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Requiring FDA Guidances Does Not Always Advance The Science, Gene Therapy Director Says

by Derrick Gingery

OTAT Director Wilson Bryan says important cell and gene therapy guidances came from clear community needs, not user fee program requirements.

A guidance mandate in the new US Food and Drug Administration user fee program may feel like a win, but it will only help industry if the agency is ready to opine on the subject, a senior official said.

The FDA must write several new guidances, including some related to cell and gene therapies, as part of the prescription drug user fee reauthorization, which went into effect on 1 October.

Wilson Bryan, director of the Center for Biologics Evaluation and Research's Office of Tissues and Advanced Therapies (OTAT), said his office will look at INDs, science and stakeholder interest to determine whether new guidance documents are necessary. He said PDUFA mandates will not produce useful guidances if the agency has nothing to say on the subjects.

Bryan said important guidances issued recently came from FDA officials listening to community needs, paying close attention to trends in INDs, and tracking evolving science.

"We put out guidance documents recently on *genome editing*, on *CAR-T cells*, guidance on the *standardizations for products*," he said during last month's American Society of Gene and Cell Therapy Policy Summit. "These I think are very important guidances, but it didn't come out of a PDUFA mandate. They came out of the agency assessing "what's needed for the community" and concluding that "we now feel like we have enough experience to write a guidance."

Listening To Stakeholders Is Most Important, Bryan Says

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Bryan suggested setting PDUFA and other user fee requirements can be difficult because they are attempting to predict future needs. He said the spirit of the commitments matter more.

"The idea is not that the folks who negotiate PDUFA now actually know what's going to be most important three years, or four years or five years from now," he said. "What's most important is that those of us in OTAT are listening to the stakeholder community and adjusting our guidance preparations and output according to the changing science."

The PDUFA VII *agreement* requires a cell and gene therapy draft guidance on evaluating efficacy in small patient populations with novel trial designs and statistical methods and how the concepts could be applied to common diseases, as well as an update to guidance on the use of expedited programs for regenerative medicine therapies for serious conditions. (*See table.*)

The story continues after the table...

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Managing PDUFA FTE Infusion Expectations

The reauthorization includes adding hundreds of new employees, many of which will go to CBER and its increasing cell and gene therapy workload. However, industry and FDA officials at the conference warned their impact likely will not be immediate.

"We need to manage our expectations as to how quickly those resources are going to offer relief," Brad Glasscock, head of global regulatory affairs at *BioMarin Pharmaceutical Inc.*, said during the conference. "I think we just have to give it time to mature and yield some benefits here for the industry."

Bryan agreed, adding that new employees usually need two years to be properly trained once they are hired.

"Seeing the impact of PDUFA VII on processes will take some years," he said. "Along with that, I'm very worried about turnover. I'm worried about turnover due to workload. I'm worried about turnover due to reimbursement and salaries."

Bryan said that many experienced people in his office are leaving and will be difficult to replace.

"I'm not losing decades of experience, I'm losing centuries of experience," he said. "And it takes time to rebuild that, to make that up."

"While the field is advancing, we're going through a lot of transitions and I feel obliged to try to

sort of dampen expectations of what you're going to see soon after any bill might be passed," Bryan added.

PDUFA VII includes adding more than 350 new employees to the FDA. Most will go to CBER and be hired during FY 2023. (Also see "*PDUFA VII Commitment Letter Outlines Real-Time Review Expansion, Hiring Goals*" - Pink Sheet, 23 Aug, 2021.)

Because FDA salaries are not competitive with industry and conflict of interest rules limit investments, hiring at the FDA often is difficult. CBER is offering permanent telework options to attract candidates who may not be willing to relocate to the Washington D.C. area. (Also see "*CBER Staffing Remains Challenging, But Permanent Virtual Work May Help Offset Expected Retirements*" - Pink Sheet, 2 Jun, 2022.)

Bryan's office will be renamed the Office of Therapeutic Products and promoted to a super office within CBER early next year in preparation for a bolus of cell and gene therapy applications. (Also see "*New Name, Old Problems: US FDA's Cell And Gene Therapy Office Still Facing Growth Challenges*" - Pink Sheet, 5 Oct, 2022.)