Introduction

The Histocompatibility Committee met in Richmond, Virginia, on 10/24/2017 to discuss the following agenda items:

1. Review of HLA Tables
2. Histocompatibility Instructional Innovations Education Series
3. Updating CPRA Calculation
4. Discrepant HLA Typing
5. Kidney Allocation System (KAS) Review
6. Histocompatibility Bylaws Clarifications

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

1. Review of HLA Tables

The Review of HLA Tables (2016) proposal was out for public comment from July 31, 2017 – October 2, 2017. The Committee reviewed the public comments at the October 10, 2017, meeting and continued their review at this meeting.

Summary of discussion:

The proposal was part of the non-discussion agenda at the regional meetings. All eleven regions voted in favor of the non-discussion agenda with no comments about this proposal. Both major histocompatibility and laboratory personnel professional societies – the American Society of Histocompatibility and Immunogenetics (ASHI) and the College of American Pathologists (CAP) – provided public comments on the proposal. The American Society of Transplantation (AST), the American Society of Transplant Surgeons (ASTS), and the Organization for Transplant Professionals (NATCO) also provided feedback on the proposal during public comment.

All professional societies supported the proposal and several gave suggestions for edits to the equivalency tables. The proposal also received several comments from individuals, who generally supported the proposal while offering suggestions for improvements.

In total, the Committee received nine public comments. The Committee discussed all comments received and made several changes to the equivalency tables in response. The following sections detail several themes from public comment and Committee discussions:

Usage of G group vs. P group for Table 4-14: HLA DPB1 Unacceptable Antigen Equivalences

Several public comments addressed using P group alleles for Table 4-14: HLA DPB1 Unacceptable Antigen Equivalences instead of G group alleles. The Committee considered this in great detail, and eventually agreed to keep the G group allele designation. While the Committee agreed with many of the comments arguing in favor of using the P group, the
Committee believed that using the P group would mean that laboratories would be required to rule out all null alleles. Since the G group includes the nulls, the Committee decided to keep the G group alleles for the equivalency table.

The Committee will work with UNOS staff to provide education to members that will detail the changes made to the equivalency tables in this proposal.

Concerns over allele level data entry

One theme that emerged from multiple public comments related to data entry. Commenters were concerned that adding more alleles will make the equivalency tables more complex, cause confusion for members, and may possibly lead to data entry errors. The Committee recognized these concerns but believed that members need to move forward with advancements in the field because many highly sensitized candidates are being disadvantaged by not considering allele-specific antibodies. The Committee is also committed to providing educational resources to help members when the proposal is implemented.

Display of Table 4-14: HLA DPB1 Unacceptable Antigen Equivalences

Several public comments referenced the layout of Table 4-14: HLA DPB1 Unacceptable Antigen Equivalences. The Committee considered several different ways to display the antigens in this table. Based on conversations that included UNOS IT, the Committee decided to list the G group allele equivalences as well as each DPB1 one-to-one equivalency (i.e. HLA-DPB1 08:01 is only equivalent to itself). This allows for implementation of this equivalency table to be similar to all other loci tables. It also follows the logic of all other equivalency tables, which list out one-to-one equivalences for all antigens in UNet.

Addition of HLA-DPA1

ASHI and AST specifically mentioned that the Committee should consider adding HLA-DPA1 into the equivalency tables. The Committee acknowledged the importance of HLA-DPA1 equivalences and will work to add those into a future equivalency table update.

In addition to these edits, the Committee agreed to change some of the equivalences that had either been mislabeled or omitted based on feedback from the public comments. These occurrences were minor, and were primarily additions of missing one-to-one equivalences for DPB1 alleles.

The Committee considered taking out several broad antigens from the equivalency tables, which would then make members have to report the split antigens. Most of the Committee voiced support for this idea, and UNOS Staff will look into the frequency of these antigens and the impact of removing them.

Next steps:

In order to look into the impact of removing the broad antigens, the Committee did not vote on approving the policy language for Board consideration at this meeting. The Committee will reconvene in the next week to review the impact of removing the broad antigens and take a vote on the final policy language.

2. Histocompatibility Instructional Innovations Education Series

UNOS Instructional Innovations staff have been working with members of the histocompatibility community (and several Committee members) on educational offerings available through the UNOS Learning Management System.

Summary of discussion:
UNOS staff presented on the development of this project and recent work done by the workgroup, including the most recent video “Predicting the Future by Virtual Crossmatch.” UNOS staff shared a timeline for providing more educational offerings over the next year. The Committee was enthusiastic about the number of video views from the community. The next video “The Basics of Immunology” is set to be available in November 2017.

