

OPTN/UNOS *Ad Hoc* Disease Transmission Advisory Committee
Report to the Board of Directors
November 14-15, 2011
Atlanta, Georgia

Summary

I. Action Items For Board Consideration

- None

II. Other Significant Items

- The Committee reviewed the new Working Agreement between Health Resources and Services Administration (HRSA) and the Center for Disease Control and Prevention (CDC) for potential donor-derived transmission event case management (Item 1, Page 3).
- The Committee prepared to discuss the soon-to-be released US Public Health Service Guidelines for Reducing Transmission of Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) through Solid Organ Transplantation (Item 2, Page 7).
- The Committee reviewed data on disease transmission reporting by both region and donor service area (Item 3, Page 7).
- The Committee continued to refine the process for reviewing and long-term follow up on potential donor-derived malignancies reported to the Improving Patient Safety portal (Item 5, Page 9).
- The Committee completed its review and classification of the first ninety-two potential donor-derived disease transmission events reported in 2011 (Item 7, Page 14).
- The Committee discussed recently implemented plans to triage case review in order to better use both staff and Committee member time (Item 8, Page 15).
- The Committee heard an update regarding work to finalize a Universal Donor Health Questionnaire appropriate for blood, organ and tissue donation (Item 11, Page 17).

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OPTN/UNOS Ad Hoc Disease Transmission Advisory Committee
Report to the Board of Directors
November 14-15, 2011
Richmond, Virginia

Emily A. Blumberg, MD, Chair
Michael Green, MD, MPH, Vice Chair

This report reflects the work of the Ad Hoc Disease Transmission Advisory Committee (DTAC) during its September 14, 2011, meeting in Chicago, Illinois, as well as all monthly case review conference calls held from June through October 2011.

1. Review of Working Agreement between Health Resources and Services Administration (HRSA) and the Center for Disease Control and Prevention (CDC) for Potential Donor-Derived Transmission Event Case Management. The Committee heard presentations from both HRSA and CDC representatives regarding the newly developed working agreement for potential donor-derived disease transmission investigations involving public health authorities. Two representatives from Health and Human Services' (HHS) Office of the Assistant Secretary of Health joined the meeting due to this office's assistance in reaching this working agreement.

Historically, the CDC's Office of Blood, Organ and Other Tissue Safety had an ex officio representative participating in the Committee's case review process and all of its meetings. It provided laboratory assistance and investigated nationally notifiable infectious diseases (**Exhibit A**) and other diagnoses of a public health interest reported to the OPTN. In September 2010, the CDC withdrew from ex officio DTAC participation, although it maintained involvement in potential transmission reports involving nationally notifiable infectious diseases and other cases that were suggested to be of public health concern. The CDC has not participated in committee conference calls or meetings since that time. At that time, the CDC did not provide an explanation for its withdrawal.

HRSA began with a brief overview regarding the Committee's charge as it relates to reviewing reported potential donor-derived disease transmissions (**Exhibit B**). The working relationship between this Committee and the CDC began informally in 2004 after a rabies transmission and an ABO mismatch event, with both events receiving wide media attention. As potential disease transmission reporting was being formulated, the role of the CDC was never clearly defined. As this Committee became formalized and the CDC became increasingly involved as case volume rose (often contacting local and state public health authorities for assistance), work load and lack of clarity in roles led to the CDC's decision to step back and re-evaluate their role in the Committee's work in the fall of 2010. HHS then became involved to help HRSA and the CDC iron out the function of public health authorities in leading or reviewing reports made to the OPTN regarding potential donor derived disease transmission based upon their statutory role as a national public health coordinating and advisory agency versus HRSA's role of overseeing the OPTN.

A CDC representative reviewed the public health aspects of investigating potential transplant associated disease transmissions (**Exhibit C**). State and local public health must invite the CDC to participate in investigations, and this is generally welcomed due to the CDC's ability to coordinate investigations that cross state lines and the lab testing available at the CDC versus most state's labs. Local public health authorities, however, are relied upon for long term follow up of individual recipients as needed (i.e. tracing of tuberculosis testing or exposure).

Public health investigations are exempt from the HIPAA authorization to release clause. It was noted that both state and local health departments make every effort to maintain patient and facility privacy, and that there has been no breach of confidentiality by local health departments since coordination of transplant-associated infection investigations began in 2005. Transplant centers were noted as more likely to present events to the media in order to maintain transparency for their program.

With the increased number of cases reported and reviewed by the Committee, there have been situations where OPOs and transplant programs were contacted by UNOS staff, CDC and local or state public health, creating duplicative work and confusion among OPTN members. The goal of this agreement is to outline responsibilities for both UNOS staff and the CDC through this agreement between HRSA and the CDC. The goal is to streamline the case investigation process while reducing ambiguity and duplicative efforts related to communicating information to multiple sources. As a result, HHS assisted HRSA and CDC in reaching an agreement on how to handle any potential organ donor-derived disease transmission investigation that involves public health authorities (**Exhibit D**). A HRSA representative outlined the objectives of the working agreement:

- No compromise in current patient safety process;
- Maintain integrity of all participating organizations;
- No change in current OPTN policies/bylaws;
- Promote optimal public health practices including cooperation and compliance by OPTN members with state reporting requirements for notifiable diseases;
- Minimize/eliminate unnecessary burden of duplicative and redundant reporting requirements; and
- Minimize/eliminate confusion and ambiguity.

Responsibilities for OPOs and transplant centers involved in a reported potential transmission event, as well as the responsibilities of CDC and UNOS staff were outlined in the working agreement and as part of the HRSA presentation. The goal is to improve communication and, ultimately, patient care.

