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September 12, 2012

James Berger
Senior Advisor for Blood Policy
Office of HIV/AIDS and Infectious Disease Policy
Office of the Assistant Secretary for Health
U.S. Department of Health and Human Services
1101 Wootton Parkway, Tower Building, Suite 250
Rockville, Maryland 20852

Re: Public Health Service (PHS) Guideline for Reducing HIV, HBV and HCV
Transmission Through Organ Transplantation

Dear Mr. Berger,

The American Society of Transplantation is pleased to comment on the most recent draft of the *PHS Guideline for Reducing the Transmission of Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) through Organ Transplantation*. We acknowledge and are grateful to the PHS for addressing many of our previously identified concerns by substantially revising many of the recommendations originally proposed in the earlier version of the Guideline.

We recognize and share the primary concern motivating the development of these guidelines – “to maximize transplant recipient outcomes while preserving patient safety with regard to risk of HIV, HBV, and HCV transmission”. The safety of the organ supply and the continued success of solid organ transplantation in saving the lives of our patients are of paramount concern.

However, it must be stated that many of the fundamental concerns regarding the overall benefit of this proposed *Guideline* and the costs involved in implementing these recommendations, as previously articulated by AST, have not been addressed. This is particularly relevant given the admittedly poor quality and limited data in this area and the current very low rate of documented unanticipated transmissions of HIV, HCV and HBV.

Moreover, given the acknowledged low quality of the evidence on which the recommendations in this *Guideline* are based, if they are ultimately implemented, AST strongly urges that the resources necessary for comprehensive collection and analysis of the results of the recommended testing of donors and recipients should be made available, thereby developing the data to allow improved identification of donors at risk for transmission of HIV, HCV, and HBV. Additionally, taking into consideration the number of gaps identified in our knowledge related to this proposed *Guideline*, AST strongly supports the Recommendations for Further Study

NATIONAL OFFICE
15000 Commerce Parkway, Suite C • Mt. Laurel, NJ 08054
856.439.9986 • Fax: 856.439.9982 • info@a-s-t.org • www.a-s-t.org

GOVERNMENT RELATIONS
William Applegate, Director of Government Relations • Bryan Cave, LLP
1155 F Street, NW • Washington, DC 20004
202.258.4989 • bill.applegate@bryancave.com

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and urges that the federal government provide adequate funding to permit investigation in these areas to proceed.

Finally and most importantly, the likely scenario that the recommendations articulated in this Guideline will rapidly transition into policy at the level of regulatory agencies remains a foremost concern. This could result in a significant negative impact on organ availability, create a significant financial burden of testing and storage that will need to be absorbed by organ acquisition costs, recipient insurance, and/or the transplant centers, and finally, may well negatively impact on transplant center performance. None of these issues have been adequately discussed or modeled in the Guideline.

As requested, below we provide specific comments related to: 1) any perceived factual errors; 2) any segments of the narrative or recommendations that are unclear; and, 3) any relevant issues that you have not been identified or commented on previously.

Page 9: Executive summary, 2nd paragraph, last line stating:

“Unexpected transmission of HIV, HBV and HCV from infected donors has been reported in heart, liver, kidney and pancreas recipients²⁻¹¹”

We completely agree that transmissions have occurred, but many of the transmissions were from a time when screening was not routinely available or performed and therefore could not have been prevented. We would recommend adding a sentence to clarify these occurrences. “While the majority of transmissions occurred prior to the availability of serologic screening it is worth noting that on rare occasions transmissions have still occurred due to limitations of the assays used.” We believe this then sets the stage for the PHS objective presented in the next paragraph. Similarly, in the Background section of the document the authors should give denominator data rather than just the numerator data on transmissions.

Page 11: First paragraph discussing recommendations and grading scheme:

It appears as though decisions to use a Grade 1 level to be based only on assumptions of the risk of not testing with NAT but there are no counter considerations to reflect the potential risk of losing organs with additional testing and the economic impact. This is especially important when the available data are not strong (As noted none of the recommendations in the Executive Summary come with a level of Grade 1A)

Page 14: Donor Testing

It would be helpful to add in a recommended algorithm for handling a positive result, particularly that which is suspected of being a false positive.

#6, Donor Testing (Living and Deceased): We are pleased that the PHS draft guideline is no longer requiring testing within 7 days. However there could be undesired ramifications using the term “as close as possible to the date of organ recovery...”

We would support the language endorsed by experts in the field at the recent AHRQ-funded consensus conference stating ... “testing be performed within 28 days but preferably within 14 days”, and to delete the phrase, “as close as possible to the date of the organ recovery operation.” We feel that this is clearer and provides a more actionable timeframe.

Bottom of page 14:

- *“Optimally, all NAT results for deceased donors should be available before the transplant occurs; however, if this is not feasible, test results can be useful to guide recipient treatment.”*
 - o The phrasing here again is somewhat nebulous and we would suggest substituting a sentence such as:

“Optimally, all NAT results for deceased donors should be available before the transplant occurs; however, if this is not feasible, and in the opinion of the transplant center the benefit of preceding with the transplant outweighs the risk of potential transmission, AND with consent of the candidate or their identified medical decision maker, the organ can be transplanted prior to the availability of results. Test results should still be obtained as they could be useful to guide subsequent recipient management “

Page 15: Section on Recipient Informed Consent:

We would ask you to consider removal of this entire section of informed consent since details are already part of OPTN policy and accordingly are redundant. Moreover, this is an area which still requires substantial research to better understand the best fashion for consenting.

Page 15, Table 7: Living Potential Organ Donor Test Recommendations Based on Risk Status for HIV, HBV and HCV Infection:

All Donors	Additional Testing When a Risk Factor is Identified	Timing of Test
antibodies to HIV (e.g., anti-HIV 1/2, OR Ag/Ab combination assay)	HIV NAT or HIV antigen (e.g., Ag/Ab combination assay)	As close as possible to the date of the donor operation, but at least within the 28 day time period prior to surgery
anti-HCV and HCV NAT	No additional testing	
anti-HBc and HBsAg		

In the first column we would add the word “or” to clarify that they could use either test methodology. In the third column we again would support the language endorsed by experts in the field at the recent AHRQ-funded consensus conference stating ... “testing be performed within 28 days but preferably within 14 days”, and to delete the phrase, “as close as possible to the date of the organ recovery operation.”

Page 16: Pre- and Post-Transplant Recipient Testing:

#15 and #16: These two sections could be clarified by stating up front that repeat Pre-transplant testing should be performed close to the time of transplantation when the donor has particular risks

#22: Would suggest that for live donors, the document clarify the duration of storage and the entity responsible for storage.

Page 18, Tracking and Reporting of HIV, HBV, and HCV:

#29: When a living donor recovery center receives information after organ recovery that a living donor is infected with HIV, HBV or HCV, the living donor recovery center should notify: 1) the OPTN; and, 2) the transplant center that received an organ from the living donor. (Category ID)

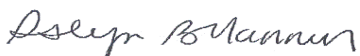
We would recommend that a statement be added that this disclosure to the OPTN and transplant center must be consistent with local law.

Pages 19-21, III: Recommendations for Further Study:

We suggest adding language that specifically includes a health economic evaluation for many of the recommendations in the *Guideline* as well as for many of the specific lines of study.

Again, on behalf of the American Society of Transplantation, I thank you for the opportunity to comment on these Guidelines.

Sincerely,



Roslyn B. Mannon, MD
President

Cc: AST Board of Directors
Ms. Susan Nelson, Executive Vice President
Mr. William Applegate, Government Relations Director