Introduction

The Histocompatibility Committee met via Citrix GoToMeeting teleconference on 10/14/2020 to discuss the following agenda items:

1. Project Updates
2. Committee Liaison Updates
4. Continuous Distribution
5. Discrepant HLA Typings Subcommittee Update
6. HLA Tables Review Subcommittee Update
7. Open Forum

The following is a summary of the Committee’s discussions.

1. Project Updates

UNOS staff presented updates to current committee-sponsored projects.

*CPRA Upgrade:*

UNOS is in contract negotiations with one of the bidders who had responded to the RFP. Committee members had no questions or concerns.

*IT Update:*

UNOS IT is planning to have the “other allele” option selectable for DPB1 available in UNet before the end of 2020. IT is discussing how to best incorporate HLA standardization across the UNet systems, and is considering incorporating the project into the 2020 HLA tables update that was approved by the Board of Directors in June.

One committee member commented that he liked the option for seeing the epitope selection separate from the allele selection for unacceptable antigens, and he thought that it would be less confusing. In addition, he liked that the user would only see the epitope and not all alleles within the epitope.

Another committee member commented that the subcommittee should discuss whether or not a lab would be able to select an epitope as unacceptable when a patient has a self allele within the epitope. He recommended a flag of some sort, but perhaps to consider not a hard stop within the system.

2. Committee Liaison Updates

Histocompatibility Committee members acting as a liaison to other committees discussed the current conversations on the represented committees and their applicability to histocompatibility.

*Organ Procurement Organization (OPO) Committee:*
No updates for the committee.

**Operations and Safety Committee (OSC):**

OSC has been discussing the DTAC US Public Health Service (PHS) proposal and the potential burden that storing living donor samples could place on programs. In addition, they’ve been discussing continuous distribution and data currently collected in relation to travel and efficiency.

**Heart Transplantation Committee:**

The Heart Committee has been discussing a potential allocation benefit for highly sensitized patients. There has been a concern expressed by committee leadership about standardization of unacceptable antigen testing and MFI, but that is likely not possible due to differences in laboratory testing and program variation in clinical practice. It would be helpful to increase education on the nuances of antibody testing, especially when they’re considering an algorithm for sensitization. This might be best to include in continuous distribution, instead of the current system.

One concern that the Heart Committee has is that they want to be able to see all offers to weight the options. They don’t want to have unacceptable antigens remove a candidate from a match run, but they’re also concerned that if that’s the case people may take advantage of the system.

One committee member proposed that thoracic allocation should follow a similar model to kidney CPRA, with unacceptable antigens determining sensitization points. There is more of a gray area in terms of what antibodies programs will allow for thoracic candidates versus renal candidates, and there’s a gray area in terms of many moderate strength antibodies. Kidneys can be more sensitive to allosensitization, and heart candidates can have a more complicated pre-transplant course that is also more dynamic. Heart candidates are often much sicker and while class II donor-specific antibodies can create a large amount of risk for vasculopathy, programs often have no choice but to accept a sub-prime offer in order to combat a patient’s mortality. If a patient is going to die in a month, programs are less concerned about 5-year graft survival rates.

The full committee would like to discuss this in more depth, and meet with the heart committee once they have had more time to discuss.

**Lung Transplantation Committee:**

The Lung Committee has been focused on continuous distribution and public comment from their proposal.

**Kidney Transplantation Committee:**

The Kidney Committee is starting to look at continuous distribution, and candidate biology will play a large role in this. They are going to be discussing sensitization, and a more granular CPRA. They may be evaluating points for DR and DQ matching instead of just points for 0 mismatch. While they’re very interested in this, we have to caution that we don’t have any data currently on the distribution of DR and DQ to see if that would disadvantage any racial or ethnic populations. There would need to be significant modeling and data before this would be feasible.

**Pancreas Transplantation Committee:**

The pancreas committee is also discussing continuous distribution and potential effects of the DTAC PHS proposal.

**Data Advisory Committee (DAC):**

Nothing relevant to the Histocompatibility Committee has been discussed at this point.


**Membership and Professional Standards Committee (MPSC):**

There have not been further meetings on Bylaws revision for Appendix C at this point. So far, the histocompatibility representatives have just been reviewing personnel/laboratory changes as needed.

3. **Kidney Paired Donation (KPD) Best Practices**

UNOS KPD Staff presented to the committee, asking if they had any recommendations for best practices for participating histocompatibility programs.

**Summary of discussion:**

The committee had the following questions:

- How many programs are involved in UNOS KPD?
  - About 80 have an active pair, but many more are signed on to participate

The committee posed the following suggestions for consideration:

- Allow the option to transfer unacceptable antigens from Waitlist as they are updated, not only when the patient is first listed for KPD (IT enhancements is currently considering this proposal)
- Require pre-screening of potential donors, and pre-refusal as appropriate, at least for donors with CPRA of 90% or greater
- Create targeted education to transplant programs with higher rates of refusal for HLA data
- Include a link to the specific candidates within UNet for the weekly preselect email, to facilitate the review
- Include HLA lab staff on the pre-screening emails
- Discussed a targeted survey on KPD listing practices to determine how people are utilizing the program

4. **Continuous Distribution**

UNOS Research staff presented on the current lung continuous distribution proposal and the biological factors and weighting under consideration.

**Summary of discussion:**

Committee members proposed that the biological attributes (sensitization, blood type, and size) may require different weights. They proposed that SRTR modeling on transplants by these different attributes would help create a better algorithm. UNOS staff reported that they are working to develop a tool to run simulations different ways using the various approaches to see if any approach disadvantages a particular group, and what approach is best for candidate access.