The CDC will take the lead on any reports involving notifiable diseases (as listed by state), disease clusters involving 2 or more infected recipients, and any cases involving public health implications (emerging pathogens or potential for person-to-person transmission). Historically, the CDC has been involved in approximately 30% of the cases reviewed by the Committee. When the CDC leads an investigation, the DTAC will receive a case summary at the end of the investigation that is anticipated to include:

- Background, including:
 - reported condition, and
 - diagnosis/discovery events, dates, etc.;
- Donor: cause of death, events, diagnostic results;
- Recipients: organs, clinical status, diagnostic results;
- Case Determination (made by the CDC. The Committee's classification may differ.); and
- Process Concerns noted during investigation: any processes that might have lead to disease transmission that if modified, or noted, may prevent future transmissions.

This agreement between the two agencies is meant to minimize or eliminate duplication of efforts that may inconvenience or overburden members involved in a reported potential transmission event.

A committee member questioned why the CDC did not want to participate in email discussion related to all cases, as part of the current practice. It was suggested that they are only interested in participating in cases involving public health interests, and the CDC does not want to give the impression of participation

in active discussion related to other types of reports. It was noted that the CDC is available for questions or potential testing assistance if needed on reports that it chooses not to pursue. A CDC representative noted that she welcomes questions and feedback from the committee on any reported event. CDC staff cannot monitor the volume of emails with its current staffing, and they choose to depend on the information that is received directly from the OPO, transplant programs and local or state health departments. HHS and HRSA indicated that when the CDC coordinates a conference call involving a potential transmission event, a Committee representative will still be included unless there are specific concerns from participating transplant professionals.

For cases where a public health investigation is pursued, the Chair or Vice Chair of the Committee will coordinate inquiries for consideration by the CDC. This is to reduce the amount of direct contact to the CDC by Committee participants. When CDC takes the lead on a report, the Committee may still evaluate the information that is available and discuss the event, but UNOS staff will not call to collect additional information, potentially duplicating the efforts of the CDC. The Committee will await the summary of the CDC's review. A member questioned whether periodic updates would be provided during the course of the CDC's investigation. HRSA suggested that interval updates would be difficult to obtain due to the way information trickles in regarding these investigations. UNOS staff initiating calls to center and OPOs in an effort to obtain the same information would duplicate CDC efforts. The Committee will have to await final summary information from the CDC before it can complete its review and classification of a reported event.

A member questioned the time frame involved in confirmation of recipient notifications when CDC leads the review of a reported event and potential impacts on patient safety. When the CDC coordinates a public health investigation, it will work through state and local health departments involved and the transplant programs and Host OPO. In addition, HRSA expects the CDC to keep UNOS staff informed if there are serious issues involving recipient safety for additional review by the UNOS Department of Evaluation and Quality.

A member also questioned the evolution in the types and numbers of cases for which the CDC has requested contact information. The CDC noted that any type of potential disease transmission could be of public health interest, but that it had no interest in investigating every event reported to the Improving Patient Safety portal. The CDC anticipates reviewing notifiable diseases (as listed by states), disease clusters (i.e. two or more recipients infected) and also diseases or conditions with public health implications such as emerging pathogens or disease with potential for person-to-person transmission. It was also noted that while UNOS staff is on call to accept potential transmission event reports, CDC staff is not. A mechanism for alerting the CDC regarding cases coming in after hours will need to be defined outside of standard email.

Confidential medical peer review concerns were also addressed. A member questioned whether sharing this information widely may cause the Committee to lose the protections that peer review provides and the authority under which the Committee works. There was also concern regarding a third arm of agency involvement in transplant- with now HRSA, CMS and CDC actively involved in transplantation with varying requirements that may be challenging to both transplant centers and OPOs. For these reasons, a member expressed concern that there may be variable levels of reporting. Currently under 20% of the reports are classified as probable or proven transmission. Will there be a dramatic change in reporting if the methodology changes for the recipient and donor information collection process?

HRSA hopes that the Committee will maintain its autonomy in reviewing and classifying potential transmission events, and it anticipates that there will be occasional discordance in classifications between the CDC and the Committee. These are expert opinions. The classifications used by the Committee and the CDC vary slightly. The Committee will have access to the CDC summary outlining its review, and

members have requested hard copies of lab results completed by the CDC. CDC representatives will look into the feasibility of sharing this information beyond what is provided on the proposed summary.

Members were concerned that the personal connections built between UNOS staff and OPO and transplant center staff that has helped increase reporting may be lost with decreased involvement of UNOS staff. Members raised concerns regarding the need to maintain the level of confidence and comfort built by UNOS staff members with patient safety contacts at OPOs and transplant programs. A member questioned whether transplant centers or OPOs will feel as comfortable communicating with health department staff as they have been after building working relationships with UNOS staff that have resulted in improved reporting and an increase in case reports.

A representative from HHS recognized the need for a coordinating location for collecting all blood, organ and tissue concerns was recognized as a way to alleviate confusion within the transplant community and better synchronize these activities. The Advisory Committee on Blood Safety and Availability (ACBSA) is expanding its responsibilities to include both tissue and organ in addition to blood, and this group will expand representation to include subject matter experts in these areas. The department recognizes the importance of this Committee for policy making and educational materials related to improving patient safety related to potential disease transmission in organ donation. The CDC's responsibilities were recognized as inherently governmental. There was concern within HHS regarding the CDC's withdrawal from the Committee, and HHS worked to help develop this working agreement that better defines roles and responsibilities related to potential organ donor-derived disease transmission events. In determining these roles, HHS recognized that there needed to be clarification of roles at the government level between HRSA and CDC. The CDC's role is that of public health, to investigate the risks and to determine how the risk can be managed to protect the public. This Committee has some overlap here for the transplant community. HHS recognized the need for the development of educational toolboxes. There is work to be done, and this is still a work in progress. The agreement is between CDC and HRSA in an effort to keep CDC at the table for Committee discussion. The process was emphasized as going forward within the OPTN contract, and there will be no exclusion of the Committee from the case review process. However, the CDC must be at the table and have bidirectional communication in order to perform both the work of the Committee and the CDC.

