American Society of Gene + Cell Therapy

September 26, 2024

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

RE: Comments for Docket No. FDA-2021-D-0789 "Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies; Draft Guidance for Industry"

Dear Sir/Madam:

The American Society of Gene & Cell Therapy (ASGCT) appreciates the opportunity to comment on the document entitled "Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies; Draft Guidance for Industry". ASGCT is a nonprofit professional membership organization of more than 6,300 scientists, physicians, clinicians, and other professionals working in gene and cell therapy (CGT) in settings such as universities, hospitals, independent research organizations and biotechnology companies.

The mission of ASGCT is to promote the advancement of knowledge, awareness, and education to support the discovery and clinical application of genetic and cellular therapies to alleviate human disease. Many of our members have spent their careers in this field performing the underlying research that has led to today's robust pipeline of transformative therapies.

General Comments

ASGCT commends FDA for taking steps to fulfill this mandate, under the Food and Drug Omnibus Reform Act of 2022 (FDORA). By creating guidelines aimed to ensure clinical trial participants better reflect the diversity of the intended patient populations of drugs, biological products, and devices, FDA is making a critical contribution to increasing the real-world applicability of clinical trial data. This initiative is vital not only for promoting more efficient and equitable healthcare outcomes, but also for improving access to clinical trials for novel therapies for patients from underrepresented communities. By fostering greater inclusion in clinical trials, the guidance helps to ensure that diverse populations are meaningfully represented, ultimately bridging the gaps in healthcare disparities and expanding the benefits of medical advancements to all.

Section 505(z) of the FFDCA, as added by FDORA Section 3601[1], does not include specific enforcement mechanisms and the draft guidance is currently silent on the actions FDA may take if sponsors do not fully meet the enrollment goals, despite their best efforts. The Society suggests FDA clarify its expectations for such situations, with a focus on key processes that represent a good faith effort in enrolling historically marginalized and underrepresented populations. By doing so, FDA can ensure diversity is prioritized while ensuring that the guidance remains flexible and supportive of sponsors' efforts.

In addition, the Society suggests offering guidance on how to use modern tools and frameworks to address underlying challenges to meeting enrollment goals. Consistent with Sections 3606 and 3607 of FDORA[1] we suggest FDA note how the use of digital health tools and decentralized clinical trials can specifically assist sponsors in meeting, or exceeding, enrollment criteria. Additionally, it would be valuable for FDA to outline how Real-World Evidence (RWE) can be leveraged in the post market phase, particularly through existing Long-Term Follow-Up (LTFU) requirements for CGT products, in order to continue data collection on key populations in a meaningful way.

Specific Comments

Section V: Content of the Diversity Action Plan

A. Enrollment Goals (Lines 225-328)

The draft guidance provides a foundation to set enrollment goals disaggregated by race, ethnicity, sex, and age group. While the guidance recognizes the need for demographic diversity, it does not adequately discuss the unique challenges and disparities influenced by a range of socioeconomic factors faced by underrepresented populations that need to be considered by sponsors, investigators, and ethics committees. The financial burden of travel, lodging, and lost wages can be significant impediments to enrollment, particularly for patients with rare diseases and participants in CGT trials.

These challenges are especially pronounced in CGT trials due to the complexity of the treatments, which often require frequent visits, extensive follow-up, and may have a limited number of clinical trial sites, resulting in a higher travel burden for patients and caregivers. While it is acknowledged that these challenges are not unique to these specific patient populations, the strong association between underrepresented populations and socioeconomic factors go hand-in-hand and merit further discussion, and guidance, to ensure effective and sustainable patient retention in clinical trials. ASGCT requests additional guidance from FDA regarding the need for advanced planning and strategies around socioeconomic factors.

1 Food, Drug, and Cosmetic Act (FFDCA), Section 505(z), as added by the Food and Drug Omnibus Reform Act (FDORA), Sections 3601, 3606, and 3607, Public Law No: 117-328 (2022). Available at: https://www.congress.gov/bill/117th-congress/house-bill/2617/text

C. Measures to Meet Enrollment Goals (Lines 385-430)

The Agency's draft guidance outlines important strategies to meet enrollment goals, such as community engagement and cultural competency training (lines 400-421). The Society suggests explicitly acknowledging the cultural and systemic barriers that have historically impeded the enrollment of certain racial and ethnic populations. Addressing these barriers through targeted community engagement, education initiatives, and training of clinical trial staff in cultural competency is essential. This need for education provided by sponsors is particularly crucial when considering novel investigational therapies, such as gene therapies, where efforts to dispel myths and build understanding are essential.

