OPTN Histocompatibility Committee
Meeting Summary
June 13, 2023
Conference Call

John Lunz, Ph.D., F(ACHI), Chair
Gerald Morris, MD, Ph.D., Vice Chair

Introduction

The Histocompatibility Committee ("Committee") met via Citrix GoToMeeting Teleconference on 06/13/2023 to discuss the following agenda items:

1. HLA Equivalency Tables Update 2023
2. Update: Data Related to Critical Discrepancies
3. Reporting Critical Discrepancies to the OPTN

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

1. HLA Equivalency Tables Update 2023

The Committee discussed the additions and updates to the HLA equivalency tables.

Presentation Overview:

Main Equivalency Table Changes and Updates:

- Addition of all IMGT/HLA p-groups with more than a single two-field allele
- Update matching tables so all HLA values within a serologic allele group match each other
- Update DPB1 tables to IMGT/HLA 3.52.0

Summary of discussion:

Decision #1: For matching equivalences, the Committee decided to strike all split alleles from DR3 to make DR3 equivalent to itself and have the remaining alleles be represented under DR17 and DR18.

Decision #2: For unacceptable antigen equivalences, the Committee decided to leave B46 and B73 out from Bw6 so individual laboratories may screen them as needed.

Decision #3: The Committee decided to separate unacceptable antigens DRB1*14:54 and DRB1*14:01 and list them as equivalent to themselves.

Vote: The Committee unanimously voted to pass and send the proposed revisions to the equivalency tables for summer public comment.

Decision #1: For matching equivalences, the Committee decided to strike all split alleles from DR3 to make DR3 equivalent to itself and have the remaining alleles be represented under DR17 and DR18.

The Committee decided that removing the specific alleles from DR3 matching equivalences and placing them with DR17 and DR18 was the best option considering the convention and practice would remain

similar to other cases. More specifically, if the same convention holds true for those specific alleles in B, they should hold true for those in DR.

Decision #2: For unacceptable antigen equivalences, the Committee decided to leave out B46 and B73 from Bw6 so individual laboratories may screen them as needed.

The Committee considered whether B46 and B73 should continue to be excluded if Bw6 is listed as unacceptable. The group decided that they should not be listed with Bw6 because it may impact organ offer access. For example, if B46 and B73 are listed within Bw6 and a transplant program receives donors that have Bw6, patients that are compatible may automatically be excluded. In addition, a member noted that there are sometimes Bw6 alternative epitopes. They did not see any harm in keeping B46 and B73 separate from the group considering that most labs will do a virtual crossmatch.

Other members suggested that the two should be grouped with Bw6 considering that it is uncommon, and some may not realize that they would need to separately list B46 and B73 as unacceptable. Despite this suggestion, the Committee decided that, to ensure access and laboratory autonomy, B46 and B73 should be left out from Bw6.

Decision #3: The Committee decided to separate unacceptable antigens DRB1*14:54 and DRB1*14:01 and list them as equivalent to themselves.

Even though these two alleles are equivalent at the p-group level, there are instances where a lab may find one positive and one negative and may wish to select one allele as unacceptable but not the other. However, if DRB1*14:54 and DRB1*14:01 are listed as equivalent, selecting one will automatically remove the other and take away choice. Listing them together may force laboratory practice by not allowing people to call one and not the other. In addition, a member noted that there is an epitope difference between DRB1*14:54 and DRB1*14:01. For these reasons, the Committee decided to list these unacceptable antigens as equivalent to themselves only.

Vote: The Committee unanimously voted to pass and send the revised equivalency table proposal for summer public comment.

Yes: 23, No: 0, Abstain: 0

Next steps:

OPTN contractor staff will finalize and submit the proposal for summer Public Comment.

2. Update: Data Related to Critical Discrepancies

The Committee discussed an update to the data pulled for critical discrepancies. The additional data was requested at the May 9th full committee meeting during discussion of the patient safety portal reports for discrepant HLA typings.

