

V. DONOR DEFERRAL ISSUES RELATED TO XENOTRANSPLANTATION

**Andrew Dayton, M.D., Ph.D., Medical Officer
Gene Regulation Section, DETTE, OBRR, CBER, FDA**

65th Meeting
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Holiday Inn, Silver Spring
8777 Georgia Avenue
Silver Spring, MD

Report of the FDA Subcommittee on Xenotransplantation
Meeting of January 13, 2000
Food and Drug Administration
Center for Biologics Evaluation and Research
CHAIRMAN'S SUMMARY REPORT
XENOTRANSPLANTATION SUBCOMMITTEE
(Subcommittee of the Biological Response Modifiers Advisory Committee)
Meeting #3: January 13, 2000
Holiday Inn, Gaithersberg,, MD

Subcommittee Participants

Hugh Auchincloss, Jr., M.D., Chair
Jonathan S. Allan, D.V.M.
Antonio Benedi
John M. Coffin, Ph.D.
F. Blaine Hollinger, M.D.
Richard J. Kagan, M.D.
Richard Kaslow, M.D., M.P.H.
Katherine E. Knowles
William G. Lawrence, J.D.
Nicholas W. Lerche, D.V.M.
Jeanne V. Linden, M.D.
Robert L. McCauley, M.D.
Claudia A. Mickelson, Ph.D.
Kenrad Nelson, M.D.
David Onions, Ph.D.
Prem S. Paul, D.V.M., Ph.D.
Daniel Salomon, M.D.
Harold Y. Vanderpool, Ph.D., Th.M.

FDA Participants

Jay P. Siegel, M.D.
Philip D. Noguchi, M.D.
Eda Bloom, Ph.D.
Carolyn Wilson, Ph.D.
Jay Epstein, M.D.
Andrew Dayton, M.D., Ph.D.
Ruth R. Solomon, M.D.
Celia M. Silverman, Ph.D., M.D.
Peter L. Hudson, Ph.D.

CDC and NIH Participants

Lousia E. Chapman, M.D.
Amy Patterson, M.D.

Executive Secretary

Ms. Gail Dapolito

Committee Management Specialist

Ms. Rosanna L. Harvey

This summary report for the January 13, 2000 meeting of the Xenotransplantation Subcommittee of the Biological Response Modifiers Advisory Committee were approved on _____.

I certify that I attended the January 13, 2000 meeting of the Xenotransplantation Subcommittee and that this report accurately reflects what transpired.

Gail Dapolito
Executive Secretary

Hugh Auchincloss, Jr., M.D.
Chairman

Introduction

The third meeting of the Xenotransplantation Subcommittee was called to order on January 13, 2000 with Hugh Auchincloss, Jr., M.D. presiding as Chairman. The subcommittee discussed three main topics: (1) Blood Donor Deferral, (2) Examination of Risks Posed by Different Xenotransplantation Products, and (3) Porcine Endogenous Retrovirus update.

A conflict of interest statement was read into the public record which stated that members with the appearance of a conflict of interest based on their work with products which could be affected in the future were given waivers to participate. Copies of the waivers are available from the FDA Freedom of Information Office.

The scientific presentations of June 13 are referenced in the attached agenda and roster. Public comment was provided by the following individuals/groups during the Open Public Hearing sessions:

Public Comment Speakers

Kay R. Gregory, American Association of Blood Banks
Chris Healy, ABRA
Becky Haley, M.D. American Red Cross
Celso Bianco, M.D. Americas Blood Centers
Michael Egan, Diacrin
Alix Fano, Campaign for Responsible Transplantation
Allan Brazel
Corinne Saville, Imutran

Topic I: Blood Donor Deferral

Background: Dr. Andrew Dayton, OBRR/CBER, provided the background and FDA perspective on the FDA draft policy on blood donor deferral for xenotransplantation product recipients and the contacts. (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 Contacts, December, 1999)

The Xenotransplantation Subcommittee, working with the FDA, had previously agreed on the principle that recipients of xenotransplants and their contacts should be deferred from blood donation indefinitely, and that this policy should be implemented primarily by the education of the recipients and their contacts by the xenotransplant team. The current discussion was initiated because the definition of xenotransplantation that has been adopted by the FDA more recently, with the agreement of the Subcommittee, is somewhat broader than it was initially.

