

**OPTN Histocompatibility Committee  
Meeting Summary  
October 16, 2019  
Chicago, IL**

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## **Introduction**

The OPTN Histocompatibility Committee met in Chicago, IL on 10/16/2019 to discuss the following agenda items:

1. Policy Oversight Committee Update (POC)
2. Committee Charge/Scope Review and Committee Liaison Role
3. Public Comment Review: Proposal to *Modify Appointment Process for Histocompatibility Vice Chair*
4. Project Discussion: HLA Equivalency Table Review Update
5. Demonstration of Critical Discrepancy Reports in Data Services Portal
6. Project Discussion: CPRA Calculation Update
7. IT Update
8. Future Project Discussion
9. Other Significant Items

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

### **1. Policy Oversight Committee Update (POC)**

The Vice Chair gave a brief update regarding the recent discussions at the OPTN Policy Oversight Committee (POC), including the selected themes: continuous distribution, more efficient donor/recipient matching to increase utilization and improved equity for multi-organ and single organ candidates.

#### Summary of discussion:

The Vice Chair shared the charge of the POC has evolved over recent months. In addition to their core responsibilities, the POC has asked OPTN committees to consider those potential projects that are aligned with three themes:

- continuous distribution
- more efficient donor/recipient matching to increase utilization, and
- improved equity for multi-organ and single organ candidates

The underpinnings for the evolution of their change due to a change in the OPTN contract that reclassified the POC as an "OPTN operating Committee". This means the POC will have an increased role in strategic planning activities, prioritize OPTN policy development, coordinate policy issues that have broad implications across OPTN committees, and ensure that all OPTN governance groups consider and justify compliance with the requirements of the OPTN Final Rule. The POC will continue to evaluate policy proposals prior to public comment. The goal of these changes are to maximize the benefit of OPTN policy changes to the transplant community.

UNOS staff indicated the “ask” of all OPTN committees was to consider new project ideas during near-term calls and meetings. These will be used by the POC to build the project plan and portfolio.

The committee had no questions or comments.

Next steps:

UNOS staff and committee leadership will include these themes in a future brainstorming session.

## **2. Committee Charge/Scope Review and Committee Liaison Role**

The committee discussed and voted on their charge. In addition, the Chair discussed future liaison responsibilities.

Summary of discussion:

### **Committee Charge Discussion**

The Committee reviewed the current charge and agreed that some improvements need to be made. Members expressed that care should be taken to keep the charge broad rather than limiting it to specifics. The committee has other requirements that are captured in OPTN bylaws and policies that do not need to be included.

Below are some suggestions members had:

- Need to add a clause to reflect more efficient candidate and donor matching
- Use the term clinical outcomes and transplant immunology
- Use the following sentence: assess, evaluate, synthesize the evolving challenges and emerging science and technology

The committee tabled this discussion to allow staff to revise the charge. Later on, a new draft of the charge was presented and the Committee voted in support of the charge below. (15 Yes; 0 No; 0 Abstain)

*The Histocompatibility Committee applies evolving science and technology in transplant immunology to develop, implement, and inform OPTN bylaws, policies, and clinical guidance for organ donation and transplantation. The committee provides subject matter expertise to the OPTN for issues related to testing, matching, allocation, personnel qualifications, and other issues in transplant histocompatibility and immunology. The committee’s goals are to promote patient safety, to strive to continuously improve clinical outcomes, and maximize the use of donated organs.*

### **Committee Member Liaison role**

Prior to the meeting the Chair asked members to volunteer as a liaison for the Histocompatibility committee. With the goal of getting input from other OPTN Committees about projects, the Committee is working on and giving input to other committees. The “ask” is that liaisons participate on their respective calls as their schedule allows and present that information during the full Committee calls every month.

Next steps:

Staff will send the revised committee charge to the OPTN Board for approval in December. In addition, members will be getting conference call invitations to their respective committees.

### **3. Public Comment Review: Proposal to *Modify Appointment Process for Histocompatibility Vice Chair***

The Committee will discuss the feedback received on the proposal to Modify Appointment Process for Histocompatibility Vice Chair. At the conclusion of the discussion, the committee voted whether to recommend this proposal to the OPTN Board of Directors.