HHS indicated that there will not be a notion of "cherry picking" by the CDC when determining cases outside of recognized nationally notifiable events. The CDC will have the opportunity to lead investigations of reported events that are emerging as public health interests by nature of the agency's charge. Additionally, this agreement should in no way change the confidential medical peer review process. This process must remain intact, and bi-directional communication should not affect this. HHS is working hard to open the lines of communication and understand where there are differences. It was noted that the ACBSA recently met with CMS to identify point people for orchestration and collaboration between blood, organ and tissue communities to improve upon other aspects of cross-communication within these groups as well.

A member questioned how the Committee is to take an active role in reviewing cases, when it appears that the CDC will lead investigations and then provide a summary for the Committee to review when the CDC's work is complete. It was noted that a Committee representative will be invited to participate on CDC-orchestrated OPO and transplant center conference calls in addition to the summary, but the Committee will no longer be actively participating and posing questions to members in these instances. A member again asked if there would be an opportunity for weekly updates that are not taxing to CDC participants. All agreed that this working agreement will need to be put into practice and then modifications can be made as all participants see ways to improve upon it.

2. US Public Health Service Guidelines for Reducing Transmission of Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) through Solid Organ Transplantation. The Committee continues to await the imminent release of a public comment proposal on updates to the US Public Health Service (PHS) guidelines related to transmission of blood borne pathogens through organ donation. The original guidelines were released in 1994, and covered only the risk of HIV transmission through organ and tissue donation. Over the course of the last three years, the CDC has worked with the Center for Evidence-Based Practice at the University of Pennsylvania Health System as well as experts in the field for review and feedback to develop an updated set of recommendations that will also include HBV and HCV in addition to potential HIV transmission.

A CDC representative noted that the draft had been approved for notification in the Federal Register, and that publication was expected in the next week or so. The public comment period was scheduled for 60 days. At the closing of the public comment period, US PHS will review and respond to all comments and post this for public viewing. Input from the expert review panel will then be requested before the guidelines are finalized. It was noted that the final document will respond to all comments, but not necessarily be modified as a result of feedback. It is not a policy or regulatory document, but provides recommendations to the organ transplant community. Ideally, the US PHS hopes that the recommendations may ultimately be used to guide policy language.

The Committee awaits the release of the public comment document that it will carefully review and respond to over the course of a series of conference calls. It is anticipated that a number of other committees will respond, and these responses will be combined into a larger OPTN response that will be signed by the OPTN/UNOS President after review by the Executive Committee.

The proposed guidelines were released for public comment on September 21, 2011. The Committee began a series of calls to review and respond to the recommendations. All feedback from this Committee and others reviewing the proposal will be combined into an OPTN response after review by the Executive Committee.

3. Disease Transmission Reporting by Donor Service Area (DSA) and Region. During its April 2011 meeting, the Committee requested additional data on the number of potential donor-derived disease transmission events (PDDTE) reported by encrypted DSA in order to identify those OPOs and regions with much fewer or greater cases reported as compared to the rest of the country (**Exhibit E**). The Committee first began reviewing reporting trends during its fall 2010 meeting, and plans to share this information for the first time at the upcoming Fall 2011 regional meetings.

A total of 646 cases were reviewed by the Committee from January 2006 through June 2011. The dramatic yearly increases in cases have stabilized over the last year, but it does appear that there will be a significant increase in 2011 as compared to 2009 and 2010. When the 646 cases are broken down by region, there is great variability in total numbers. Region 5 reported the largest number of cases with 124, followed closely by Region 3 with 116. Region 1 had the fewest cases reported with ten during the same five and a half year time period. The next smallest numbers of reports received were from Regions 6 and 8, both with 25 reports each in the same time period.

All reported cases are tracked by donor ID. When the data from the same time period is broken down by Host OPO, there was one OPO with no events reported during this five and a half year period. The greatest number of reported cases for one DSA was 47, followed by 46 for another.

When the data was broken down by a single year, July 2010 through June 2011, to look for reporting patterns, Region 3 donors resulted in the greatest number of cases reported (26), followed by Region 5 (22) and Region 2 (20). Two donors recovered in Region 1 were reported during this time period, which

is an increase from the previous report. The Committee opined that this may have been the result of increased efforts in outreach and education related to the rewrite of Policy 4.0 that was implemented in January 2011 and the e-newsletter. In looking at the same one year time period by individual DSA, there was still great variation in reporting. Eleven of the 58 DSAs did not report any cases during this time period, but this compares favorably with the 14 without any reported cases in calendar year 2010.

The percent of deceased donors recovered in 2009 and 2010 and reported as a PDDTE varies by region. Results were somewhat similar for Regions 2, 3, 5, 6, 9, and 11, which ranged from reporting 1.8 to 2.8% of their recovered donors. Somewhat lower reporting was noted in Regions 1, 4, 7, 8, and 10, which ranged from 0.4 to 1.2%.

The data indicate that more than two-thirds of all reported PDDTE involve infectious disease. Region 5 has the largest percentage of cases at 2.6% for the same two year time period, with Region 9 at 1.6%. Region 1 had the smallest percentage of infectious disease reports, with only 0.2% of its donors reported.

When the same two year period is reviewed for malignancy reports, the numbers are much smaller and vary greatly. Where Region 5 had the highest percentage of infectious disease reports, it is the second lowest for reported malignancies, with only 0.18% of its deceased donors. The only region with a smaller percentage is Region 4 at 0.14%. The regions with the highest percentage of reported malignancy cases are Regions 9 (0.99%) and 6 (0.8%).

When comparing the percent of deceased donors reported as PDDTE between those donors indicated to be US PHS “high risk” for HIV and all other donors, six of the eleven regions have a higher percentage of cases reported for “high risk” donors while the opposite is true for the other five regions. It is important to remember that in some regions the number of “high risk” donors recovered is quite small. Region 6 had the highest percentage, but there were a total of 33 “high risk” donor recovered during the two year review period resulting in three reported events.