Next steps:
The Committee will continue to hear updates on the progress with the education series at future meetings as necessary.

3. Updating CPRA Calculation
The Committee sent a project idea that involves changing the way CPRA is calculated to the Policy Oversight Committee (POC) in October 2017.

Summary of discussion:
The Committee Liaison briefly updated the Committee on the current status of the CPRA project. The POC prioritized the project highly amongst the Goal 2 project ideas that had been submitted as of the POC’s October 2017 meeting. The Committee Liaison articulated that the POC will review all Goal 2 projects at a meeting after the Board of Directors Meeting on December 4-5, 2017.

The Committee reviewed data previously presented to the Committee on the September 26, 2017, call that broke down the donor count CPRA more granularly. One Committee member brought up that it is important to consider those candidates who will not get offers as a result of changing how CPRA is calculated and by adding HLA-DQA1 and DPB1 to the CPRA calculation. While the Committee agreed that this is important to consider how the changes will affect all candidates, some Committee members articulated that it is a center’s decision whether or not they list certain antigens as avoids in UNetSM and have those candidates get fewer offers. One Committee member brought up the idea that CPRA may not be the best way to weigh disadvantage for candidates. While there was not a clear alternative, the Committee member thought it was important to think about whether CPRA is the best measure for prioritizing individuals.

Next steps:
The Committee will move forward with this project if approved by the POC and Executive Committee.

4. Discrepant HLA Typing
The Discrepant HLA Typing Subcommittee (Subcommittee) has been discussing methods for decreasing the number of HLA data entry errors in UNet as part of the Addressing HLA Typing Errors project.

Summary of discussion:
The Committee heard an update from a Subcommittee member on recent discrepancy rates from the first two quarters of 2017. Overall rates remained relatively the same compared to past quarters, though there was a slight reduction in the number of errors in 2017. One Committee member commented that the educational letters that were sent out in the fall of 2016 to labs with error rates around 10% may have helped reduce the overall discrepancy numbers. UNOS Staff also articulated that the Subcommittee and Committee leadership had recently altered the definition of a discrepancy that UNOS Research Staff uses in the calculation for the discrepant reports provided to the Subcommittee. The new definition better reflects reporting for DQA1 and DPB1 by not counting allele level differences as discrepant (for example, DQA1 01:01 and
DQA1 01:02 would not be counted as discrepant). Since reporting at the allele level is not required by policy, this discrepant definition also aligns more with some center practices. This lowered the overall discrepant rates; when previous quarters were recalculated with the new discrepant definition, the 2017 quarters were still slightly lower overall.

The Committee discussed ideas for improving discrepant reporting. UNOS Staff presented an idea to produce reports for labs on a regular basis, such as annually or biannually. These reports could show statistics like the lab’s overall discrepant rate, the lab’s discrepant rate compared to the average rate across all member labs, and a lab’s historical discrepancies. The Committee was very receptive to this idea and UNOS Staff will look into the logistics of this going forward. The Committee also discussed developing a “threshold” for reporting certain labs to the Membership and Professional Standards Committee (MPSC). While the Subcommittee previously used a 10% discrepant rate for sending centers specific communication about their discrepancies, the Subcommittee is interested in better defining a measure for when a lab should potentially be referred to the MPSC for review. The Subcommittee previously reported labs in the Patient Safety Portal that appeared to have typed the completely wrong donor. The Subcommittee will continue to define this threshold. The Committee agreed that education for labs is going to be an outcome of this project.

As part of the Addressing HLA Typing Errors project, the Subcommittee will be distributing a survey to better understand lab specific practices. Due to limitations of the OPTN data, the Subcommittee is hoping to get more qualitative data from the survey to identify ways to limit the number of data entry errors and to identify educational opportunities. The Committee brainstormed some questions for the survey and provided the following possible questions:

- Who enters the HLA data at your center?
- What testing method does your center use?
- Does your center have a process for verifying the data? If so, what is that process?
- Does your center use middleware (HistoTrac, mTilda, iTransplant)?
- How does your center report parents/splits for ___?
  - Committee will include several examples of splits that are frequently at the parent level.

Next steps:
The Subcommittee will create a final draft of the survey questions and present it to the full Committee before distributing the survey in early 2018.

5. KAS Review

The Kidney Committee is discussing a couple of project ideas that have histocompatibility components.

