At-a-Glance

- **Proposal to Require Collection of Human Leukocyte Antigen (HLA) Type for Thoracic Organs**

- **Affected Policy:** 3.7.12.1 Essential Information for Thoracic Offers

- **Thoracic Organ Transplantation Committee**

- Clinical practice and review of the literature suggest that knowledge of donor HLA type allows for a sensitized candidate to receive the most suitable thoracic organ offer. The proposed policy states that if a transplant center requests donor HLA type when its candidate receives a thoracic organ offer, the OPO must provide HLA type for each thoracic organ offered prior to the organ's final placement. The proposed policy change does not require that a thoracic transplant center request donor HLA type for its candidate. However, if the transplant center seeks donor HLA type, then it is responsible for communicating this request to the relevant OPO.

  Coupled with recently developed techniques to determine HLA antibody specificity and perform virtual crossmatching, donor HLA data provided at the time of a thoracic organ offer will allow transplant centers to consider offers for sensitized candidates in circumstances where prospective crossmatch is not practical. Enabling virtual crossmatching for thoracic organs also has the potential to reduce post-transplant morbidity and mortality by preventing unanticipated positive crossmatches.

- **Affected Groups**
  Directors of Organ Procurement Organizations (OPO)
  Lab Directors/Supervisors
  OPO Executive Directors, Medical Directors, and Coordinators
  Transplant Administrators and Program Directors
  Transplant Physicians/Surgeons
  Organ Recipients
  Organ Candidates
  General Public

- **Number of Potential Candidates Affected**
  This policy proposal has the potential to affect all sensitized thoracic transplant candidates.

- **Compliance with OPTN Strategic Goals and Final Rule**
  - Operational Effectiveness (Strategic Goal)
  - "§ 121.8 Allocation of organs. […] (a) Policy development. […] (1) Shall be based on sound medical judgment; […] (5) Shall be designed to avoid wasting organs, to avoid futile transplants, to promote patient access to transplantation, and to promote the efficient management of organ placement; (6) Shall be reviewed periodically and revised as appropriate;" […]

Proposal to Require Collection of HLA Type for Thoracic Organs

Affected Policy: 3.7.12.1 Essential Information for Thoracic Offers

Thoracic Organ Transplantation Committee

Summary and Goals of the Proposal:

Clinical practice and review of the literature suggest that knowledge of donor HLA type allows for a sensitized candidate to receive the most suitable thoracic organ offer. The proposed policy states that if a transplant center requests donor HLA type when its candidate receives a thoracic organ offer, the OPO must provide HLA type for each thoracic organ offered prior to the organ's final placement. The proposed policy change does not require that a thoracic transplant center request donor HLA type for its candidate. However, if the transplant center seeks donor HLA type, then it is responsible for communicating this request to the relevant OPO.

Coupled with recently developed techniques to determine HLA antibody specificity and perform virtual crossmatching, donor HLA data provided at the time of a thoracic organ offer will allow transplant centers to consider offers for sensitized candidates in circumstances where prospective crossmatch is not practical. Enabling virtual crossmatching for thoracic organs also has the potential to reduce post-transplant morbidity and mortality by preventing unanticipated positive crossmatches.

Background and Significance of the Proposal:

In 2008 and 2009, the Thoracic Committee discussed the advantages of providing HLA data with each deceased donor thoracic organ offer. Initially, this discussion centered on the data required in DonorNet® when making thoracic organ offers. Although the Thoracic Committee would prefer HLA type to accompany each thoracic organ offer, this cannot be achieved until it is required of OPOs as part of their process. Thus, the first step would be to add HLA type to Policy 3.7.12.1 per the Thoracic Committee.

In July, 2009 the Thoracic Committee discussed this addition to the policy with the leadership of the OPTN/UNOS Histocompatibility Committee. The Histocompatibilty Committee's leadership supported the proposed requirement. The Thoracic Committee then discussed the feasibility of OPOs being able to provide HLA data when making deceased donor thoracic organ offers. Policy 3.5.9 (Essential Information for Kidney Offers) requires the following HLA data accompany each deceased donor kidney offer: "HLA A, B, Bw4, Bw6, and DR antigens." Therefore, OPOs already submit deceased donor tissue to laboratories for HLA identification. Representatives of the OPO community who are members of the Thoracic Committee commented that providing HLA information for deceased thoracic donors may not be an extraordinary effort for some OPOs. Further, knowledge of deceased donor HLA type prior to the recovery of thoracic organs equips clinicians with necessary information to accept or refuse thoracic organ offers on behalf of their candidates.

The medical management of a candidate involves laboratory tests to identify the candidate's HLA type and the presence of preformed anti-HLA antibodies. A positive anti-HLA antibody crossmatch between donor and candidate tissue is undesirable, i.e., the candidate's immune system is more likely to reject the organ. This rejection can lead to graft failure and possibly, recipient mortality. A negative anti-HLA antibody crossmatch between the donor and candidate tissue is desirable, i.e., the recipient's immune

system is more likely to accept the organ. Improved solid phase assays for the detection of anti-HLA antibodies in transplant candidates has made possible the use of a "virtual crossmatch" if the donor HLA type is known and the candidate does not have preformed antibodies to the donor's specific HLA antigens.

