June 15, 2012

James Berger
Senior Advisor for Blood Policy
Office of HIV/AIDS and Infectious Disease Policy
Office of the Assistant Secretary for Health and Human Services
1101 Wooton Parkway, Tower Building, Suite 250
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RE: Transplant Community Questions and PHS Revised Guidelines for Reducing HIV, HBV, and HCV through Organ Transplantation

Dear Mr. Berger:

On behalf of the American Society of Transplantation (AST) and American Society of Transplant Surgeons (ASTS), representing the majority of professionals caring for people awaiting or receiving lifesaving organ transplants, we remain grateful for the opportunity to work closely with the U.S. Department of Health and Human Services (HHS) as the Agency updates the 1994 document *PHS Guidelines for Preventing Transmission of HIV through Transplantation of Human Tissue and Organs.* The overall safety of patients and ensuring the availability and success of transplantation as a treatment option is of the highest priority and importance to our organizations.

The safety of our organ supply is paramount. As you know, during our long history of collaborative work with HHS and other federal agencies, our primary goal has always been to achieve safe and successful transplantation. We know that HHS shares this goal and are encouraged by the recent revisions made to the PHS guideline document in response to our voiced concerns. We applaud the Agency and HHS Assistant Secretary for Health Dr. Howard Koh for engaging in a dialogue that will hopefully ensure that the revised document achieves its stated purpose of strengthening public health. We are hopeful that this dialogue will continue until these stated goals are realized in the final product.

Although each society has attached a separate document with suggested edits and comments regarding specific sections of the revised proposed PHS guidelines, we also have several shared, overarching concerns and questions regarding the document – concerns that we consider to be essential and that have yet to be addressed. In an effort to truly achieve the outcomes stated by HHS at the onset of this rulemaking process, ASTS and AST believe that it is imperative that the Agency consider these issues.

First, as we all have recognized throughout this process, there is a natural tension between seeking to ensure the absolute safety of the organ supply and reducing unnecessary organ wastage. Do the revised Guidelines strike the appropriate balance? The answer depends on two other questions:

> *What is the estimated effect that these guidelines would have, if implemented, on reducing donor-transmitted HIV, HCV, and HBV?*
>
> *What is the estimated impact on deceased donor organ availability and overall transplant and waitlist outcomes?*

It is only when the appropriate balance is achieved that this document will be ready to be published in final form, and achieving this balance necessarily requires close consultation with the transplant community.

Second, it is unclear to us whether the PHS has evaluated the significant cost (in addition to the potential impact on organ availability) associated with implementing the revised Guidelines, especially the cost of collecting, monitoring, and storing multiple donor and recipient specimens over a 10-year period for each transplant performed. We believe these costs should be quantified before the agency moves to the next stage of finalizing the Guidelines, especially since it appears likely that the Medicare program will bear a significant portion of these costs through organ acquisition centers. In light of the critical need to curb rising health costs in both the private and public sectors, we would hope that the agency will not move forward without a comprehensive impact analysis.

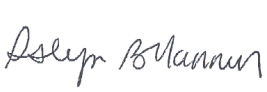
Third, although the Agency has indicated that this document is a "guidance tool," because the OPTN final rule requires OPTN policies to reflect CDC guidance, it highly likely that these guidelines will actually be binding on both OPOs and transplant centers. Under these circumstances, we urge PHS to ensure that there is a realistic plan and timetable for implementation of the Guidelines before the process proceeds further.

Fourth, although the Agency has stated in conference calls and meetings that the revision process will continue until a majority of the expert stakeholders in the transplant community are satisfied with the process and outcome, the Expert Panel has not been reconvened nor have there been any other opportunities for meaningful dialogue beyond a limited conference call and very brief future opportunity for final comment in mid-summer. What additional opportunities will there be for the Agency's expert panelists and transplant stakeholders to review the final guidance document? As concluded at the recent AHRQ conference supported by the AST and ASTS, consensus takes time and careful deliberation when there is such a broad spectrum of opinion regarding risk assessment.

Finally, and along similar lines, given that we all share the common goal of revising, improving, updating, and enhancing the guidelines to produce as strong a document as possible, why does there now appear to be such a fast-track and limited opportunity for review following the re-constituted Expert Panel (now termed "Technical Advisors") and review committee?

The ASTS and AST continue to believe strongly that this process should result in recommendations based on clearly stated goals, with comprehensive analysis of overall risk and benefit to transplant candidates and patients based upon current and accurate data. In the absence of data, we believe that gaining community consensus is the best path to reducing the risks of transmission of HIV, HCV, and HBV through organ transplantation. We recognize and very much appreciate the recent revisions made by PHS in response to the public comment. As leaders and stakeholders in the transplant community, we welcome the opportunity and look forward to continuing to work with you cooperatively and collaboratively to "get this right" and improve the health of our patients and the outcomes of those with end-stage organ failure. In this spirit, we thank you in advance for answering the concerns and questions we have summarized in this letter. We look forward to hearing from you in the near future. If you have any questions or require additional information, please do not hesitate to contact either of us directly.

