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MEMORANDUM

To: Dr. Carl Berg, UNOS President
Mr. Brian Shepard, UNOS CEO

From: Ms. Libby McDannell, AST Executive Vice President

RE: AST Comments on OPTN Policy Proposals

Date: March 27, 2015

On behalf of the American Society of Transplantation Board of Directors, I am enclosing the Society's comments on the ten OPTN policy proposals currently out for public comment.

Thank you for the opportunity to provide feedback on these policy proposals.

Cc: AST Board of Directors
Dr. Yolanda Becker, AST UNOS Board Representative

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Proposal #1: Proposal to Require the Re-Execution of the Match Run when a Deceased Donor's Infectious Disease Results Impact Potential Recipients based upon Screening Preferences

UNOS Summary of Proposal: The purpose of Policy 2.9 (Required Deceased Donor Infectious Disease Testing) is to determine whether deceased organ donors have evidence of infection with a number of potentially transmissible pathogens. For some of these specific pathogens, organ transplant candidates may choose not to receive offers from positive donors. In this case, these candidates do not appear on a match run. Current policy does not require the host OPO to re-execute the match run if new results become available after execution of the initial match run. This updated donor information could screen certain candidates from receiving organ offers. Review of OPTN data indicates that a large number of organ allocations take place using match runs executed prior to receipt of all test results. This presents a potential patient safety concern, as organs could unintentionally be allocated to a candidate who is not willing to accept offers from organs who are positive for a specific infectious disease. This could result unintended donor-derived disease transmission. Better defining in policy the processes that should be followed when new results are learned after the initial match run will reduce the opportunity for error and enhance patient safety.

AST Comments:

The AST supports this proposal. When possible, OPOs should have the required serology and NAT testing results prior to the match run. However, the current policy, which does not require the host OPO to re-execute the match run if new results become available after execution of the initial match run, should be updated so that either the match run is redone, or centers are notified, when new results are made available. It is imperative that donor offers be flagged so that the accepting transplant center understands that some of the infectious disease testing has not yet been done, and there should be a systematic way to notify accepting transplant centers of the updated results. We the one-hour timeframes mentioned.

As written, this proposal will require the host OPO to re-execute the match run if new results become available for donor HBV, HCV, HIV or CMV. Although we strongly support the requirement to re-execute the match run for new HIV, HBV or HCV results, re-executing the match run for new CMV results should be restricted to intestine recipients. The risk of post-transplant CMV can effectively be mitigated in the majority of recipients with the use of universal prophylaxis or pre-emptive monitoring; as the result of the success of these interventions, CMV matching is not currently utilized in non-intestine recipients. As a result, the match run should only be re-executed for new CMV results for intestine recipients.

The AST also appreciates the opportunity to respond to the 3 specific questions DTAC asked during the public comment period:

1. Provide a reasonable point in time in the organ allocation and recovery process where results might be required for sharing with the recipient transplant hospitals:

   For kidney recipients, the deceased donor crossmatches are generally reported within 6 hours of the organ offer. Generally, serologic results should be made available within 6 hours of receipt of blood, therefore suggesting a reporting window of approximately 6 hours so that the match run can be re-executed seems reasonable. NAT requires longer, typically 12 hours after blood is received in the laboratory, although there is significantly more variability in the turn-around-time (Theodoropoulos *et al*. ***Am J Transplant***. 2013;13:2186-2190). If NAT is to be included, a

slightly longer duration might be appropriate. Policy on appropriate turn-around-times should be driven by data, derived from regular surveys of OPOs, not expert opinion.

2. How much will delayed entry of HCV results, which is part of the KDPI calculation, impact kidney match run order for those candidates willing to accept an HCV positive donor kidney?

   Per HRSA's "A Guide to Calculating and Interpreting the Kidney Donor Profile Index (KDPI)" "the KDPI provides no assessment of the likelihood of disease or malignancy transmission from a deceased donor. Even though the formula includes HCV as a factor, its inclusion was strictly due to the association of HCV positivity with (lower) graft survival. Further, the KDPI can be calculated if HCV status is not available. It appears that less than 20% of the match runs occurred with HCV status pending. A small percentage of these donors will actually have a positive result that will require the match run to be re-executed and may result in an increase in cold time. HCV NAT will require longer to obtain results but provides a shorter window period – and as such, will likely inform acceptance of organs if there are new results. The impact of donor-derived disease transmission seems to be greater than the information provided to calculate KDPI.