At its meeting on November 4, 2009, the Thoracic Committee voted in favor of submitting the addition of HLA as required data for all deceased donor thoracic organs. UNOS staff drafted a public comment proposal that included HLA type in Policy 3.7.12.1, and presented it to the Thoracic Committee for its review in the first quarter of 2010. The Thoracic Committee determined that it needed further deliberation on the proposed policy.

On March 23, 2010, the Thoracic Committee discussed its proposal to add HLA to Policy 3.7.12.1. Currently, Policy 3.7.12.1 requires an OPO provide the following data with each deceased donor thoracic organ offer:

> *"i) The cause of brain death;*
> *ii) The details of any documented cardiac arrest or hypotensive episodes;*
> *iii) Vital signs including blood pressure, heart rate and temperature;*
> *iv) Cardiopulmonary, social, and drug activity histories;*
> *v) Pre- or post-transfusion serologies as indicated in 2.2.7.1 (pre-transfusion preferred);*
> *vi) Accurate height, weight, age and sex;*
> *vii) ABO type;*
> *viii) Interpreted electrocardiogram and chest radiograph;*
> *ix) History of treatment in hospital including vasopressors and hydration;*
> *x) Arterial blood gas results and ventilator settings; and*
> *xi) Echocardiogram, if the donor hospital has the facilities.*
>
> *The thoracic organ procurement team must have the opportunity to speak directly with responsible ICU personnel or the on-site donor coordinator in order to obtain current first-hand information about the donor physiology."*

During its March meeting, the Thoracic Committee discussed the proposal with the Chair of the OPTN/UNOS OPO Committee. The Thoracic Committee explained its intent to add HLA to Policy 3.7.12.1: knowledge of deceased donor HLA would:

- Enable transplant centers to screen thoracic organ offers for unacceptable donor antigens;
- Enable sensitized thoracic candidates to receive suitable organ offers; and,
- Promote the practice of virtual cross-matching.

The Thoracic Committee asserted that current laboratory technology allowed for HLA typing of thoracic donors. The Thoracic Committee sought commentary from the OPO Committee's leadership on:

1. When OPOs could provide HLA typing for thoracic donors, i.e., at the time of the organ offer or before performing a match run;
2. The specificity of HLA typing the OPOs could provide for thoracic organ donors; and,
3. The operational issues the OPOs would encounter with such a policy requirement.

(Prior to the meeting, both the OPO Committee's leadership and the Thoracic Committee reviewed a draft of the HLA policy proposal.)

During the meeting, the OPO Committee's leadership cautioned that obtaining HLA typing for thoracic donors before running a match, as indicated in the early draft of the policy proposal, could be burdensome operationally to some OPOs. The group discussed that there is indeed only anecdotal knowledge on the number of OPOs that could or could not readily provide HLA data for thoracic organs. However, OPOs already provide HLA typing when running kidney matches. The Thoracic Committee recollected the leadership of the Histocompatibility Committee's Vice-Chair, who had attended the July, 2009 meeting, commenting favorably on the feasibility of histocompatibility laboratories to perform HLA typing tests and provide the results for thoracic organs.

One Thoracic Committee member informed the group of having conducted an informal telephone survey of 15 OPOs to understand how quickly these organizations could test for and provide HLA typing for thoracic organs. Most of the organizations responded that they received HLA typing information within 6-8 hours. Nevertheless, as this member commented, it is necessary for the Thoracic Committee to understand logistical issues encountered by OPOs that do not receive HLA typing information within the 6-8 hour time frame.

The group also discussed if blood or lymph nodes was the more appropriate sample to submit for receiving accurate typing of deceased donor HLA; and, what impact a hemodiluted blood sample could have on the accuracy of HLA typing.

The OPO Committee's leadership supported the concept of HLA typing for thoracic organs, but suggested the Thoracic Committee collaborate with the OPO Committee first to understand the availability of HLA typing for thoracic organs. The OPO Committee's leadership recommended the Thoracic Committee conduct this formative research before making a policy recommendation. The Thoracic Committee needed to identify how readily the proposed policy could be applied by OPOs and engage the Histocompatibility community or Committee, or both, in this discussion. The OPO Committee's leadership commented that should such a survey indicate that the majority of OPOs responding could provide HLA typing on thoracic donors within short time frame, then the OPO Committee and community would provide operational guidance to the minority of organizations needing assistance in reducing the length of time it takes them to receive HLA typing. The Thoracic Committee agreed that a survey could provide salient information about OPO operational practices regarding HLA typing for thoracic organs.