“Xenotransplantation: any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (a) live cells, tissues, or organs from a nonhuman animal source, or (b) human body fluids, cells, tissues or organs that have had ex vivo contact with live nonhuman animal cells, tissues or organs.”

Working with this definition (which includes the ex vivo contact provision), it had become apparent that the number of xenotransplant recipients that currently exist is significantly larger than had previously been recognized, and that many of these individuals are probably not aware that they are such recipients. Thus, the original policy for blood donation deferral adopted by the Subcommittee and the FDA could not possibly be effective. Therefore, the FDA sought guidance from the Subcommittee about how to handle both previous blood donations that may have been made by xenotransplant recipients and the management of future blood donation deferral.

Committee Discussion: The Subcommittee asked the FDA for information about the scope of the potential problem. Recognizing that there is no exact answer to this question, and that new recipients of xenotransplants may be identified in the future, the FDA indicated that over the past ten years there may have been around 750 individuals who have received human cells that had ex vivo contact with cell lines derived from nonhuman sources. No evidence has appeared during that time of any ill consequences as a result of blood donors that were xenotransplant recipients.

In discussing the appropriate response to the FDA’s questions, the Subcommittee recognized a number of factors that contribute to the risk/benefit analysis of blood donor deferral policy. Some important considerations include:

- Because plasma derivatives are created from pooled sources, the withdrawal of these products, on the basis of a single donor having been a xenotransplant recipient, would have an enormous immediate impact on the plasma supply.
- The techniques used to generate plasma derivatives destroy many of the infectious agents that have been of greatest concern to the Subcommittee in the past. However, members of the Subcommittee pointed out that this safety feature would not apply to all possible infectious agents.
- The transmission of potential zoonotic infections between humans is most likely to occur by exposure to body fluids, implying that “contacts” of xenotransplant recipients would most likely involve truly “intimate” contacts, rather than all members of a household. The Subcommittee voted **12 yes, 1 no, and 3 abstentions** to consider “intimate” rather than “close” contacts of xenotransplant recipients.
- The Subcommittee members agreed with the principle that it might well be possible to characterize established cell lines from animal sources such that ex vivo contact with these cells would not generate an infectious risk that was sufficient to warrant

blood donor deferral. Discussion of what that characterization might involve took place later in the day under Topic II.

- Subcommittee members felt that contact with xenotransplant recipients by health care workers that would generate an infectious risk would most likely have to involve an exceptional contact with body fluids that would be recognized as a concern under existing standards of universal precautions.
- The members of the Subcommittee did not feel that additional questions regarding exposure to xenotransplants (which might be added to the questions that are already used to screen potential blood donors) would be useful because they would be poorly understood. In addition, the subcommittee recognized the potential negative impact of such additional questions on blood donation. The Subcommittee voted **16 yes, 0 no**, in favor of not including additional questions on the blood donor donation questionnaire. The Subcommittee continued to focus on the need to achieve blood donation deferral by education of the xenotransplant recipients and their intimate contacts.

Based on these and other considerations, the Subcommittee voted on a number of questions posed by the FDA. The outcome of those votes is as follows:

