

**INTERIM REPORT OF THE
OPTN/UNOS AD HOC DISEASE TRANSMISSION ADVISORY COMMITTEE**

**April 6, 2011
Chicago, Illinois**

The OPTN/UNOS Ad Hoc Disease Transmission Advisory Committee met in Chicago, Illinois on April 6, 2011 and considered the following items:

1. Dr. Emily Blumberg, Chair, reviewed the Committee's 2010-2011 goals, and what had been done to meet these goals to date:
 - Recommend modifications to OPTN policies 2.0 and 4.0 to improve screening and diagnostic testing for donor disease transmission.
 - The Committee's rewrite of these policy sections was approved by the Board of Directors during its November 2010 meeting, and implemented on January 10, 2011.
 - Remove the list of frequently transmitted disease from OPTN Policy and instead develop a guidance document that can be updated more frequently and easily.
 - The Committee will present this document to the Board of Directors during its June 2011 meeting.
 - Produce a DTAC newsletter twice per year for OPTN members to share information regarding disease transmission concepts.
 - This communication tool continues to be used effectively, and receives positive feedback from the transplant community.
 - Conduct a follow-up survey of all OPOs regarding current screening practices to determine how practices have changed based upon changing test kit availability and the new CDC/US Public Health System guidelines that are expected in Fall 2010.
 - The timeline for releasing this survey remains on hold, as it is dependent on the CDC's efforts to update the current high risk guidelines.
 - Publish disease transmission data in journals, abstracts and at professional meetings to increase community awareness of disease transmission.
 - The Committee continues to publish and present its work in a number of professional journals and meetings, both nationally and internationally.
 - Produce OPTN/UNOS guidance documents based on bacterial transmissions, TB transmissions, fungal transmissions and malignancy to promote practices that reduce disease transmission.
 - The Committee received updates on each of these projects, as they continue to develop based upon review of the aggregate potential transmission data collected in each of these areas.

- Review potential donor-derived transmissions since HTLV screening requirements were eliminated in November 2009 and develop a guidance document to help OPOs and transplant centers understand: (1) when to report a potential HTLV transmission to the Patient Safety System, and (2) what confirmatory testing is available and appropriate.
 - The Committee will present this document to the Board of Directors during its June 2011 meeting for consideration.
- 2. The Committee discussed the recently publicized living donor transmission of Human Immunodeficiency Virus (HIV). The CDC's March 18, 2011 Morbidity and Mortality Weekly Report (MMWR) and a New York State Department of Health Advisory related to a reported transmission of HIV from a living donor to a kidney recipient were reviewed by the Committee during its April 2011 meeting. Both of these documents included specific recommendations for prevention and screening of HIV infection in potential living donors. Currently there is no specific policy language related to screening potential donor organs for conditions that may be transmitted to recipients, though there are guidelines that recommend testing for both living kidney and liver donors.

During the spring of 2010, the Committee formed a Living Donor Screening Subcommittee to provide recommendations to the Living Donor Committee regarding testing that it believed should be required for all potential living donors. This information was shared with the Living Donor Committee in a June 30, 2010 memo. Last year, all potential policy language under development and consideration by the Living Donor Committee was shared with a Joint Societies Working Group consisting of representation from the American Society of Transplantation (AST), the American Society of Transplant Surgeons (ASTS) and The Organization for Transplant Professionals (NATCO). This group was given a year to consider all of the language to date, as there were concerns that there was concern that some of this potential policy language may dictate medical practice. The Working Groups is in the late stages of review and will report its recommendations to the OPTN before the Living Donor Committee then takes up these recommendations to complete the policy development process.

The Living Donor Committee requested assistance from the Committee in developing policy related to potential living donor screening. Any language proposed by this Committee will include input from the Living Donor Committee as well as the Joint Societies Working Group.

The Chair recognized that timelines for potential living donor screening were not included in the Committee's original recommendations memo. Because screening timeline was so critical in the case outlined in the MMWR, this is an area that may be considered in the policy development process. Members noted that there is very little standardization in the area of living donor screening currently, perhaps due to the lack of policy requirements in this area.