The group also noted that the OPO community was concerned about the need to perform nucleic acid testing (NAT), but over time accepted this requirement. The Thoracic Committee's focus is to improve organ allocation to sensitized thoracic candidates, and this is best accomplished by the addition of an HLA requirement to Policy 3.7.12.1. Many transplant centers already perform virtual cross-matching to identify medically suitable donor organs for their candidates.

Knowing that there are sensitized candidates who could benefit from the addition of an HLA requirement to Policy 3.7.12.1, the Thoracic Committee considered how best to proceed. The Thoracic Committee opined that it should do its best to abide by the needs of the sensitized patient. Literature supports the benefit of identifying donors' unacceptable antigens, performed through virtual or prospective crossmatching. Thus, the Thoracic Committee considered proceeding with its intent to add an HLA type requirement to Policy 3.7.12.1.

Some members of the Thoracic Committee argued for building consensus on the proposed policy change before distributing it for public comment. This approach could increase the likelihood of the proposal's acceptability to the OPO community. Other members argued that the Thoracic Committee need not "sell" its idea of adding HLA typing to Policy 3.7.12.1. Rather, given the time that exists between this meeting and the next public comment cycle (October, 2010), the Thoracic Committee could collaborate with the OPO, Histocompatibility, and Operations and Safety Committees to conduct the aforementioned survey, i.e., build consensus without losing sight of the need to improve thoracic organ allocation for the sensitized candidate. The Thoracic Committee could apply the survey results to further develop the proposal.

In an effort to consider possible operational difficulties facing OPOs following the addition of HLA requirement to Policy 3.7.12.1, the Thoracic Committee considered addressing the survey to histocompatibility laboratories as well. Thus, it might be easier to understand whether the operational difficulties in HLA typing reside in fact in laboratories affiliated with said OPOs.

The group also discussed the possibility that operational issues faced by some OPOs are more cultural or historic in nature than practical.

The Thoracic Committee also commented that the policy language in the initial draft of the proposal did not state clearly when OPOs should provide HLA typing to transplant centers. While the proposal stated OPOs could not conduct a match run without having deceased donor HLA typing, the policy did not. Further, the Thoracic Committee members opined that it was not their intent for HLA typing information to be ready before a match run. Rather, the Thoracic Committee members commented that they would be comfortable with the receipt of HLA typing from OPOs at the time thoracic organs were offered for transplant.

One member proposed the following policy alternative: require HLA typing only if the OPO is offering a thoracic organ outside of its local area. Another member countered that if in the future, the Thoracic Committee were to eliminate "local" as a geographic factor in allocation, then the proposed alternative would require revisions.

The Thoracic Committee also recommended that the proposed language should focus on unacceptable antigens and virtual crossmatching. The initial draft of the proposal mentioned virtual crossmatching, but focused more on prospective crossmatching.

Having learned that the OPO Committee would meet on April 20, 2010, the Thoracic Committee requested that a few of its members be present at that meeting as the proposal would be discussed, and possibly, the results of the aforementioned survey. The Thoracic Committee requested that UNOS staff develop a working group representing the following Committees to develop the survey: Thoracic, OPO, Operations and Safety, and Histocompatibility. This working group would draft and distribute the survey to the OPO and histocompatibility communities, and prepare a final draft of the proposal for review by the Thoracic Committee. The survey would include the following statement and questions:

1) An introduction that educates the survey participant on the Thoracic Committee's intent for collecting HLA from thoracic donors, the significance of unacceptable donor antigens to sensitized thoracic candidates, and the evidence for their proposal; and

2) Questions listed below.
    a. How much time does your laboratory require to provide deceased thoracic donor HLA typing?
    b. How much time does your OPO currently need to collect blood or tissue sample for HLA typing of thoracic donors?
    c. What operational impact would your OPO experience if the Board of Directors approves the addition of HLA to 3.7.12.1?
        i. If the impact is potentially unfavorable, how can the OPO community assist your organization in complying with the policy and your organizational needs?
    d. Which sample provides accurate typing of deceased donor HLA: blood or lymph nodes?
    e. What impact does a hemodiluted sample have on the accuracy of HLA typing?
    f. When a sample is hemodiluted, what tests can a laboratory apply to determine the accuracy of HLA typing?
    g. How often does HLA mistyping occur for a thoracic donor?
        i. What is the magnitude of the impact of this mistyping?

Consensus Building

The Chair of the Thoracic Committee attended the OPO Committee meeting on April 20, 2010. As the survey was not in its final form, the OPO Committee recommended that the draft of the survey to the OPO community also include the following question: Does the OPO receive HLA typing information prior to allocating thoracic organs? The OPO Committee emphasized that the OPO community may not favor a mandate on providing HLA type for each thoracic organ at the time an OPO performs a thoracic match run.

