

8606 '01 JUL 30 A8:26



GlaxoSmithKline

July 27, 2001

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

South Eden Park Road  
Beckenham  
Kent  
BR3 3BS

Tel. +44 (0)20 8658 2211  
Fax. +44 (0)20 8639 6114  
www.gsk.com

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**Re: Docket No. 00D-1662:** Draft Guidance for Industry on Source Animal, Product, Preclinical and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans.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

01D-0162

C11

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

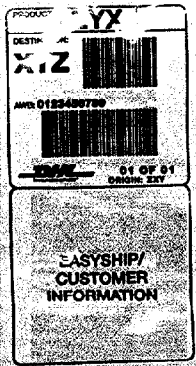
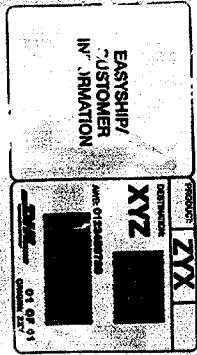
Helen Edwards

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

DEPEND UPON DHL FOR FAST DELIVERY-BUSINESS TO BUSINESS WORLDWIDE



PLEASE PLACE AIR WAYBILL IN POUCH WITH THE BAR CODE AT THE TOP



OR

SENDER'S A/C: 131026182  
 S/REF: L0907  
**FROM**: GLAXO SMITHKLINE  
 KEVIN GALLAGHER  
 SOUTH EDEN PARK ROAD  
 BR3 3BS  
 UNITED KINGDOM  
 PHONE: 0181-639-6302 FAX: 0181-639-6114  
 VAT : C/RTE: CR07

**TO**: FOOD & DRUG ADMINISTRATION  
 DOCKETS MANAGEMENT BRANCH  
 5630 FISHERS LANE, R001061  
 ROCKVILLE MARYLAND 20852

USA  
 UNITED STATES **20852**

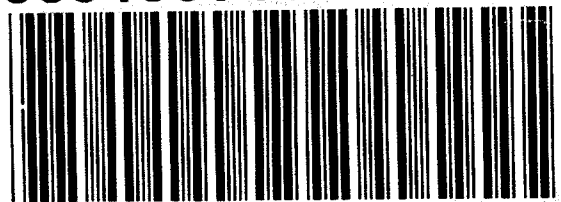
PHONE: FAX:  
 VAT :

VALUE: GBP	INSURANCE [NO]
WGT: 0.50 kg	IV : 0.00
VOL. WGT: 0.00	DIM: 0x0x0
IMP/EXP TYPE:	DATE: 27/07/01
<b>DESC</b> : DOCUMENTS	DUTIES/TAX
	DDU [X]
	DDP [ ]
	SAT DEL [NO]

PRODUCT: **DOC**

DESTINATION: **GAI**

AWB: 3665483544



**DHL**  
 WORLDWIDE EXPRESS

1 OF 1  
 ORIGIN: IWR