

OPTN Histocompatibility Committee**Meeting Summary****June 14, 2022****Conference Call****Peter Lalli, PhD, F(ACHI), Chair****John Lunz, PhD, D(ABHI), Vice Chair****Introduction**

The Histocompatibility Committee (the Committee) met via Citrix GoToMeeting teleconference on 06/14/2022 to discuss the following agenda items:

1. Update to Histocompatibility Policies/Guidance

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

1. Update to Histocompatibility Policies/Guidance

- Candidate antibody screening

A committee member reviewed sections of the 2017 Histocompatibility Guidance Document. The content suggested for removal is standard complement-dependent lymphocytotoxicity (CDC) and Enzyme-Linked Immuno Sorbent Assay (ELISA)-based from [Table 3 Assays to Identify Antibody to HLA: Screening, Specificity, or Crossmatching](#). The presenting member also suggested the removal of the reference to multi-antigen beads and "For PRA without background from cell membranes" under Flow cytometry-based assays in Table 3, since they are not effective in determining single antigen specificities. The presenter recommended to remove "crossmatches" under "is used" regarding determination of isotype of antibody and questioned the explicit mention of C1q in solid phase assays. Finally, the presenting member suggested removing "treatment of serum" and "crossmatches" from "to rule out contribution by auto-antibody."

- Candidate HLA typing

Committee members discussed [OPTN Policy 4.3.B HLA Typing for Candidates](#), "Laboratories must perform HLA typing on a kidney, kidney-pancreas, pancreas, or pancreas islet candidate and report results for HLA A, B, Bw4, Bw6, and DR to the transplant program prior to registration on the waiting list." Members discussed whether the requirement should be molecular typing or are serologic equivalents acceptable for candidate HLA typing. Additionally, members examined whether HLA typing should be completed for other organs.

Summary of discussion:

- Candidate antibody screening

The committee members agreed that standard complement-dependent lymphocytotoxicity should be removed from guidance because it is antiquated and there is a lack of routine crossmatch trays being conducted to assess antibodies. The same was decided for anti-human Globulin- enhanced cytotoxicity.

The Chair voiced concern about the removal of ELISA because AT1R is ELISA based, and as non-HLA antibody field grows it may become important. The presenting member suggested the guidance

specifies this - table is labeled 'Assays to identify candidate antibody HLA' - which means there may need to be a new table. The guidance could provide a test for anti-AT1R or reflect emerging new non-HLA antibodies. The Chair urged a title change of 'Transplant related antibody testing' to encompass everything.

The Vice Chair stated if we add reference to non-HLA more types of testing would need to be incorporated to be inclusive. Committee members voiced concern about whether the guidance document should be comprehensive or be best practice focused. The more the committee includes, the more it looks like these types of testing are the recommended options. A committee member noted there is not a recommendation for routine monitoring on non-HLA antibodies, so the concern is that what is missing will be viewed as not recommended with unnecessary additions. The guidance document should reflect what the best practice is to meet the policy requirements. A committee member noted the importance of making sure we are consistent with current policies and with ASHI. UNOS staff noted we are running these changes by ASHI staff. ASHI uses 'solid phase' terminology, so it makes sense to remove ELISA and use this language to avoid confusion. ELISA and various Flow cytometry assays could be grouped under solid phase to create better guidance.

Regarding the removal of language from Flow cytometry-based assays, members stated a lot of labs still use these methods for screening. A member stated it is the primary specificity mold used by the Hopkins HLA lab. A committee member reiterated this is not guidance for optimization, but rather guidance for compliance. UNOS staff noted we do not have a routine requirement for routine sensitization.

Members agreed to remove the assay regarding the determination of isotype of antibody and explained it is outdated.

Regarding "to rule out contribution by auto-antibody," members brought up labs that keep cytotoxicity antibody panel up and running in the lab that are willing to cross cytonegative antibodies. Members posed this as an adjunct method of screening, rather than a primary method of screening. Members concluded that knowing a solid phase method must be used and that no other organs besides kidney require antibody screening, this should be removed.

- Candidate HLA typing

A member stated there is sufficient data to experiment with molecular typing, but it is not widely practiced in the U.S. This would also prove too costly to labs, and physicians do not have current understandability of the results. Members argued typing should move towards a P Group and keep it molecular. Another member stated it is difficult to narrow down typing into a singular P Group.

The Chair stated the discussion should be how will we deal with WHO nomenclature regarding serologic equivalence. A member stated there is an increased cost and time to get patients listed, and there needs to be a significant enough reason to require programs to take this on. A member asked if you are required to do a DNA based typing, why are you not required to do a molecular recording. The member responded recipients do not have to and heart and lung does not require it. It is a heavy lift to move away from serologic nomenclature as a requirement. The Chair noted if labs are adding unacceptable antigens into Continuous Distribution schema for lung and heart and people can input unacceptable antigens - hypothetically they could potentially put in all types of antibodies and it would not be able to filter this out, which could cause this to unnecessarily exclude donors.

A member stated a molecular method to get to a serologic equivalent typing result at the very minimum should be required for recipients, since this is required for donors. A member agreed typing should be molecular, but reporting can be serologic equivalent or follow the WHO nomenclature. A member questioned whether there is sufficient evidence to require typing at ABDR or all loci. The member stated the lack of the ability to collect data to evaluate outcomes is a real consideration and may pose an argument. The member argued that with no molecular typing the number of labs that may report a false positive DQ5 DSA is too high. The original member agrees with this, but notes that this is a huge change.

UNOS staff suggested pulling a data pool to inquire which labs are using serologic typing. Members voiced support for this because it would be deemed inappropriate to only use serologic typing methods. A member asked if the committee should survey HLA labs to make sure we are driving forward best practices, but not hindering transplants by stopping lab operations that are performing serologic typing. A member noted serologic typing is used for disease association, etc., so this would need to be pulled out. UNOS Staff agreed to reach out to ASHI to see which labs are using serology for candidate typing and if when molecular typing is used, a full genotype is pulled. A member requested this additional data because a full genotype may be needed in post-transplant setting to accurately assess DSA presence or absence. The member is also curious to see if this is completed for other organs as well.

Upcoming Meeting

- July 12, 2022, 12PM ET, Teleconference

Attendance

- **Committee members**
 - Amber Carriker
 - Andres Jaramillo
 - Annette Jackson
 - Bill Goggins
 - Evan Kransdorf
 - Gerald Morris
 - Idoia Gimferrer
 - Jennifer Schiller
 - John Lunz
 - Karl Schillinger
 - Laurine Bow
 - Manu Varma
 - Omar Moussa
 - Peter Lalli
 - Qingyoung Xu
 - Reut Hod Dvorai
 - Valia Bravo-Egana
 - Vikram Pattanayak
- **SRTR Staff**
 - Katherine Audette
- **HRSA Representatives**
 - Jim Bowman
 - Marilyn Levi
- **UNOS Staff**
 - Amelia Devereaux
 - Courtney Jett
 - Sarah Scott
 - Rebecca Brookman
 - Taylor Livelli