In the second quarter of 2010, the Thoracic Committee collaborated with the leadership of the Histocompatibility, OPO, and Operations and Safety Committees to understand – through a survey – the nationwide practice of obtaining HLA type on deceased donor thoracic organs. On June 16, 2010, the Thoracic Committee surveyed the OPO executive directors and the histocompatiblity laboratory directors. The appendix to this proposal shows the questions to and responses from the OPO executive directors and histocompatiblity laboratory directors. The objectives of the survey were to understand the:

1. Specificity of HLA typing that could be provided by histocompatibility laboratories;
2. Time when OPOs must provide HLA type information to transplant centers, i.e., at the time of the organ offer or before a match run;
3. Amount of time histocompatibility laboratories require to type HLA of thoracic organs; and,
4. Business impact that OPOs and histocompatibility laboratories may experience if the proposed policy to add HLA type to Policy 3.7.12.1 were approved by the OPTN/UNOS Board of Directors.

The Thoracic Committee prepared and distributed the surveys via e-mail using SurveyMonkey™,[A] a web-based survey tool. The Thoracic Committee leadership e-mailed all directors of OPTN member histocompatibility laboratories (N=156) and executive directors of OPOs (N=58). Several histocompatibility laboratory directors served in this capacity at more than one laboratory.

[A] http://www.surveymonkey.com/

The survey distributed to histocompatibility laboratory directors included the following questions:

1) What is the deceased donor sample you HLA type at your laboratory most frequently? Please select one answer from the options provided below:

    a) Peripheral blood
    b) Lymph nodes
    c) Spleen
    d) Buccal swab

2) What primary method do you use for deceased donor typing of Class I HLA? Please select one answer from the options provided below:

    a) Serology
    b) Sequence-specific primers (SSP)
    c) Sequence-specific oligonucleotides (SSO)

3) What primary method do you use for deceased donor typing of Class II HLA? Please select one answer from the options provided below:

    a) Serology
    b) SSP
    c) SSO

4) Do you require a different deceased donor sample than indicated above if the donor has received multiple blood transfusions?

    a) Yes
    b) No

5) What is the average time from receipt of deceased donor blood or tissue to reporting the HLA type to the OPO? Please respond in hours to the nearest half hour.

6) Which HLA loci do you currently type for deceased thoracic donors? Please select all applicable answers from the options below.

    a) HLA-A
    b) HLA-B
    c) HLA-Bw4/6
    d) HLA–Cw
    e) HLA–DR
    f) HLA-DR51/52/53
    g) HLA–DQ
    h) HLA–DP

7) What general comments do you have about the proposed addition of HLA type to Policy 3.7.12.1? Please write below.

The survey distributed to OPO executive directors included the following questions:

1) Upon receipt of typing specimen, how much time, on average, does your affiliated HLA laboratory require to provide HLA of thoracic deceased donors? Please respond to the nearest half hour and elaborate on your response.

2) Does your OPO currently attempt to obtain HLA of thoracic deceased donors before making thoracic organ offers via DonorNet®?

3) Does your OPO receive HLA of thoracic deceased donors before it begins the organ allocation process (i.e., before making organ offers)? Please elaborate on your response.

4) What percentage of the time is the HLA of thoracic deceased donors available before thoracic organ allocation?

5) How much time, on average, does your OPO need to gather blood or tissue samples for the purposes of HLA from thoracic deceased donors? Please respond to the nearest half hour and elaborate on your response.

6) If your OPO does not currently receive HLA prior to allocation of thoracic organs, what is the time lapse between your OPO's performance of a thoracic match run and its receipt of the deceased donor's HLA?

7) What operational impact would your OPO experience if the Board of Directors approves the addition of HLA to 3.7.12.1? Please elaborate on your response.

8) Should this proposed change become policy, what negative impact or situations might your OPO encounter?

9) If the impact is potentially unfavorable, how can the OPO community assist your organization in complying with the policy and your organizational needs?

10) What additional comments do you have about the proposed addition of HLA to Policy 3.7.1.12?

Survey Results

Of the 58 OPO executive directors surveyed, 34 responded – one by e-mail and 33 in SurveyMonkey™ (59% response rate). Of the 135 lab directors surveyed, 73[B] responded in SurveyMonkey™ (54% response rate). The results of the survey follow.

Analysis of Responses Provided by Histocompatibility Laboratory Directors

Histocompatibility laboratory directors responded that their laboratories primarily (81%) use peripheral blood as sample for testing donor HLA type. The remaining 19% of responses were lymph nodes; none of the lab directors reported using spleen or buccal swab as samples.

[B] A few directors responded that their laboratories were affiliated with transplant centers, and not OPOs.

The majority of the directors (65%) stated that their laboratories perform Class I HLA typing using the sequence-specific primers method, with the remaining responses split almost evenly between serology and sequence-specific oligonucleotides. Likewise, some directors reported that their laboratories use the serology and sequence-specific oligonucleotides methods to perform typing of Class II HLA, but the majority (70%) stated that their labs perform Class II HLA typing using the sequence-specific primers method. One third of the directors reported that they require a sample other than the original sample if the donor received multiple blood transfusions. Of the 64 laboratory directors who responded to question 5, 53 (83%) indicated it took 5 hours or less to report HLA type test results to the OPO after the receipt of donor blood or tissue. (If a range was reported, the mid-point of the range was used.) Only 3 respondents stated that the average time was longer than 6 hours: 2 directors reported 8 hours and one reported 72 hours.

