AMERICAN SOCIETY of GENE & CELL THERAPY

February 2, 2018

Tami Belouin
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 71, Rm. 7301
Silver Spring, MD 20993-0002

Dear Ms. Belouin:

Thank you for the opportunity to comment on the draft guidance for industry entitled "Expedited Programs for Regenerative Medicine Therapies for Serious Conditions." The American Society of Gene and Cell Therapy (ASGCT) appreciates CBER's provision of guidance to sponsors engaged in the development of regenerative medicine therapies for serious or life-threatening diseases or conditions on the expedited development and review of these therapies.

ASGCT is a professional membership organization for gene and cell therapy, consisting of approximately 2,500 scientists, physicians, patient advocates, and other medical professionals working in a variety of settings including academic medical centers, hospitals, and patient advocacy organizations. 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.

Guidance on the Regenerative Medicine Advanced Therapy (RMAT) designation is particularly beneficial because this program could contribute to the efficient, safe development of more products for currently untreatable or inadequately treated diseases than other expedited pathways provide alone. In addition, ASGCT is in favor of the provision of FDA input to sponsors at the earlier point in development that the guidance outlines for therapies with expedited designations. The Society has three recommendations below for modifications to the guidance.

Inclusion of gene therapy in RMAT designation

ASGCT recommends the consistent inclusion of gene therapy in the definition of regenerative medicine, and supports the resulting eligibility of gene therapies for consideration for RMAT designation. The Society is therefore pleased that in this guidance CBER includes gene therapies that lead to a durable modification of cells in the definition of regenerative medicine. The following statement on p. 2, however, is somewhat unclear and potentially limiting: "As FDA interprets section 506(g), gene therapies, including genetically modified cells, that lead to a durable modification of cells or tissues may meet the definition of a regenerative medicine therapy."

The durability of modifications of cells and tissues that gene therapy provides, referenced above, is difficult to concisely and accurately delineate. The Society therefore recommends clarifying this statement, and the resulting implications related to RMAT designation, by stating, "As FDA interprets section 506(g), gene therapies, including genetically modified cells, meet the definition of a regenerative medicine therapy. As such, gene therapies are also eligible for consideration for RMAT designation."

If further detail is desirable, ASGCT would recommend utilizing the following definition of gene therapy: a set of strategies that modify the expression of an individual's genes or repair abnormal genes, involving the administration of a specific nucleic acid (DNA or RNA) through viral or non-viral vectors. Clarifying that gene therapies are consistently eligible for consideration for RMAT designation could encourage the development of such therapies, which hold the potential to provide treatment for significant unmet need for multiple rare diseases. Offering this potential additional pathway for efficient development of gene therapies could assist in overcoming the challenges of rare disease drug development.

Determination of meaningful number of sites

One of the provisions for RMATs to be eligible for accelerated approval is reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites as appropriate. The guidance indicates on p. 9 that the determination of whether the number of investigational sites is meaningful will be a BLA review issue that will be considered on a case-by-case basis. While the Society supports this determination being made on a case-by-case basis, sponsors would be assisted by obtaining this information at an earlier point during the more collaborative drug development process between the FDA and the sponsor for RMAT-designated programs.

Innovative design example

ASGCT supports the concept of innovative clinical trial design, noted on p. 11. The example of innovative design offered in the guidance is of "trials that compare several different investigational agents to each other and a common control." The execution of this example seems, on a practical basis, to lack feasibility, especially for small biotechnology companies, due to issues related to development costs and potentially differing enrollment and dose escalation criteria. ASGCT recommends offering an alternate example of innovative design, or including more details about the execution of the example provided.

Thank you again for the opportunity to provide comment on this guidance. ASGCT is extremely appreciative of the efforts of CBER to provide guidance that facilitates the efficient, safe development of disease treatments that include gene and cell therapies. The Society is especially grateful for the inclusion of certain gene therapies in the definition of regenerative medicine, and their resulting eligibility for consideration for RMAT designation. Please feel free to contact us with any questions you may have regarding this input.

Sincerely,

Helen E. Heslop, MD
President

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Chair, Clinical Trials & Regulatory Affairs Committee