When comparing the number of cases reported across regions and 18 month time periods from January 2007 to June 2011, there were four regions that should a decline in the number of cases reported (Regions 3, 4, 7, and 10). Regions 1, 6, and 9 remained exactly the same, and Regions 2, 5, 8, and 11 showed an increase in the number of cases reported.

The Committee recognized that these data could be skewed in many ways based upon population make up (urban population versus rural) and also the aggressiveness of an OPO in pursuing donors. Members also questioned whether the varying number of donors in a year might also influence the data. In considering the types of reports that are received, the need for continued education and guidance regarding what types of cases to report will be helpful in collecting meaningful data and tracking outcomes that may guide future policy development.

The Committee will continue to follow these data, and requests that staff continue to follow up on events reported on the Post-Transplant Malignancy Form (PTM Form) without being reported as a PDDTE. Data will be updated and presented at the March 2012 meeting.

4. Donor Related Malignancies Not Reported to the Improving Patient Safety Portal. Over the course of the last four face-to-face meetings, the Committee has reviewed data related to donor-related malignancies reported on the PTM Form, but not to the Improving Patient Safety portal as a PDDTE (**Exhibit F**). For this meeting, the Committee asked for updated information and follow-up with transplant centers to identify reasons cases not reported to PSS. Specifically, the Committee requested an update on the number of cases reported to both the PTR forms and the Improving Patient Safety portal. Staff was to contact reporting transplant centers to validate the information provided on donor-related tumors reported

on the PTM form but not to the portal. Data on the number of recipient deaths related to these donor related malignancies was also requested.

A total of 63 donor-related malignancies were reported with a diagnosis date of January 2007 through June 2011 on the PTM Forms. Of these, 25 (39.7%) were also reported as a PDDTE. All nine cases reported within the last year (July 2010 through June 2011) were also reported as a PDDTE. There were additional cases noted during this one year period and originally reported as Donor Related. Calls made to transplant centers by staff determined that several were five or more years from donation, one was EBV related, and one case involved a tumor related to organ from a different donor. Forms were corrected as necessary.

There were a total of 183 recipients stemming from the 63 donors reported. Recipient outcomes included a total of 75 recipient deaths from 48 of these donors. Twenty-seven of the deaths from 26 donors had cause of death listed as malignancy related. It is possible that the other reported deaths may have been indirectly related to malignancy as well (multi organ failure, cardiovascular, etc.)

In summary, there continue to be some cases reported as donor related tumors on PTM forms but not reported to portal, but improvement have been noted in the past year. The Committee's newsletter article on what should be reported as a PDDTE was well received by the transplant community and was used as a teaching tool during the staff calls to follow up on discrepancies between reporting on the PTM and not on the portal. Staff is optimistic that additional updates to the UNetSM definition of donor related malignancy will also be helpful in this area, and will work with the Malignancy Subcommittee to finalize the updates to this definition.

5. Continuing to Refine the Process for Reviewing and Following Malignancies reported as PDDTE. Classification issues related to malignancies were reviewed by the Committee, as there are still minor differences between the current classifications used for infection versus neoplasia.

In reviewing the development of the classifications (**Exhibit G**), it was noted that malignancies were included as almost an aside when the classification system was developed. The original classifications as published by Ison et al (Am J Transplant 2009; 9: 1929-35) did not provide language specific to malignancies. As the definitions have been slowly modified to address the increasing number of malignancy PDDTE reported, all confirmed categories (proven, probable, possible) require positive recipient infection (or tumor). Excluded is constructed to "explain away" the donor origin of recipient infection as due to other reasons. There was no specific incorporation of situation in which donor disease/tumor is present, but no tumor arises in the recipient. A new category, intervention without documented transmission (IWDT), was added in 2010, and has limited application to tumors. Should this category be used when a tumor is resected from an organ (i.e. small RCC excised prior to transplant), or when an organ is explanted?

Another issue arising within malignancy PDDTE discussion involves whether a tumor is donor-transmitted or donor derived. When is it reasonable to conclude that a tumor arose after transplantation? The Committee believes there is no easy answer, but 10 years has been used as a conservative estimate for Committee discussion purposes and also was adopted by the Israel-Penn Tumor Registry. This is an area that will require in depth discussion in the coming years. A suggested functional definition offers that donor transmitted, in retrospect, could have been avoided; while donor derived, in retrospect, could most likely not have been detected at time or transplant

If no tumor is noted in the recipient (no confirmed transmission), should a malignancy PDDTE be classified as excluded or unlikely? The excluded category includes cases that are "thrown out" because

they should not have been reported in the first place. Cases classified as unlikely include events in which transmission is documented, but logically improbable.

A Committee member recommended the use of the “Excluded” category to apply to cases in which no recipient disease develops. Since there is always a tumor risk, a follow-up interval should be specified. The “unlikely” category could then be utilized to document cases in which recipient, and not donor, origin is strongly suspected but not proven. Further, a suggestion was made to introduce a new category, “Inappropriate Report,” to isolate those cases that need not have been reported in the first place. This could allow staff to remove the cases classified as Inappropriate Report from statistics without removing all “excluded” cases, and also allow for education regarding what not to report.

Manuscript Regarding Relative Risk of Tumor Transmission. The Committee’s Malignancy Subcommittee’s developed a manuscript that was published in the American Journal of Transplantation in June 2011 regarding the relative risk of tumor transmission. It adopted a three-pronged approach to:

- Define an overall framework to categorize relative transmission risk (tumor independent);
- Populate risk categories with individual tumors according to best available data; and
- Address special emphasis topics based on PDDTE reviewed by the Committee.

The overall approach is similar to the European approach to this issue. There are two independent parts to the definition. At present, almost everything fits under the nominal definition because of data limitations. Quantitative frequency estimates serve several purposes in the paper. First, it gives an idea of what is meant by the minimal, low, etc. categories used to define groups of risk. Second, as prospective data gets collected, the Subcommittee may be able to switch over to quantitative definitions in some cases. Third, and important to point out, is that this is a log scale, not a linear scale. It is quite conservative, and the Subcommittee considered a significant (intermediate) risk at anything 1% or over. The clinical recommendations were worded in such a way that they do not demand or prohibit use (i.e., they do not interfere with the doctor-patient relationship). They are clear while leaving room for clinical judgment. Overall, this is meant to be a resource document and does not replace clinical judgment based on a specific recipient’s situation.