All directors reported that their laboratories typed the following HLA loci for deceased thoracic donors: HLA-A, HLA-B, and HLA-DR. The majority of the directors reported that they type the following HLA loci: HLA-Bw4/6 (95%), HLA-Cw (86%), HLA-DR51/52/53 (93%), and HLA-DQ (96%). Only 10 (14%) directors reported that their laboratories type thoracic donors at the HLA-DP locus.

Sixty-five histocompatibility directors responded to the following question: What general comments do you have about the proposed addition of HLA type to Policy 3.7.12.1? All supported the addition of HLA type in policy. In general, the directors commented that requiring HLA typing of thoracic donors would benefit sensitized thoracic candidates as well as enable virtual crossmatching. The majority of the directors were in favor of requiring HLA typing for thoracic organs, whereas one director commented that policy should make HLA typing of thoracic organs desirable. One comment was cautionary: it is possible that requiring HLA typing of thoracic organs could cause delays in procurement and transplant.

The comments also expressed included the need for mandating molecular typing, and a recommendation to type for HLA-DP. The latter recommendation was made by a few directors, some of whom commented that HLA-DP typing was not commonplace and may need to be required in the future. The directors also commented that HLA typing on thoracic organs should be performed as early as possible in the donor management process. Further, while many directors recommended that HLA typing of thoracic organs should be ready at the time of the match run, some suggested that providing these data to transplant centers at the time of an organ offer may be appropriate.

Analysis of Responses Provided by OPO Executive Directors

All of the OPO executive directors reported that on average, it took 6.5 hours or less for their laboratories to provide HLA typing.[C] Over half of the respondents indicated that the average time was 4 hours or less to provide HLA typing.

Half of the executive directors responded that their OPOs attempted to obtain HLA type of thoracic organs before making offers, and the other half reported that they did not. Some executive directors commented that their OPOs make offers while HLA type testing is being

[C] In analyzing the survey data, if a range was reported, the mid-point of the range was used.

performed; and, OPOs will accept a "provisional yes" from transplant centers while the typing is being identified. Some executive directors commented that their OPOs wait for HLA typing before performing a match run. One respondent commented that HLA typing was performed on thoracic organs before an organ offer, but only for recipients in the local area.

According to the responses of the thirty-four executive directors, it appears that those who receive and those who do not receive HLA typing prior to making organ offers are split near 50/50. While some executive directors reported that their OPOs waited for HLA typing results before running a match, the other OPOs, in general, reported that they began to offer organs while HLA typing results are pending.[D]

Nine executive directors (26%) reported receiving HLA typing before allocation less than half of the time. An additional eight executive directors (24%) reported having HLA typing before allocation 50% to 80% of the time; and, the remaining 17 OPO executive directors (50%) reported having HLA typing 80% or more of the time.

Most OPO executive directors reported that they needed about 2 hours to gather the sample necessary for HLA typing. Some directors commented that recovery of lymph nodes increased the time needed to obtain the sample. The reported increase in time ranged from 4 to 12 hours.

Eighteen out of 34 OPO executive directors responded that the length of time between the running of a thoracic match and the receipt of HLA typing results appears to vary – anywhere from one or two hours to 15 hours. (The remaining 16 executive directors either did not respond or reported that the length of time was "not applicable," as they had responded on an earlier survey question that HLA typing was available before allocation in a very high percentage of cases.)

Twenty executive directors (59% of the respondents) commented that requiring HLA typing of thoracic organs would either have no impact or minimal impact to the operation of their OPO. Some executive directors commented that a policy that requires HLA typing of thoracic organs would significantly delay the allocation process. Two respondents commented that the potential delay may not be favorable to the deceased donor's family: "Families are beginning to complain about how long the process takes from the time they consent to when they can get their loved one's body to [the] funeral home." One executive director wrote that "[t]his would significantly impair an OPO['s] ability to effectively allocate hearts in an expeditious way…[n]eed for donor HLA prior to allocation will impair an OPO to effectively plan for an OR." Another executive director commented that the proposed policy would require the OPO to submit blood samples to the histocompatibility laboratories at an earlier point in the donor management phase, and "[t]this would be a good thing."

[D] In current practice, approximately 70% of heart matches in the first four months of 2010 did have HLA type entered prior to the match run. So the practices reported in this survey of OPOs do not appear to be consistent with current data entry patterns in DonorNet®. The OPOs participating in this survey may differ from those who did not participate; or, the responses provided may reflect historical rather than current practice patterns.