Summary of discussion:
The Committee heard details about a recent Kidney Committee project idea that looks into the impact of the recent kidney allocation system on high CPRA candidates. As part of this project, the Kidney Committee is considering reworking the points candidates receive for their CPRA value. The Kidney Committee may also consider desensitization as part of the point allocation. The Histocompatibility Committee will be involved in this project if it is approved by the POC and Executive Committee.

The liaison to the Kidney Committee presented information on an active project that is looking at allowing deceased donor initiated chains for kidney paired donation. The Kidney Committee had
a concept paper out for public comment from July 31, 2017 – October 2, 2017, which outlined several possible scenarios for how this concept would work.

Next steps:
The Histocompatibility Committee is interested in the project and will hear updates from the Kidney Committee as necessary. A member of the Histocompatibility Committee joined the workgroup for this project and will also provide updates to the Histocompatibility Committee as necessary.

6. Histocompatibility Bylaws Clarifications

The MPSC sent two memos to the Committee seeking clarifications on sections of the bylaws related to histocompatibility laboratory personnel.

Summary of discussion:
The Committee briefly discussed the clarifications that the MPSC outlined in the two memos to the Committee. One memo dealt with key personnel requirements (specifically the amount of time key personnel had to spend at their lab if they were listed as key personnel at more than one lab). The second memo sought clarification on a section of the bylaws related to qualifications for a histocompatibility technologist. A couple other ideas for bylaws changes were discussed. One of these ideas included changing or clarifying what needs to be submitted when there is a change in key personnel as part of Bylaw C.5 Changes in Laboratory Personnel; currently, labs must send a complete list of lab personnel employed at the lab and not just the key personnel that has been changed. Committee members expressed that it is burdensome to complete this task and think that they should only have to provide the name of the person or persons who have changed positions. Another idea for a bylaw change was to add language that specifies how long a laboratory director can be out of practice and then return to practice. The Committee discussed current American Society for Histocompatibility and Immunogenetics (ASHI) and College of American Pathologists (CAP) standards for this, and will consider adding it in as a bylaw change.

The Committee Liaison discussed where a project like this would fall in the Strategic Alignment, and the Committee agreed that it is a Goal 5 (promote the efficient management of the OPTN) project.

Next steps:
The Committee agreed that a subcommittee should be created to discuss all bylaw changes and clarifications.


The Expanding HLA Typing Requirements project and the Annual Equivalency Table Update (2015) project both had post-production monitoring components to measure the impact of the implemented changes.

Summary of discussion:
UNOS Research Staff presented the results of the post-production monitoring on both projects. Some of the goals of the Expanding HLA Typing Requirements project were improving virtual crossmatching, preventing unexpected positive crossmatches, and promoting transplant safety by adding HLA-DQA1 and DPB1 unacceptable antigens in UNet. The project was implemented on January 21, 2016, and the post production monitoring showed a steady increase in the number of registrations with DQA1 and DPB1 reported. As of January 31, 2016, there were
2,772 registrations with DQA1 and/or DPB1 unacceptable antigens. By August 31, 2016, there were 8,800 registrations. The percentage of kidney offers refused due to positive crossmatch went down; previous to implementation, the rate of refusals was 0.48% and one year after implementation the rate went down slightly to 0.42%. Similarly, the rate of kidney offers accepted but not transplanted was lower one year post implementation. In the year prior to implementation, the rate was 10.3%; one year after implementation, the rate dropped to 8.65%. The Committee talked in detail about looking more deeply into the rate of kidneys that were accepted, turned down due to positive crossmatch, and then shipped to another center. This may become a future data request.

**Upcoming Meeting**

- November 14, 2017
Attendance

- **Committee Members**
  - Bob Bray
  - Cathi Murphey
  - Adam Bingaman
  - Laurine Bow
  - Cathy Gebhardt
  - Steve Geier
  - Peter Lalli
  - Chantale Lacelle
  - Mayra Lopez-Cepero
  - John Lunz
  - Gabriel Maine
  - Allen Norin
  - Rajalingam Raja
  - Carley Shaut
  - Craig Van De Walker
  - Melissa Yeung

- **HRSA Representatives**
  - Joyce Hager
  - Marilyn Levi

- **SRTR Staff**
  - Katie Audette

- **OPTN/UNOS Staff**
  - Alison Wilhelm
  - James Alcorn
  - Jason Chicirda
  - Emily Kneipp
  - Anna Kucheryavaya
  - Liz Robbins Callahan
  - Chad Southward