Committee members and research staff agreed that the goal for CPRA is to include as granular of results as possible for point assignment.

One committee member asked if any donor characteristics would be taken into consideration for a composite score, such as ABDR matching like for kidney. Donor characteristics could also be beneficial to consider for pediatrics, or differences between DCD and non-DCD donation.

Committee members discussed linear and non-linear approaches to point assignment for CPRA. One member proposed that the non-linear approach will help the most disadvantaged patients, and that it would help with system efficiency by encouraging programs to submit all appropriate unacceptable antigens.
Committee members were concerned about how to assign sensitivity points for thoracic candidates, as well as the current OPTN policy that does not require HLA typing be complete prior to executing thoracic match runs. They proposed that showing programs how many offers they decline for sensitized patients may also help them when discussing the benefit of inputting unacceptable antigens.

**Next steps:**
The Committee would like to continue the discussion on sensitization point assignment at a later date.

5. **Discrepant HLA Typings Subcommittee Update**
The Histocompatibility Committee Chair presented on the findings of the discrepant typings subcommittee and the current progress on their policy proposal.

**Summary of discussion:**
Committee members were disappointed that the early data after implementation of double HLA data entry did not show decline in the number of errors. Committee members also wanted more answers on why errors occur, what is submitted as the reason for the error.

Committee members discussed when errors occur pre- or post-allocation. Members were divided on whether or not a match run would be re-executed, as there is the potential for organ loss due to delay. Their primary concern with the project is to make sure that all updated HLA typing information is communicated quickly.

Committee members discussed the definition of a “critical” HLA discrepancy. They agreed that it would be a discrepancy that could potentially change a candidate’s ability to be transplanted with the donor typing, in whether or not an unacceptable antigen was appropriately evaluated.

Members were concerned about the potential for negative virtual crossmatch if the typing entered is incorrect. There is the potential that a program will not have a sample for a physical crossmatch until after an organ has been accepted.

Committee members agreed that any time an HLA typing is changed, there should be notification, whether or not that change is critical. Committee members agreed that there are too many variables, and that the best and safest practice would be to require a notification with every change.

**Next steps:**
The subcommittee will present their policy proposal to the full committee on December 8th, for the committee to vote on sending to public comment in January.

6. **HLA Tables Review Subcommittee Update**
The Histocompatibility Committee Vice Chair presented on the work of the HLA Tables Review subcommittee, and their intended direction.

**Data summary:**
The subcommittee is interested in including a table for null alleles, a table for DPA1, and all common and intermediate alleles from CIWD 3.0 in the next version of the HLA equivalency tables update.

**Summary of discussion:**
Members agreed that labs should be able to define common null alleles, but that the CIWD 3.0 list of null alleles includes ones that do not currently have reagents. They agreed that the committee should come up with a list of nulls to define for solid organ transplant, instead of leaving it to an outside organization such as ASHI. They want to make sure that there is guidance on how these are entered and
reported in DonorNet, since there has been confusion on this in the past and it could change matching for potential recipients. It may be less confusing to make it a policy requirement to define null alleles without entering them in DonorNet, especially if non-laboratory staff are entering the donor typings.

Committee members agreed that common and intermediate alleles should be stable for a significant period of time, since the CIWD 3.0 included a very large reference population. One of the concerns from the community has always been that there aren’t enough alleles present in DonorNet and Waitlist. Now the community has the ability to define alleles more precisely, and the community wants the ability to enter this information for more precise matching and allelic antibodies.

A committee member brought forward a concern that allocation based on allele specificities could be difficult or incorrect if labs only have low-resolution typing. However, another said that it would be caught on proficiency testing, and that rapid next generation sequencing (NGS) is becoming more available and affordable for donor HLA typings. The committee would like to allow programs to enter allele-level data if they have it available.

**Next steps:**
The subcommittee will take the comments back from the committee and continue to discuss possibilities for inclusion of null alleles.

7. **Open Forum**

**Summary of discussion:**
Members brought up concern on CMS’s lack of guidance on the acceptability of virtual crossmatching, especially with the upcoming removal of donor service area (DSA) in kidney allocation. They are concerned that the community is implementing a very large change without the well-defined guidance needed, in spite of it being over two years since the original request for information given by CMS.

**Next steps:**
HRSA representative is following up with CMS to see if there are any developments in their definition of compliance for crossmatching.

**Upcoming Meetings**
- November 10, 2020, 12 PM, Teleconference
Attendance

- **Committee Members**
  - Cathi Murphey
  - Evan Kransdorf
  - Idoia Gimferrer
  - Jennifer Schiller
  - Jerry Morris
  - John Lunz
  - Karl Schillinger
  - Manu Varma
  - Marcelo Pando-Rigal
  - Peter Lalli
  - Phyllis Weech
  - Reut Hod Dvorai
  - Taba Kheradmand
  - Tracy McRacken
  - Valia Bravo-Egana
  - Vikram Pattanayak
  - William Goggins
  - Yvette Chapman

- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi

- **SRTR Staff**
  - Katie Audette

- **UNOS Staff**
  - Adel Husayni
  - Betsy Gans
  - Courtney Jett
  - Darren Stewart
  - Emily Ward
  - James Alcorn
  - Kelsi Lindblad
  - Kiana Steward
  - Leah Slife
  - Nicole Benjamin
  - Rebecca Goff
  - Ruthanne Leishman
  - Susan Tlusty

- **Other Attendees**
  - Medhat Askar
  - Melissa Yeung
  - Vincent Casingal