The draft guidance discusses monitoring enrollment during the conduct of the clinical study and suggests that sponsors may need to take prompt action if they are not on track to meet these goals (lines 422-430). While this implies a level of adaptability, the Society suggests FDA explicitly allow for flexibility in adjusting enrollment strategies and goals as necessary. This will ensure that diversity plans remain relevant and achievable as circumstances evolve.

The Society notes that sponsors developing drugs to treat rare and ultra rare diseases may encounter challenges when collecting diversity data in ex-U.S. countries, where data protection laws may prevent collection of this information. As a result, this data may also not be readily available. The Society requests clarity on how global efforts to recruit patients from diverse ethnic groups will be evaluated within the overall diversity plan, especially in the context of international regulatory environments. In addition, it would be beneficial if the final guidance addressed these international challenges and provided clarity for sponsors to navigate these complexities by referencing existing guidance such as *E17 General Principles for Planning and Design of Multi-Regional Clinical Trials*.

Section VI: Timelines for Submitting Diversity Action Plans (Lines 433-460)

The draft guidance recommends that sponsors discuss their Diversity Action Plan (DAP) with FDA no later than at the end-of-phase-2 meeting (lines 438-445). While this is an important backstop, the guidance also encourages earlier discussions regarding the DAPs (lines 316-318). However, obtaining these early meetings can be challenging for sponsors. Opportunities for earlier, and more frequent, engagements regarding the DAP would be beneficial to sponsors.

To address this, the Society suggests FDA give additional structured opportunities for sponsors to engage in meaningful discussions about their DAPs earlier in the clinical development process. This could include more flexible options for scheduling meetings outside of the traditional milestone sessions and guidance on how, and when, sponsors can initiate these early discussions. Through these interactions, FDA could provide sponsors with timely feedback to guide their efforts throughout the development process.

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Section VII: Procedures for Submitting the Diversity Action Plan and Receiving Feedback (Lines 462-620)

The Society appreciates the information on timelines provided in the draft guidance. To ensure success, ASGCT suggests greater clarity on the internal review process, interactions with sponsors, timing of feedback to sponsors, and the definitive approval process for DAPs. We suggest FDA provide additional details in a timetable for submitting DAPs, as well as timing for feedback from the Agency to sponsors. If feedback is not necessary, the Society suggests FDA provide a statement of concurrence to sponsors.

Section VIII: Requesting Diversity Action Plan Waivers (Lines 623-688)

The criteria to request a waiver should be more clearly defined, particularly in the context of rare diseases where the patient population is inherently limited. The Society suggests FDA align this section of the guidance with recommendations in the "Postmarketing Approaches to Obtain Data on Populations Underrepresented in Clinical Trials for Drugs and Biological Products" guidance, which provides a framework to collect data post-approval in populations that are a challenge to enroll in large pivotal trial(s).

Given the unique challenges associated with rare diseases, we suggest the final guidance include illustrative examples of DAPs for diseases with small patient populations, such as those with only a few hundred patients in the U.S. The Society requests examples of cases where a waiver may be approved, and clarification the justifiable circumstances. Clear guidelines on the waiver process, including the criteria for approval, and examples of justifiable circumstances, would help sponsors navigate this complex area and avoid unnecessary delays in the development of therapies addressing high unmet needs.

ASGCT commends the spirit of the draft guidance to ensure diversity is better reflected in clinical trials. This is in alignment with the mission of the Society, and we would welcome the opportunity to provide any additional detailed information the Agency may be interested in considering.

Thank you for the consideration of these comments. If you have any questions, please do not hesitate to contact Margarita Valdez Martínez, Chief Advocacy Officer, at mvaldez@asgct.org.

Sincerely,

David Barrett, J.D.
Chief Executive Officer