3. Do you believe that screening criteria should be broadened to include HBV sAg?

   Yes. Most likely, a positive result for either HBV NAT or HBVsAg would result in significant clinical decision making for the transplant team. Risk of HBV transmission from HBcAb donors to non-liver recipients is low, especially if the recipient is HBsAb seropositive (Huprikar *et al*. ***Am J Transplant***. 2015 Feb 23. doi: 10.1111/ajt.13187. Epub ahead of print) whereas the risk of disease transmission from a HBsAg or NAT positive donor would be significant and likely would only be acceptable in recipients with active or treated HBV infection. Knowing the infectious status of the donor would be of great value and should be included as a screening criteria.

Proposal # 2: Proposed Membership and Personnel Requirements for Intestine Transplant Programs

UNOS Summary of Proposal: The proposed bylaw will define a designated intestine transplant program and establish minimum qualifications for primary intestine transplant surgeons and physicians. The proposal includes a full approval pathway and a conditional approval pathway for intestine transplant programs. The intent is to set minimum standards where none currently exists without compromising quality or restricting new program formation.

AST Comments:
The AST supports this proposal. We acknowledge the need for the Membership and Professional Standards Committee (MPSC) to have a set of minimum standards for qualification as a designated intestine transplant program and minimum qualifications for primary intestine transplant surgeons and physicians with which to assess whether or not an Intestinal Transplant program qualifies for membership in the OPTN. Additionally, the AST acknowledges the challenges of creating balanced and fair criteria for a sub specialty of transplantation that performs a limited number of transplants in a limited number of centers. However, the AST would like to express the following concern for consideration by the Liver and Intestinal Transplantation Committee.

1. The AST is concerned that focusing on number of transplants in a field that in total performs very few, will result in a few programs having designation as a 'high volume program' or a 'center of excellence.' The AST believes it is important to avoid these designations because patients may not be able to obtain insurance authorization and this could significantly limit patient access to care. Additionally this approach could initiate a downward spiral that results in successive program closure and intestinal transplantation be concentrated in a few centers. This would further impede access to care in socio-economically and geographically disadvantaged patients.

Proposal #3: Proposal to Address the Requirements Outlined in the HIV Organ Policy Equity Act

UNOS Summary of Proposal: Current federal rules and OPTN policy prohibit the recovery and transplantation of organs form deceased donors infected with the human immunodeficiency virus (HIV). The HIV Organ Policy Equity Act (HOPE Act), enacted on November 21, 2013, will allow for the development and publication of criteria for the conduct of research relating to transplantation of organs from donors infected with HIV into individuals who are infected with HIV before receiving such organ. The goal of this proposal is to continue to amend OPTN policies to allow members to participate in the research study in accordance with upcoming changes to the Final Rule and criteria developed by the Secretary of Health and Human Services (HHS).

AST Comments:
AST supports this proposal with the following reservations:
Although the AST strongly agrees with the need for additional research into the safety and efficacy of HIV+ to HIV+ transplantation, as recommended by the HOPE Act, we have 2 major concerns for the proposal as written:

1. The AST strongly feels that HIV+ individuals should not be used for living donors.
   Similar to diabetics, we would not recommend the use of donors at higher risk for kidney disease. Literature has shown that the risk of HIV-associated nephropathy (HIVAN), especially among blacks, is significant. While the rate of HIVAN varies across different populations, it is significant. In addition, focal segmental glomerulosclerosis, arterionephrosclerosis and diabetic nephropathy are increasingly common in individuals who have been on HIV therapy for years; such diseases are associated with metabolic syndrome, obesity and premature ageing. (Rosenberg *et al*, ***Nat Rev Nephrol***. 2015 Mar). While the true risk of ESRD in the individual HIV+ potential donor may be hard to calculate, clearly the overall risk of ESRD is higher in this population.
2. The AST agrees with the prohibition of storing of HIV vessels for later use other than the originally intended recipient. Iliac vessels are sometimes used for complex reconstruction and for this purpose it is best to have the vessels of the donor from which the organ came for the intended recipient.

