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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852
Docket No. 2005D-0310

Re: Comments on "Guidance for Industry; Gene Therapy Clinical Trials – Observing Participants for Delayed Adverse Events"

October 19, 2005

To Whom It May Concern:

The US Department of Health and Human Services, Food and Drug Administration (FDA), Center for Biologics Evaluation and Research, issued in the Federal Register on Aug. 23, 2005 a Draft Guidance entitled "Guidance for Industry; Gene Therapy Clinical Trials – Observing Participants for Delayed Adverse Events". This guidance is intended to represent the FDA's current thinking on this topic. The guidance, while addressed to the sponsors of gene therapy studies, will, non the less, be a document of referral for all involved with Gene Therapy Trials, including Institutional Review boards (IRBs, IBCs). Comments on this guidance are being accepted through December 9, 2005

The following comments represent the views of Stanford University's Institutional Biosafety Committee (IBC) with regards to the above-mentioned Guidance.

1. Section IV Item C: Vector Integration Potential and Reactivation as Risks for Delayed Adverse Events

Biology decrees that most vectors used in Gene Therapy trials can be categorized according to their propensity to integrate into host cell DNA. The ability to integrate and/or become reactivated can be used as a matrix that can be tied into requirements for long-term follow-up necessity.

We agree with the logic behind this matrix. However, we believe it vital that all involved interpret the matrix equivalently.

- a. We ask that the FDA set parameters on the definitions used to discuss integration potential or reactivation. Examples of these include:
 - i. "propensity to integrate or reactivate"
 - ii. "low propensity"
 - iii. "persistent transgene expression"

2. Section V Item B: Suitability of Clinical Trial Populations for Long-term Follow-up Observations

2005D-0310

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The Guidance proposes that long-term follow-up observations on trial participants with "widespread disease, or extensive exposure to agents with potential for delayed adverse events such as radiation or chemotherapy" may have limited scientific value.

a. We ask that the FDA define 'extensive', with reference to both qualitative and quantitative measures.

b. The ultimate purpose of long-term follow-up is to identify consequences of persistent biological activity following exposure to gene transfer. As such, we believe it vital to capture adverse events, regardless of the potential difficulties of causal interpretation. It is understood that parallel treatments and disease progression will have their own effects on subjects. The purpose of monitoring and reporting is to obtain any and all information that may be important to the study; it would be impossible to make any scientific judgment if the data is not collected. Due to the often-limited number of subjects in Gene Therapy trials, all observations must be considered and scientifically analyzed for cause and effect. As such, we request that Section V Item B be removed from the Guidance.

Thank you for the opportunity to comment on this very important guidance. If you have any questions, please do not hesitate to contact me.

Sincerely,



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