

May 8, 2002

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket #99D-5347: "Draft Guidance for Industry Precautionary Measures to Reduce the Possible Risk of Transmission of Zoonoses by Blood and Blood Products from Xenotransplantation Product Recipients and Their Intimate Contacts"

Dear Docket Officer:

The American Association of Blood Banks (AABB) is the professional society for over 8,000 individuals involved in blood banking and transfusion medicine and represents approximately 2,000 institutional members, including blood collection centers, hospital-based blood banks, and transfusion services as they collect, process, distribute, and transfuse blood and blood components and hematopoietic stem cells. Our members are responsible for virtually all of the blood collected and more than 80 percent of the blood transfused in this country. For over 50 years, the AABB's highest priority has been to maintain and enhance the safety and availability of the nation's blood supply.

The AABB appreciates the opportunity to comment on this "Draft Guidance for Industry Precautionary Measures to Reduce the Possible Risk of Transmission of Zoonoses by Blood and Blood Products from Xenotransplantation Product Recipients and Their Intimate Contacts." Our major points follow:

- We accept the necessity to defer recipients of xenotransplants but respectfully suggest that the transplant programs have primary responsibility to initiate this process as part of the xenotransplantation consent process. We also suggest that transplant programs must educate the transplant product recipient and their intimate contacts about the risks of xenotransplantation, and this education should include information advising them that they should not donate blood or tissue.
- Blood collection facilities can reinforce this with written information provided to all potential donors.

99D-5347

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- We suggest that the addition of unvalidated donor interrogation questions for the theoretical risks of xenotransplantation may, at worst, paradoxically increase other risks of transfusion, and at best will further contract an already shrinking donor base.
- Deferral for contact with xenotransplant recipients is unwarranted at present and the risk of such contact is amenable to study in populations with occupational exposure to the relevant species

Deferral of Xenotransplant Product Recipients

The AABB reiterates its position stated in numerous public meeting and written comments, that the information that xenotransplantation product recipients are prohibited from allogeneic blood and tissue donation should be included in the informed consent process associated with xenotransplants, and should not require specific blood donor questions.

Recognizing the potential risk of transmitting zoonotic pathogens to patients by xenotransplantation, the AABB agrees that xenotransplant recipients are unacceptable donors of allogeneic blood and tissue. Under current donor restrictions regarding health and medication use, virtually no xenotransplant recipient would be a qualified blood donor at this time.

The current number of xenotransplantation product recipients was estimated at the March 12, 2002 HHS Secretary's Advisory Committee on Xenotransplantation (SACX) as 1000 to 1500 in the United States, with at least 550–1000 of these being autologous transplants of cells grown for prolonged periods of time on a monolayer of a well characterized murine tissue culture line. Thus, only 450-500 recipients are truly of concern. As suggested at the SACX, an educational program for transplant recipients and their intimate contacts should be established and part of that educational program should discuss why blood donations are prohibited. Asking millions of blood donors questions about xenotransplantation is akin to looking for a needle in the haystack, and protection of the blood supply can be accomplished by other means.

Blood collection facilities can reinforce the prohibition on donation by including the xenotransplant exclusion in the written materials blood donors are required to study before each donation. This avoids addition of time-consuming, confusing, and unvalidated questions that FDA suggests adding to the donor interview in this guidance.

Donor Questions

According to the draft guidance, the Blood Products Advisory Committee (BPAC) recommended "that the blood donor questionnaire be carefully modified to appropriately capture xenotransplantation product recipients and their intimate contacts without increasing the complexity of the questionnaire or detracting from known risk behaviors." It should be noted that the Xenotransplantation Subcommittee of the Biological Response

Modifiers Advisory Committee did not recommend addition of donor interview questions. At its meeting on March 12, 2002, the HHS Secretary's Advisory Committee on Xenotransplantation also declined to endorse the proposed donor questions.

The proposed questions clearly do not meet the criteria identified by BPAC. The proposed questions are far too complex to be understood by donors. In fact, the questions are difficult to interpret even for blood banking professionals. The first FDA proposed question — “In the past 12 months, have you received blood, an organ, skin graft or other tissue transplant from a human donor?” — is described in the draft guidance as a modification to the currently asked questions. While this was correct at the time the draft guidance was written, the blood banking community has already taken steps to revise this question on the current questionnaire. Recognizing the need to simplify the current donor screening questionnaire, an AABB-sponsored interorganizational task force on streamlining the donor history questionnaire has recently submitted an improved questionnaire for FDA approval.