Additionally, the AST feels strongly that the proposal should include collection of the donor and recipient antiretroviral regimens on page 9 under "additional data collection".

Proposal #4: Proposal to Modify the Sterile Internal Vessels Label

UNOS Summary of Proposal: This proposal seeks to modify the requirements for the sterile internal vessels label. The amount of information required on this label will be reduced. Currently all infectious disease results are required by policy to be handwritten on a "2 x 4" or "2 x 5" label in a sterile field. This process is difficult for OPOs to complete and prone to transcription errors. Infectious disease results on this label will be reduced to whether the donor is positive for Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), or Hepatitis C Virus (HCV) and whether the donor is at increased risk in accordance with US Public Health Service Guidelines for HIV, HBV, or HCV. Requirements for the hangtag poly-plastic internal label attached to the outermost layer of the triple sterile barrier will not change and all infectious disease results still must be completed on this label.

AST Comments:
The AST supports this proposal, but recommends that the positive results for HBV be more specific on the label for the reasons noted in the comment below.

The proposed label is more simplistic than prior:
"These vessels are from a donor:
1. With positive test results for HIV, HBV, or HCV
   ☐Yes ☐No ☐Pending"

There is a much lower risk for transmission of HBV from HBV core antibody positive donors compared with donors who are positive for HBV by either sAg or NAT. Our understanding of policy is that all HBV sAg or NAT positive donor vessel are not stored. If HBV cAb+ vessels are used, then this current labeling does not allow for differentiation between cAb+ (lower risk) and sAg or NAT (high risk). This new label would seem to result in loss of more vessels. If they changed the new label to make it clear as to whether the HBV positive test were cAb+ (lower risk) or sAg or NAT (high risk), that might provide for less loss of vessels. Also, this new label would technically include HBV surface antibody positivity (not always checked, but maybe sometimes checked or known), which is not a risk factor for possible disease transmission. Thus, although this may work well for HIV and HCV, where any positive result is significant, this new label should probably be more specific for the exact HBV assay that was positive.

An additional issue is the 'pending' box for infectious disease tests. If this box is checked – the requirement would be that receiving OPO would have to revise the box to yes or no, prior to storage of the vessels. The AST is aware that the data on HIV, HBV & HCV may not be available at the time of the procurement, however, it would be available at the time of storage. A clear hand-off of this data, and checking the final yes, no box will again, be the responsibility of the recipient OPO.

Proposal #5: Clarify Policy Language and Process for Individual Wait Time Transfer

UNOS Summary of Proposal: Policy 3.6.C: Waiting Time Transfer does not completely and accurately describe the process that occurs when a candidate transfers primary waiting time from one transplant program to another. The Patient Affairs Committee proposed modifications to Policy 3.6.C so that it details the process and defines waiting time that is eligible for transfer. This proposal promotes the efficient management of the OPTN by describing the responsibilities of both transplant programs and the OPTN Contractor in the individual waiting time transfer process. By defining waiting time that is eligible for transfer, this proposal also ensures that the waiting time transfer calculations are accurate and that the process is fair for all candidates.

AST Comment:
The AST supports this proposal. In the proposal, it states that "The OPTN Contractor will not include time between removal at the earlier transplant program and registration at the new program in the candidate's waiting time."

The above statement in the proposal requires additional clarification. For patients on dialysis, this statement is in conflict with the recently implemented policy where the wait time is calculated based on the date the patient starts dialysis. The above statement may only be applicable to patients who are pre-emptive and have not started dialysis. KPCOP asks that the Committee reviews the above language and ensure that it is consistent with the wait time calculation policy.