Concerns related to implementation of a seven day window for living donor screening, as recommended in the MMWR, were voiced by multiple members. Issues related to time constraints and psychological stresses related to false positive test results were also briefly discussed. Members also questioned whether screening or diagnostic testing would be most appropriate for this population, as what is required for potential deceased donors may not necessarily be appropriate for potential living donors due to the differences in both donor health status and time available to complete testing.

A recommendation was made to re-establish the Living Donor Screening Subcommittee to use the June 2010 memo as a starting point for updated recommendations based upon this recent transmission. Several members noted their interest in participating in this process.

3. The Committee discussed concerns related to deceased donor HIV screening requirements that arose after the January 2011 implementation of changes to Policy 2.0. The Committee's proposed modifications to policy sections 2.0 and 4.0 were approved by the Board of Directors during its November 2010 meeting. The intent of this rewrite of the policy sections was to clarify and/or improve current OPO and transplant center requirements for screening for, communicating and reporting all potential or confirmed donor-related disease and malignancy transmission events. Members agreed that one goal of this effort was to move any language related to donor evaluation and screening out of policy 4.0 and into 2.0. This would place all donor evaluation language up to the point of recovery in one policy section, making locating language easier for OPOs. Though the majority of donor screening language resided in policy section 2.0 prior to the rewrite, much of the language related to HIV screening, including what is now policy 2.2.3.2, was located in Policy 4.0. The list of tests and laboratory requirements for OPOs screening potential deceased donors outlined in what is now policy 2.2.4.1 were essentially unchanged other than to specifically clarify that the use of diagnostic tests for HIV is not permissible. In this section, all potential deceased donors are to be tested for the presence of HIV antibody, using a FDA licensed screening test for Anti-HIV-1 and HIV-2.

During its November 2010 monthly conference call, the Committee discussed an announcement from a large corporation that an enzyme immunoassay HIV-1/HIV-2 test kit that was commonly used by OPOs for donor screening that was to be retired in March 2011. This retirement had been discussed within the OPO community for some time prior to the announcement, and most OPOs were prepared for this change. The Committee's 2008 donor screening survey indicated that less than half of the OPOs were using the soon-to-be retired test kit at that time, as there were already indications that the test would soon be eliminated. As a result the Committee was optimistic that this test elimination would not require actions similar to that for HTLV screening in 2009. To follow up on whether OPO Community was aware of this upcoming change and prepared to remain in compliance with current OPTN policy that allows only for screening (and not diagnostic) HIV tests for potential organ donors, the committee partnered with the AOPO to release a short email survey to all OPOs in September 2010. Though not all

OPOs completed the survey, the results received overwhelmingly indicated that OPOs were aware and prepared for this change.

After the test kit was eliminated, only one other FDA-approved antibody screening test remained for detecting HIV-1 and HIV-2 in potential deceased donors. In considering options for donor testing, a question arose regarding whether nucleic acid testing (NAT) would be an appropriate alternative. NAT is currently FDA-approved for testing potential deceased donors for HIV-1. A review of current policies related to this specific area of policy language indicated that, as currently worded, this option may be considered as permissible in Policy 2.2.3.2.

As part of the Committee's rewrite, a more general HIV testing requirement previously located in policy section 4.0 was moved up to section 2.0, and now appears as policy 2.2.3.2. This policy requires FDA-licensed HIV-1 and HIV-2 screening for all potential deceased donors, but does not specifically indicate that antibody screening is the specific type of test necessary to meet policy requirements. Because this section of policy now appears before the specific list of required tests to be completed by the Host OPO on any potential deceased donor, there is concern that this inconsistency could create confusion within the OPO community. While NAT is FDA licensed for HIV-1 screening, it is not available for HIV-2 screening at this time and does not meet the more specific requirement in section 2.2.4.1 for antibody screening.

The Committee did not intend to allow NAT as a substitution for antibody screening tests to rule out HIV in potential donors. Further, policy 2.2.4, which appears later in policy, clearly states "All donor laboratory testing must be performed in an appropriately accredited laboratory utilizing FDA licensed, approved, or cleared serological screening tests" and policy 2.2.4.1 clearly requires "FDA licensed Anti-HIV I, II (diagnostic testing not acceptable)." The Committee did not recognize this potentially confusing language in policy during its proposal development, but wishes to amend this language to eliminate any potential confusion between policies 2.2.3.2 and 2.2.4.1 to make it clear that its intentions were to maintain the requirement that HIV antibody screening be completed for all potential deceased donors. The Committee believes that including the term "anti" in the policy language so that it mirrors what is already present in section 2.2.4.1 will more clearly indicate the expectation that antibody testing is required for HIV-1 and HIV-2 screening.