One of the cornerstones of the task force approach was to simplify the questions, and to eliminate compound and complex questions. Based on focus group studies and cognitive interviews conducted by the National Center of Health Statistics of the Center for Disease Control and Prevention, it is clear that donors tend to focus on only one element of compound questions and do not pay attention to the entire question. The format and language for this question are significantly different in the proposed questionnaire. The proposed questionnaire now asks three separate questions, each very short and addressing only one concern:

In the past 12 months have you
Had a blood transfusion?
Had a transplant such as organ, tissue, or bone marrow?
Had a graft such as bone or skin?

The second proposed question “Have you, any sexual partner, or any member of your household ever had a transplant or other medical procedure that involved being exposed to organs, tissues, or living cells from an animal?” is too long, addresses too many issues and is unlikely to elicit an accurate response. The same is true of all of the follow-up questions.

This task force conducted focus group evaluation of the xenotransplantation questions proposed by FDA. The focus groups made multiple recommendations for editing and shortening the questions, splitting questions into their component parts, and more precise definition of such terms as "repeatedly" and "deep kissing." The UDHQ task force examined these suggestions but was unable to devise better language without putting undue emphasis on this theoretical risk by making the number of questions and explanations about xenotransplantation out of proportion to the number of questions about other well known risks. However, the overall reaction of the focus groups is even more telling. The focus groups concluded that it was “impractical and foolish to ask

these questions of all donors in order to detect a small number of individuals who are theoretically at risk.”

The proposed donor questions in this draft guidance remain too arcane to add to the current screening process and will produce donor confusion. This could result in unneeded deferrals at a time of borderline blood supply adequacy.

Donor screening is already lengthy and complex. Increasing the complexity of the donor screening process for marginal theoretical risks will detract from its efficacy for documented risks like traditional viral transfusion associated infections and malaria. The result may be a paradoxical decrement in transfusion safety, in addition to any unintended donor loss. REDS investigators have reported that 1.8% of anonymously surveyed accepted blood donors admit to deferrable risks, and we suspect that a substantial proportion of that percentage is due to the length and complexity of the donor interview.

If donor questioning about xenotransplantation is to be mandated, at a minimum, additional questions proposed by FDA for the reduction of this *hypothetical* risk must be validated for comprehension before being added to what is already referred to as the "donor interrogation" process.

Deferral of Intimate Contacts

The AABB wishes to reiterate its opposition to the deferral from blood donation of “intimate” contacts of xenotransplantation products. The requirement for deferral of sexual, household, and other close contacts is unsupported by any evidence of transmission of potential or unrecognized pathogens to such contacts after exposure to xenotransplant recipients. The AABB understands that the xenotransplantation recipient will be immunosuppressed and be at theoretically increased risk from zoonoses. We do not accept that the contacts are at increased risk and object to their inclusion. In the prior draft, deferral of “health care workers, laboratory personnel, and other individuals who have had contact with blood and body fluids from a xenotransplantation product recipient...” was subject to the same criticism, and this language has been dropped from this most recent draft. Furthermore, it is a slippery slope from such donor deferrals to disqualification of larger populations with significant occupational animal exposures, such as abattoir workers, farmers, veterinarians, and medical researchers.

The AABB suggests that a risk assessment be undertaken among non-xenotransplant individuals with close contact to the relevant animal species for evidence of disease associations that would support concerns of zoonotic transmission of disease causing organisms by donor blood. Given the small numbers of xenotransplants currently being performed, and the potentially large populations with contact to nonhuman primates and swine, these epidemiological studies can be carried out before xenotransplantation becomes prevalent, constituting a zoonotic threat to significant numbers of patients and their contacts.

The AABB appreciates this opportunity to comment. Please direct any questions to Kay Gregory, Director Regulatory Affairs at kayg@aabb.org or 910-842-2790.

Sincerely,

A handwritten signature in black ink that reads "Dale R Malloy". The signature is written in a cursive style with a large, prominent initial "D".

Dale Malloy, DPA, MT(ASCP)SBB
President