Proposal #6: Proposal to Establish Pediatric Training and Experience Requirements in the Bylaws

UNOS Summary of Proposal: Pediatric transplantation is a subspecialty within the field of transplantation. In the current OPTN Bylaws, the primary surgeon and primary physician are not required to have pediatric training or experience in order to serve as key personnel at programs that perform pediatric transplants. The Bylaws' silence on pediatric program requirements means that there is not a universal standard of quality in pediatric care, which, in the most rare and serious of circumstances, could post a risk to patient safety. While the Pediatric Transplantation Committee, the MPSC, and others have attempted to establish pediatric requirements since 1993, the project has gained momentum since 2010, when the MPSC set an annual goal of developing qualification criteria for pediatric organ transplant approval. In 2012, the Board of Directors included developing separate program requirements for pediatric programs as a key initiative under Goal 4: Promote Patient Safety of the OPTN/UNOS Strategic Plan. To fulfill this key initiative, the committee proposes that a designated transplant program must have an approved pediatric component in order to perform transplants in patients less than 18 years old. To be approved for a pediatric component, a program must identify a qualified primary pediatric surgeon and a qualified primary pediatric physician to serve as key personnel.

AST Comments:
The AST agrees that minimum standards for qualification are desirable but we do not support this proposal as written. The premise of this proposal is sound but the proposal itself is not perfect. There were significant concerns by the AST constituency as follows:

1. The estimate of the number of programs that would no longer meet approval is unclear. We would like to see more granular data on the anticipated impact to geographical distribution of available transplant services for patients, particularly in more sparsely populated areas, where higher volumes are difficult to achieve based on population demographics. The proposed volume criteria for the pediatric programs set a high bar that we suspect will have a more detrimental effect to access to care than the offsetting benefit in improved outcomes from increasing the volume criteria to the extent noted.
2. The proposal does not acknowledge any differences in complexities between infant and adolescent surgery.
3. There may well be cases where experienced high-volume adult surgeons may be more appropriate to perform adolescent transplantations than a pediatric surgeon with a lower volume of transplants. However, other aspects of the program infrastructure would need to be in place such as child life, psychosocial support and nursing expertise.
4. The proposal also lacks detail in regard to the supporting staff and QI.

Proposal #7: **Proposal to Collect Ex Vivo Lung Perfusion (EVLP) Data for Transplant Recipients**

UNOS Summary of Proposal: Ex vivo lung perfusion (EVLP) is an emerging technology that can be used during transport, and to preserve and condition lungs prior to transplantation. The utilization of EVLP is not currently reported to the OPTN, so the OPTN cannot determine how many lungs have been perfused and then transplanted. In the spring of 2015, the OPTN will implement changes to the OPTN Tiedi forms, including the Deceased Donor Registration form (DDR). Through the modified DDR, Organ Procurement Organizations (OPOs) will report whether an accepting transplant programs intends to perfuse the lungs prior to transplant. However, there is no corresponding field on the Transplant Recipient Registration form (TRR) for transplant programs to report whether lungs were perfused prior to transplant. The thoracic committee believes it is important to capture this information to monitor lung allocation, recipient safety, and organ and patient outcomes. This information will also be important for future policy development and risk adjustment for member-specific performance measures.

AST Comments:
The AST supports the policy proposal as written.

Proposal #8: Membership Requirements for Vascularized Composite Allograft Transplant Programs

UNOS Summary of Proposal: Vascularized Composite Allografts (VCAs) were included in the OPTN Final Rule (42 CFR part 121) as covered human organs effective July 3, 2014. In response to this change, the OPTN Board of Directors approved minimal VCA membership requirements that will expire on September 1, 2015. Under the current rules, there are no specific membership requirements with regard to VCA transplant experience for the primary physician and surgeon at a VCA program. The VCA Committee is proposing minimal certification, training, and experience for individuals serving as VCA primary physicians and surgeons. If approved, these new requirements will replace those requirements that will expire in September 2015.

AST Comments:
The AST supports this proposal as written.

Proposal #9: Proposal to Improve UNet Reporting of Aborted Procedures and Non-Transplanted Organs

UNOS Summary of Proposal: To clarify and simplify reporting requirements for aborted living donor recovery procedures and incidents when a living donor organ is recovered but not transplanted and to ensure that follow-up forms are generated so no living donor is lost to follow-up.

AST Comments:
AST supports this proposal. We offer three additional comments to approve the policy proposal.