Though not all executive directors reported that the proposed policy would negatively affect OPO operations, some expressed concerns that include the following (in addition to delays in the thoracic allocation process):

- Possible impact on multi-organ allocation;
- Longer time period for managing donors;
- Possible violations of policy;
- Possible loss of donors;
- Decrease in the utilization of hearts;
- Increase in donor management cost due to the potential delays; and,
- May prohibit allocation of hearts from unstable donors;

If the Thoracic Committee were to pursue the proposed policy modification, one executive director requested that transplant centers enter candidates' unacceptable antigens,[E] while another suggested that the Thoracic Committee not pursue this policy modification. Some executive directors commented that they were uncertain what actions the OPO community could take to mitigate any negative operational issues.

In general, while some OPO executive directors commented favorably on the proposed policy, a few urged the Thoracic Committee not to pursue the modification. If the proposal were to be pursued, a few executive directors recommended that the proposed policy be written so that if an organ had to be offered without HLA typing, this would not constitute a policy violation on the part of the OPO. A few directors were opposed to the proposed policy concept, whereas one director commented, "I am in favor of this policy but would even[t]ually like it to screen out unacceptable antigen patients so that they do not even print on our list."[F]

Policy Concept Proposed

To be consistent with the HLA typing requirements proposed by the Histocompatibility Committee during the March 19 to July 16, 2010 public comment cycle, the Thoracic Committee decided to propose the following:

1) The policy recommends but does not require that OPOs provide HLA type for each thoracic organ at the time of the initial organ match run;
2) However, an OPO *must* provide HLA type for each thoracic organ offered prior to the organ's final placement if a thoracic transplant center requests donor HLA type after indicating provisional acceptance through DonorNet®;
3) If the transplant center seeks donor HLA type, then it is responsible for communicating this request in the most expeditious method (telephone, etc.) to the relevant OPO; and,
4) If requested, the OPO must provide the following HLA type for a thoracic organ: HLA-A, HLA-B, HLA-Bw4, HLA-Bw6, HLA-Cw, HLA-DR, HLA-DP (only if available through the OPO's affiliated laboratory), and HLA-DQ antigens.

[E] Centers have the ability to report unacceptable antigens in UNet^{SM}.

[F] If the donor's HLA type is entered into UNet^{SM} prior to the match run, candidates with unacceptable antigens reported in UNet^{SM} are screened for antibodies found in the donor. DonorNet® does not currently screen candidates dynamically; therefore, if donor HLA type is added to DonorNet® after the match is run, candidates with unacceptable antigens will not automatically be screened from that match run.

Further, the Thoracic Committee requests that OPOs continue to comply with the following statement in Policy 3.2.4 (Match System Access) and not bypass sensitized candidates who appear at the top of a given thoracic match run:

> "The final decision whether to use the organ will remain the prerogative of the transplant surgeon and/or physician responsible for the care of that candidate. This will allow physicians and surgeons to exercise judgment about the suitability of the organ being offered for the specific candidate. If an organ is declined for a candidate, a notation of the reason for the decision refusing the organ for that candidate must be made on the appropriate form and promptly submitted."

Implicit in Policy 3.2.4 is that the match run be followed.

While the Thoracic Committee prefers that results of donor HLA type tests accompany initial thoracic organ offers, the proposed policy continues to allow OPOs to make initial thoracic organ offers without donor HLA type provided. Similarly, the proposed policy continues to allow transplant centers to accept organ offers on a provisional basis without knowledge of donor HLA type. For each thoracic organ offered to its candidate, the transplant center decides whether or not to request donor HLA type and whether or not to accept an organ offer without HLA typing results.

The proposed policy would only require OPOs to supply HLA data if a transplant center requested donor HLA type following its entry of "provisional yes" to a thoracic organ offer in DonorNet®; and, in such a case, the OPO must provide the donor HLA type described above prior to the transplant center's final acceptance of the organ. If requested HLA type cannot be provided for a thoracic organ, the OPO must provide a rationale, e.g., unstable donor.

Finally, the proposed policy will not affect the donor's family's wish to expedite the organ donation process.

At its meeting on September 2, 2010, the Thoracic Committee voted in favor of the proposed policy, and submitting it for public comment: (22-Supported, 0-Opposed, and, 0-Abstained).

Strengths and Intended Consequences

The proposed policy modification:

- Assists clinical efforts in identifying candidates with negative anti-HLA antibody crossmatch, which promotes the success of an organ transplant;
- Has the potential to improve equity by allowing sensitized patients access to appropriate organs; and,
- Has the potential to decrease mortality on the waiting list for sensitized thoracic candidates.

There is a greater potential that the transplant center will be aware of a suitable organ for the candidate as well as being aware of the potential for a negative virtual crossmatch.

Weaknesses and Unintended Consequences

The proposed modification may have no impact or have a negative impact on the utilization of deceased donor thoracic organs. Further, rates of graft failure may continue to occur regardless of favorable humoral immunity.