After careful review, the Committee voted to recommend the following resolution to clarify the intent of this policy for consideration by the Board:

***** RESOLVED, that Policies 2.2.3.2 shall be modified as set forth below, effective pending notice to the membership:**

2.2.3.2 All potential donors are to be tested by use of a serological screening test licensed by the U.S. Food and Drug Administration (FDA) for Human Immune Deficiency Virus (Anti-HIV-1 and Anti-HIV-2).

If the sample is qualified, the screening test for HIV is negative, and blood for subsequent transfusions has been tested and found to be negative for HIV, re-testing the potential donor for HIV is not necessary.

Committee vote: 15 in favor, 0 opposed, and 0 abstentions

4. The Committee reviewed proposed guidance for HTLV-1 screening and confirmation in potential donors and reporting potential HTLV-1 infection. On October 23, 2009, the Executive Committee eliminated the requirement for pre-transplant deceased donor Human T-cell lymphotropic virus (HTLV) 1/2 screening. This policy change was implemented on November 23, 2009. The basis for this decision included considerable organ wastage due to false positive results using HTLV screening tests, the very low prevalence of HTLV-1 in the United States, and the impending lack of availability of an FDA licensed HTLV-1 screening test that could practically be used in most OPO laboratories.

As one of its 2010-2011 goals, the Committee was charged with developing a guidance document to assist OPOs and transplant programs with ongoing testing issues and questions related to HTLV-1 in the organ transplant community. The HTLV Screening Subcommittee was formed to develop this document. Some OPOs continue to test for HTLV on a case-by-case basis, and there are still questions regarding how to confirm infection or effectively rule out a positive result in donors or recipients. After reviewing the Committee's previous work on this topic, including a journal article¹ outlining the data reviewed as part of the 2009 policy modification process.

The Subcommittee met during a series of conference calls and reviewed:

- specific tests appropriate for screening, monitoring and confirming HTLV 1/2;
- circumstances in which HTLV donor screening may be performed;
- symptom driven testing in recipient;
- management and monitoring of recipients of organs or vessels from confirmed screen positive donors; and
- when to report recipients found to be HTLV-1 positive post-transplant.

This information was compiled into a guidance document meant to aid the transplant community.

The Subcommittee presented the guidance document to the full Committee during its April 6, 2011, meeting. A member stressed the importance of a yearly review of this and any other guidance document developed by the committee in order to keep information

¹ Kaul DR, Taranto S, Alexander C, Covington S, Marvin M, Nowicki M, Orłowski J, Pancoska C, Ison MG. Donor screening for human T-cell lymphotropic virus 1/2: changing paradigms for changing testing capacity. American Journal of Transplantation 210:207-213, 2010

current and up to date. Testing availability is ever changing, and therefore it is critical that guidance documents be accurate upon review. Concerns were also raised regarding the location of where guidance documents are posted on the OPTN website. Members noted that the current location is not easily accessible- especially if information is needed quickly or in the middle of the night. Staff will determine whether a new website tab can be created specifically for guidance documents or whether they could also be posted in Secure Enterprise for ease of accessibility.

After careful review, the Committee voted to recommend the guidance document for consideration by the Board of Directors:

***** RESOLVED, that the “Guidance for HTLV-1 Screening and Confirmation in Potential Donors and Reporting Potential HTLV-1 Infection” document be posted on the OPTN and UNOS websites for member education.**

Committee vote: 17 in favor, 0 opposed, and 0 abstentions

5. The Committee reviewed proposed guidance for reporting potential donor-derived disease transmission events (PDDTE). A draft guidance document was prepared to assist members in determining what types of situations should be reported as a PDDTE. This document was a 2010-2011 goal for the committee. After review, a committee member recommended reviewing the draft alongside similar guidance from Europe on reporting adverse events, including disease transmissions. This document will be revised based upon this review and shared with the full committee again during its May 2011 monthly conference call. The Committee plans to take this document to the Board for consideration in June 2011.

