Alliance for Regenerative Medicine

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Dockets Management Staff (HFA-305)
US Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Comments for FDA Docket No. FDA-2020-N-1529 "Independent Third-Party Assessment of Investigational New Drug Food and Drug Administration-Sponsor Communication Practices in Prescription Drug User Fee Act VI; Public Meeting; Request for Comments."

The Alliance for Regenerative Medicine (ARM) appreciates the opportunity to provide its comments regarding the Independent Third-Party Assessment of Investigational New Drug (IND) FDA-Sponsor Communication Practices in the Prescription Drug User Fee Act (PDUFA) VI, FDA Docket No. FDA-2020-N-1529, published in the Federal Register on July 21, 2020.

ARM is the leading international advocacy organization dedicated to realizing the promise of regenerative medicines and advanced therapies. ARM promotes legislative, regulatory and reimbursement initiatives to advance this innovative and transformative sector, which includes cell therapies, gene therapies and tissue-based therapies. Early products to market have demonstrated profound, durable and potentially curative benefits that are already helping thousands of patients worldwide, many of whom have no other viable treatment options. Hundreds of additional product candidates contribute to a robust pipeline of potentially life-changing regenerative medicines and advanced therapies. In its 11-year history, ARM has become the voice of the sector, representing the interests of 360+ members worldwide, including small and large companies, academic research institutions, major medical centers and patient groups.

ARM commends the FDA's initiative to convene the public meeting on August 11, 2020, to discuss the Independent Third-Party Review Assessment (Assessment) of FDA-sponsor communication practices during the IND stage of new drug/biologic development. The public meeting and the Assessment helped characterize current communication practices and identify best practices and challenges, as well as offering suggestions for improvement. ARM appreciated the opportunity to hear directly from Eastern Research Group (ERG), the authors of the Assessment, as well as the FDA and other stakeholders. ARM's specific comments follow.

<u>CBER Representation in Commercial IND Phase</u>

ARM appreciates that ERG used a systematic process to identify, collect, and analyze data for the PDUFA VI IND Assessment and took efforts to include a range of INDs in its analysis. ARM

commends ERG for replacing a number of the randomly selected INDs with INDs that met desired distribution traits; specifically INDs submitted to the Center for Biologic Evaluation and Research (CBER) which led to greater representation and more data from INDs for biological products. ARM further appreciates that ERG extended the assessment period for the CBER INDs by one month, through August 31, 2019.

However, CBER's overall representation in the Assessment was still much less than the Center for Drug Evaluation and Research's (CDER) representation. In addition, CBER's Office of Tissue and Advances Therapies (OTAT) represented only 11% of the total INDs reviewed, and more generally CBER represented only 19% of the total INDs. The lack of CBER IND representation is concerning to ARM because CBER submissions have drastically increased. As of July 2020, there are more than 1,000 active gene therapy INDs in-house at CBER, and 134 INDs submitted in 2020. FDA officials have predicted that INDs for cell and gene therapy products will continue to dramatically increase, and the questions these products pose will become more complex. Therefore, ERG should have included more such INDs in its Assessment to get an accurate picture of current practices and should consider to include in its future assessments an evaluation by each Center – CDER, CBER, and the Center for Devices and Radiological Health – in order to recommend general and center-specific policies to support FDA in the days ahead.

In light of the resource constraints and staggering number of active INDs with CBER, ARM requests a follow-up report dedicated to CBER practices. In this report, ARM suggests a review also be conducted assessing FDA and sponsor interactions prior to IND submission.

Patient Voice is Absent from the Assessment

ARM believes FDA should actively use patient perspectives in the drug review process, and that the process should be more transparent. However, the patient voice was missing from the Assessment.

Patient Focused Drug Development (PFDD) should remain a high priority for FDA, and the collection of Patient Experience Data (PED) by sponsors must be a part of the product development process to not only inform clinical development but also regulatory decision making. FDA should more aggressively communicate opportunities for patients to participate and make public the outcome of these interactions. This will broaden the understanding of how the Agency is using patient data, and how this informs drug approval.

