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July 27, 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Dear Sir/Madam,

Re: Docket No. 00D-1662: Draft Guidance for Industry on Source Animal, Product, Preclinical and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans. **Federal Register,** February 7, 2001 (66FR 26).

At a recent meeting of the HHS Secretary's Advisory Committee on Xenotransplantation, Anthony Lubiniecki, Sc.D. was asked by Dr Eda Bloom to formally respond to the above Docket outside the published closure date of May 8. Dr Lubiniecki's comments are as follows:

In general the document is very thoughtful, however please consider the following:

Section III.E.1., Page 16. The second and third sentences describe the need to validate the harvesting process. "Validation" is probably not the exact term that is appropriate here since these processes are similar to surgery and likely to be carried out by human hands in a low bioburden environment or in a biological safety cabinet. Most validation experts would argue that this type of operation is not capable of validation, just as the asepticity of hand filling for parenteral products is generally regarded as not validateable. Control of this process is important, and should include calibration of the HVAC and/or biological safety cabinet, SOPs on gowning and harvesting, environmental monitoring, and documentation, as you mention. However, it is just not possible to achieve a state that would typically be regarded as "validated", especially to the point of being able to avoid the introduction of infectious agents during harvesting. The request for "validation" also seems to exceed the standards used to surgically implant the xenograft into the human recipients. "Control" or "controlled" are words that may be more appropriate.

Section VI.C.5., Page 32. The first sentence states that all processes should be validated. It is typically required that all *critical* steps in a process be validated for other types of drugs and biologicals. To not clarify that this only applies to critical steps would be to require a higher standard than that accepted for any other product type. Secondly, some

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attributes of some steps may be critical, but incapable of validation (see the above comment regarding harvesting procedures). E.g., it may be possible to validate that the harvesting procedure provides usable organs which function as desired after transplantation, but it will not be possible to validate that a human working in a surgical suite or biological safety cabinet can harvest organs that are free of infectious agents. Consider adding the words "critical" and "where appropriate" to the first sentence.

Thank you for the opportunity to comment on this document.

Sincerely

Helen Edwards

Helen Edwards
Principal Registration Executive
BioPharmaceutical New Submissions
On behalf of:
Anthony Lubiniecki, Sc.D.
Vice President
BioPharmaceutical Development
GlaxoSmithKline

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