American Society of Gene + Cell Therapy



August 27, 2024

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

**RE: Comments for Docket No. FDA-2024-D-1829 "Platform Technology Designation Program for Drug Development; Draft Guidance for Industry"**

Dear Sir/Madam:

The American Society of Gene & Cell Therapy (ASGCT) appreciates the opportunity to comment on the document "*Platform Technology Designation Program for Drug Development; Draft Guidance for Industry.*" ASGCT is a nonprofit professional membership organization comprised of more than 6,200 scientists, physicians, patient advocates, and other professionals working in cell and gene therapy (CGT) in settings such as universities, hospitals, and biotechnology companies.

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. 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**

In 2023, the pipeline of CGT, and RNA therapies grew by 6%. Currently, there are over 4,000 gene, cell, and RNA therapies in development ranging from preclinical through preregistration. The pipeline includes over 2,000 gene therapies (including genetically modified cell therapies such as CART-cell therapies), and globally 32 gene therapies have been approved. As more products receive approval, the ability to scale up and streamline development and manufacturing processes to meet the needs of patients is critical.

The Society was therefore pleased to see the Platform Technology Designation Program for Drug Development included in the Food and Drug Omnibus Reform Act (FDORA) in 2022. The adoption of more standardized platforms across drug development programs will reduce burden for both developers and regulators alike and reduce uncertainty in new products for patients. We believe this pathway can encourage more adoption of platforms in the industry.

Given the great potential of this specific pathway and platform approaches in general (including leveraging prior knowledge and the Advanced Manufacturing Technologies designation program), the Society especially urges FDA to embrace the spirit of the law. While new innovative laws and positive commentary from agency leadership are appreciated, this spirit is not always evident in sponsor interactions and recent guidance documents, including this one, which is highly relevant to the field.

For example, regarding the treatment of post-approval changes to platforms across products, the current requirements for making changes after products are on the market were developed with small molecule chemistry in mind. However, for CGT, manufacturing process improvements may occur at any time during product development, including post market. For many CGT development programs, process changes are made to scale up manufacturing during late stages after demonstration of early clinical benefit. In this respect, chemistry, manufacturing, and controls (CMC) data for gene and cell therapy products often come throughout the product lifecycle. The spirit of the program is intended to allow a single application for a major CMC change to a designated platform to facilitate, and permit, that change to be effectuated across all products using the platform. We urge that this single application provides a streamlined process and not simply an umbrella of what is essentially multiple individual applications as the draft guidance currently reads. As multiple gene therapies come to market on designated platforms, this program can enable the latest CMC learnings to be applied across products to ensure timely patient access to these transformative therapies.

We would also like to reiterate comments previously submitted regarding the final rule *Biologics License Applications and Master Files (89 FR 9743)* ('BLA DMF rule'). The BLA DMF rule codifies FDA's policy that BLAs cannot incorporate information about drug substance, drug intermediate or drug product through referencing a drug master file. This implementing guidance also cites this rule as the reason that, for BLAs of products based on a designated platform, all information on the platform must be submitted with the BLA and cannot cite a DMF. FDA has repeatedly noted that bespoke manufacturing processes in the CGT field lead to long and complex CMC reviews – leading to high regulatory burden on both the agency and CGT developers. Eliminating the ability for BLAs to reference DMFs that contain information about a designated platform technology diminishes the value of the designation and keeps the reviewer burden high – as the information already reviewed and designated is not clearly delineated. We suggest, at minimum, the guidance be amended to include information on how to delineate data that has already supported an approved platform in a new application. More broadly, we believe that the BLA DMF rule should be reexamined in the context of CGTs, especially those based on designated platforms or advanced manufacturing technologies.

Additionally, many CGT developers are start-up companies, small biotech companies, and academic sponsor-investigators who do not have a currently approved product. ASGCT understands that CGT sponsors who do not have an approved product (and thus are not eligible for this designation program) can leverage prior knowledge. However, these product candidates could benefit from better understanding how to use the principles of Designated Platform Technologies in the initial program to streamline the designation process after approval for subsequent products. The Society was pleased to see a new proposed guidance "*Use of*

*Platform Technologies in Human Gene Therapy Products Incorporating Human Genome Editing; Draft Guidance for Industry*" on CBER's updated guidance agenda for 2024. We hope that these topics will be addressed in this new draft guidance.

Finally, the Society understands and appreciates the challenges the FDA faces and the agency's efforts to prepare for the future – like the establishment of the OTP Super Office. ASGCT scientists and professionals stand at the ready to assist the agency with addressing key scientific questions pertinent to the field that will enable more standardized approaches that will eventually reduce the scientific uncertainty and regulatory burden of each new product.

