American Society of Gene + Cell Therapy

June 23, 2025

Dockets Management Staff
Food and Drug Administration
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

Re: Comments for Docket No. FDA-2025-N-0287: Exploration of Health Level Seven Fast Healthcare Interoperability Resources for Use in Study Data Created From Real-World Data Sources for Submission to the Food and Drug Administration; Establishment of a Public Docket; Request for Comments

Dear Sir/Madam,

The American Society of Gene and Cell Therapy (ASGCT) appreciates the opportunity to submit comments on the public docket for "Exploration of Health Level Seven Fast Healthcare Interoperability Resources for Use in Study Data Created From Real-World Data Sources". ASGCT is a nonprofit professional membership organization comprised of 6,400 scientists, physicians, and other professionals working in cell and gene therapy (CGT) in settings such as universities, hospitals, and biotechnology companies. 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. The mission of ASGCT is to advance knowledge, awareness, and education leading to the discovery and clinical application of genetic and cellular therapies to alleviate human disease.

Currently, there are over 4,000 gene, cell, and RNA therapies in development globally[1] ranging from preclinical through preregistration. The pipeline includes over 2,000 gene therapies (including genetically modified cell therapies such as CAR T-cell therapies). In the US, 22 gene therapies and a number of genetically-based therapies have been approved.[2]

ASGCT would like to thank the Agency for organizing this public docket to collect information to advance the CGT field and improve patient outcomes regarding the use of real-world data.

[1] American Society of Gene and Cell Therapy, Citeline (April 2025). *Gene, Cell, & RNA Therapy Landscape: Q1 2025 Quarterly Data Report*. https://www.asgct.org/global/documents/asgct-citeline-q1-2025-report.aspx

[2] U.S. Food and Drug Administration (May 2025). *Approved Cellular and Gene Therapy Products*. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products

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For CGT development, ASGCT believes it is critical to consider the totality of evidence by leveraging all possible data sources, including biomarkers, comparison to natural history, real-world data (RWD), and real-world evidence (RWE) in a consistent and predictable manner.[3] Previously, ASGCT commented on the draft guidance document "Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products."[4] In our comments, ASGCT requested that FDA issue a new draft of that guidance with clear recommendations on how external controls, including those utilizing RWE, can be used to support product development. ASGCT also requested that FDA make recommendations on the collection, analysis, and submission of control data that would best support regulatory approval, particularly when traditional trial design is unethical or unfeasible. ASGCT understands this docket may play a role in addressing some of these requests; we appreciate FDA's continued attention to these important issues. We respectfully request that future guidance documents and Agency resources recognize and respond to the unique features of RWD for CGTs. It is critical that FDA provide transparent, consistent pathways for RWD use and distribution, including external controls and registry data for submission in both clinical development and post-marketing surveillance.

ASGCT's response to specific questions in the docket are below. If you have questions about any of the information provided, please contact Margarita Valdez Martínez, Chief Advocacy Officer, at mvaldez@asgct.org.

Sincerely,

David Barrett, JD
Chief Executive Officer
American Society of Gene & Cell Therapy

Exploration of Health Level Seven Fast Healthcare Interoperability Resources for Use in Study Data Created From Real-World Data Sources for Submission to the Food and Drug Administration

1. **What challenges do you see for the pharmaceutical industry regarding the current state of submitting clinical study data collected from RWD sources to FDA?**

[3] American Society of Gene and Cell Therapy (2024). Optimizing Regulatory Frameworks for Gene Therapies in Rare Diseases: Challenges and Solutions. *Molecular Therapy Methods and Clinical Development.* https://www.asgct.org/advocacy/policy-statement-landing/2024/optimizing-regulatory-frameworks-for-gene-therapie

[4] American Society of Gene and Cell Therapy (2023). *Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products Guidance* [Regulatory Comment]. https://www.asgct.org/advocacy/policy-statement-landing/2023/considerations-for-the-design-and-conduct-of-exter

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ASGCT recognizes the growing value of real-world data (RWD) collected through electronic health records (EHRs), registries, and digital health technologies in assessing patient outcomes, post-approval safety, and in facilitating therapy development.[5] However, challenges remain. Variability in the quality of data and unstandardized processes for submissions, specifically related to registries and electronic medical records, limits the integration of RWD into submissions.