A number of shortcomings in the paper were highlighted, including:

- Limited data; no high level evidence
- Some tumor groups may be too general; e.g., “lymphoma”, “leukemia”
- Resected RCC between 2.4 and 4 cm not specifically mentioned (an oversight)
- Prostate adenocarcinoma discussed but not included in category list
- Many tumors not specifically mentioned
 - “Active cancers not considered elsewhere” = potential high risk

Additional Areas for Consideration and Study. As the Committee continues to refine its methods for reviewing the increasing number of malignancies reported as PDDTE, a number of areas were recognized as requiring additional consideration:

- Living donors were not specifically included. Living donors may develop tumor after donation, and a small number of cases have been reported as both living donor adverse events and PDDTE. The Malignancy Subcommittee is interested in what the risk is to recipients and how long to follow living donors for reported malignancies.
- Follow-up on all PDDTE reviewed by the Committee was originally limited to 45 days, but now malignancy reports are followed for 2 years. Patient survival and tumor development is still collected. What is long term survival, disease free survival of these patients?

- Some tumors preferentially metastasize to certain organs (e.g., colon cancer → liver). Are some organ allografts more prone to develop tumor? Does risk vary among tumor/allograft type? Increased follow up and classifying cases by individual recipient as well as an overall classification assigned to donor will be helpful in monitoring organ specific data for these purposes.
- The Subcommittee's first study focused on Renal Cell Carcinoma (RCC). Subsequent studies will focus on lessons related to other tumor types (e.g., clinical features of patients with Central Nervous System (CNS) tumor misdiagnosed as a stroke).
- Additional studies will be conducted to determine whether there are certain high risk patient categories for which screening tests should be recommended (or specifically not recommended) (e.g., prostate cancer screening)).

A huge amount of work has already been done within the Malignancy Subcommittee and there are still many areas that can be considered and reviewed more closely as the Committee continues to determine the best way to consider aggregate data in providing policy input and education to the transplant community.

6. Review of Policies and Bylaws Issues for Public Comment. The Committee reviewed the fourteen policy proposals released for public comment on September 16, 2011, during its face-to-face meeting.

- 1) Proposal to Clarify Requirements for Waiting Time Modification Requests (Kidney Transplantation Committee)

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

- 2) Proposal to Extend the "Share 15" Regional Distribution Policy to "Share 15 National" (Liver and Intestinal Transplantation Committee)

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

- 3) Proposal for Regional Distribution of Livers for Critically Ill Candidates (Liver and Intestinal Transplantation Committee)

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

- 4) Plain Language Modifications to the Adult and Pediatric Heart Allocation Policies, Including the Requirement of Transplant Programs to Report in UNetSM a Change in Criterion or Status within 24 Hours of that Change (Thoracic Organ Transplantation Committee)

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

- 5) Proposed Revisions to and Reorganization of Policy 6.0 (Transplantation of Non-Resident Aliens), Which Include Changes to the Non-Resident Alien Transplant Audit Trigger Policy and Related Definitions (Ad Hoc International Relations and Ethics Committees)

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

- 6) Proposed Update to the Calculated PRA (CPRA) (Histocompatibility Committee)

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

- 7) Revision of the UNOS Bylaws, the OPTN Bylaws and the OPTN Policies that Govern HLA Laboratories (Histocompatibility Committee)

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

- 8) Proposal to Establish Requirements for the Informed Consent of Living Kidney Donors (Living Donor Committee)

The Committee reviewed the proposal and supports the proposal as written, but recommends the addition of a statement that consent should include language regarding the fact that donor behavioral risks could have an impact on recipient outcomes (15 in favor, 0 opposed, 0 abstentions). Potential donors should be informed of this as part of the evaluation process. The Committee believes it is important that potential living donors understand that pre-donation behaviors could potentially harm the recipient who is meant to benefit from transplant.

A recommendation was also made that language related to potential impacts on future insurability or healthcare be included in section 12.2, letter j of the proposal document. The Committee recognized that additional language related to this also appears in letter k and in letter l, sections iv and v, but it believes that it may be helpful to have this language in one specific area for ease of reference to more clearly inform potential living donors of these issues prior to donation.

- 9) Proposal to Establish Minimum Requirements for Living Kidney Donor Follow-up (Living Donor Committee)

The Committee reviewed the proposed language. The need for specific language regarding requirements for reporting potential living donor-derived disease transmission events through the Improving Patient Safety portal has been discussed, and will be developed for future inclusion in Policy section 12.8.4. Policy 4.5 will be used as a model, but consent to share living donor information related to potential disease transmission will also have to be carefully considered and included in policy language regarding to donor consent in order to recognize the differences in this area of policy between living and deceased donors when it comes to donor-derived disease transmission.

The Committee agreed that there is a great risk for creating a burdensome follow-up process for donors for an extended period of time. A member noted that the temptation is great to continue to add data items within the two year period of required follow-up, and that guidance is needed to control this issue appropriately. The Joint Societies Working Group was comfortable with the two year follow up period and list of minimum data points to be required. A member questioned whether concentrated funded research might be a better route for seeking the information that may be required of the full living donor transplant community.

The Committee will select members to participate in a joint subcommittee with the Living Donor Committee to develop language related to reporting potential living donor-derived disease transmissions. A joint public comment proposal is anticipated to be the end result of this effort.

Because the public comment period was not officially open at the time of the Committee's meeting, discussion and final recommendations were completed at the Committee's October 13th teleconference. After review of discussion that took place in Chicago, the Committee voted to support the proposal as written, but recommends that a Joint Subcommittee be formed with the Living Donor Committee to develop potential policy language related to reporting requirements for potential living donor-derived disease transmissions (11 in favor, 0 opposed, 0 abstentions).