Supporting Evidence

OPTN/UNOS Policy:

The Thoracic Committee's proposal to add HLA type to Policy 3.7.12.1 is supported by the existing Policy 2.6 (Initiating Organ Procurement and Placement), which states the following:

> "In order to maximize the number of transplantable donor organs, tissue typing and crossmatching of an organ donor shall commence as soon as possible, ideally pre-procurement."

Literature Review and Survey Results

A very brief survey of peer-reviewed medical literature informs that:

- Virtual crossmatching is a useful tool in identifying unacceptable donor antigens for a sensitized thoracic candidate[2, 13];
- Crossmatch for anti-HLA antibody is a necessary clinical step in determining the suitability of a deceased donor organ offered for a given candidate, if the candidate is sensitized[1-14];
- Positive anti-HLA antibody crossmatch increases the likelihood of thoracic graft failure and recipient mortality post-transplant[1-14];
- Heart candidates with ventricular assist devices tend to have high (>10%) panel reactive antibodies (PRA), and are less likely to have negative anti-HLA crossmatches with offered deceased donor thoracic organs[2, 12];
- Lung transplant candidates with high PRA levels (>10%) are more likely to experience graft failure due to their sensitization[5, 7, 9]; and,
- Presence of Class I and Class II anti-HLA antibodies in a thoracic recipient post-transplantation increases the likelihood for graft failure[1, 3, 4, 9, 10, 12].

As in allocation of deceased donor kidneys, the literature reviewed here supports the prospective provision of HLA data on deceased thoracic donors. The literature reviewed indicates that some thoracic candidates have pre-formed anti-HLA antibodies, and this occurrence is likely to continue and possibly grow among candidates with ventricular assist devices[2, 12]. Thus, there exist challenges for managing or reducing the likelihood of post-transplant rejection due to anti-HLA antibodies. The mitigation of this challenge can occur, in part, through required submission of HLA data with all deceased donor thoracic organ offers.

Previously prospective crossmatches have been required for candidates with known preformed antibodies. One improvement to this clinical effort, however, rests with the provision of HLA data at the time of a deceased donor organ offer. With this proposed practice, donors with unacceptable antigens for a sensitized candidate can be identified and excluded from consideration for that candidate without requiring a prospective crossmatch. The availability of virtual crossmatching for thoracic organs

also has the potential to reduce post-transplant morbidity and mortality by preventing unanticipated positive crossmatches. Therefore, based on the literature as well as clinical expertise of its members, the Thoracic Committee recommends the provision of Class I and Class II HLA data for all deceased donor thoracic donors at the time of an organ offer.

Results of the survey of the histocompatibility laboratory directors and OPO executive directors suggest that these groups recognize the need to better serve sensitized thoracic candidates. While the histocompatibility laboratory directors commented favorably on the proposed policy, the support from the OPO executive directors was not unanimous – comments reported reflected about 60% of the OPOs, and therefore, it is possible that the practices and patterns reported may not be reflective of all OPOs. Some of the OPO executive directors expressed concern about delays in thoracic organ allocation and possible loss of thoracic donors. Also expressed was a concern that a requirement to provide HLA typing results on thoracic organs may result in policy violations. All OPOs who responded to the survey appear to be able to provide HLA typing results on thoracic organs prior to an acceptance (not provisional) of the organs.

During its June 7, 2010 meeting, the Thoracic Committee reviewed favorably (18-Supported; 0-Opposed; and, 0-Abstained) the following proposal distributed by the Histocompabitibility Committee: Proposal to Require that Deceased Donor HLA Typing be Performed by DNA Methods and Identify Additional Antigens for Kidney, Kidney-pancreas, Pancreas, and Pancreas Islet Offers. The Thoracic Committee opined that:

- HLA typing should be performed on donors, regardless of the organs offered; and
- HLA typing proposed for collection will be part of the Thoracic Committee's proposal to require HLA type information on all donor hearts and lungs. The typing proposed is "Identified splits of HLA-A,-B, Bw4, Bw6,-Cw,-DR and -DQ antigens."

To be consistent with the HLA typing requirements proposed by the Histocompatibility Committee, the Thoracic Committee decided to propose that the following HLA types be required: HLA-A, HLA-B, HLA-Bw4, HLA-Bw6, HLA-Cw, HLA-DR, and HLA-DQ antigens. In addition, the Thoracic Committee proposed provision of HLA-DP if it is available through an OPO's affiliated laboratory.

Adherence to OPTN Strategic Plan and the OPTN Final Rule:

The following strategic plan supports this policy modification: "to achieve the best use of donated organs, the OPTN will refine allocation policies by incorporating objective, measurable criteria related to concepts of donor risk/quality and recipient benefit." The accompaniment of HLA type data with each thoracic organ offer, combined with the transplant community's existing practice of recording anti-HLA antibody data for their candidates, promotes identification of candidates with negative anti-HLA antibody crossmatch with the donor's HLA.