Currently, the evaluation of whether a given RWD source is fit for a specific research question is left to the sponsor. This case-by-case approach creates uncertainty and inefficiencies for industry stakeholders who must repeatedly assess each registry or dataset without clear standards or expectations from regulators.

Additionally, there are common elements of data reliability including data collection processes, audit trails, procedures to track data completeness, and management of loss to follow-up, that could be evaluated independently of any specific study design. These foundational data practices significantly impact whether RWD can support regulatory submissions, and yet there is no consistent process or framework for evaluating or validating these characteristics across data holders.[6]

2. **What opportunities and/or challenges do you see for the pharmaceutical industry on reaching a future state of clinical study data submissions collected from RWD sources using HL7 FHIR (e.g., business processes, technical considerations)?**

ASGCT has not taken a formal position on the use of HL7 FHIR standards versus other data interoperability systems for regulatory submissions. The Society is not a product sponsor, so we would defer to other subject matter experts on the specific technical opportunities and challenges of the HL7 FHIR system. In general, however, the Society supports opportunities to facilitate secure, standardized data exchange between sponsors, providers, and the FDA, and we support enhanced data processes to collect, store, and trace sources in alignment with regulatory standards. Challenges for the field for any RWD system include harmonization across sponsors and providers to understand the diversity of data formats and sources. Particularly in rare disease and CGT contexts, there can be significant challenges to standard mapping and consistency of data.

[5] American Society of Gene and Cell Therapy (2023). *Methods and Approaches for Capturing Post-Approval Safety and Efficacy Data on CGT Products Listening Session* [Regulatory Comment]. https://www.asgct.org/advocacy/policy-statement-landing/2023/post-approval-cgt-products-listening-session

[6] American Society of Gene and Cell Therapy (2022). *Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products* [Regulatory Comment]. https://www.asgct.org/ASGCT/media/about/ASGCT-comments-on-FDA-2021-D-1146-Assessing-Registries.pdf?ext=.pdf

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3. **What are your suggestions on how, from a data standards perspective, FDA might reach a future state of clinical study data submissions collected from RWD sources that aligns with ASTP/ONC health IT goals for HL7 FHIR-based exchange?**

As FDA considers ways to build and/or strengthen RWD systems for regulatory submissions, FDA should consider that CGTs often have unique characteristics and considerations compared to small molecule therapies. ASGCT's recommendations include that FDA should:

- Develop and publish clear, CGT-specific data element standards and implementation guides that reflect the durable treatment effects and long-term follow-up requirements characteristic of gene and cell therapies.[7]
- Coordinate cross-center (CDER, CBER, OCE) collaboration to harmonize standards and regulatory expectations for externally controlled trials using RWE and registry data.[8]
- Increase transparency of FDA-collected data and facilitate access through standardized FHIR APIs to reduce additional data capture by sponsors.[9]

5. **Under TEFCA (Trusted Exchange Framework and Common Agreement), a variety of "Exchange Purposes" are authorized. If "Research" was added as an "Exchange Purpose," what role could TEFCA play with using RWD for clinical research? How could TEFCA support more efficient collection and exchange of RWD for clinical research purposes? What challenges might exist with this approach?**

ASGCT does not have a position at this time on Question 4 (USCDI v 3) or Question 5 (TEFCA). We defer to other subject matter experts, while generally recognizing the challenges involved in collecting and exchanging RWD for clinical research.

[7] American Society of Gene and Cell Therapy (2023). *Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products Guidance* [Regulatory Comment]. https://www.asgct.org/advocacy/policy-statement-landing/2023/considerations-for-the-design-and-conduct-of-exter

[8] Ibid.

[9] American Society of Gene and Cell Therapy (2022). *Real-World Data* [Regulatory Comment]. https://www.asgct.org/ASGCT/media/about/ASGCT-comments-on-FDA-2021-D-1146-Assessing-Registries.pdf?ext=.pdf

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