Specifically, we urge CBER to facilitate program-specific patient engagement meetings so that patients can provide perspective about their experience with a particular therapy. For example, CBER should consider creating a program similar to CDER's Standard Core Sets Clinical Outcome Assessments and Endpoints Grant Program to encompass the patient perspective. Such input provides different and necessary patient input outside of what is gleaned from the general patient perspective in general PFDD meetings, and this input is invaluable to inform benefit-risk decisions for specific programs.

Establish Best Practices

ARM encourages FDA to establish best practices to promote greater consistency between CBER and CDER, and the divisions within each review center regarding their communications practices. ARM urges the Agency to take steps such as greater consistency in the use of email and other technologies. For example, FDA should outline best practices for sending courtesy copies of communication to sponsors, and the implementation of live meeting minutes so that the Agency and sponsors are in agreement on discussions and next steps at the conclusion of meetings. This would not only shorten the time lapse, but it would streamline the end of meeting process. ARM encourages the Agency to ensure these meetings have the appropriate allotted time and suggests the Agency increase meeting time to reflect any time impact these best practices may have. We propose that the Agency formalize this with updating the existing guidances and MAPPs.

Moreover, given the extensive and unprecedented use of virtual meetings, ARM encourages FDA to establish best practices for virtual meetings. For example, FDA should establish a best practice for review of the sponsor's technology and materials, such as use of video conferencing and ensuring all participants are on the conference prior to starting the meeting. Sponsors are prepared to video conference and benefit from the use of video conferencing by improving interactions and mirroring face-to-face interactions for example the Agency should limit use of the "mute" function during the meeting. This is a beneficial aspect of a face-to-face meeting, that is slowly being lost, and sponsors are now subject to long periods of silence during the meeting, as FDA goes on "mute".

ARM appreciates all of the efforts the Agency has taken in light of the unprecedented workload FDA is facing as a result of COVID-19. ARM commends the Agency on its responsiveness to sponsors and IND submissions.

However, during the COVID-19 pandemic, CBER has shifted to using written response only (WRO) more often and being available less frequently for meetings. This has forced sponsors to lose the important opportunity for discussions with CBER in a live meeting and caused official meeting minutes to be lost. For example, only the WROs are considered by FDA as official meeting minutes. Unlike in person meetings, where the comments and agreements during the meeting are captured and included in the official meeting minutes, WRO only captures the written responses and does not capture a follow-up call or correspondence with a WRO. Thus, any clarification or subsequent agreements will not be a part of the official minutes, and this can become problematic if FDA relies only on the official minutes and not the subsequent commentary. We recommend that the Agency consider aligning these practices so that they are consistent and include any WRO follow up in the official minutes. These should be shared with the sponsor within a defined period of time.

While ARM recognizes CBER's resource constraints, FDA should establish best practices for granting meetings or requiring a WRO format. FDA should establish these best practices to ensure the WRO interactions are meaningful without adding delay. ARM further suggests the Agency consider providing a sponsor the opportunity to follow up on a WRO, and making this response follow a time-mandated response time.

ARM encourages the Agency to establish best communication practices related to COVID-19 and to assess and share the impact and mitigation strategies to address the impact from the ongoing COVID-19 pandemic on the Agency's communication practices.

Conclusion

The regenerative medicine sector is the next frontier in the fight against some of society's most devastating diseases and disorders. These therapies have just begun to demonstrate their power to improve patient lives, but there is still much work to be done. ARM is looking forward to continuing to work with FDA, and other key stakeholders, to address the policies needed to advance the sector so that these cutting-edge treatments can meet their potential and be accessible to patients in need.

Thank you for the consideration of our recommendations.

Sincerely,

Robert J. Falb
Director, U.S. Policy and Advocacy