

**t. Breeders, Inc.**  
One Innovation Drive  
Worcester, MA 01605  
508/793-1566  
508/831-3521 – Fax

January 20, 2000

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Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane  
Room 1061  
Rockville, MD 20852  
Dear Sir/Madam:

**Re: Request for Proposed Standards for Unrelated Allogeneic Peripheral and Placental/Umbilical Cord Blood Hematopoietic Stem/Progenitor Cell Products (Docket No. 97N-0497)**

Dear Sir/Madam:

On behalf of t. Breeders Inc., Worcester, Massachusetts ("t. Breeders Inc."), I would like to respond to the Food and Drug Administration's ("FDA's") request for comments on the development of uniform product standards for minimally manipulated hematopoietic stem/progenitor cells from peripheral and placental/umbilical cord blood for use in unrelated allogeneic hematopoietic reconstitution (hereinafter referred to as Standards) (63 Fed. Reg. 2985, January 20, 1998). t. Breeders Inc. is a Cellular Therapy company with a proprietary technology platform for the *ex vivo* expansion of peripheral and placental/umbilical cord blood hematopoietic stem cells. Since its inception, t. Breeders Inc. has recognized the importance of the development of a uniform FDA policy for the regulation of all institutions that collect and process peripheral and cord blood stem cells for subsequent transplantation into humans.

**A. t. Breeders Inc. Supports FDA's Approach**

FDA's proposal to develop product standards and establishment and processing controls for unrelated allogeneic products, as opposed to requiring individual license applications containing clinical data, is consistent with the tiered approach first articulated by FDA in 1997 in its "Proposed Approach to Regulation of Cellular and Tissue-Based Products." 62 Fed. Reg. 9721 (March 4, 1997). t. Breeders Inc. is strongly supportive of FDA's proposals for the uniform regulation of human cellular and tissue-based products and applauds FDA's attempt to balance the need for new

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technologies to be demonstrated safe and effective, while ensuring that medical advances are not unnecessarily impeded by regulatory concerns.

To that end, FDA has acknowledged that Standards developed by private sector could provide the basis of its Standards development activities as long as they were in accordance with FDA's regulatory goals. We feel that Standards from expert groups such as the American Association of Blood Banks ("AABB") should be granted substantial consideration by FDA. t. Breeders Inc. believes that these Standards and others, appropriately modified by FDA, could provide sufficient guidance for the development of uniform establishment and processing controls and product Standards for all unrelated allogeneic peripheral and placental/cord blood products.

The utilization of existing private sector Standards however, does not mean that FDA should adopt such Standards without modification or substantive expert input. Indeed, as noted below, t. Breeders Inc. has substantive concerns that it requests the FDA to address regarding certain Standards for unrelated allogeneic products. Further, t. Breeders Inc. believes that once FDA develops a draft guidance, it should be published for comment and a public meeting should be held consistent with the agency's Good Guidance Practices for Level 1 guidance documents. (See 62 Fed. Reg. 8961, February 27, 1997). This will ensure that FDA's final guidance setting forth controls and Standards for unrelated allogeneic products benefits from full review and participation by all interested persons.

**B. General Observations About FDA Standards Development**

FDA is uniquely positioned to evaluate the various proposals of Standards that will be submitted to the Agency. While t. Breeders Inc. anticipates that each private sector Standards proposal will certainly represent the best efforts of the organization involved, these individual proposals cannot be expected to reflect the multiplicity of approaches or technologies that could be used successfully to achieve FDA's primary goal of developing establishment controls, processing controls, and product Standards, as well as to ensure that unrelated allogeneic products are safe and effective. Thus, in developing regulatory and licensing Standards for unrelated allogeneic products, t. Breeders Inc. requests that FDA be cognizant of the following concerns.

**1. FDA should follow the precedent set by its current Good Manufacturing Practice ("cGMP") regulations for blood, drug and medical device products, and develop controls and Standards based on performance goals and not on design Standards.**

The long term success of FDA's cGMPs for blood, drug and medical device products may be attributed, in large part, to the Agency's recognition that such

regulations must be suitable for a wide variety of products and must be flexible enough to allow the use of sound judgment and permit technological innovation. For reference, see preamble to the final rule amending the cGMPs for human drug products and 43 Fed. Reg. 45014, September 29, 1978. In the context of developing process and control Standards for unrelated allogeneic products, for instance, FDA should not engage in the business of determining Standard Operating Procedures for facilities. For example, FDA should not mandate the use of a particular laboratory machine, collection device or collection process. Rather, FDA should follow its existing cGMP precedent and focus on identifying performance objectives or goals (the "what" of must be achieved) and not design Standards (the "how" of achieving it).

By establishing performance goals, FDA will provide entities with the freedom to reach compliance in any appropriate manner, as is currently permitted for other regulated product categories. For example, FDA's drug cGMPs do not specify the educational degrees required of particular personnel but rather state that they "shall have education, training and experience" necessary for performance of assigned functions. Consistent with that example, t. Breeders Inc. strongly opposes, as highly inappropriate, the development of any Standard or process that would "lock in" particular technologies or other requirements for unrelated allogeneic products.

**2. FDA's development of performance goals should have sufficiently broad applicability to accommodate different types of blood banking models, programs and facilities.**

FDA's development of establishment and processing controls and product Standards for unrelated allogeneic products will apply to a variety of banking models, programs and facilities. There are public banks, private banks, academic banks, and hospital banks, all of which currently vary the techniques used with regard to unrelated allogeneic products. t. Breeders Inc. urges FDA to ensure that its development of draft Standards does not support any single model, to the exclusion of others that are equally capable of maintaining the same level of quality assurance and product safety. For example, FDA should not dictate Standards designed solely to accommodate select academic institutions (*e.g.*, by mandating IRB approval) when unrelated allogeneic banking conducted by smaller hospitals and nonacademic centers is equally capable of generating quality product that is both safe and effective and within the institutions standard of care as determined by appropriate medical review.

**3. FDA's development of controls and Standards should not freeze innovation or the use of new technologies or processes as they become available.**

t. Breeders Inc. urges FDA to devise controls and Standards that will not inhibit the development of new technologies or collection processes in the future. A major

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component of FDA's policy development in this area has been to encourage innovation, not to impede it. t. Breeders Inc. strongly supports FDA's intent to formulate an approach to the regulation of human cellular and tissue-based products that will: "maintain or improve protection of the public and increase public confidence in these new technologies, while permitting significant innovation to go forward unfettered by unnecessary regulatory requirements. (FDA's Proposed Approach to the Regulation of Cellular and Tissue-Based Products, February 28, 1997)."

t. Breeders Inc. shares with FDA the paramount concern of ensuring the safety and health of patients using unrelated allogeneic products. In that regard, t. Breeders Inc. urges FDA to be careful that in developing Standards and controls the agency does not usurp the basic tenets of the practice of medicine.

t. Breeders Inc. continues to believe that many issues surrounding Standards and proposed controls for unrelated allogeneic products fall within the jurisdiction of the doctor patient relationship. For example, the suitability and ultimate use decisions for unrelated allogeneic products should be decided by the treating physician in conjunction with the informed patient (with informed consent). Again, t. Breeders Inc. appreciates this opportunity to have input with FDA on the development of Standards and controls for unrelated allogeneic products proceeds.

Sincerely,



Morey Kraus  
President and CEO