- Deferral for certain ex vivo exposures, such as exposure to a well-characterized cell line, or exposure across a physical barrier, may be exempted by FDA on a case-by-case basis. **16 yes, 0 no.**
- Persons who have received xenotransplantation products should be indefinitely deferred from donating whole blood and blood components including Source Plasma and Source Leukocytes. **16 yes, 0 no.**
- Persons who are intimate contacts of xenotransplantation product recipients should be indefinitely deferred from donating Whole Blood, blood components, including Source Plasma, and Source Leukocytes. **9 yes, 7 no.**
- Health care workers, including laboratory personnel, and other individuals who have had contact with blood and body fluids from a xenotransplantation recipient, through percutaneous inoculation (such as accidental needle stick) or through contact with an open wound, non-intact skin, or mucous membranes should be indefinitely deferred from donating Whole Blood and blood components, including Source Plasma, and Source Leukocytes. **0 yes, 16 no.**
- Whole Blood and blood components (including unpooled plasma and Source Leukocytes) intended for transfusion or for further manufacturing into injectable products, if made from donations obtained from persons eligible for deferral, should be withdrawn from distribution and held in quarantine or destroyed. **16 yes, 0 no.**
- In-date plasma derivatives (including pooled plasma) that have been made from plasma containing a donation obtained from persons eligible for deferral should be withdrawn from distribution and quarantined or destroyed regardless of the animal species involved in the xenotransplantation product. **16 yes, 0 no.** (Note that the actual voting on this issue was conducted in two stages involving different possible animal species.)
- Plasma derivative withdrawal is recommended for donors who are intimate contacts of recipients of xenotransplantation products regardless of the animal species involved. **4 yes, 9 no, 3 abstentions.**
- Withdrawal and quarantine may not be warranted for certain ex vivo exposures, such as exposure to a well-characterized cell line, or exposure across a physical barrier, and may be considered by FDA on a case-by-case basis. **16 yes, 0 no.**

The voting on these questions reflects a high degree of consensus among members of the Subcommittee regarding the questions posed by the FDA. The exceptions involved the issue of how far donor deferral should extend to intimate contacts of xenotransplantation recipients with slightly more than half of the members voting that it should extend to intimate contacts in the case of Whole Blood and blood components, and only a quarter of the members voting that it should extend to intimate contacts in the case of plasma derivatives.

However, the critical unresolved issue from this discussion was what type of characterization of well established animal cell lines would be sufficient to allow the FDA to exempt xenotransplant recipients (and their contacts) from donor deferral based on ex vivo contact with these cell lines.

Topic II: Examination of Risks Posed by Different Xenotransplantation Products

Information regarding Epicel3 (cultured epidermal autografts, Genzyme Tissue Repair (GTR)), indicated for the treatment of burn injuries, was provided to the committee. The essence of this product, from the point of view of xenotransplantation, is that it is generated by culturing human epidermal cells on a feeder layer of irradiated 3T3 cells, a cell line derived from a mouse strain more than 30 years ago. Thus, it involves "human body fluids, cells, tissues or organs, that have had ex vivo contact with live nonhuman cells, tissues or organs" and is, therefore, a xenotransplantation product.

Background on the product and the characterization of the mouse cells used in the production of Epicel3, and information on the use of well-characterized, non-human cell lines in the production of medical products was provided by Ms. Doris Peterkin and Dr. Bruce Wentworth (GTR), and Dr. Alan Moore (Primedica Corp.). A patient perspective was offered by Mr. Michael Doucey as part of the GTR presentation.

The FDA perspective was provided by Dr. Eda Bloom. She briefly reviewed many of the FDA guidelines on xenotransplantation that would be applied to this product that might not be necessary in view of the use of well-characterized cell line. The Subcommittee then discussed many of these guidelines and offered their opinions.

The first issue addressed by the Subcommittee was whether the very extensive and excellent characterization of the mouse 3T3 cell line that was being conducted by the company and that had been conducted in the past was sufficient to protect against the infectious risks of xenotransplantation. Without criticizing the excellent testing that had been conducted in the past, several members of the Subcommittee indicated that additional testing or improved assays should be considered in the future. These included co-culture experiments (already now required by the FDA), updated PERT and PCR-based assays for retroviruses, and further testing for other agents, not just viruses, such as non-cultivable bacteria. In addition, the Subcommittee discussed the need to "test procedures, not just product", the importance of determining the degree of inactivation of the feeder cell line, and the need for validation of the final product when any key reagent is changed. The Subcommittee also noted that it was appropriate for the FDA to consider a number of variables when considering the characterization of nonhuman cell lines including: the particular strain of origin (not just the species), the number of nonhuman cells that might be in the final product, the life span of the cells, the immune competence of the intended recipient, and the overall history of ex vivo contact with the particular cell line.