This policy is clarifying and simplifying the reporting requirements for aborted living donor recovery procedures and incidents where a living donor organ is recovered, but not transplanted. It is essentially aligning process with policy. The proposed changes will ensure the OPTN is aware within 72 hours of either an aborted living donor surgery (after anesthesia is commenced) or when a living donor organ is recovered, but not transplanted into any recipient. Currently, the OPTN is made aware of these events through the Patient Safety Portal. The new policy describes a process by which the transplant center will notify the OPTN via the Living Donor Feedback Form in addition to the Patient Safety Portal. However, the Living Donor Feedback (LDF) mechanism will ensure the living donor follow-up forms are generated.

We recommend the AST support the policy proposal as stated. Because the proposed policy requires the transplant center to contact the OPTN to modify the LDF form, a function that the transplant center is able to perform now within the Tiedi system, we offer two recommendations to assist centers in following policy:

1. The functionality in the Tiedi LDF should be disabled at the time the policy goes live rather than the proposed 'if and when possible' proposal. In addition, and ideally, this question could be placed in the registration form rather than the LDF.
2. The Patient Safety Portal should be developed to identify the two procedures as options in reporting a living donor adverse event. Currently only loss of native organ function and living donor death are options in the Improving Patient Safety Living Donor Adverse Event portal. The system should be set to remind the transplant center to contact the OPTN ***in addition to reporting through the Patient Safety Portal*** for either of these events to support transplant center compliance with policy that requires reporting the same event in two places.
3. There should be clear distinction between the living donor whose case was aborted prior to donor nephrectomy and the case in which the living donor who actually underwent donor nephrectomy but the kidney was not transplanted.

Proposal #10: Proposed ABO Blood Type Determination, Reporting, and Verification Policy Modifications

UNOS Summary of Proposal: This proposal seeks to: 1) Clarify requirements related to ABO blood type determination, reporting, and verification for donors and candidates; 2) Strengthen current key system safety components to ensure the correct organ is transplanted into the correct recipient and that the match is ABO compatible or planned incompatible; 3) Align OPTN/UNOS and Centers for Medicaid and Medicare Services (CMS) blood type requirements more closely. This proposal was originally released in the spring 2014 public comment cycle and has been modified to address concerns raised by the transplant community.

AST Comments:
The AST does not support the revised ABO verification policy as written. As noted during the previous comment period, existing policy has been effective in preventing these exceptionally rare events. The additional burden of further regulation is not justified given the lack of preventable adverse events. Specifically:
1) Adding yet another verification at time of organ check-in is duplicative of existing verification which is required prior to implantation of the organ. It offers no likely gain in safety, while increasing the burden on centers and further moving OPTN regulations out of step with CMS regulations, which have no such requirement. The AST will not support this additional, unnecessary step.
2) Requiring a policy for resolution of blood type mismatches and subjecting it to survey will create further confusion and move OPTN regulations further out of step with CMS regulations. We are aware of no incidents in which a center has identified a blood-type discrepancy but failed to adequately resolve it. The handling of these rare events should be left entirely to the judgment of the extremely capable transplant centers who handle it well now. Extremely rare events are better handled by the judgment of professionals who can assess the individual circumstances rather than by attempting to develop policies capable of addressing all rare possibilities. Absent evidence this is solving an actual problem and that policies will be more effective than case-by-case resolution, this requirement lacks any basis for inclusion. Given surveyor history of variable interpretation of general requirements, we are further concerned this requirement will lead to further confusion and ambiguity on the content of such policies.
3) Defining qualified healthcare professionals is unnecessary for listing verification, which can be performed by any center staff member. While a center could make such a designation in its policy, this would create risk of surveyor interpretation on this term.
4) Requiring pre-donation verification occur in the OR is unnecessarily proscriptive. Completing the verification in the pre-op area is no less safe given the safeguards in place in the recipient OR.

At this time, and given no evidence the current extensive regulations are inadequate, the OPTN should confine its regulatory changes on this topic to reduction of unnecessary or ambiguous requirements and harmonization with CMS. Any expansion or increase in specificity is an unwarranted diversion of effort from areas with much greater likelihood of improving safety and outcomes.