This group will need to carefully consider issues related to a living donor's right to privacy in transplant center and recipient communications regarding potential disease transmission.

10) Proposal to Establish Requirements for the Medical Evaluation of Living Kidney Donors (Living Donor Committee)

The Committee was asked to review this proposal prior to public comment release due to its previous recommendations regarding specific screening tests for potential living donors. The Living Donor Committee chose not to accept the recommendations from this Committee because it did not want to oppose recommendations already received from the Joint Societies Working Group (comprised of representatives from the American Society of Transplantation (AST), the American Society of Transplant Surgeons (ASTS), and National Alliance of Transplant Coordinators (NATCO)) that the public comment proposal was based upon after a year of review.

The Committee raised concerns regarding the proposed language. Its recommended additions appear in underline and recommendations for removing language are shown in strikethrough:

In the section labeled "Social History":

- The Committee believes this section should include a bullet to reference the US Public Health Service Guidelines for Reducing Transmission of Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) through Solid Organ Transplantation. The guidelines reference both living and deceased donors, and it would be appropriate to reference this in living donor policy, as it is referenced in deceased donor evaluation policy language.

In the section labeled "Screening for Transmissible Diseases":

Add underlined language for clarity and remove language that is struck through as shown:

- HIV 1,2 (Human Immunodeficiency Virus) antibody testing
- HCV (Hepatitis C Virus) antibody testing
- Screening for Tuberculosis (intradermal PPD or Interferon Gamma Release Assay (IGRA) testing)

Screening for transmissible diseases must be repeated if there is significant delay between evaluation and the eventual donor nephrectomy, especially in donors considered as having increased risk for disease transmission ~~per the US PHS Guidelines~~¹. Transplant centers should consider additional testing based on donor risk profile such as:

- Strongyloides for donors from endemic areas
- Trypanosoma cruzi for donors from endemic areas
- West Nile for endemic areas

¹ The "Exclusionary Criteria" in Rogers MF, Simonds RJ, Lawton KE, et al. Guidelines for Preventing Transmission of Human Immunodeficiency Virus Through Transplantation of Human Tissues and Organs. CDC MMWR Recommendations and Reports. 1994; May 20/43 (RR-8):1-17.
<http://www.cdc.gov/mmwr/preview/mmwrhtml/00031670.htm>

- Toxoplasmosis: ~~Transmission is low if recipients are treated with trimethoprim-sulfamethoxazole~~

In the section labeled “Exclusionary Criteria”:

- Persistent infections ~~or infections with drug resistant organisms~~

The Committee feels strongly that the language noted as struck above be clarified. As written, it is too vague and may lead to the failure to pursue recovery of an organ due to confusion over what is meant in this section. A clearer definition will be helpful to practitioners regarding what can and cannot be used. The vagueness could lead to rejection of donors that are still appropriate.

Because the public comment period was not officially open at the time of the Committee’s meeting, discussion and final language recommendations were completed at the Committee’s October 13th teleconference. After careful review of its discussion in September, the Committee voted to oppose the proposal as currently written (0 in favor, 11 opposed, 0 abstentions).

The Committee noted that it understands the Living Donor Committee’s desire to propose potential policy language as approved pre-public comment by the Joint Societies Working Group, but believes that the modifications it recommended prior to public comment release are critical to making the policy language more clear for implementation and may have been an oversight by the Joint Societies Working Group in their earlier review. The Committee also noted that all policy related to evaluation of both living and deceased donors may have to be reviewed and modified based upon the final version of the US Public Health Service Guidelines for Reducing Transmission of Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) through Solid Organ Transplantation.

- 11) Proposal to Eliminate the Use of an “Alternate” Label when Transporting Organs on Mechanical Preservation Machines and to Require the OPTN Distributed Standardized Label (Organ Procurement Organization (OPO) Committee)

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

- 12) Proposal to Change the Term “Consent” to “Authorization” Throughout Policy When Used in Reference to Organ Donation (Organ Procurement Organization (OPO) Committee)

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

7. Review of Reported Potential Donor-Derived Disease Transmission Events. The Committee completed its semi-annual review of potential disease transmission events reported to the Patient Safety System. Ninety-two cases were reviewed and classified based upon the probability of donor-derived transmission. Of these cases, eighteen were classified as proven or probable transmissions.

The Committee continues to review and refine the case classification list that will more clearly represent both infectious disease and malignancy transmissions. Anticipated changes will allow for case follow-up beyond 45 days as needed. In 2012, the committee will begin to assign a classification for each organ recipient involved in a case review rather than an overall case classification to better determine measure the organ specific effects of potential donor derived disease transmission.

The Committee voiced concerns regarding the need for Toxoplasma screening requirements for deceased donors. There have been poor outcomes reported for recipients where Toxoplasma testing was either not

completed or missed by the transplant center. The Committee believes that this is a completely avoidable scenario, and does not believe that the expense of testing would be prohibitive. Equally, it would not be a test result required prior to recovery or even transplant. A Toxoplasma screening requirement was recommended in the Committee's Policy 2.0 rewrite, but received a great deal of negative feedback from the OPO Community. Based upon review of reported cases, the Committee feels that it will be appropriate to pursue this as a policy requirement again, with evidence to support it based upon aggregate case data.

The Committee also hopes to begin assigning case classifications in individual recipients in addition to the overall donor report in an effort to make aggregate case data easier to study specific to the effects of a certain diagnosis on a specific organ group. This practice is planned to be adopted in 2012, and the new case management software being developed will allow for this function.

