

**OPTN/UNOS Ad Hoc Disease Transmission Advisory Committee (DTAC)**  
**Meeting Summary**  
**October 21, 2016**  
**Chicago, IL**

**Cameron Wolfe, MBBS (Hons), MPH, FIDSA, Chair**  
**Marian Michaels, MD, MPH, Vice Chair**

*Discussions of the full committee on October 21, 2016 are summarized below. All committee meeting summaries are available at <https://optn.transplant.hrsa.gov>.*

**Committee Projects**

**1. Guidance on Explaining Risk Related to Use of Increased Risk Donor Organs When Considering Organ Offers**

The DTAC project to develop “Guidance on Explaining Risk Related to Use of Increased Risk Donor Organs When Considering Organ Offers” is currently under the Joint Society Work Group (JSWG) process. The JSWG contains representatives from the American Society for Transplantation (AST), American Society of Transplant Surgeons (ASTS), and North American Transplant Coordinators Organization (NATCO). It is being led by Dr. Michael Ison, an AST representative.

The project arose due to education needs in the community to understand and communicate the “true” relative risk of donors designated as US Public Health Service (PHS) Increased Risk (IR). There has been a general feeling that organs have been declined due to this status that might have been used with better understanding. Research presented last year at American Transplant Congress (ATC) conducted by DTAC members did demonstrate a statistically significant difference in use based on PHS IR status.

It is hoped that the guidance will provide useful information for clinicians to use themselves as well as links to materials that can be used for patients. The project does not encompass informed consent questions. It was noted that other Committees such as Pediatrics and Vascularized Composite Allograft (VCA) have talked about these issues and would find this type of guidance very helpful.

At this point, several JSWG calls have been held and a very collaborative process has led to the development of “draft” guidance. It is required that all society members of the JSWG vote to approve and send the document back for their individual organization’s approval. Due to one organization not being represented on the last call, this motion was changed to an email vote. Virginia law requires 100% participation and 100% approval. One member voted by email to abstain due to use of the term “increased risk”. It was explained that the Final Rule requires the OPTN to follow Centers for Disease Control and Prevention (CDC) recommendations and that the term was developed and published by the CDC (PHS) so this term is not up for discussion. Another call may be held soon for a revote as it anticipated that the broad group does support sending the document along in the process.

A DTAC member, who also serves as the AOPO medical Director, expressed serious concerns that AOPO is not a named JSWG member. It was expressed that this type of guidance can impact OPOs and their society should have a seat at the table. It was shared that the original agreement drafted by US Health Resources and Services

Administration (HRSA) and the three societies was done in 2010 due to living donor policy concerns which did not involve OPOs. The HRSA representative at the meeting indicated that this concern would be taken back and shared.

It was also noted that both DTAC and APOPO have opportunities for involvement later in the process. Once approved by the JSWG, the draft guidance will go back to each of the three respective societies for their individual consideration. If approved by all three respective societies, then the draft guidance with comments from AST, ASTS, and NATCO will then come back to DTAC and follow the OPTN guidance document process.

DTAC will make their comments and guidance documents now follow a public comment pathway. The liaison working on the project explained that it is hoped that spring 2017 public comment will work, however, it was also shared that guidance documents can go out for special public comment periods that only need to be at least 30 days long. The Executive Committee can approve guidance documents on behalf of the OPTN/UNOS Board of Directors. If deadlines are missed to the JSWG process, then there are options besides waiting for the fall cycle.

DTAC did not review the document text but they were asked to share a draft and start gathering feedback from colleagues with the aim of making useful edits once DTAC receives JSWG feedback.

## **2. Education to Reduce Unnecessary Discard of Kidneys with Small Renal Cell Carcinoma (RCC) Found Pre-Transplant**

The Committee still plans to send this project for Policy Oversight Committee (POC) consideration in December 2016. Research on unilateral versus bilateral early stage renal cell carcinoma is still being conducted to add to the supporting evidence section.

### **Committee Projects Pending Implementation**

## **3. Modifications to How New Donor Information Received Post-Transplant is Reported to Recipient Centers (PDDTE New Policy Debrief)**

The toxoplasmosis screening requirement for deceased donors is the only part of the potential donor-derived disease transmission event (PDDTE) policy changes that did not go into effect on September 1, 2016. This portion will require IT programming in DonorNet® and the Deceased Donor Registration (DDR) form. DonorNet programming will be scheduled for some time in 2017. Once the DonorNet portion is completed, then the policy to require toxoplasma IgG screening on all deceased donors will go into effect. The community will be notified through a system notice. DDR programming will require Office of Management and Budget (OMB) approval by the federal government and the policy change can move ahead without this component that will be completed at a later unknown date.