#### Summary of discussion:

Staff presented the sentiment of this proposal by OPTN region and member type. Overall, the proposal was supported in all regions and across member types. There was minimal opposition. Members had no questions or comments. The committee voted to recommend this proposal to go to the OPTN Board of Directors for approval in December 2019. The vote was as follows 15 Yes; 0 No; 0 Abstain.

#### Next steps:

UNOS Staff will prepare the briefing paper consistent with the Committee's discussions.

- Consideration by OPTN Board Policy Working Group in early November
  - Review & offer recommendation to the Board
  - Recommend either the consent or discussion agenda
- OPTN Board consideration December 2019

### **4. Project Discussion: HLA Equivalency Table Review Update**

The full Committee will receive a brief summary of this project and discuss action items. This project is slated for January 2020 Public Comment.

#### Data summary:

The Chair of the subcommittee gave a brief overview of the project details and the timeline for this project.

- Timeline
  - Full committee vote on 12/10/19
  - Public comment 1/22/20-3/22/20
  - Board June 2020

#### Summary of discussion:

##### **Expedited Pathway discussion**

This project would like to include an expedited policy process per OPTN *Bylaw 11.8 Expedited Actions* to apply to future table updates. Policy language was presented to the committee and they had the following questions and concerns:

- When would this pathway apply?
  - For example if we are adding DPB1 epitope it would not, as epitopes are a substantive addition to policy.
- The HRSA representative mentioned the possibility of five individuals that could be recruited to submit objections and derail this expedited process.
  - Example: a vendor within the industry with commercial interest in derailing the expedited process.
  - The committee did not think this was realistic given where the vendors are in their testing capabilities.

- Members asked the cadence at which IMGT-HLA is updated, which was found to be quarterly. However many of these changes are not substantive.
- In the future, the Committee would like to use IMGT-HLA tables as a source for future table updates.
  - IT expressed some concerns about not having a reference for programming purposes.
- Another suggestion was to have a separate appendix of values that could be updated more frequently.
- The committee voted to approve the expedited pathway languages ( 16 Yes; 0 No ; 0 Abstain)

### **Shortened DPB1 unacceptable antigen table discussion**

The Committee is proposing to shorten the current DPB1 unacceptable antigen (UA) table in policy. The rationale for this change:

- To include meaningful content in policy
- Not limit the antigens available for members to select
- Allow the ability to select prior donor antigens in a relisted candidate
- This short list would include the G groups and the top 35 common and well-documented antigens, this approach should capture nearly 100% of possibilities for donors.

The committee had the follow questions or concerns about this proposed change:

- Asked about the inclusion of National Bone Marrow database (NMDP) data for DPB1 loci and that was reviewed by the subcommittee.
- The chair stated that this loci (DP) is unlike the others (A, B or DR) and therefore transplant programs may want the option to select UAs without a documented test result.
  - Another member chimed in that the interactions overtime in UNet<sup>SM</sup> may necessitate the need for a “not tested” option. A candidate is registered first then the HLA information is entered later.

### **Epitope Discussion**

The committee is proposing to add epitope based UAs assignment for the DPB1 loci. The rationale for this change is to introduce this concept to the field.

Members had some questions and concerns regarding the use of certain epitope and format of the proposed table:

- Is this an option for transplant programs to use? If the donor testing does not enter epitopes, does this need to change? The subcommittee chair showed the committee a slide that illustrated what it would look like and explained that transplant programs can select individual UAs rather than epitopes.
- IT staff expressed the need to be mindful, as these updates result in many questions.
- A member asked if this would this work with other lab information systems (LIS) that are out there.
  - IT staff commented that vendors are working with the OPTN on APIs (application programming interface).
  - The subcommittee chair also commented vendors usually make changes between OPTN Board approval and implementation.
- A member asked if the OPTN could put their tables in a central place such as GitHub. To make them more widely available for hospitals with their own “home grown” LIS?