8. Reported PDDTE Not Posted for Full Committee Review. As case volume workload continues to increase, staff and Committee leadership worked together to develop a triage system for case management. Preparing a reported event for Committee review generally takes 2-3 hours of staff time. After discussing the effort involved in posting a case on SharePoint for Committee review, it was determined by Committee leadership that some reports do not warrant this level of effort because there is little for the Committee to discuss that relates to its charge. Examples of these types of reports include:
- Duplicate reports (OPO and one or more transplant center report the same event)
 - OPO notifies recipient of new information (usually a final culture result covered by standard peri- or post-operative antibiotics. All recipients are doing well and receiving appropriate coverage for the new finding.)
 - False positive test results (i.e. HTLV 1/2 screening was positive, but confirmatory testing was negative)
 - Reported disease or malignancy developed 5+ years post-transplant
 - Event is misreported (should have been reported as a patient safety situation or living donor adverse event)
 - Non-transmissible or benign tumor is reported
 - A suspected contaminant in a culture is reported, all recipients are well
 - A potential donor with a positive test result is not pursued or all organs are discarded
 - A reported transmission involving a blood product (not an organ donor)

In order to maintain case work load for both staff and Committee members, Committee leadership supported the creation of a triage system to eliminate such cases from full committee review. When such a case is reported (or any other questionable situation), staff notifies the Chair, Vice Chair and any other subject matter expert on the committee (frequently members with malignancy background) to determine if full committee case review if all recipient centers have been notified and all recipients are well. In any event where a full case review is not completed, centers are encouraged to contact staff with questions or concerns or even re-report if concerns related to the original report arise.

From January 1 to August 31, 2011, 160 PDDTE were reported on the Improving Patient Safety portal. Of these reports, 36 of these events were not reported to the full DTAC for review. All fell within the scenarios outlined above. Six more reports received either by phone or email (and not entered into the Improving Patient Safety portal by members) that were not reported to full DTAC based upon DTAC Leadership review during the same time period.

As a result of the new triage plan, 42 reports did not require full DTAC review. The majority of these events were duplicate reports and OPO reports of positive cultures such as Staphylococcus aureus in

sputum when lungs were not used and post-transplant Toxoplasma positive results where recipients received prophylaxis and had no related problems.

Staff will continue to provide summary data of cases not reported at each of the committee's face-to-face meetings (**Exhibit H**).

9. Updates to the Improving Patient Safety Portal. The Committee was provided with screen shots demonstrating the latest proposed updates to the Improving Patient Safety portal's PDDTE reporting page (**Exhibit I**). The Committee reviewed and discussed these modifications during its August 2011 teleconference, and the latest documentation was provided for a final review and vote. Due to time constraints, members were asked to look over the screen shots independently, and vote electronically on approving the modifications.

The Committee will cast a formal vote during its October 13 meeting via LiveMeeting and teleconference in support the modifications to the PDDTE reporting page on the Improving Patient Safety Portal (11 in favor, 0 opposed, 0 abstentions).

The modifications to PDDTE reporting will be part of a larger project that will update the living donor adverse event and patient safety situation reporting pages as well within the Improving Patient Safety portal.

10. Review of 2010-2011 Goals as Assigned by the Board. The committee reviewed its 2011-2012 goals, and what had been done to meet these goals to date:

- 1) Proposed Minimum Screening Requirements for Potential Living Donors

The Committee provided feedback to the Living Donor Committee on its proposed living donor screening requirements draft prior to release of public comment. The Living Donor Committee did not accept all of this Committee's recommendations, but both groups are committed to continued partnership to get minimum policy requirements in place and then modify language in the future to continue to build patient safety protections into this population. In addition, the two committees will work together to develop policy language regarding requirements for reporting potential living donor-derived disease transmission events within Policy 12.0.

Two Committee members co-chaired the July 2011, Potential Living Donor Screening Consensus Conference in Baltimore, Maryland, while two additional members attended and participated in planning subcommittees. The goal of this group was to look at issues related to pre-recovery donor testing for blood borne pathogens, risk group analysis, the consent process and developing a framework for implementation of testing practices and/or policy. The meeting included diverse participation from professional societies, government representatives, as well as living donor and living donor recipient representation. At the end of the meeting, there was limited consensus on how to move forward. Participants agreed that testing should be completed, but disagreed on the type of testing and timing of testing that should be held as a minimum requirement in policy language. It was almost universally recognized that completing nucleic acid testing (NAT) on a living donor within seven days of organ procurement, as recommended by the CDC in a recent Morbidity and Mortality Weekly Report (MMWR) outlining a confirmed living donor-derived Hepatitis C transmission, was not feasible or supported by data, and was therefore opposed by the group.

Related discussion is taking place in multiple arenas. Another consensus conference, sponsored by the Agency for Healthcare Research and Quality (AHRQ), is anticipated to cover these same

topics. It has also been noted that the US PHS Guidelines are expected to reference living donor screening recommendations as well that mirror the CDC's MMWR recommendations.

Members agree that it would be wise for the community to attempt to find common ground on how to proceed with living donor testing before perhaps less desirable and more restrictive policy language is implemented. The living donor evaluation and testing process will have to be closely reviewed as a minimum set of standards is developed into policy. Concerns were raised during the conference that inefficiencies may be introduced into the system (additional cost to transplant centers and potentially unnecessary testing and frustration for potential living donors) if the process become too proscriptive.

2) Guidance for Considering Donors with Meningoencephalitis of Unknown Etiology

The Committee's Encephalitis Subcommittee continues to review reported potential donor derived disease transmission events involving diseases related to meningoencephalitis and the outcome of recipients of these donor organs. The group will utilize its findings to develop a guidance document that is anticipated to help OPOs when considering donors that fall into this category as well as transplant programs considering these organ offers. New members were encouraged to participate in this effort.

3) Bi-annual DTAC Electronic Newsletter

The Committee's Newsletter Subcommittee has drafted several articles, and anticipates its next edition of the DTAC News to be released in October 2011 as part of the larger monthly UNOS e-newsletter. New members were encouraged to participate in this effort, and reminded that the articles are brief, but informative to the general transplant community.