### **Implemented Committee Projects**

## **4. Modifications to How New Donor Information Received Post-Transplant is Reported to Recipient Centers (PDDTE New Policy Debrief)**

The Committee received an early debrief on the new policies impacting potential donor-derived disease transmission events (PDDTE) that went into effect on September 1, 2016 (with the exception of the toxoplasmosis screening requirement as noted above).

Once per year the DTAC will review the Pathogens of Special Interest list. The Committee reviewed the list that is referenced in policy but maintained outside of policy

to allow the DTAC and CDC to make changes in real time and respond to emergent health concerns such as Zika. Some in the community have questioned why hepatitis B (HBV) is not on the list yet hepatitis C (HCV) and HIV are on the list. The intent is not review expected transmissions or irrelevant clinical findings such HBV core positive only. Leadership discussed that we want to make modifications that will not lead to unnecessary reporting without missing unexpected donor-derived disease.

The group discussed HBV and agreed that they would want to know about accidental transmissions meaning those where the results were not known prior to transplant or unexpected transmissions despite negative testing (e.g. window period cases). One member questioned what if people do not end up not on appropriate anti-viral therapy or when appropriate treatment gets stopped too early. The emerging studies of knowingly transplanting HCV positive organs into hepatitis C negative recipients was discussed. It was noted that there is an upcoming conference on when to use Hep C positive organs. It was suggested that DTAC could be mechanism to collect this type of data and it might be useful to have this kind of data. Then the discussion shifted back to the original purpose of the list. The list is designed so that CDC can view what is going on in donors where their able to get involved that can help recipients with diagnostic capabilities, public health investigations, and clinical advice. These are things that DTAC cannot and does not provide. Ultimately, it was decided to add active HBV to the list. A note has also been added to clarify that expected transmissions where the transplant hospital is aware of positive results prior to transplant do not need to be reported.

Another suggestion was made to consider the audience of the list. It was requested that all names and possible synonyms be listed (not just scientific names) so that anyone using the list could better identify a pathogen that needs to be reported. It was noted that labs vary in their reporting and often a user may use a search function. It was noted that actual users and coordinators should vet the list to minimize risk of not clearly communicating the pathogens and risking one slipping through the cracks. The list will be edited with this concern in mind.

The other note about resolved or remote disease that does not need to be reported was discussed. It was noted that the DTAC does want to allow some deference to OPOs for items reported by family members such as malaria at age 25 or donor history of Lyme Disease five years ago. In situations like these, the note allows OPOs to use their expertise on reporting.

Whether histoplasmosis should be added to the list was discussed. The CDC representative noted that CDC would not get involved in these cases. These cases can also be tricky with the diagnosis and that we have to be careful not to reintroduce noise back into the system. Ultimately, it was decided not to add this condition to the list.

The DTAC member who also serves as the AOPO medical director volunteered to have it posted in the AOPO portal, as it could be helpful and reach more OPO personnel in this location.

It was reported that 15 reports since September 1<sup>st</sup> had been made but were not necessary reports according to the new policy guidelines. When this happens, DTAC staff do provide feedback to the reporting OPO and let them know these conditions are no longer required to be reported. The DTAC is moving away from donor culture reporting and focusing on recipient illness through the policy changes. One OPO received that feedback and stopped filing unnecessary reports. Another OPO has received the feedback but continued to report. It was noted that previous policy was vague and it is now purposely more detailed to help OPOs know what needs to be

reported. Another member noted that some OPOs have said they will report everything because they are afraid of missing something. DTAC members agreed there will be a learning curve and the Committee will continue to educate the community.

## **Other Significant Items**

### **5. Pilot to Use DonorNet to Communicate Results Received After Transplant**

Members received a progress update from Amy Putnam, UNOS Customer Council Director, on a pilot information technology (IT) project that will allow OPOs to notify transplant hospitals of updated test reports through DonorNet®. The pilot is being led by the UNOS IT Customer Council. Preliminary work was completed during a SONU day with the assistance of a former DTAC member, Chris Curran who is with New England Organ Bank. The pilot programming will be completed sometime in 2017. This will be done in a manner that is similar to how organ offers are communicated currently. Patient safety contacts (on call) using the current on call contact management system would be selected or indicated and OPOs would then choose the test type results that are available for view in DonorNet. Following the pilot and evaluation, the project would then be ready for Committee sponsorship.

