endpoints developed through the RDEA pilot may be presented by FDA, such as in guidance documents, on a public-facing website, or at public workshops as case studies. FDA staff capacity will also be expanded to enable and facilitate appropriate development and use of these types of novel endpoints. This staff will support the complex and intensive review work necessary to evaluate novel endpoint development with a focus on the challenges of trial designs utilizing small populations.

2. Dr. Vereshchagina, can you provide the number of new products the user fee agreements have helped bring to market overall, and how many have specifically been brought under Accelerated Approval?

Since 1992 when the program was first enacted, PDUFA has provided more timely patient access to more than 1,700 new drugs and biologics including treatments for cancer, rare diseases, cardiovascular, neurological, and infectious diseases. Before PDUFA, it often took FDA more than two years to review new medicines. In 2021, the Center for Drug Evaluation approved 50 novel drugs. 86% were approved on the first cycle. 76% were approved in the United States before any other country. 52% were for rare or orphan diseases. 54% were First-in-Class.[ii]

Medicines approved under accelerated approval address unmet medical needs for serious and life-threatening diseases and conditions and meet FDA's high standards for safety and effectiveness. This pathway has provided timely access to hundreds of treatments for HIV/AIDS, cancers and rare diseases, leading to better health outcomes for millions of patients.
Since the inception of accelerated approval in the early 1990s, over 250 new drugs and biologics to treat serious or life-threatening illnesses have been approved through the accelerated approval pathway. From 1992 through about 2010, accelerated approval was primarily used for drugs indicated for the treatment of HIV (39.7% of approvals), cancers (35.6% of approvals) and other rare disease treatments and specialty drugs (24.7% of approvals). In 2021, CDER approved 14 of the 50 novel drugs (28%) under Accelerated Approval.[iii]

The upcoming PDUFA VII efforts are aimed at modernizing the U.S. regulatory and drug development paradigm and improving efficiencies in drug review, including for post-marketing requirements (including those for accelerated approval drugs). For example, FDA will update their review processes to provide timelier discussions between sponsors and the Agency to help ensure earlier agreement on post-marketing requirements, including for drugs and biologics approved under the accelerated approval pathway.

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[i] Real Time Oncology Review (RTOR) is separate from the STAR pilot program. Sponsors developing oncology products can still utilize the RTOR program.

[ii] FDA New Drug Therapy Approvals 2021. Available at https://www.fda.gov/media/155227/download

[iii] FDA New Drug Therapy Approvals 2021. Available at https://www.fda.gov/media/155227/download