- IT asked the committee to expand on how adding these epitopes would be similar to how BW4 and BW6 are in policy.
  - The subcommittee chair commented that this change does not change donor typing. It expands on the relationship between the epitopes and related antigens and alleles.
- Asked if KPD would change, and staff commented that it would.
- A member commented that future table updates to other loci would shift to this format due to less emphasis on serological equivalents and more emphasis on allelic values.

Overall, the Committee was supportive of using the expedited policy process, shortening the DPB1 UA table and the use of epitopes. They also expressed interest in using a second table or appendix for other DPB1 values. Lastly, the subcommittee chair stressed the importance for a quality assurance check of all the tables in policy to ensure no omissions.

Next steps:

Staff and subcommittee leadership will send out a doodle poll for scheduling an upcoming subcommittee call. On the next subcommittee call, members will do a comprehensive table review.

**5. Demonstration of Critical Discrepancy Reports in Data Services Portal**

Summary of discussion:

Research conducted a demonstration on the use of the Discrepancy Reports in the Data Services Portal. Members suggested developing education on the description/ definition of reasons why typing is marked as discrepant. It was also remarked that a future policy changes should include mandating all typing be done by molecular methods.

**6. Project Discussion: CPRA Calculation Update**

The committee received an update on the status of this project, heard two data presentations.

Data summary:

1. Staff gave a brief update and a timeline on the status of the project.
  - New project timeline of Fall 2020 Public Comment
2. A committee member gave a research presentation about CPRA data.
  - Background
    - Current OPTN CPRA calculator includes HLA-A, -C, -B, -DQB1, -DRB1
    - Many sensitized candidates have unacceptable antigens (UA) for HLA-DQA1, -DPA1, -DPB1
    - In a Canadian regional cohort, 18% of total had HLA-DQA1 UA; 27% of total had HLA-DPB1 UA
    - Earlier data showed that a haplotype reference panel constructed from HLA typing obtained from volunteer stem cell donors is suitable for use in calculation of CPRA for solid organ transplant candidates
  - Summary:
    - Approximately 13-14% of candidates have HLA-DQA1 or HLA-DPB1 UA-HLA
      - African American patients are more likely to have these UA-HLA
    - Many candidates with HLA-DQA1 or HLA-DPB1 UA-HLA are highly sensitized
    - Inclusion of HLA-DQA1 or HLA-DPB1 UA-HLA will lead to a substantial reclassification of candidates within the existing CPRA categories
    - A genotype-based or haplotype-based strategy for CPRA calculation yield similar values

3. Research staff gave a presentation on the projected impact of *Adding DQA1 and DPB1 to CPRA on Offer Metrics*
  - Background
    - Proposed CPRA calculation will incorporate DPB1 and DQA1
    - Currently, candidates receive no CPRA “credit” for listing DPB1 or DQA1 as unacceptable
    - In this presentation:
      1. DPB1/DQA1 UAs and refusal due to positive cross match
      2. DPB1/DQA1 UAs and organs accepted but not transplanted into the intended recipient
  - Summary
    - Adding DPB1 and DQA1 to CPRA is unlikely to have large impact on offer refusals system-wide
      1. For high CPRA candidates, potential for large impact on number of undesired offers received
    - 13% of waitlist modifications included DQA as UAs and 15% of waitlist modifications included DPB as UAs
    - Adding DQA1 and DPB1 to CPRA is unlikely to affect the rate of accepted offers not transplanted into the intended recipient

Summary of discussion:

**Staff update discussion**

- There were no comments or questions.

**CPRA data presentation discussion**

The presenter recommended a single table format going forward for gains in efficiency of calculations as well as using genotype (counts) methodology for future CPRA calculation. The committee had the following questions and comments:

- Will this impact waiting time or just accuracy of CPRA.
  - The presenter responded by saying both, this may affect some candidates waiting time if they move to a higher classification for allocation priority.
- HRSA representative ask if there is a risk of losing organs.
  - The presenter responded by saying no, a transition to an 11 loci calculation will not affect the number of organs transplanted and increase the number of sensitized candidates who are transplanted.
- Is there linkage between blood groups (and relative size of the population of each blood type) and CPRA?
  - The presenter responded by saying that there is some relationship, e.g. there is a higher frequency of ABO “AB” are highly sensitized.
- This model gives this the ability to better account for ethnicity and is a prudent change.
- Candidates make antibody to the genotypes, not the haplotypes.
- Would be interesting to see the modeling with the new calculation; would the shift up in CPRA yield an increase in the number of kidney transplant candidates that are so highly sensitized they receive no organ offers.
  - Another member suggested that a bolus of transplants in highly sensitized candidates would occur after the implementation of a new change to CPRA.
- A member commented that in the future the OPTN should collect data on loci DPA1.