Based on these considerations, the Subcommittee found itself discussing two different xenotransplant products: 1) Epicel3 that had been produced in the past (using the recommended assays at that time), and 2) Epicel3 that might be produced in the future using the "best testing" as recommended by the Subcommittee. The Subcommittee recognized that some of its recommendations regarding these two products would appear to be confusing or even contradictory, since in some cases members recommended relatively stringent application of the FDA guidelines for the future, "best-tested" Epicel3 product, even though they did not feel that it would always be necessary to go back to recipients of the old Epicel3 product (with its less advanced testing) and seek to apply the same stringent guidelines or to rectify the failure to apply those guidelines (by blood product withdrawal, for example).

The Subcommittee did not see this position as contradictory since future application of stringent guidelines would often be simple and have little impact on society, while retroactive application of the same guidelines would often be extremely difficult and highly disruptive. In the face of the Subcommittee's judgement that the infectious risks associated with even the old Epicel3 were extremely small, its members did not see its recommendations as being inconsistent when considered on the basis of a risk/benefit analysis.

The Subcommittee then considered the need to apply some of the particular FDA guidelines to recipients of Epicel3. These included:

- Blood donor deferral of Epicel3 recipients, and intimate contacts: The Subcommittee voted **6 yes, and 10 no** that future recipients of Epicel3, after institution of the best available testing, should be deferred indefinitely from blood donation. The Subcommittee appeared to be in agreement, however, that withdrawal of blood or plasma products based on past donations by recipients of the old Epicel3 product was not necessary, and that deferral of blood donations by recipients of future Epicel3 products did not need to extend to the intimate contacts of these recipients. The Subcommittee did not take a formal vote on these last two points, however, and it should be noted that in this case the presumed agreement of the Subcommittee on these points may be in conflict with some of the formal votes taken during the discussion of Topic I. Since it would appear that the Subcommittee believes that recipients of the old Epicel3 product should be considered eligible for deferral, and since during the earlier discussion the Subcommittee had been unanimous in recommending withdrawal of both blood products and plasma derivatives under these circumstances, it might seem that the Subcommittee should have recommended withdrawal of blood products if donors had been recipients of the old Epicel3. This difference may reflect the evolution of the Subcommittee's thinking based on further reflection and/or on the examination of the particular example provided by Epicel3. Alternatively, it may be that the majority of Subcommittee members believe that even recipients of the old Epicel3 do not need to be subject to blood donor deferral. Whatever, the explanation, no member of the Subcommittee disagreed when it was specifically stated that our position was that withdrawal of blood products was not necessary if previous donors had been recipients of Epicel3.
- Education and Surveillance of Epicel3 Recipients:
- Informed Consent: the Subcommittee voted **6 yes, 6 no, and 2 abstentions** that Epicel3 recipients be informed that they received a xenotransplant.
- Extent and Frequency of Follow-up: The Subcommittee discussed the need for a database of patients who had received Epicel3. The members did not recommend any particular follow-up testing.
- Archives of Patient Samples: The Subcommittee agreed with the FDA recommendation that patient samples be archived. The Subcommittee indicated that active monitoring of these patients was not necessary but it voted **13 yes, 1 no**, that "passive" monitoring should be conducted.
- Animal Procurement Sources and Source Facility Controls: The Subcommittee agreed with the FDA recommendation that this category of safeguards need not be applied to Epicel3.
- Archive samples of the cells, tissues, or organs involved in the manufacture of Epicel3: The Subcommittee agreed that archiving of the xenotransplant product is appropriate.

Following this discussion of the Epicel3 product in particular, the Subcommittee considered a number of more general questions that might apply to other “well characterized cell lines” in an effort to provide the FDA with guidance for their review of other potential xenotransplant products. In general, this discussion by the Subcommittee indicated that its members were often in agreement that certain factors might affect the risks associated with xenotransplant products, but that members had trouble identifying any factors that would automatically be sufficient to exempt the products from the safeguards the FDA has established for xenotransplantation. Particular issues discussed by the Subcommittee included:

- Species of source animal: The Subcommittee agreed with the FDA recommendation to exclude nonhuman primates as source animals.
- Non-primate mammals: The Subcommittee agreed with the FDA that the “use of species or strains lacking infectious endogenous retrovirus may lower concerns about latent infection but not to the extent that changes in lifelong follow-up or deferral of intimate contacts from blood donation would be prudent at this time”.
- Non-mammalian animals, including invertebrates: The Subcommittee urged some caution when considering non-mammalian animals since the required testing of their cell lines may be different and there may be other possible risks such as retroposons that are not considered in mammalian cases.
- Cell line vs. fresh tissue: The Subcommittee felt that the earlier discussions and recommendations regarding Epicel3 are generalizable and agreed with the FDA position that “extensive testing and experience with a long-term cell line may obviate most or all need for animal procurement sources and source facility controls. Additionally, definitive exclusion of various pathogens, (e.g. herpesviruses and retroviruses) could lead to less intensive long-term monitoring and sample archiving and could obviate the need to inform contacts or defer them from blood donation”.
- Use of barriers and/or encapsulation, transient or low dose exposure: The Subcommittee felt that approaches such as these might lower the infectious risks associated with xenotransplantation but that there needed to be a presumption of failure at this time for these types of approaches and that therefore their use would not change the current monitoring recommendations for recipients of xenotransplants.
- Immunosuppression: The Subcommittee recognized that the absence of immunosuppression in the recipient might alter the infectious risks associated with xenotransplantation but that, in view of the difficulty in determining the degree of immunosuppression in any given individual, the Subcommittee would not alter the current monitoring recommendations for recipients of xenotransplants on the basis of a lack of exogenous immunosuppression.

Topic 3: Porcine Endogenous Retrovirus Update

The Subcommittee heard a presentation by Novartis of recently published data from a retrospective study of patients treated with living pig tissues. About 160 patients were studied and no evidence of PERV infection was encountered. Although the assays used were felt to represent a state-of-the-art approach to this analysis, the Subcommittee recognized the need for on-going acquisition of data of this sort as xenotransplantation trials proceed.

The Subcommittee also heard a presentation by Dr. David Onions, Q-Biotech, who showed preliminary results from a single unpublished experiment involving transmission of PERV to guinea pigs. The experiment was designed to raise antibodies against PERV. Eight guinea pigs were inoculated subcutaneously with PERV-B prepared in human 293 cells. Following this treatment, infection by between 3,000 and 70,000 copies of the provirus was demonstrated per million guinea pig cells in all eight guinea pigs, and the number of proviral copies suggested that at least one round of viral

replication had occurred. Expression of the virus was demonstrated in one of eight guinea pigs at the single time point tested. There was no evidence of viremia. Both the Subcommittee and the FDA welcomed this information since it suggests that an animal model can be developed that might allow for testing of some of the consequences of PERV infection in vivo. Nonetheless, it remains true that no animal model will necessarily predict the consequences of a possible infection of human recipients of xenotransplant products.

**Implementation of Precautionary
Measures to Reduce the Possible Risk
of Transmission of Zoonoses by
Blood and Blood Products from
Xenotransplantation Product
Recipients and Their Contacts**

By Andrew I. Dayton, M.D., Ph.D.
LMV/DETTD/OBRR/CBER/FDA

Xeno Definitions

- Zoonoses are infectious diseases of animals that can be transmitted to humans through exposure to, or consumption of animals.

Xeno Definitions

- Xenotransplantation is any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (a) live cells, tissues, or organs from a non-human animal source, or (b) human body fluids, cells, tissues, or organs that have had *ex vivo* contact with live non-human animal cells, tissues, or organs.

Xeno Definitions

- Xenotransplantation products include live cells, tissues or organs used in xenotransplantation.
- Biological products, drugs, or medical devices sourced from nonliving cells, tissues or organs from nonhuman animals, including but not limited to porcine insulin and porcine heart valves, are not considered xenotransplantation products.

Risk of Transmission of Zoonoses by Xenotransplantation

- Because transplantation necessitates disruption of the recipient's usual protective physical and immunologic barriers, xenotransplantation may facilitate transmission of known or as yet unrecognized zoonotic agents to humans.

Risk of Transmission of Zoonoses by Xenotransplantation

- Some Xenotransplantation product sources (particularly pigs) are being genetically modified in ways that may foster adaptation of zoonoses to human receptors.