Several Committee members again noted concerns regarding the current location of guidance documents on the OPTN website. It was suggested that a separate tab should be created to make these important reference items more accessible to the transplant community.

6. The Committee reviewed the thirteen proposals released for public comment on March 11, 2011, during its April 6, 2011, meeting in Chicago.
 - 1) Proposal for Improved Imaging Criteria for HCC Exceptions (Liver and Intestinal Organ Transplantation Committee)

Upon review, the Committee determined that it had no comment regarding this issue.

- 2) Proposal to Reduce Waiting List Deaths for Adult Liver-Intestine Candidates (Liver and Intestinal Organ Transplantation Committee)

Upon review, the Committee determined that it had no comment regarding this issue.

- 3) Proposed Committee-Sponsored Alternative Allocation System (CAS) for Split Liver Allocation (Liver and Intestinal Organ Transplantation Committee)

Upon review, the Committee determined that it had no comment regarding this issue.

- 4) Proposal to Encourage Organ Procurement Organizations (OPO) to Provide Computed Tomography (CT) Scan of Requested by Transplant Programs, and to Modify Language in Policy 3.7.12.3 for Currency and Readability (Thoracic Organ Transplantation Committee)

Upon review, the Committee determined that it had no comment regarding this issue.

- 5) Proposal to Require Updates of Certain Clinical Factors Every 14 Days for Lung Transplant Candidates with Lung Allocation Scores (LAS) of at least Fifty, and to Modify Policy 3.7.6.3 for Currency and Readability (Thoracic Organ Transplantation Committee)

Upon review, the Committee determined that it had no comment regarding this issue.

- 6) Proposal to Allow Outpatient Adult Heart Transplant Candidates Implanted with Total Artificial Hearts (TAH) Thirty Days of Status 1A Time (Thoracic Organ Transplantation Committee)

Upon review, the Committee determined that it had no comment regarding this issue.

- 7) Proposal to Improve the Reporting of Living Donor Status (Living Donor Committee)

After review, the Committee chose not to vote on this proposal because it does not have the expertise to respond to the practicalities of meeting such a policy requirement. It was noted none of the data other than cause of death would benefit the Committee's potential donor-derived disease transmission case review process. Recognizing that collecting additional data may be very difficult for transplant centers that recover living donors, additional information regarding potential living donor-derived disease transmission (e.g. development of malignancy within the established two-year follow-up period) would be beneficial to the DTAC's charge.

- 8) Proposal to Improve the Packaging, Labeling and Shipping of Living Donor Organs, Vessels and Tissue Typing Materials (Living Donor Committee)

After review, the Committee chose not to vote on this proposal. It was noted that the Living Donor should address issues related to:

- Transportation of organs (NOTA makes OPOs responsible for transport of organs, should this be the case for living donor organs as well?)
- Labeling of vessels (the Committee believes that vessels should be labeled in the same way that donor organs are- both on the external triple barrier and the innermost container or bag that holds the organ)

- Keeping this policy updated as deceased donor organ policies are updated.

The Committee suggests consistency to minimize contamination of organs, and standardizing the overall process as much as possible between deceased and living donor organs for consistency and simplicity within the transplant community.

- 9) Proposal to Require Confirmatory Subtyping of Non-A₁ and Non-A₁B Donors (Operations and Safety Committee)

Upon review, the Committee determined that it had no comment regarding this issue.

- 10) Proposal to Standardize Label Requirements for Vessel Storage and Vessel Transport (Organ Procurement Organization (OPO) Committee)

After hearing the presentation, the Committee had a number of questions. It was recognized that if only the outermost layer of the triple sterile barrier is labeled, there would be no requirement for a label on the actual jar that holds the vessel. This would produce an opportunity for patient safety to be compromised. Without a label on the rigid container that holds the vessels, there is no information available to OR staff during time out procedures meant to promote patient safety. Labeling this internal container at the transplant center introduces opportunity for omission of important information (such as HCV or HBV positive donor status, as seen in at least one donor-derived disease transmission event) or transcription errors regarding donor ID or blood type. Members suggested that requiring an internal and external label would be more appropriate, as the triple sterile outermost barrier/bag is frequently discarded and not kept with a stored vessel.