## **Adding DQA1 and DPB1 to CPRA on Offer Metrics discussion**

During the presentation, staff announced the need to put out an RFP (Request for proposal) to assist the OPTN on this project.

- Members encouraged the OPTN to make sure NMDP is aware of this and that this work is within their scope.
- Other members encouraged the Committee to consider the respondents and to assess whether they are capable to doing the work.

Members had the following questions and comments regarding this presentation:

- If an offer is made to a 100% CPRA potential recipient at a distance and the importing program is given local back up, is this counted in the data for a transplant into a different recipient that originally accepted?
  - The presenter responded that this is correct.
- Having these two loci in the CPRA may not influence program behavior. It is the program's decision whether to enter the UAs. That said it is still an important change to make because it will allow greater equity in access to transplantation.
- Need to be careful about offer refusals by CPRA as some transplant programs do not list UAs and opt to see how positive the cross match result is.

## **7. IT Update**

UNOS IT staff will update the committee on upcoming IT initiatives

### Summary of discussion:

- IT staff profiled their experience at ASHI.
- They shared the need to standardize HLA data collection across all Secure Enterprise apps. This is a value-add initiative to be prioritized over the programming with addressing HLA typing errors project.

Members had the following comments:

- Some of the errors seen in the discrepancy reports are critical in nature and can present a safety issue. As a result, there is substantial patient safety improvement by programming the addressing HLA typing errors project.
  - IT staff responded by asking if it would be of value to address the enhancements to HLA data collection in order of priority, e.g. in DonorNet®?
  - Members responded by saying yes and suggested the next priority would be Waitlist<sup>SM</sup> then KPD<sup>SM</sup>.
- Expressed disappointment to hear the delay in the implementation of addressing HLA typing errors project.
  - IT staff commented that this is being addressed and there is a dedicated programming team. The work will begin at the end of October with an implementation target in February 2020. Future touch points with the Committee will be occurring to ensure the programming is on-point.

## **8. Future Project Discussion:**

The Committee had a discussion on future project ideas.

### Summary of discussion:

The committee discussed several future projects:

1. Revisions to OPTN Bylaws, Appendix C Membership Requirements for Histocompatibility Laboratories
  - This a project is a component of larger Bylaws review initiative by OPTN Membership & Professional Standards Committee.
  - Below are the current proposed changes:
    - Clarify Functional Inactivity for histocompatibility laboratories
    - Agreement across requirements for key personnel
    - Update reference to ASHI standards
  - Members had the following comments:
    - Overall members felt this was straightforward and approved of this project
    - Need to ensure that CAP is appropriately referenced in the Appendix C.
2. Enhance Donor-Recipient Matching - DR & DQ Mismatches and Transplant Outcomes
  - The committee has previously looked at this a few times. It had been found that DR matching had more impact on outcomes as compared to zero mismatches.
  - Members had the following comments:
    - Not convinced that it makes sense from an equity standpoint. The ethics view could say this approach would potentially disadvantage minorities.
    - This would disadvantage homozygous population
    - This would help look at the longevity of the organ/graft.
  - Overall members were not in consensus on this project and determined this requires more insight and research.
3. Other projects
  - Members discussed continuous distribution and were concerned about physical versus virtual cross match, limited donor material and the difficulty in predicting cross matching when serving multiple transplant programs.
  - Expressed interest in working on ABO projects
  - A process or guidance document for when a transplant recipient (whether solid organ or bone marrow) becomes an organ donor. There is a need to capture the HLA information from the index donor and to know if the transplanted organs are being transplanted again into another recipient.

#### **Upcoming Meeting(s)**

- November 12, 2019 Full Committee Call
- December 10, 2019 Full Committee Call