The pilot is designed to be a proof of concept to help ease communication and acknowledgement of results received post-transplant. The demonstration showed a notify button used by the OPO that calls back to waitlist for all recipients transplanted from a specific donor. The OPO can then choose which transplant hospitals by organ groups to notify. OPOs can enter any free text (max 500 characters). The transplant hospital will receive the same type of notification that they have chosen to receive for organ offers. A log of notifications sent, received, and by what method is kept. A more detailed audit log is planned for future with date/time stamps for points of communication marked by user log on.

It was noted that they are also working with the Operations and Safety and Transplant Administrators Committees. They have also spoken to a number of OPO groups who have had positive reactions. It was suggested that an alert be built in if results have not been reviewed within a certain timeline.

It was noted that the pilot purpose is to make more urgent communication easy, efficient, and traceable. It was mentioned that this could make data searchable and trackable as well as provide a denominator for DTAC PDDTE data. It was also suggested that the notification have an identifier to help with research or a link that could go straight into UNet authentication to minimize searching.

The cases where transplant hospitals are conducting testing on behalf of OPOs (e.g. bronchoscopy) were brought up. It was suggested that the transplant hospital report to the OPO who can then report out using the system. It was asked if the system could be built to have functionality like I2B2, which systematically searches databases available results at regular time intervals to help cut down on missing results that may take some time to come back.

It was noted that UNOS has been doing work on application programming interfaces (APIs) to help enhance the electronic flow of data between electronic medical records and other databases. In 2016, the focus was on OPOs and in 2017; more work will be done to build transplant hospital APIs. The vision is to become an information hub in more real time.

One member related a concern about typing in culture sensitivities. It was noted that results will also be uploaded as pdfs and there will be a check box to indicate that a pdf result is available. Susceptibilities could be uploaded as well from an .xml file in the OPO computer system.

It was reiterated that the pilot is a proof of concept. The goal is to get the basic functionality and use out there among some pilot sites and then work to build some of add ons such as those mentioned by DTAC.

It was noted that DTAC will request an update at their next face-to face meeting and that they support this effort.

## **6. Policy Oversight Committee Updates**

Vice Chair, Dr. Marian Michaels, relayed information regarding the latest work of the Policy Oversight Committee (POC). She provided members with an overview of what the POC does and what types of items must be approved by the POC. The 2015-2018 OPTN Strategic Plan goals were reviewed along with the level of effort (LOE) assigned to each. Members were shown how the actual project portfolio LOE by goal fits against the plan benchmarks. They were also shown how to access the dashboard should they want to review it on their own. It was noted that space would become available in the safety bucket after the next BOD meeting.

The status of DTAC projects was discussed. Case review is just part of normal Committee work so DTAC is different in that respect in that basic review does not go through the POC. Next project review will likely be in December and will talk about RCC. We make a stronger proposal if we know how it will be evaluated.

The new guidance document process was shared that went into effect as of the June 2016 OPTN/UNOS Board of Directors (BOD) meeting. Guidance documents will now be submitted as project proposals and the POC and Executive Committee will need to approve the work. The Joint Societies have the opportunity with every project to indicate that they want to make it a JSWG project. Guidance documents must go out for public comment but if needed they can go out under a special public comment session. Guidance documents can be approved by either the full BOD or the Executive Committee at their monthly meeting on behalf of the BOD. It was noted that clinical guidance, member obligations not readily apparent, and controversial issues are within scope. It was also noted that FAQs, educational offerings, updates to existing documents, and guidelines related to operations would not be within scope for this process.

The DTAC RCC project under development would fit within scope of this new guidance process. The current focused review of granuloma/histoplasmosis cases would not be within scope because only a scientific paper is planned at this point. There are fiscal implications as going to the POC and receiving approval does result in time being approved or assigned to projects such as research time.

The new fiscal impact process for proposals was also discussed. Fiscal impacts to small, medium, and large organizations (e.g. transplant hospitals, OPOs) will now be part of information sent to the OPTN/UNOS BOD when considering policy proposals. The fiscal impacts are high-level estimates developed by an ad hoc fiscal impact group that contains both Committee and non-Committee members. The pilot process has both OPTN member as well as UNOS staff input in developing high-level fiscal estimates for low, medium, and high volume organizations impacted by the proposal.

