**OPTN Histocompatibility Committee**
**Meeting Summary**
**November 8, 2022**
**Conference Call**

**John Lunz, PhD, D(ABHI), Chair**
**Gerald Morris, MD, PhD, Vice Chair**

**Introduction**

The Histocompatibility Committee (the Committee) met via Citrix GoToMeeting teleconference on 11/08/2022 to discuss the following agenda items:

1. Welcome
2. CPRA Calculator and Update
3. HLA Confirmatory Typing Discussion and Vote
4. Kidney and Pancreas Continuous Distribution Discussion
5. New Project Follow-up from In-person Meeting
6. Closing Remarks

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

**1. Welcome**

The Chair welcomed Committee members.

Summary of discussion:

There was no further discussion by the Committee.

**2. CPRA Calculator and Update**

United Network for Organ Sharing (UNOS) staff gave an update and an overview of the changes to the calculated panel reactive antibody (cPRA) calculator. She explained that entering the unacceptable antigens will still look the same as it currently does in production. The change that will be seen is when an unacceptable antigen is selected from one of the loci added to the calculation, or an allele-level unacceptable antigen is selected, the cPRA change is seen after selecting 'calculate' or 'save.' Having no unacceptable antigens entered will result in NULL rather than '0.' In the OPTN Computer System and on reports, a cPRA of NULL will appear as blank. CPRA will be calculated and stored for all organs.

UNOS staff noted that a contractor confirmed his IT group incorporated the OPTN cPRA application programming interface (API) changes out on Beta into their system. The contractor ran some test cases and found OPTN results to be matching with their expected results. She stated a data report for Change in cPRA is on the Data Services Portal. The report is built off transplant center data. The largest drops in total cPRA will likely be due to misrepresentation of linkage disequilibrium in 2013 cPRA.

Summary of discussion:

A member asked if the cPRA tables will be available similar to the availability of the 2013 tables. UNOS staff responded that the genotype frequency tables are two million rows, so she will need to follow-up on availability. The member noted it may be good to have a reference on how to outsource these tables.

The Chair asked if there will be a footnote to denote the change from '0' to NULL. UNOS staff explained there is not a footnote currently, but additional education can be created. She suggested education explaining that if no unacceptable antigens (UAs) are entered, there will be a blank field, but if UAs are entered then there should be some value, either 0 or more. The Chair agreed. A member asked if it is possible to have a 0 when a patient has no UAs or antibodies. In the match run, a NULL is converted to a '0' but for research purposes no UAs entered will show up as NULL to show nothing is calculated.

**3. HLA Confirmatory Typing Discussion and Vote**

The Chair gave an overview of the proposal the Committee will send to January 2023 public comment. The policy change will require HLA confirmatory typing tests. Confirmatory tests may be conducted simultaneously. This will require two separate samples and best practice is to use two different test kits. Discrepancies should be handled according to current policy in place.

This proposal stems from a letter received by the Committee and the OPTN Membership and Professional Standards Committee from John Hopkins.

The OPTN Membership and Professional Standards Committee asked if a typing could be performed with lymph node samples and blood samples. The Committee recognized this would be optimal, but it may not be available by laboratories to routinely analyze. The ASHI Directors Meeting allowed ASHI members to vocalize concern for timing and staffing, but the Committee has incorporated this into their decision process for moving forward and during the public comment period these concerns should be submitted.

The Committee reviewed the final policy language for this proposal and 13 members voted to approve this language, while four members abstained from voting.

Data Summary:

The number of critical discrepancies related to donor typings reported quarter to quarter are significant. There were 33 critical discrepancies within 2021 and this resulted in a rerun of the match run 19 times. From the incorrect sample/sample integrity, 18 have occurred since 2015. 12 have been reported through the patient safety portal. This policy aims to minimize the errors as much as possible.

Summary of discussion:

The Scientific Registry of Transplant Recipients (SRTR) staff stated most discrepancies come from using one typing assay. He suggested mandating two different vendor assays. He explained most of the issues lie with DQB1 typings and using the same vendor will not resolve this discrepancy. He noted most labs already do this, so the burden would not be large on laboratories. The Chair responded that some laboratories use only one technology, and it will create unnecessary burden on them to use two different vendors. A member stated using two vendors will be safer, and workload will double by requiring two typings. The Chair stated that if a vendor has difficulty producing their reagents, then laboratories would have issues complying with policies. The member argued a lab could use real time polymerase chain reaction (PCR) and sequence-specific oligonucleotide (SSO), but the Chair stated his lab does not have SSO.

