www.bioworld.com/articles/511849-pdufa-vii-keeping-pace-with-the-present-prepping-for-the-future

PDUFA VII keeping pace with the present, prepping for the future

By Mari Serebrov
Sep. 28, 2021

The PDUFA commitment letter negotiated between industry and the U.S FDA every five years provides an inside look at the future of drug development. The PDUFA VII letter, which is to be presented to Congress by Jan. 15, is no exception.

With a focus on gene and cell therapies, rare diseases, real-world evidence (RWE), and digital and cloud technologies, the proposed commitments presented at the FDA's Sept. 28 public meeting have evolved light years from the first agreement in 1992 that dealt primarily with user fees to support the drug review program. And they show where both regulators and sponsors expect increased action over the lifespan of PDUFA VII, which would go into effect in fiscal 2023.

Already stretched beyond capacity by COVID-19, the FDA's Center for Biologic Evaluation and Research (CBER) likely will be at the center of the activity. Offering a public stakeholder perspective during the meeting, Ed Neilan, chief medical and scientific officer for the National Organization for Rare Diseases, noted that CBER had received more than 200 investigational new drug (INDs) applications for cell and gene therapies in 2018 and again in 2019, doubling the 100 submitted in 2017.

That growth is expected to continue, even as CBER is seeing an increase in other applications due to the pandemic. In fiscal 2020, CBER received nearly 7,000 INDs, Neilan said. Its load would be further stretched under PDUFA VII, which calls for allergenic extract products approved after Oct. 1, 2023, to be subject to the user fee program.

To prepare CBER for the future, the commitment letter calls for the center to hire 160 additional staff who would provide direct and indirect support for the rapidly growing cell and gene therapy space, CBER's Chris Joneckis said. Along with the funding to hire that staff, PDUFA VII would give CBER the resources needed to onboard and train the new employees while modernizing its reviews and engagement with sponsors of cell and gene therapies.

The letter also would commit CBER and the FDA's Center for Drug Evaluation and Research (CDER) to modernizing their information technology (IT) infrastructure. Although both centers have been accepting submissions electronically for years, their systems have a lot of problems accepting large datasets, CDER's Mary Ann Slack said. She noted that it's tough to extract and triage data because of the way the information

comes in. The agency's current environment also doesn't support shared content, so there's limited support for sponsor-regulator collaborations and information requests.

The increasing volume and complexity of biologics submissions place CBER in a unique position, Slack said, as "the trains need to keep running while this modernization takes place."

The PDUFA VII letter addresses some of those IT issues by providing resources to shift to cloud-based operations, create demonstration projects to promote innovation, and improve data management and analytics, Slack said.

A related commitment is for CBER and CDER to assess the performance of digital health technologies (DHTs) in drug development. While DHTs have helped sponsors keep clinical trials on track during the pandemic, CBER and CDER need to build the capacity to address the challenges the technologies present and help realize their potential.

Other lessons from COVID-19 included in PDUFA VII involve greater use of RWE and alternative inspection tools. While RWE is woven throughout the commitments, the FDA is continuing to learn and understand what's possible with inspections. The commitment letter calls for the agency to issue guidance on alternative inspection tools as it moves beyond the pandemic, CBER's Carol Rehkopf said.

Reaction

Some of the proposed commitments didn't sit too well with a few advocacy groups. While industry and the FDA touted how PDUFA VII would advance cell and gene therapies, increased patient engagement, the use of RWE, digital tools and innovations in drug manufacturing, those groups worried that the commitment letter, hammered out between industry reps and FDA officials behind closed doors, ignored the agency's role as a public health gate-keeper by leaning too far into the idea of a public/private partnership.

The commitment letter encourages fast approval at the expense of careful approvals, said Michael Abrams, a senior health researcher at Public Citizen. Noting that the FDA's performance measures included in the agreement are all timeline-focused, Abrams suggested that short- and long-term public health impact measures – such as the number of applications rejected and tallies for withdrawals and recalls – be included as well.

He also encouraged the FDA to develop performance measures based on surveys of content experts, including its review staff and advisory committee members. Their thoughts are germane to the efficacy of the program, Abrams said, adding that it would be useful to see the percentage of FDA reviewers who felt they were free from pressure in making regulatory decisions.

Abrams also called for the FDA to establish procedures to separate the staff involved in pre-approval proceedings with sponsors from those who review an application.

Speaking during the public comment period, Kim Witczak, founder of Woodymatters, agreed that PDUFA VII's priority is expedited approvals. While acknowledging the pandemic lesson that highlighted the need for a strong regulatory agency that can act quickly, she said the agency's performance also should be built on safety. "It shouldn't be an either/or," Witczak said.

Rather than relying on risk evaluation and mitigation strategies (REMS) as a safety catch-all, the FDA should focus on premarket safety concerns and investigate safety signals as soon as they arise, as it has done with COVID-19 therapies and vaccines, Witczak said.

Diana Zuckerman, president of the National Center for Health Research, agreed that the REMS program needs to be completely overhauled or discontinued. The FDA's analysis of the opioid REMS shows how ineffective it was, she added.

Zuckerman and Witczak both called for a return to in-person inspections. Remote inspections should be the exception in the future, Zuckerman said.

In concluding the public comment meeting, Zuckerman reiterated that the FDA should be a public health agency, and it needs to ensure that industry user fees do not interfere with that mission. When decisions, such as the PDUFA VII commitments, are made behind closed doors, it's hard for the public to have confidence in the agency, she said.

Comments on the commitment letter are due by Oct. 28.