Best Regards,



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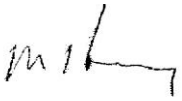

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RE: ASTS Comments – PHS Revised Guidelines for Reducing HIV, HBV, and HCV through Organ Transplantation

Dear Mr. Berger:

On behalf of the American Society of Transplant Surgeons (ASTS), I am writing to thank you for including ASTS on the recent call with the Technical Advisors for the revisions to the proposed PHS "Guideline for Reducing HIV, HBV, and HCV through Organ Transplantation" (the "Draft Guidelines"). We very much appreciate your including us in the process and applaud the significant substantive changes made by the agency in response to the public comments submitted by ASTS and others—changes that will address many of the concerns raised in our prior communications.

ASTS shares PHS's commitment to the twin goals of minimizing unanticipated transmission of communicable diseases through transplantation and ensuring that the Draft Guidelines do not exacerbate the already critical shortage of organs available for transplantation. We appreciate PHS' recognition that both minimizing unanticipated disease transmission and increasing the availability of organs for transplantation are critical public health objectives that must be balanced carefully and pursued thoughtfully.

We believe that the changes made to the Draft Guidelines that were shared with us during the recent call will go a long way toward ensuring a more appropriate balance between these goals. We particularly appreciate the agency's reconsideration of the need for universal NAT testing and revisions to the definition of high risk donors.

At the same time, we would be remiss if we were to fail to express our continued concerns about the process to be used in finalizing the Draft Guidelines. In addition, we have a number of continued substantive concerns related to the "Donor and Recipient Specimen Collection and Storage" recommendations, as set forth in greater detail below. These concerns are exacerbated because, as set forth in our prior comments, while the CDC considers the Guidelines to be voluntary, the OPTN is bound by regulation to make its rules consistent with CDC guidelines, and for this reason, the Guidelines, once incorporated into OPTN policy, may have binding effect.

Timing and Process

We remain extremely puzzled by the agency's haste in finalizing the Draft Guidelines, providing the Technical Advisors only a few days to comment on the revised document before circulating it for interagency review and finalization. In a letter dated January 19, 2012, Secretary Koh wrote to ASTS and to the American Society of Transplantation:

> I am pleased your organization was able to meet with Dr. Ronald Valdiserri, Deputy Assistant Secretary for Health for Infectious Diseases, and Dr. Joanne Cono, Centers for Disease Control and Prevention (CDC), on January 6, 2012 to discuss the details of the remaining steps in the process. The PHS Guidelines working group is currently drafting proposed edits suggested through more than 100 public comments received during the open period ending on December 23, 2011. Once that step is complete, members of the original expert review panel, several of whom represent your organization, will be invited back to review and consider those edits and also to examine relevant safety data made available by CDC. It is anticipated other stakeholders may be afforded an opportunity to contribute alongside the expert review panel. I remain confident we will keep the PHS Guidelines public comments review process transparent and inclusive.

Providing the Expert Panel "a few days" to review the revised Draft Guidelines before interagency review (when further substantive changes can be made) most certainly does not constitute the type of comprehensive "transparent and inclusive" process that we anticipated based on the Secretary's January 19 correspondence. Based on this letter and on our prior discussions, we understood that the Expert Panel would be "invited back" and potentially expanded; that the process of finalizing the document would be an open one; and that the final document would reflect expert consensus. While we very much appreciate and strongly support the changes made in the revised Draft Guidelines thus far, allowing the Technical Advisors a few days to review the revised Draft Guidelines and accompanying text before the document undergoes interagency review is inconsistent with our understanding of the process that was to be used moving forward, based on Dr. Koh's January 19, 2012 correspondence.

The basic question here is, "What's the rush?" In the aftermath of the publication of the prior Draft Guidelines, it became clear that while disease transmission through transplantation is a serious issue that warrants attention both from the agency and from the transplant community, it

most certainly does not present a public health crisis. In fact, as you may recall, OPTN has clarified that, during the period from 2007-2011, there were an estimated two donors per year with proven or probable transmission of HIV, HBV, or HCV, and it is extremely unclear whether some, all, or any of these disease transmissions would have been prevented by the revised Draft Guidelines or by the Draft Guidelines as they were initially published.

While we most certainly concur that the Guidelines should be updated, we remain convinced that it is more important to get it done right than to get it done fast. And while we understand and share the agency's frustration with the protracted process involved here, we believe that the current efforts to hasten finalization of this document are likely to result in unnecessary controversy that could be easily avoided through a more thoughtful and consensus-based approach involving all of the affected parties, including not only the ASTS and AST but also the OPOs and the OPTN, which will play crucial roles in implementing the final Guidelines.