The member suggested two different kits from the same vendor. The Vice Chair stated the Committee can tell people what needs to be done, but they should not tell them how to do it. A member agreed with requiring two different assays, and she asked to abstain from the vote. She asked to include a caveat that states if two reagents are available then the laboratory would have to use two different assays. She stated if the Committee hopes to address the issue, two assays must be required because

most of these errors are not sample switches. SRTR staff agreed that using two different reagents is critical for virtual crossmatch.

The Chair encouraged members to submit their concerns in public comment.

**4. Kidney and Pancreas Continuous Distribution Discussion**

UNOS staff explained that the Review Boards Workgroup will establish a review board for kidney and pancreas and identify exceptions that can be requested in continuous distribution. The Review Boards Workgroup is developing recommendations, which will be sent to the OPTN Kidney Transplantation Committee and the OPTN Pancreas Transplantation to approve for the continuous distribution proposal going to August 2023 public comment. Over the past few weeks, the Review Boards Workgroup has been evaluating each attribute to determine whether an exception could appropriately be submitted for each attribute. Exceptions are attribute-based, candidate-specific, and known prior to the time of match. They are typically submitted where the allocation system or rating scale may not be appropriately representing the candidate.

UNOS staff noted the Review Boards Workgroup did not feel that, clinically, there would be cases where it would be appropriate for a candidate to request an exception based on cPRA or blood type. UNOS staff requested feedback from the Committee on this.

Summary of discussion:

The Chair explained the Committee discussed an exception for patients that undergo desensitization and have a reduction in their antibodies. Their cPRA may be lowered with desensitization, but some centers may want to keep their candidate's cPRA points. The Ex-officio said this should not move forward as an exception.

The Ex-officio stated that there are patients that have had a stem cell transplant that was ABO mismatched, and their blood type changes afterwards. He has debated how to list this blood type, and this would be a situation where a center determines how to list this patient. Members agreed this is a common occurrence, and perhaps molecular typing should be accepted as a supporting document for an exception. UNOS staff noted that is covered under Policy 2.6 Deceased Donor Blood Type Determination and Reporting for deceased donors and Policy 3.3 Candidate Blood Type Determination and Reporting before Waiting List Registration for candidates. She explained methodologies to address blood typing discrepancies when forward and reversed blood typings do not match can be found in guidance. The member explained the exception would fall under complications of listing and whether organs should be considered for a candidate with a reverse typing against the donor's blood type. Members agreed this should be left up to policy created by individual transplant programs. The Committee agreed there should not be any exception pathways based on cPRA or blood type for kidney and pancreas continuous distribution.

**5. New Project Follow-up from In-person Meeting**

The Committee reviewed projects discussed at their in-person meeting on 10/7/22. The Committee discussed which projects should be prioritized and additional ideas that should be submitted. The Chair noted the Policy and Guidance Update will move to August 2023 public comment after CMS proposed changes to CLIA are implemented. This will also look at adding As to BW4 or keeping AW4 separate. The Committee discussed removing the cPRA signatures for the greater than 98% cPRA candidates' medical records. The Committee aims to require HLA typing for any organ allocated and requires a crossmatch with the appropriate materials to improve the efficiency of the match run.

Summary of discussion:

The Ex-officio noted that requiring HLA typing for any organ allocated is essential. He stated there is a very small number of match runs executed without a typing, so the burden would be small on organ procurement organizations.

**6. Closing Remarks**

The Chair thanked the Committee for their participation and encouraged members to send any additional project ideas to UNOS staff or Committee leadership.

Summary of discussion:

There was no further discussion by the Committee.

**Upcoming Meetings**

- December 13, 2022, 12 p.m. EST, teleconference

**Attendance**

Committee members:

- Amber Carriker
- Andres Jaramillo
- Caroline Alquist
- Gerald Morris
- Hua Zhu
- John Lunz
- Kelley Hitchman
- Lenore Hicks
- Laurine Bow
- Manu Varma
- Marcelo Pando
- Omar Moussa
- Peter Lalli
- Qingyoung Xu
- Reut Hod Dvorai
- Valia Bravo-Egana
- William Goggins
- Yvette Chapman

SRTR Staff

- Katherine Audette
- Rajalingam Raja

HRSA Representatives

- Jim Bowman
- Megan Hayden

UNOS Staff

- Amelia Devereaux
- Alex Carmack
- Karen Wooten
- Kayla Temple
- Krissy Laurie
- Matt Belton
- Susan Tlusty
- Taylor Livelli
- Thomas Dolan