**Specific Comments**

| I. **Platform Technology Designation Request** | | |
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| Lines/Section/Text Reference | Text Recommendation | Comment |
| 89-90<br><br>"However, BLA sponsors seeking to leverage data and information from a platform technology in a prior application should include the full information in their subsequent application." | N/A | As discussed in detail above, the Society suggests that since a designated platform technology will have had related BLA information submitted for previous products that it should not be necessary to resubmit such information for follow on products by the sponsor or anyone with right of reference.<br><br>In addition, if sponsors are required to resubmit all platform information in the BLA along with new product specific information, it will greatly reduce the ability to meet the "significant efficiency" threshold (discussed in more detail below). Requiring re-review of already platform-designated data reduces the potential regulatory efficiencies this provision of law seeks to achieve. |
| 105-113 | N/A | We respectfully request the |

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| "Under section 506K(h)(1) of the FD&C Act, a platform technology is a well-understood and reproducible technology, which may include a nucleic acid sequence, molecular structure, mechanism of action, delivery method, vector, or a combination of any such technologies that FDA determines to be appropriate, where the sponsor demonstrates that the technology (1) is incorporated in or used by a drug or biological product and is essential to the structure or function of such drug or biological product; (2) can be adapted for, incorporated into, or used by, more than one drug or biological product sharing common structural elements; and (3) facilitates the manufacture or development of more than one drug or biological product through a standardized production or manufacturing process or processes." | | Agency provide clarification as to how the agency will interpret the statutory definition of 'well understood', as the term is used in the definitions but not extrapolated on with regard to eligibility. Considering a designation request should include a description of how a technology meets the 'well understood definition,' this is a critical attribute.<br><br>For instance, is 'well understood' used in the context of scientific understanding of the technology or to denote an established or proven use of the technology? |
| 168-173 and associated bullet points (175-199)<br><br>"Information about a designated platform technology may be leveraged in a subsequent application when supported by sufficient preliminary evidence. The application should be from the sponsor that was originally granted the platform technology designation. Alternatively, it can be from a sponsor that has full rights of | N/A | Overall, the Society appreciates the added benefits for recipients of a designated platform technology.<br><br>The ability for other sponsors to potentially gain the right of reference to data associated with the platform can help expedite the development of therapies for patients with unmet needs. |

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| reference to that information. Potential benefits to a sponsor that is granted a platform technology designation for a subsequent application may generally include one or more of the following, as deemed appropriate by FDA …" | | |
| 186-191<br><br>"Leveraging data from a prior product that used the designated platform technology, such as leveraging batch and stability data from a related product as prior knowledge that can supplement product development studies (e.g., in-use stability studies to define administration conditions and/or light exposure studies to inform the design of the container closure system), or support shelf-life extrapolation and determination for structurally alike products." | N/A | The Society requests additional detail regarding what information the agency will require from submissions leveraging data from a designated platform technology.<br><br>For example, will sponsors be expected to recreate studies, or simply resubmit findings from prior studies? Will batch and stability data from prior products require additional supplementation, and if so, how much? |
| 240-247<br><br>"Information to justify why the use of the platform technology would bring significant efficiencies to the drug development or manufacturing process and to the review process for the application (e.g., allow testing or validation performed as part of developing one of the products to reduce some testing or validation for the other products and thus increase efficiency). | Information to justify why the use of the platform technology ~~would~~ ***has a reasonable likelihood to*** bring significant efficiencies to the drug development or manufacturing process and to the review process for the application (e.g., allow testing or validation performed as part of developing one of the products to reduce some testing or validation for the other products and thus increase efficiency | The Society requests that the standard set forth in the guidance mirrors that in the statute in Section 506K(b)(3)[2]. The types of data and information to support a reasonable likelihood standard and a definitive effect are different, and it would be nearly impossible to prove an efficiency in the review process for the first follow on product (when the platform is initially eligible) before the first follow on is approved. |

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| The ability to reduce certain testing and validation for manufacturing and/or analytical methods will depend on the drug class. Whether the reduction of certain testing or validation | | FDA defines "significant efficiency" in the appendix as "…help streamline drug development or manufacturing and review." However, given the critical nature of the interpretation of "significant efficiency" by the Agency, the Society requests clarity on how to leverage this information, and what the threshold is for 'significant efficiencies.'<br>If it is simply to streamline development or review, reduction in testing and validation should meet the standard.<br><br>However, if that is not the case, as the draft guidance is currently written, we then respectfully request examples of things that are and are not 'significant efficiencies.' For instance, an increased efficiency to a sponsor may not increase efficiencies for the Agency. Information on how process improvements to either the sponsor or Agency will be measured would be appreciated.<br><br>As noted above, we believe that review efficiencies will be blunted if all information must be resubmitted in a BLA for follow-on products, and therefore recommend that platform information not be required to be resubmitted. |
| **II. Post Approval Changes to Designated Platform Technology** | | |

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| Lines/Section/Text Reference | Text Recommendation | Comment |
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| 371-372<br>“A new supplement should be submitted as appropriate for each.” | N/A | The Society requests the agency redraft this sentence to clarify whether it refers to a post approval supplement with a comparability protocol, or for the change itself. |
| **III. General Considerations for Eligibility** | | |
| Lines/Section/Text Reference | Text Recommendation | Comment |
| 378-379 and associated bullet points (381-394)<br><br>“Included below are examples of potential platform technologies, with examples of key elements of each technology:” | N/A | The Society appreciates the breadth of examples provided by the Agency along with the relevant elements. |

The Society would welcome the opportunity to work with the Agency on further developing this pathway to meet its goals for the CGT field. 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