After discussion, the Committee voted unanimously to oppose this proposal as written (0-Support, 17-Oppose, 0-Abstentions). Committee members believe that OPOs should provide the same type of labeling for vessels as what is required for organs. The Committee recommends that this proposal be modified to require that both the external triple barrier and the internal rigid container in which the vessels are actually stored be labeled by the OPO prior to shipping.

- 11) Proposal to Update and Clarify Language in the DCD Model Elements (Organ Procurement Organization (OPO) and Organ Availability Committees)

Upon review, the Committee determined that it had no comment regarding this issue.

- 12) Proposal to List All Non-Metastatic Hepatoblastoma Pediatric Liver Candidates as Status 1B (Pediatric and Liver and Intestinal Organ Transplantation Committees)

Upon review, the Committee determined that it had no comment regarding this issue.

13) Proposal to Eliminate the Requirement that Pediatric Liver Candidates Must be Located in a Hospital's Intensive Care Unit to Qualify as Status 1A or 1B (Pediatric Transplantation Committee)

Upon review, the Committee determined that it had no comment regarding this issue.

7. UNOS Research Staff presented data the Committee requested during its September 2010 meeting regarding:
 - An update on donor-related malignancies not reported to the Improving Patient Safety portal in Secure Enterprise;
 - A summary of renal cell carcinoma (RCC) cases reported to the Improving Patient Safety portal; and
 - A review of potential donor-derived disease transmission events reported by donor service area (DSA) and region.
8. The Committee completed its semi-annual review of potential disease transmission events reported to the Patient Safety System. Seventy-six cases were reviewed and classified based upon the probability of donor-derived transmission. Of these cases, nine were classified as proven transmissions. A summary review of all cases reported in 2010 indicated 18 cases classified as proven.

The Committee reviewed and adopted modifications to the case classification list that will more clearly represent both infectious disease and malignancy transmissions. This new list, combined with modifications to policy that allow for case follow-up beyond 45 days as needed will allow for additional monitoring of possible transmission events and more appropriate classification of reports.

Also discussed were new challenges discovered during case review. Areas of concern included:

- the use of tests not approved for screening potential deceased donors and how results should be shared with and considered by transplant programs (*it should be noted that these tests were not required by current policy but additional testing that an OPO was completing by choice*);
- research testing- should unverified results be shared with transplant programs, and how are they to be interpreted/utilized; and
- tracking reported events that may not necessarily need full committee assessment as a potential donor-derived disease transmission event.

The Committee will be discussing these issues in greater detail in the coming months and will develop subcommittees as needed to address concerns.

9. The Committee received an update from its Confidential Medical Peer Review Subcommittee and learned about a resource developed by staff to assist members in preparing educational materials, presentations and other publications without compromising the protections afforded to both reporting members and committee members by the confidential medical peer review process. This will be an ongoing effort,

and specific events that require immediate alerts or education of the transplant community will be considered and addressed on a case-by-case basis to promote patient safety.

10. The Encephalitis Subcommittee Chair presented an update on this group's work to the full Committee, including an abstract to be presented at the May 2011 American Transplant Congress and a guidance document that will be developed for the transplant community.
11. Committee members heard an overview of the World Health Organization's (WHO) work on biovigilance. Members learned about how potential donor-derived disease transmission events were reported and tracked in several European countries. Several members of the Committee are actively involved in these global discussions and will continue to update this group regarding progress made.
12. OPTN patient safety staff briefly outlined preliminary efforts to update the Improving Patient Safety portal available to members for reporting: (1) potential donor-derived disease transmissions; (2) patient safety situations; (3) living donor adverse events; and (4) best practices. Several departments will be working together to develop updates to the portal that will streamline the reporting process and provide staff with more detailed information regarding incoming reports.
13. Members whose terms end on June 30, 2011 were recognized for the service and dedication.

Dr. Emily A. Blumberg, Chair
University of Pennsylvania Medical Center
Philadelphia, PA

Dr. Michael Green, Vice-Chair
Children's Hospital of Pittsburgh
Pittsburgh, PA

Shandie Covington
UNOS Staff/Professional Services Coordinator
Richmond, VA