Substantive Concerns

We have two significant substantive concerns about the revised Draft Guidelines: (1) the "Donor and Recipient Specimen Collection and Storage" recommendations #1 and #2, which mandate the collection of two specimens both for deceased donors and for living donors, transplant candidates and recipients, and the "New Recommendation" in this section relating to storage of archival plasma or serum; and (2) the "Donor and Recipient Specimen Collection and Storage" recommendation #7, which precludes use of vessel conduits from donors who are infected with HIV, HBV, or HCV, unless needed for the initial transplantation procedure in the recipient.

We urge PHS to reconsider the Specimen Collection recommendations #1 and #2. While such extensive specimen collection may be useful to the CDC in tracking the extent of disease transmission through transplantation, and therefore may serve some research purposes, it is not clinically necessary or consistent with OPTN rules on this subject. The costs involved will be borne in the first instance by transplant centers in the case of living donors, and by OPOs in the case of deceased donors; however, ultimately, these costs would be borne to a large extent by the Medicare Program (in the form of increased organ acquisition costs), private payers (and their insureds, in the form of increased premiums), and transplant patients (in the form of increased charges). Moreover, these recommendations are not drafted clearly: For example, it is unclear whether the recommendations apply to all donors or only high risk donors; nor is it clear whether specimens are to be collected and archived from all transplant "candidates" or only for transplant "recipients."

The New Recommendation regarding storage of archival plasma and serum specimens is also extremely problematic. We urge PHS to consider the significant costs of implementing this new recommendation. To the extent that HBV, HCV, or HIV is transmitted through transplantation, it is highly unlikely that it would take 10 years for the disease to emerge. Nor is it clear that even the best run of facilities can prevent freezer malfunctions and other technological mishaps that

would preclude effective implementation of this recommendation for 10 years. See http://www.cbsnews.com/8301-504763_162-57450310-10391704/freezer-malfunction-thaws-150-brains-at-harvard-research-hospital/ (involving freezer malfunction at a Harvard laboratory).

Finally, we recognize that current OPTN rules preclude the use of blood vessel conduits from donors infected with HCV, HBV, or HIV; however, in response to concerns raised by ASTS, the Operations and Safety Committee of the OPTN is considering an interim action that would allow storage of blood vessel conduits solely for use in the original recipient. As discussed further below, the OPTN regulations require the OPTN to adopt CDC guidelines, so if recommendation #7 is included in the Guideline but the OPTN Operations and Safety Committee recognizes an exception authorizing storage of these vessels solely for use in the original recipient, an unnecessary conflict is created. Moreover, since this subject is already fully addressed by OPTN policy, it is unclear what the inclusion of Recommendation #7 in the Guidelines is intended to accomplish—other than limiting the flexibility of the OPTN to craft appropriate exceptions to the current policy as may be necessary to save the lives of already-exposed transplant recipients who may develop a critical need for these blood vessel conduits.

The Status of the PHS Guidelines

The legal status of the PHS Guidelines is complicated as a result of the overlapping authority of the OPTN and CDC in this area. The National Organ Transplantation Act (1984 Pub.L. 98-507), which governs most aspects of organ transplantation in the United States, specifically authorizes the OPTN to:

> **adopt** and use standards of quality for the acquisition and transportation of donated organs, including **standards for preventing the acquisition of organs that are infected with the etiologic agent for acquired immune deficiency syndrome.**

At the same time, the OPTN Final Rule (42 CFR § 121.4(a)(2)) specifically provides that the OPTN policies for "testing of organ donors and follow-up of transplant recipients to prevent the spread of infectious diseases" shall be "consistent with recommendations of the Centers for Disease Control and Prevention."

In other words, federal law mandates transplant center membership in the OPTN; OPTN members are required to comply with OPTN policies (including those related to the transmission of communicable diseases through transplantation); and OPTN policies with regard to disease transmission are required by regulation to be consistent with CDC Guidelines. Thus, while the CDC formally may consider the Guidelines "voluntary," as a practical matter they are likely to be binding on transplant centers—albeit indirectly, through OPTN policy. It is for this reason that we strongly urged PHS to include the OPTN (as well as OPOs) in the process used to formulate the final Guidelines. It is our understanding that this has not been done. We also urge you to include specific language in the accompanying narrative that clarifies that donors with risk factors can be used as organ donors.

To summarize, we are extremely concerned about the haste and lack of true transparency of the process being used to finalize the Draft Guidelines and believe that the result is likely to be counterproductive. In addition, we have serious concerns about the new and revised Specimen Collection and Storage requirements and the lack of flexibility of the prohibition on the use of infected blood vessel conduits for the initial recipient. We stand ready and willing to assist in any way, and respectfully suggest that a less hasty process, while potentially frustrating, would better serve our common goal of promoting both disease transmission reduction and organ availability. We very much appreciate your consideration of these comments, and again urge you to make this the truly open and collaborative process envisioned in Dr. Koh's January correspondence.

Sincerely,

Kim M. Olthoff, MD
President

Cc The Honorable Kathleen Sebelius
Secretary, Department of Health and Human Services

The Honorable Howard Koh, MD, MPH
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