



Monday, August 23, 2004

Division of Dockets Management (HFA-305),  
Food and Drug Administration  
5630 Fishers Lane, rm.1061  
Rockville, MD 20852

Re: [Docket No. 2004D-0193]

To Whom It May Concern:

Please accept these comments on the draft guidance entitled **Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)**. The Seattle Cancer Care Alliance and the Fred Hutchinson Cancer Research Center have a rich history using hematopoietic stem cell therapies to save lives. The draft guidance intends to limit the potential for communicable disease transmission via these treatments. Accordingly, we appreciate the opportunity to work in cooperation with the FDA to ensure the safety and efficacy of cellular-based therapies.

It is our mission to cure cancer. Each year, over 1000 autologous and allogeneic peripheral blood stem cell products are collected and distributed by the Seattle Cancer Care Alliance in concert with the Fred Hutchinson Cancer Research Center. These products may be minimally manipulated or modified to select for certain cell populations or extended storage. Our treatment relationship with the patient and their families compels us to submit the following insights:

*Balancing the Risks and Benefits—Consider the blood donor*

We understand that the draft guidance was written to address cellular and tissue-based products from both cadaveric and living donors. For the cadaveric population, it is impossible to directly query the donor regarding risk factors and prior medical history. Thus, we fully support the completion of (1) a current **donor medical history interview** with individuals knowledgeable in the donor's history; (2) a current report of the **physical assessment** of the donor and (3) the evaluation of **other available records** for the cadaveric donors.

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However, in the case of a living donor, the requirement for **a physical examination** of a donor for purposes of revealing high risk behavior and the evaluation of **other available records** should be employed *only* to augment or clarify the donor's response to direct questioning. Attempts to collect more and different information are unlikely to reveal anything other than discrepancies of questionable merit. Though the guidance is clear in delimiting the pursuit of additional records to avert delay in the usefulness of the product, most of the records listed in the guidance would only be of value for cadaveric donors. The labor required to fulfill this requirement should be weighed against expected beneficial yield when the living donor is available to provide primary information.

Looking to blood donors as an example, a medical history interview is coupled with a limited physical examination and serological testing to determine suitability. Approximately 27 million blood transfusions occur each year in the United States<sup>1</sup>. All use this technique to minimize the risk of disease transmission. The FDA has not cited any evidence suggesting that living peripheral blood stem cell donors pose greater hazard for communicable disease than blood donors. Therefore, if the information collected by direct questioning of blood donors is currently sufficient to protect the public from infectious disease by blood products then these measures should also be sufficient to protect HCT/PS recipients who are infused at a much lower frequency. Moreover, the physical examination of a stem cell donor is designed to ensure safety for the recipient (regarding possible transmission of communicable disease or malignancy) as well as the safety for the donor (regarding hematopoietic growth factor administration and apheresis or anesthesia and bone marrow harvest). The comprehensive examination required for stem cell donation, therefore, greatly supplements the historical database and far surpasses the evaluation required for volunteer blood donors.

Because the minimum requirements for hematopoietic stem cell donor evaluation already exceeds those for routine blood donors, we recommend that examination of the living donor should *not* necessitate probing for<sup>2</sup>:

1. Physical evidence for risk of sexually transmitted diseases such as genital ulcerative disease, herpes simplex, syphilis, chancroid;
2. Physical evidence of anal intercourse including perianal condyloma;
3. Physical evidence of nonmedical percutaneous drug use such as needletracks, including examination of tattoos, which may be covering needle tracks;
4. Physical evidence of recent tattooing, ear piercing, or body piercing;
5. Disseminated lymphadenopathy;
6. Oral thrush;
7. Blue or purple spots consistent with Kaposi's sarcoma;
8. Unexplained jaundice, hepatomegaly, or icterus.
9. Physical evidence of sepsis, such as unexplained generalized rash;
10. Large scab consistent with recent smallpox immunization;
11. Eczema vaccinatum;
12. Generalized vesicular rash (generalized vaccinia);
13. Severely necrotic lesion consistent with vaccinia necrosum; and/or
14. Corneal scarring consistent with vaccinia keratitis.

## *Labeling—Respecting Privacy and the Need to Know*

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We are in agreement with the requirements to test and appropriately label HCT/P's. It is also reasonable for products that have been untested to be marked "NOT EVALUATED FOR INFECTIOUS SUBSTANCES" and "WARNING: Advise patient of communicable disease risks." We concur that the recipient must be informed of any additional risk associated with the use of HCT/P's that do not meet the defined eligibility requirements.

We are, however, highly concerned with the requirement that HCT/P's be labeled with specific test results identifying the presence of certain communicable disease agents and/or risk factors for or clinical evidence of relevant communicable disease agents or diseases. Prominently divulging testing abnormalities does not serve to communicate this information in a manner that benefits patient care. In fact, it may interfere with the care relationship.

In our experience, the infusion of stem cells is a momentous occasion often attended by family and friends. If, for example, a sibling is the donor of the HCT/P, there is no reason that other family members present for the infusion should be privy to the testing or behavioral risk factors. Despite the fact that the donor is not named on the label, the donation is hardly anonymous when derived from a relative. All inherently know the identity of the HCT/P donor. Alerting all in attendance to the disease state of the sibling is insensitive. We feel it objectionable to conspicuously advertise the particular details of the donor's status outside of the care relationship that requires the consent of the patient.

As an alternative, we encourage the FDA to consider "associated materials" as labeling and allow the specific testing or risks to be contained in paperwork accompanying the product rather than prominently displayed. We believe it acceptable to label the unit(s) with biohazard label(s) and perhaps, refer the infusionist to review associated materials. This would achieve the objective of assuring that the risks are communicated without advertising the risk to those outside of the patient-provider relationship.

Again, blood components are not labeled with positive infectious disease results when required by a patient for overriding medical reasons. A biohazard label suffices. In no way does this allowance erode the importance of informed decision-making between the provider and the patient.

We thank you for the opportunity to comment and await the final guidance.

Sincerely,



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Fred Hutchinson Cancer Research Center  
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<sup>1</sup> Ensuring Blood Safety and Availability in the U.S.: Technological Advances, Costs, and Challenges to Payment, The Lewin Group, September 2002

<sup>2</sup> Draft Guidance for Industry, Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-based Products (HCT/Ps), U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research (CBER), [Docket No. 2004D-0193] May 2004, p. 25.