December 10, 2018

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Comments for Docket No. FDA-2018-D-2173: Long Term Follow-Up After Administration of Human Gene Therapy Products

Dear Sir/Madam:

The American Society of Gene & Cell Therapy (ASGCT) appreciates the opportunity to comment on this guidance document. ASGCT is a professional membership organization for gene and cell therapy with over 3,000 members. Membership consists primarily of scientific researchers, physicians, other professionals, and students in training. Members work in a wide range of settings including universities, hospitals, biotechnology and pharmaceutical companies, and government agencies. 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.

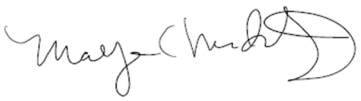
ASGCT appreciates the opportunity to comment on this guidance document. FDA's recommendations in this draft guidance are generally welcomed and will provide clarity for long-term follow up after administration of gene therapy products. The Society supports vector- and disease-specific requirements for long-term follow-up reporting, as this guidance document proposes. The Society agrees that the 15-year reporting requirement for many gene therapy applications is no longer relevant to many *in vivo* DNA vector applications because of a 25-year experience with *in vivo* administration of DNA vectors. The following specific comments are provided for FDA consideration:

Section/ Lines	Comment/Issue	Proposed Change
IV.	**Preclinical Data Used for Assessment of Delayed Risks in Gene Therapy Clinical Trials**	
	B. Considerations for Preclinical Study Design to Assess Biodistribution and Persistence of Gene Therapy Product	
361 – 362	Guidance Text: "We recommend that you perform preclinical biodistribution studies using methods shown to be sensitive and quantitative to detect product sequences."	"We recommend that you perform preclinical biodistribution studies using methods shown to be sensitive and quantitative to detect

Section/ Lines	Comment/Issue	Proposed Change
	Comment: ASGCT recommends that when a sponsor utilizes a different transgene in the same capsid as that sponsor's previous data, the sponsor may use its prior biodistribution data, without a requirement to repeat biodistribution studies.	product sequences, except when the biodistribution of the vector being used has been well defined and well characterized. If the product differs only in the transgene encoded, biodistribution studies do not need to be repeated."
	C. Vector Persistence, Integration, Reactivation and Genome Modification: Assessing Long-Term Risks	
523 – 525	Guidance Text: Table 1. Propensity of Commonly Used Gene Therapy Products/Vectors to Modify the Host Genome Comment: Clarify or exemplify the meaning of long-term follow-up observations being product specific for transposon elements and microbial vectors for gene therapy.	
V.	**Recommendations for Protocols for Long Term Follow-Up Observations: Clinical Considerations**	
	D. Elements of Long Term Follow-Up Observations	
	3. Annual Reports to the IND/Summary Information	
768 – 773	Guidance text: "In that report, you should submit information obtained during the previous year's clinical and nonclinical investigations, including a summary of all IND safety reports submitted during the past year, and a narrative or tabular summary showing the most frequent and most serious adverse experiences by body system." Comment: Clarity is needed on the degree of reporting for expected side effects, since the guidance implies that sponsors should collect and report all adverse events, which may be numerous in patients proceeding to other therapies.	
VI.	**General Considerations for Post-Marketing Monitoring Plans for Gene Therapy Products**	
1054 – 1055	Comment: Within this section, we recommend that FDA clarify that use of patient registries are allowable for use in long-term reporting.	

Thank you for consideration of these comments. Please do not hesitate to let ASGCT know if you have questions.

Sincerely,



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Chair, ASGCT Clinical Trials and Regulatory Affairs Committee