Xenotransplantation Across Barriers

- Some xenotransplantation procedures maintain a barrier between host and foreign tissue.
- Even when such barriers are non-permeable for virus, the risks of barrier failure require consideration.

Considerations in Deferral Policy

- The risks of zoonotic transmission to xenotransplant recipients, and their contacts, remain undefined.
- The risks to the public health of blood or plasma becoming unavailable are immediate and significant.
- Withdrawal of plasma derivatives to address even small numbers of unsuitable donations could cause serious product shortages.

Xenotransplantation issues impacting the blood supply.

How many xenotransplantation recipients are there?

- about 1000 in the US
- at least 550 of these have had autologous transplants of cells grown for prolonged periods on a monolayer of a well characterized murine tissue culture line.
- about 50-100 “classic” recipients.

Recent Chronology I

12/23/99 Publication of Draft Guidance Document:

**“Precautionary Measures to Reduce the Possible Risk
of Transmission of Zoonoses by Blood and Blood
Products from Xenotransplantation Product Recipients
and Their Contacts”**

Recent Chronology II

1/13/2000 Biological Response Modifiers Advisory
Committee Subcommittee on Xenotransplantation

("XAC" or Xeno Advisory Committee)

Discussed the highlights of the Draft Guidance Document
and voted on several recommendations.

Xeno Advisory Committee Vote on Draft Guidance for Blood

1. Indefinite deferral for xenorecipients:

Yes = unanimous

2. Contacts of significance for deferral/withdrawal
policy are limited to "intimate" contacts ("close
contacts", as a defined term, was too broad).

Yes= 9; No=1; Abstain = 3

(However, "intimate" was never defined.)

Xeno Advisory Committee Vote on Draft Guidance for Blood

3. Defer intimate contacts of xenotransplantation product recipients:

Yes = 9; No = 7

4. Defer Healthcare Workers etc. who have mucosal or percutaneous exposure to xenorecipients:

No = unanimous

Xeno Advisory Committee Vote on Draft Guidance for Blood

5. Allow case-by-case exceptions for deferral (such as when exposure has been to a well characterized cell line):

Yes = unanimous

6. Withdraw whole blood and unpooled blood components for donation by xenorecipient (e.g. unpooled plasma, source leukocytes):

Yes = unanimous

Xeno Advisory Committee Vote on Draft Guidance for Blood

7. Withdraw plasma derivatives (pooled plasma) for donation by xenorecipient (any animal):

Yes = unanimous

8. Withdraw plasma derivatives (pooled plasma) for donation by intimate contact of a xenorecipient

Yes = 4; No = 9; Abstain = 3

Xeno Advisory Committee Vote on Draft Guidance for Blood

10. Case-by-case exceptions to withdrawal of pooled products for exposure *ex vivo* (e.g. to well characterized cell lines or across a physical barrier):

Yes = unanimous

Xeno Advisory Committee Vote on Draft Guidance for Blood

11. Add the series of Xenotransplantation questions to the donor deferral questionnaire:

No = unanimous

Factors distinguishing exposure of HCW to
xenotransplantation product recipients from exposure
of abattoir workers & veterinarians etc. to animals.

1. The xenotransplantation product recipient represents, generally, a long term, intimate apposition of xenogeneic tissues.
2. This apposition is generally under conditions of host immuno-suppression, which may allow abnormal amounts of xenozyoonotic replication, thereby favoring adaptation
3. In some xenotransplantation scenarios, genetic modifications of the transplanted material may pose the risk of additional avenues of xenozyoonotic adaptation.

PLANNED CHANGES TO GUIDANCE

I

OLD

Close Contacts:

“...household members and others with whom the [xenotransplantation product] recipient participates in activities that could result in exchanges of bodily fluids.

NEW

Intimate Contacts:

Includes “...persons who have engaged repeatedly in activities that could result in intimate exchange of body fluids with a xenotransplantation product recipient. For example ... sexual partners, household members who share razors or toothbrushes and health care workers or laboratory personnel with repeated percutaneous, mucosal, or other direct exposures...”

PLANNED CHANGES TO GUIDANCE II

OLD

NEW

Deferral of Close Contacts.
(HCW not in definition)

Deferral of Intimate Contacts.

