FUEHRING Stefan (ENTR)

From: ENTR /F/2 PHARMACEUTICALS
Sent: lundi 20 octobre 2008 9:36
To: FUEHRING Stefan (ENTR)
Subject: FW: Draft Amendments to the Clinical Trial Application Form as regards Advanced Therapy Medicinal Products
Importance: High

A/25823

From: IXA and TTS HQ (Filomena Picciano) [mailto:dso@transplantation-soc.org]
Sent: Friday, October 17, 2008 7:09 PM
To: ENTR /F/2 PHARMACEUTICALS
Cc: RPIERSON@smail.umaryland.edu; 'Jeremy Chapman'; 'Emanuele Cozzi'
Subject: Draft Amendments to the Clinical Trial Application Form as regards Advanced Therapy Medicinal Products
Importance: High

INTERNATIONAL XENOTRANSPLANTATION ASSOCIATION

a section of The Transplantation Society

October 14th, 2008

Subject: European Commission Public Consultation on "DRAFT AMENDMENTS TO THE CLINICAL TRIAL APPLICATION FORM AS REGARDS ADVANCED THERAPY MEDICINAL PRODUCTS"

Dear Sir or Madam,

I am writing on behalf of the current Council and former Presidents of the International Xenotransplantation Association (IXA). IXA is a section of the international Transplantation Society (TTS), and its membership is comprised of the leading investigators, ethicists, and key opinion leaders in the field of cross-species or "xeno-" transplantation.

We have read the "DRAFT AMENDMENTS TO THE CLINICAL TRIAL APPLICATION FORM AS REGARDS ADVANCED THERAPY MEDICINAL PRODUCTS" [2 July 2008 version]. The revised data form reflects that applications proposing the use of cell, tissue, or organ xenografts as "advanced therapy investigational medicinal products (ATIMPs)" are expected, and suggests an expectation that such proposals will be actively considered for approval. In response, the opinions below reflect the consensus opinion of the IXA Council, with the concurrence of TTS leadership.

While IXA strongly supports efforts to improve human health through the use of xenografts, we are equally enthusiastic in our insistence that any such trial be securely founded upon peered-reviewed preclinical data suggesting that efficacy is likely (i.e., that therapeutic benefit for the recipient may be expected). Although significant progress is being made, we are not aware of any evidence to support initiation of a clinical xenograft trial at this time.

It is the consensus opinion of the xenotransplantation community that cross-species transfer of living cells and tissues involves potential risks not only to xenograft recipients, but also to their close contacts, and others. These risks must be specifically managed to prevent unlikely but potentially serious and avoidable harms. In addition to surveillance of the xenograft recipient, the special risks that may accompany xenotransplantation also likely will require consent by and surveillance of the xenograft recipient's close contacts. At a minimum, we feel it is very important that the final EC documents should clearly acknowledge that oversight and regulation of xenograft trials will likely be different than for autologous or allogeneic cells and tissues, and should be performed by a national health authority.

Of note, the IXA is working with international experts to develop consensus recommendations to define the circumstances when xenotransplant trials should go forward. These consensus guidance documents will be available for islet transplantation by the end of 2008, and for other organs by the end of 2009. (Interim guidance for islets can be found at http://www.transplantation-soc.org/sections.php?s=01.) In addition, we are strongly supporting a WHO initiative to internationally coordinate the regulation of xenotransplantation by national health authorities, through a WHO-sponsored meeting scheduled for November 18-21 in Changsha, China.

Once clinical xenotransplant trials receive scientific, ethical, and regulatory approvals, the "ATIMP" vehicle (or one like it) may indeed be appropriate to implement clinical xenograft trial oversight within the EC. Meanwhile, reference to xenografts may more safely be omitted from the proposed form. Preferably, if the form will contain reference to xenografted cells, tissues, or organs, clear reference should be incorporated to indicate that 1) WHO, EU, and IXA guidelines will be considered and 2) oversight by a national health authority with a specific framework for xenotransplantation be implemented as conditions for approval.

We hope that these comments will be constructive, and will help further improve this important document. Please let me know if IXA can be of any further assistance, now or in the future.

Sincerely yours,

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