



CORCELL

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January 20, 2000

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

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

Dear Sir/Madam:

On behalf of CorCell, Inc. ("CorCell"), I am writing in response to the above-referenced request ("the Request") published at 63 Fed. Reg. 2985 (January 20, 1998).

Initially, CorCell is concerned with the scope of the proposed standards. In particular, while CorCell believes that in its proposed regulatory approach the Request properly differentiates between use of cellular and tissue-based products for autologous use or family-related allogeneic use, on the one hand, from other products and applications, on the other, CorCell believes that the FDA's definition of family-related allogeneic use is unduly restrictive. The term is defined in the Request as limited to the administration of such products to "a first-degree blood relative" of the donor. 63 Fed. Reg. at 2986, n.6.

CorCell believes that current scientific data strongly supports broadening the definition of "family-related" to include all ancestral relations, siblings and collateral relations to the fourth degree by blood or marriage. This is important because the current standard of care in stem cell transplantation extends to the extended family where there is an appropriate HLA match (aunts, uncles, first cousins, grandparents, grandchildren). Kaufman, Bone Marrow Transplant, 1995 Feb; 15(2):279-82 and 1996 Jun; 17(6):1013-20 and Shipper, Blood, vol. 87, No. 2, pp. 800-804. Recent scientific reports on haploidentical transplantation tolerance also support greater utilization within the family. Guinan, Eva Transplantation of Anergic Histoincompatible Bone Marrow Allografts, New England J. of Medicine 1999 June 3; 340(22):1704-14. Dr. John Wagner, at the American Society of Hematology Meeting, December, 1999, presented on the acceptable use of mismatched cord bloods in transplant outcomes in unrelated cord blood donor transplantation. See Wagner, Kurtzberg article in press at the New England Journal of Medicine. Further, Dr. Kurtzberg, in testimony before the FDA's Biological Response Modifiers Committee Meeting in November 1998, noted the importance of the use of

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mismatched cord bloods and matched cord bloods in the effort to broaden ethnic access to such resources and the important role of such products in providing therapies and future treatments related to sickle cell anemia and to other rare genetic diseases. See Transcript of FDA's Biological Response Modifiers Committee Meeting (November 1998) at pages 149-50.

Aside from the scientific support, compelling policy reasons also dictate that FDA broaden the definition of "family related" as CorCell requests. Indeed, the FDA has previously recognized that "it is appropriate to leave it up to the family and their physician to decide whether to use such tissue, and would not prohibit use even of contaminated material from closely-related donors." CorCell agrees with and strongly supports FDA's explicit recognition that where cells or tissue are obtained from related donors, the decisions to use such materials should be left to the family and the family's physician. Individuals who bank privately for their family should have access to utilize the unit within the family if there is a suitable HLA match.

To limit the definition of family related as FDA proposes is to deny access to a valuable and suitable cell source material within the extended family. Limiting such access has even greater implications for certain ethnic groups where finding an unrelated donor is extremely difficult. Also, transplant experience shows half siblings are often used in the transplant setting. Recent scientific reports show the acceptance of mini-allogeneic transplants for older populations. With the increase in application of stem cells, the definition of family including extended family members is increasingly important for stem cell therapies using umbilical cord blood ("UCB"), mobilized peripheral blood stem cells, and bone marrow. Thus, CorCell proposes that family-related use be defined to include all ancestral relations, siblings, and collateral relations to the fourth degree by blood or marriage.

CorCell also supports inclusion of adopted relations within the definition of family related. While we recognize that such relations do not share any blood lineage, we believe that to the extent FDA grants families and their physicians the discretionary choice to use product with a suitable HLA match, it is appropriate to include adopted family members within the scope of that decision and to permit families that have chosen to bank the cord blood of adoptive children to use those units within the family.

This distinction is significant to CorCell because CorCell's business is the collection and storage of umbilical cord blood so that it may be available, at the option of the donor or the donor's parent, for appropriate transplantation into the donor or a relative of the donor, subject to the medical judgment of a treating physician. Application of a licensing requirement conditioned upon compliance with standards otherwise appropriate for suppliers of tissue for unrelated allogeneic transplantation (such as requiring the destruction of specimens that test positive for viral contamination) could impose unnecessary regulatory constraints and resulting costs upon CorCell and its patient/customers and improperly interfere with the right of individual donors to exercise control over their UCB and to provide for autologous or family transplantation based upon their evaluation of considerations of their own safety. It is CorCell's understanding

could impose unnecessary regulatory constraints and resulting costs upon CorCell and its patient/customers and improperly interfere with the right of individual donors to exercise control over their UCB and to provide for autologous or family transplantation based upon their evaluation of considerations of their own safety. It is CorCell's understanding that the right of a blood donor to store HIV contaminated blood for autologous transfusion has been upheld under the Americans With Disabilities Act. CorCell believes that an individual patient thus has the right to store infectious disease-positive and false positive stem cells, so long as the tissue is properly labeled and stored to prevent risk of cross contamination. Moreover, given proper labeling and storage protocols, CorCell believes that the use of even infected samples should be permitted based upon the [informed] consent of the donor (or parent) and the recipient (or parent) and the judgment of the treating physician. Imposition upon an entity such as CorCell of standards that might, would unduly restrict the rights of patients who choose to store UCB with CorCell and/or unnecessarily chill the interest of patients who might otherwise do so.

CorCell agrees that certain basic standards for prevention of cross contamination must be observed if any untested samples, or samples that have tested positive for disease contamination, are to be stored. CorCell's procedures require that prior to being placed in long term storage, UCB cells are placed in a quarantine tank, which are in vapor phase. Once testing is completed, the specimen is labeled and placed in one of two tanks. If testing shows the specimen free of viral contamination, the specimen is placed in a liquid nitrogen tank for permanent storage. On the other hand, if the test for viral contamination yields a false or true positive result, the specimen is labeled appropriately and maintained in a vapor quarantine storage tank. Parents are notified of the results and the limitations of the product.

The fundamental requirement of a proper regime for the storage of potentially contaminated specimens is appropriate procedures for labeling and segregation, such as those presently observed by CorCell.

In conclusion, CorCell supports the FDA's effort to develop appropriate standards as reflected in the Request, provided that those standards do not unnecessarily interfere with CorCell's business or with the options of patients for autologous and family-related uses.

Very truly yours,



Marc Laleman
Acting President and CEO