Deferral for HCW with
percutaneous/mucosal
exposure.

HCW with
percutaneous/mucosal
exposure now included in
definition of Intimate Contact,
but only if the exposure has
been repeated.

The “XAC” votes on 1/13/2000:

Defer intimate contacts (“intimate” had not been rigorously
defined, however): yes=9; no = 7

Defer HCW with percutaneous/mucosal exposure (exposure was
not required to be “repeated”) no=unanimous

PLANNED CHANGES TO GUIDANCE III

OLD

Withdrawal of plasma derivatives (pooled material) for donation by a xenorecipient **only if** product is from non human primate.

Withdrawal of plasma derivatives (pooled material) for donation by a **close contact** of xenorecipient **only if** product is from non human primate.

NEW

Withdrawal of plasma derivatives (pooled material) for donation by any xenotransplantation product recipient (certain exceptions).

No withdrawal of plasma derivatives for donation by “intimate contacts” of xenorecipients.

“XAC” votes on 1/13/2000:

Withdrawal of plasma derivatives (pooled plasma) for donation by any xenorecipient. yes = unanimous

Withdrawal of plasma derivatives (pooled plasma) for donation by intimate contact of NHP Xenorecipient: yes=4; no = 9; abstain=3

Withdrawal of plasma derivatives (pooled plasma) for donation by intimate contact of Xenorecipient (animals other than NHP): yes=4; no = 9; abstain=3

PLANNED CHANGES TO GUIDANCE IV

NEW:

Case by case exceptions to deferral and/or withdrawal for donation by xenotransplantation product recipients may be considered when the exposure has involved only well characterized cell lines or when the exposure occurred only across a physical barrier.

Proposed Modification of Screening Procedures

I

Include the following information in the educational material presented to donors before donation:

Do not donate blood or blood products if you have ever been exposed to animal organs, tissues or cells during a medical procedure or treatment.

An individual may be exposed to animal organs, tissue or cells by one of the following medical procedures or treatments:

- receiving a transplant of a living organ, tissues, or cells from an animal.
- having blood or other body fluids removed from your body, passing it through a machine or procedure which exposes your blood or body fluids to living organs, tissues, or cells from an animal and then returning it to your body.

Do not donate blood or blood products if you have ever had intimate contact with an individual who has been exposed to animal organs, tissues or cells during a medical procedure or treatment.

Examples of intimate contact activities include:

- sexual intercourse.
- sharing of needles, toothbrushes or razorblades.
- laboratory or health care workers who may experience repeated, direct injection or mucosal exposure to body fluids.

Proposed Modification of Screening Procedures II

Modify the existing donor questionnaire section on transplantation:

OLD: See series of questions in draft Guidance

FDA proposes to modify the current AABB Standard Donor Questionnaire question on transplantation/transfusion.

The current question reads as follows:

“In the past 12 months, have you received blood or had an organ or tissue transplant or graft?”

NEW:

FDA proposes:

I. Replace the current question with the following:

“In the past 12 months, have you received blood or had an organ or tissue transplant or graft from a human?”

II. Insert the following after the one above:

A. “Have you or any one you know ever been exposed to animal organs, tissues, cells or transplants as part of a medical treatment?”

1. If the answer to II.A above is yes, were you the one who received the medical treatment?

a) If the answer to II.A.1 above is no, did you engage with the treated individual in behaviors which could involve the repeated exchange of body fluids, such as sexual intercourse or sharing of razors or toothbrushes, or were you repeatedly exposed to cells tissues organs or body fluids from such individuals through your mouth or eyes or open wounds or sores?

III. Prospective donors answering yes to any of questions I, II.A or II.A.1 above should be deferred..

Questions for this Committee IV:

We have proposed language concerning Xenotransplantation deferral issues to be added to educational material required to be read by blood/plasma donors before donation.

Does the committee agree that donors should be required to read this material, before donation?

(Committee members wishing to modify the proposed language are requested to submit revised language to the FDA within the next two weeks.)

Questions for this Committee V:

We have proposed modifying the blood donor questionnaire to intercept Xenotransplantation product recipients and their "intimate contacts."

Does the committee agree with the proposed modification to the questionnaire?