The following constructs in the OPTN Final Rule support this proposal.

> "§ 121.8 Allocation of organs. […] (a) Policy development. […] (1) Shall be based on sound medical judgment; […] (5) Shall be designed to avoid wasting organs, to avoid futile transplants, to promote patient access to transplantation, and to promote the efficient management of organ placement;" […]

The Thoracic Committee's policy proposal, which is based on the literature, capability of histocompatibility laboratories to perform HLA typing, and the operational ability of OPOs to provide HLA typing results to transplant centers before acceptance of organ offers, promotes access to transplantation for sensitized thoracic candidates.

Committee's Plan for Evaluating the Proposed Policy:

Following implementation, the Thoracic Committee will monitor the provision of HLA type data, for thoracic organs offered to transplant centers, and requested by transplant centers. The Thoracic Committee will monitor reporting of HLA type to requesting transplant centers through data collected during the OPTN contractor's site audits.

Additional Data Collection:

This proposal does not require additional data collection in UNet[SM]. However, this proposal does require OPOs to provide donor HLA type if requested by a transplant center receiving a thoracic organ offer on behalf of its candidate. The proposal also requires OPOs and transplant centers to document communications with each other about, and provision and receipt of, donor HLA type as applicable.

Expected Implementation Plan:

This policy will be implemented 60 days after the Board of Directors approves this proposal.

Communication and Education Plan:

Communication and Education Activities			
Type of Activity	**Audiences**	**Deliver Method**	**Timeframe**
Policy Notice	• Directors of Organ Procurement Organizations • Lab Directors/Supervisors • OPO Executive Directors, Medical Directors, and Coordinators • Transplant Administrators and Program Directors • Transplant Physicians/Surgeons • Organ Recipients • Organ Candidates • General Public	Email	Submitted 30 days after approval by the Board of Directors
Training	• Directors of Organ Procurement Organizations • Lab Directors/Supervisors • OPO Executive Directors, Medical Directors, and	Telephone and Internet	Two weeks before implementation

	Coordinators • Transplant Administrators and Program Directors • Transplant Physicians/Surgeons		

Monitoring and Evaluation:

During on-site reviews, the OPTN contractor will review a sample of donor records based on the number of donors the OPO had in the previous year, and verify that donor HLA information was entered into both DonorNet® and Tiedi if it was requested for a thoracic organ offer by a transplant center.

Specifically, the OPTN contractor's Department of Evaluation and Quality (DEQ) will review the following to assess policy compliance:

- Transplant center's documentation in the patient's medical record of its request for HLA type for a thoracic organ offer;
- OPO's documentation in the donor's medical record stating receipt of the transplant center's request for HLA type for a thoracic organ offer;
- OPO's documentation in the donor's medical record that the OPO provided HLA type to the requesting transplant center;
- Transplant center's documentation that it received its requested HLA type from the OPO for a thoracic organ offer; and,
- OPO policy on the provision of HLA type for a thoracic organ offer when a transplant center requests HLA data.

DEQ staff will request a corrective action plan if the transplant center's documentation does not comply with the requirements of this policy and forward the survey results to the OPTN/UNOS Membership and Professional Standards Committee (MPSC) for review.

Policy Proposal:

3.7.12.1 Essential Information for Thoracic Offers. The Host OPO or donor center must provide the following donor information to the recipient center with each thoracic organ offer:

(i) The cause of brain death;
(ii) The details of any documented cardiac arrest or hypotensive episodes;
(iii) Vital signs including blood pressure, heart rate and temperature;
(iv) Cardiopulmonary, social, and drug activity histories;
(v) Pre- or post-transfusion serologies as indicated in 2.2.7.1 (pre-transfusion preferred);
(vi) Accurate height, weight, age and sex;
(vii) ABO type;
(viii) Interpreted electrocardiogram and chest radiograph;
(ix) History of treatment in hospital including vasopressors and hydration;
(x) Arterial blood gas results and ventilator settings; ~~and~~
(xi) Echocardiogram, if the donor hospital has the facilities~~.~~; and,
(xii) Human leukocyte antigen (HLA) type if requested by the transplant center.

If a transplant center requires donor HLA type prior to submitting a final organ acceptance, it must communicate this request to the OPO; the transplant center must document this request. If a transplant center requests donor HLA type prior to submitting a final organ acceptance, the OPO must provide the following, identified splits before the organ's final acceptance: HLA-A, HLA-B, HLA-Bw4, HLA-Bw6, HLA-Cw, HLA-DR, and HLA-DQ antigens. The transplant center may request HLA-DP type, but the OPO need only provide it if its affiliated laboratory performs related testing. The OPO must document provision of HLA type to the requesting transplant center.

The thoracic organ procurement team must have the opportunity to speak directly with responsible ICU personnel or the on-site donor coordinator in order to obtain current first-hand information about the donor physiology.

[There are no further changes to this policy.]

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