March 4, 2024

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

Regarding Docket No. FDA-2023-N-5653-0002, *Food and Drug Administration Draft Report and Plan on Best Practices for Guidance*

Dear Sir or Ms.:

The Alliance for Regenerative Medicine (ARM) appreciates the publication of this draft report, in accordance with section 2505(a) of the Consolidated Appropriations Act, 2022, to identify and plan for implementation of best practices for the efficient prioritization, development, issuance, review, clearance, and use of guidance documents.

The Alliance for Regenerative Medicine (ARM) is the leading international advocacy organization championing the benefits of engineered cell therapies and genetic medicines for patients, healthcare systems, and society. As a community, ARM builds the future of medicine by convening the sector, facilitating influential exchanges on policies and practices, and advancing the narrative with data and analysis.

We actively engage key stakeholders to enable the development of advanced therapies and to modernize healthcare systems so that patients benefit from durable, potentially curative treatments. As the global voice of the sector, we represent more than 400 members across 25 countries, including emerging and established biotechnology companies, academic and medical research institutions, and patient organizations.

The Importance of Comment Periods for Guidance Documents for Cell and Gene Therapies

Although we understand FDA's efforts aim to improve efficiencies, ARM believes it is in the interest of the public to retain the public's right to review federal guidance in all but extraordinary circumstances, such as some that arose during the COVID-19 pandemic. As an organization representing a nascent field with complex products, such as cell and gene therapy (CGT), ARM finds FDA guidance documents to be critical to efficient development since they identify Agency expectations for trials of these new product types. Streamlining the processes for guidance development is a laudable goal to maximize the use of Agency resources and to provide its expectations to sponsors in the timeliest way. However, small nuances

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in changes to policy or requirements in an emerging field could have unintended consequences.

FDA requested comments on whether there are any additional circumstances, categories, or topics for which it may be appropriate for FDA to consider issuance as a Level 1 guidance document for immediate implementation without prior public comment. ARM's response is that it supports the maintenance of the comment period, typically of 60 days, required prior to implementation of most Level 1 guidance documents (i.e., those that include initial interpretations of a statute or regulation, changes in interpretation or policy that are of more than a minor nature, complex scientific issues, or highly controversial issues).

The comment period offers an opportunity for sponsors to provide beneficial input into the feasibility of regulatory policies and FDA interpretation of policies for these newer product types before implementation, given sponsor experiences during development of CGTs, which are unique and complex products. Leveraging public stakeholder expertise can effectively address critical issues and bridge scientific gaps. Sponsor insights may be able to assist the Agency when finalizing guidance in addressing additional areas not initially considered in draft guidance and in providing clarifications to content that is unclear to sponsors, which is helpful to the whole field in development of therapies for patients awaiting treatments, or improvements in treatment options, for their diseases.

We recognize that under section 701(h)(1)(C) of the FD&C Act, the FDA may make exceptions to its need to ensure public participation prior to the implementation of Level 1 guidance when it determines that such prior public participation is not feasible or appropriate. However, we appreciate FDA's indication in the preamble to the final GGP rule, that it anticipated this exception would generally be applicable when there are public health reasons for the immediate implementation of the guidance document; there is a statutory requirement, executive order, or court order that requires immediate implementation; or the guidance document presents a less burdensome policy that is consistent with public health. ARM generally supports these reasons for exceptions, although for public health reasons, only when there are extraordinary public health reasons. We recommend continued application of *only* these exceptions for guidance issued related to CGT development.

FDA will also consider whether there are additional categories of guidance that would meet the definition of Level 2 guidance, for which the FD&C Act and FDA's GGP regulation require that FDA provide for public comment upon implementation (without a prior comment period). ARM recommends that CGT-related guidance should be excluded when considering additional categories that may meet the Level 2 guidance definition. For the reasons stated above, a comment period prior to implementation of CGT-related guidance may be valuable in identifying whether existing practices are feasible and whether changes in policy that may seem minor are indeed minor in practice.

Additional or Revised Practices for the Agency To Consider To Further Improve Its Processes for the Issuance of Guidance Documents

The long period of time that it often takes for guidance documents to be finalized leaves sponsors with uncertainty of the status of FDA expectations, which can prolong development timelines. ARM therefore recommends that CBER establish a performance goal within this report of finalizing guidance documents within a certain length of time, ideally within 18 months of the close of the comment period. The FDA agreed to finalize, or issue revised draft, guidance documents within this time frame for draft guidance documents to be developed per the PDUFA VII commitment letter. ARM supports this approach, which will prevent reliance of sponsors on draft guidance that may be outdated. While we understand the resource constraints within CBER, we hope that the growth of the Center that federal appropriations and PDUFA VII provide over the next few years will enable such timely finalization of draft guidance documents.

The FDA may also want to consider issuing a summary of comments received on a draft guidance, as some other agencies do. Such summary reports could be helpful in providing public understanding of the Agency's collective interpretation of comments received.

In addition, ARM is supportive of amending GGP regulation to provide information to ease the process for external stakeholders to suggest topics for new guidance, as the draft report offers as an example of a GGP amendment the FDA is considering. While the FDA indicates in an attachment to a web page that interested persons have an opportunity to provide input to FDA on topics for guidance documents in various ways, including by submitting comments on the topics on the annual guidance agenda, these mechanisms are not widely known, nor are there clearly identified procedures for doing so. We encourage CBER to open a docket for comments in response to the issuance of its annual guidance agenda, soliciting input on guidance topics annually. Doing so would give sponsors the opportunity to provide input on topics needing policy development, which could be mutually beneficial, especially in new fields such as cell and gene therapy.

Novel Guidance Document Formats That Would Be of Particular Utility in Streamlining Guidance Document Development, Such as Q&A Formats

ARM supports the use of question and answer and bulleted guidance formats in many instances to facilitate earlier issuance and/or revision of guidance documents on the many CGT topics in need of new or revised guidance. We suggest that FDA consider soliciting stakeholder questions prior to issuance of a Q&A format guidance to assist in offering as thorough guidance as CBER can offer at the time of issuance. We would recommend establishing realistic timelines for public review of these Q&A formats to facilitate inclusion of necessary updates as the field moves forward. Additional use of a brief, bulleted guidance format (similar to disease-specific guidance) is often appropriate and helpful in understanding FDA's current thinking. As FDA gains additional experience, these guidance documents can be revised to include additional detail. But to be clear, there are some topics that are of greater

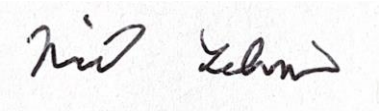
significance and/or complexity that will continue to require the more traditional detailed guidance document format that allows inclusion of illustrative examples. However, we generally support the appropriate use of these concise formats.

We also encourage the FDA to consider methods and mechanisms in addition to guidance documents to share their evolving thinking on a particular topic. For example, ARM members find the transcripts of Town Hall meetings delivered in a Q&A format to be quite helpful which, for certain topics, could form the basis for Q&A guidance documents.

ARM appreciates the efforts of the FDA to plan ahead and consider ways of streamlining guidance development and providing advice to therapeutic developers. We encourage such efficiencies that can be done without sacrificing needed public input. This topic is a good one for a public conversation or workshop to drive forward-leaning ideas.

Thank you for your consideration of these comments.

Sincerely,



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