## **7. Zika Update**

The Committee, along with the AST and ASTS, has proposed edits to the current Zika recommendations originally released in February 2016 to give opinions on what transplant hospitals should consider. When the original publication was released, there had been no mainland spread. In addition, the landscape has changed with regard to blood donor recommendations as well as testing. It was decided in light of those changes, to review the document and consider some edits.

At this time though the group recognizes that the science is imperfect and that we have not experienced the pathology to date as was seen with other mosquito-borne disease such as West Nile Virus (WNV). There has been one documented case of Zika transmission in Brazil published on a liver transplant recipient who contracted the virus through blood transfusion.

The proposed edits try to be careful not to automatically exclude donors based on travel history and the aim is to have clinicians use their judgement and weigh the risks of potential infection versus not accepting an organ. More information was added regarding available testing and the considerations of each test. Many questions remain and there are not clear answers at this time particularly with the impact to transplant recipients. HRSA is currently reviewing the document.

DTAC members shared their experiences. One member spoke of how they are not currently testing in Puerto Rico because of uncertainty of what to do with positive results or fear of false positives. It was noted that they had amended their donor screening questionnaire. It has not been an issue that organs are being turned down from this area. It was noted that Zika is on the Pathogens of Special Interest list and would be reported if found. There has only been one offer where a Zika concern was voiced on the other end. There have been a few evaluations that were halted due to possible concerns of Zika symptoms. There are roughly 100 donors annually from Puerto Rico. Some struggles regarding Zika were noted at the last regional meeting and it was noted that DTAC must continue communications with those on the front line.

Another transplant hospital member noted that they had testing capability but had not yet had reason to use on transplant patients. They have tested pregnant patients and CDC employees who have traveled to endemic areas. Their testing is confirmed by CDC.

DTAC members noted that they would like to do a retrospective study of donor samples from endemic areas and trace to recipient outcomes or potential disease. It was also noted that we might not have a complete or accurate sexual history, which could confound some of the data. It was noted that CDC was in discussions with HRSA regarding what types of studies could be funded. CDC noted that they were not certain that banked samples would be the way to go with current testing capabilities and they were still considering the best ways to investigate possible incidence. One DTAC member did note that studies did help identify Chagas but that some Zika testing can also have some cross reactivity with other viruses.

## **8. Donor Granuloma Case Review**

The Committee is conducting a specific focused review of potential histoplasmosis cases including cases where granulomas or other potential evidence such as nodules is noted in the donor record. Dr. Marilyn Levi discussed that the purpose is to review the cases and possibly develop some points of clinical guidance as these cases can be challenging to determine risk and true disease. The review process will examine whether it is safe to use organs from donors with granulomas on lymph nodes or other tissue.

The review will include donor cases of reported histoplasmosis, coccidiomycosis, mycobacterial disease or granulomas reported to DTAC between 2006-present. The case review group will be combing the data to answer a set of specific review questions in hopes of identifying organ transplants most associated with active infection and identifying the utility of donor histopathology, serologies, cultures or PCR to predict primary infection or reactivation.

The study could help identify what symptoms or testing could be helpful in telling whether a donor has an active infection that could be transmitted. DTAC recognizes the importance of this study. A member stated that it could help to increase transplants through decreasing unnecessary discards. It was noted that the risk of disease is probably low and the results could shed light on effective prophylaxis. This is important to growing lung transplant programs.

It was noted that the keywords “nodule” and “blasto” could be added to the search for cases to review. The group wants to make the list as inclusive as possible. Currently there are 71 cases of mycobacterium tuberculosis (+ 4 unclassified + 2 unlisted); 34 cases of coccidiomycosis (+ 1 unclassified), 32 cases of histoplasmosis: (+ 5 unclassified) as well as some sarcoid and other extraneous cases scheduled for the small group review.

## **9. DTAC Data Requests**

Marissa Clark, UNOS Research Analyst reviewed post-implementation evaluation data from three proposals that had been combined into one IT implementation on August 10, 2015. The first related to the project on “Reporting Whether Donor Screening Tests are Completed Using Qualified Specimens”. Data on 9,499 deceased donors recovered between 8/10/2015 – 7/31/2016 were reviewed for the analysis. There were eight donors among five OPOs with hemodiluted specimens for HIV antigen/antibody testing during that time. In addition, there were 166 donors among 46 OPOs with hemodiluted specimens for HIV NAT testing during that same time. Three related reports to the OPTN/UNOS Improving Patient Safety PDDTE portal were identified in association with the hemodiluted samples. The three reports will be researched to examine whether there was any disease transmissions. It was noted that hemodilution calculations must be done according to a formula and that it can be complex to identify all products given to a donor. It was noted that the actual numbers of hemodiluted specimens could be greater but not identified due to these complexities.