4) Improvement to Potential Donor-Derived Disease Transmission Reporting Page (the Improving Patient Safety Portal on Secure Enterprise)

The Committee has completed its review or modifications and additions suggested by staff and OPTN members who complete the disease transmission report form on the portal. The Committee is in support of programming of these changes, and a final vote will be taken on the October 13, teleconference. The modifications and additions are part of a larger effort to update all sections of the Improving Patient Safety portal, including reports for living donor adverse events and patient safety situations.

5) OPO Screening Practices Survey

The Committee's work on this effort has been on hold, awaiting the release of the US Public Health Service Guidelines for Reducing Transmission of Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) through Solid Organ Transplantation. The Federal Register notice of public comment regarding this document was released on September 21, 2011. The Committee believes that it is important for the new guidelines to be put into place before surveying OPOs on changes to screening practices since its Fall 2008 survey. This project remains on hold for this reason.

11. Universal Donor Health Questionnaire Review. The Committee continues its involvement in the finalization of a Universal Donor Health Questionnaire (UDHQ) that is expected to be implemented for collecting medical and social history for potential blood, organ and tissue donors. This effort was spearheaded by the American Association of Tissue Banks (AATB) with a goal of creating document

with questions that would collect information pertinent and useful to OPOs as well as blood and tissue banks. A single questionnaire would also be expected to reduce the emotional burden on family members of potential organ and tissue donors, who are sometimes asked to complete more than one history form. Two draft questionnaires were circulated for public comment by the AATB in late 2010 (adult and pediatric less than 12 years of age), and the Committee provided feedback regarding its concerns that some questions may be too general to collect the type of information on risk needed to allocate organs appropriately (**Exhibit J**).

The AATB received an incredible amount of feedback during the public comment period, and opted to establish a group with wide representation from all three areas of donation in addition to those well versed in the development of questionnaires to review all the comments received and revise the proposed questionnaire as appropriate based upon these comments. The Committee's chair was asked to serve on this review group alongside a former member of the Committee with an OPO background.

The review group has been meeting twice a month to review each question on the proposed questionnaire alongside the feedback received in each area. Committee members were provided a brief snapshot regarding what was to be discussed at each of these meetings, with a request for feedback to be taken to the larger multi-disciplinary review group. To date, the Committee Chair has received little to no feedback regarding this effort, but recognized the limited notice given for this review and feedback. Based upon the diverse knowledge base within the Committee, all were requested to take some time to review the document updates as they are provided and share feedback to be taken back to the larger group.

A face-to-face meeting for the larger AATB-sponsored review group will be taking place, and the Committee's input is needed on this form. While it is meant to be functional and not comprehensive in that it would be burdensome to the donor or donor family member, the goal is to develop questions that may ultimately guide the surveyor to follow up on specifics raised upon completion of the general questionnaire.

12. Transplant Community Outreach. The Committee briefly discussed ways to continue to educate the transplant community regarding reporting requirements and what it has learned from review of the aggregate case data. The Committee's newsletter and abstract presentations at various professional society meetings were highlighted. Members briefly shared ideas for abstracts for presentation in 2012. Staff outlined deadlines for submissions for the American Transplant Congress 2012 for both malignancy and infectious disease. All members were reminded of the Committee's charge to improve upon transplant patient safety through the development of policy and educational efforts as they develop thoughts or ideas regarding abstracts.
13. Welcoming New Committee Members. The Chair welcomed new members who started their terms with the Committee on July 1, 2011, and asked all members to introduce themselves and share some background regarding what skills they brought to the Committee. A new members training session was provided by LiveMeeting and teleconference in late June, but a slide set outlining basic OPTN and HRSA functions and committee member expectations was provided to all within the meeting materials packet.

**AD HOC DISEASE
TRANSMISSION
ADVISORY
COMMITTEE (DTAC)**

	MONTH	JULY	AUGUST	AUGUST	SEPTEMBER	SEPTEMBER
	DAY	13	11	18	8	14
FORMAT (select)	Live Meeting/ Teleconference	Live Meeting/ Teleconference	Live Meeting/ Teleconference	Live Meeting/ Teleconference	Teleconference	In Person
NAME	COMMITTEE POSITION					
Emily Blumberg MD	Chair	x	x	x	x	x
Michael Green MD, MPH	Vice Chair	x		x	x	x
Carrie Comellas BS, RN, CPTC	At Large					x
Edward Dominguez MD , FACP, FIDSA	At Large	x	x		x	
Afshin Ehsan M.D.	At Large		x			x
Barry Friedman RN, BSN, MBA, CPTC	At Large	x	x			x
Thomas Gross MD, PhD	At Large	x	x	x	x	
Daniel Kaul MD	At Large	x	x		x	x
Shimon Kusne MD	At Large	x				x
George Lyon III, MD, MMSc	At Large	x	x			x
Rachel Miller MD	At Large	x	x	x	x	x
Samantha Mitchell RN, CCRN, CTBS	At Large	x			x	
Michael Nalesnik MD	At Large		x	x	x	x
Volker Nিকেleit MD	At Large					x
Martha Pavlakis MD	At Large	x		x	x	x
Timothy Pruett MD	At Large		x		x	x
Phillip Ruiz Jr , MD	At Large		x			
Michael Souter	At Large		x		x	x
J. Elizabeth Tuttle-Newhall M.D.	At Large					x
Linda Weiss	At Large	x	x			x
Russell Wiesner MD	At Large					x
James Bowman III, MD	HRSA	x	x	x	x	x
Bernard Kozlovsky MD, MS	HRSA		x			
Raelene Skerda, RPh, Bpharm	HRSA		x	x	x	x
Matt Kuehnert, MD	CDC					x phone
Susan Hocevar, MD	CDC					x
Shandie Covington BS	Committee Liaison		x	x	x	x
Kimberly Parker	Support Staff	x	x	x	x	x phone
Sarah Taranto	Support Staff	x	x			x
Kimberly Taylor RN	Support Staff	x	x	x	x	x
Stacey Burson	Support Staff	x	x			
Jerry Holmberg, PhD	HHS					x
James Berger	HHS					x