It was noted that some of the high NAT numbers might be due to triplex NAT testing. It was noted that samples from hospital admissions may not be accepted by labs for NAT testing but they are more likely to be accepted for serology tests.

Post policy implementation evaluation data related to the project on “Review of Minimum Screening Requirements for Deceased Donor Evaluation” were also presented and discussed for the same cohort as above. All 58 OPOs are performing NAT testing some of the time (9,380 donors) and 56 OPOs are using HIV antibody screening at least some of the time (9,246 donors). HIV antigen/antibody combination testing is reported as used by 25 OPOs in 299 donors.

Data below were shared for the following evaluation questions:

*How many OPOs are using HIV antigen/antibody combination diagnostic testing versus HIV antibody screening?*

HIV Antigen/Antibody Combination Testing	HIV Antibody Screening	No. of Donors	No. of OPOs
Yes	Yes	47	22
Yes	No	252	4
No	Yes	9,195	56

*How many OPOs are using HIV antigen/antibody combination diagnostic testing instead of NAT testing?*

HIV Antigen/Antibody Combination Testing	HIV NAT Testing	No. of Donors	No. of OPOs
Yes	Yes	184	25
Yes	No	115	1
No	Yes	9,192	56

Other post policy implementation evaluation data for the project “Aligning OPTN Policy with 2013 PHS Guidelines” were presented. The evaluation plan was to look at HBV, HCV, and HIV cases reported since 8/10/2015. One proven/probable case of HBV and one for HCV were identified. Nine organs were transplanted all nine recipients were reported as alive with functioning grafts.

	Reported	Reviewed	Proven/ Probable
<b>HBV</b>	<b>12</b>	<b>7</b>	<b>1</b>
<b>HCV</b>	<b>11</b>	<b>6</b>	<b>1</b>
<b>HIV</b>	<b>3</b>	<b>3</b>	<b>0</b>

A HOPE Act update was also given. There are currently 20 approved transplant hospital programs. A total of 33 matches have been run to date (none since 7/19/16). There 81 HIV positive candidates (73 kidney, 8 liver) on the waitlist willing to accept a HIV positive organ. There have been four donors and ten deceased donor transplants (7 kidney, 3 liver) HOPE Act transplants (none since 7/20/2016).

It was noted that it might take awhile for HOPE Act transplants to get up and running. One member asked about false positive but it was clarified that there is not a standard data field to track these. Dr. Wolfe discussed a recent AOPO webinar in which he participated to help get the word out. It was noted that that for some transplant hospitals active viremia or co-infections would not be automatically ruled out but that some may believe that to be the case. The need for more education was identified.

Amber Wilk, UNOS Biostatistician, showed the Committee a new interactive Tableau dashboard that takes DTAC case report and review data and displays by a variety of variables. The user interface allows the user to make multiple choices in how to view the data. It allows filtering by year, gender, ethnicity, cause of death, region, DTAC classifications, HCV positive donors, PHS Increased Risk status, and other variables. It can also provide data by specific conditions. It was noted that it is not an official database for abstracts but is meant to be an idea generator.

DTAC members noted how helpful this could be for posters and power point presentations. It was suggested to allocate time on a future call once all members have access to practice with the tool. Although requested, it was noted that former DTAC members would not be able to access due to security issues. It was suggested that as the product develops it could be very helpful if different levels of security were developed or a more public facing tool to help researchers in moving the field forward.



It was noted that December 2, 2016 is the deadline for ATC abstracts. HRSA does not have to approve abstracts but must approve any presentations that would be given on behalf of DTAC.

#### **10. 2016 Case Reviews**

The Committee reviewed potential donor-derived disease transmission events reported through the Improving Safety Portal. This is completed as a confidential medical peer review activity. Aggregate results are reported later through articles, abstracts, and presentations.

#### **Upcoming Meetings**

- November 8, 2016 Teleconference
- December 13, 2016 Teleconference
- January 10, 2017 Teleconference
- February 14, 2017 Teleconference
- March 15, 2017 Chicago, IL