Data summary:

Main Findings:

- Between 2015 and 2021, there was a total of 471 HLA typing error cases reviewed by the subcommittee, and between 2015-2023 there were 91 total cases of HLA typing errors submitted through the patient safety portal
    - There are significantly more cases for critical discrepancies for the HLA discrepant typing subcommittee than they are seeing for the Patient Safety Portal Reports
- In 2022, there were 14,763 donor HLA typings reported and 66 total critical discrepancies

- 84 total labs reported at least one donor typing during this period, and 37 unique labs were the initial typing lab for donor critical discrepancies during this period

- Counts of Discrepancies
  - Range: 1-8
  - Mean: 1.9
  - Median: 1
- Percentages of Discrepancies
  - Range: 0.1-3.8%
  - Mean: 0.95%
  - Median: 0.55%

Labs with more than 1 discrepancy

Total N donors typed by lab 2022	Total N discrepancies 2022	Percent Total Discrepancies 2022
280	8	2.857142857
487	4	0.821355236
668	4	0.598802395
124	4	3.225806452
344	3	0.872093023
254	3	1.181102362
170	3	1.764705882
140	3	2.142857143
162	3	1.851851852
442	3	0.678733032
353	2	0.566572238
267	2	0.74906367
253	2	0.790513834
278	2	0.71942446
328	2	0.609756098
52	2	3.846153846

Summary of discussion:

The Committee did not make any decisions.

The Committee discussed the potential to report labs with high numbers of critical discrepancies to the MPSC, but did not make any decisions on thresholds for referral.

3. Reporting Critical Discrepancies to the OPTN

The Committee further discussed what should happen with critical discrepancies and whether policy should be implemented to report critical discrepancies and their causes to the OPTN.

Presentation Overview:

OPTN Policy *4.4.A.i Donor HLA Critical Discrepancies* requires laboratories to notify Organ Procurement Organizations (OPOs) and transplant hospitals of critical discrepancies based on the specified timeline criteria. Currently, labs are not required to report critical discrepancies to the OPTN or perform Root Cause Analyses (RCAs). However, collection of this information regarding critical discrepancies is valuable, as it may address patient safety concerns and inspire policy improvements.

Current reporting pathways to the OPTN include the OPTN Patient Safety Portal and a TIEDI Discrepancy form. The Patient Safety Portal consists of voluntary reporting and can occur at any time relative to transplant. The TIEDI Form encounters limitations in terms of its set triggers, however, it automatically detects critical discrepancies. There may be a delay in the information collected from TIEDI forms considering it may take upwards of 60 days for submission and to run the reports. Through either of the reporting pathways, the Membership & Professional Standards Committee (MPSC) or the MPSC

Histocompatibility Subcommittee can review and report in aggregate to the Histocompatibility Committee.

Summary of discussion:

Decision #1: The Committee agreed that the definition of a critical discrepancy was appropriate for defining such incidents.

Decision #2: The Committee did not come to a consensus regarding which reporting structure would be best to pursue in policy but agreed to continue this discussion in future meetings.

Decision #1: The Committee agreed that the definition of a critical discrepancy was appropriate for defining such incidents.

To further discuss a potential reporting process to the OPTN, the Committee first reviewed the relevance of the existing definition of a critical discrepancy. For the purposes of this topic, an HLA critical discrepancy is a difference among non-equivalent values, according to *Policy 4.10: Reference Tables of HLA Antigen Values and Split Equivalences,* at one or more loci in a candidate's, donor's, or recipient's HLA typing. Considering none of the Committee members expressed dissatisfaction or rejected the proposed definition, the group determined that the definition of a critical discrepancy was appropriate.

Decision #2: The Committee did not come to a consensus regarding which reporting structure would be best to pursue in policy but agreed to continue this discussion in future meetings.

The Committee reviewed the current reporting pathways and considered potential alternatives. The group agreed that the most meaningful aspects to focus on were the gaps in current policy where this reporting requirement and structure are not specified. The Chair asked the Committee to also consider what the purpose of root cause analyses would be and the importance of including those in the identification of critical discrepancies. The Committee will continue to consider and discuss this topic in future meetings.

Next steps:

The Committee will continue to discuss this matter in future meetings.

Upcoming Meeting(s)

- July 11, 2023

Attendance

- **Committee Members**
  - John Lunz
  - Gerald Morris
  - Caroline Alquist
  - Laurine Bow
  - Valia Bravo-Egana
  - Amber Carriker
  - Yvette Chapman
  - Reut Hod Dvorai
  - Manish Gandhi
  - William Goggins
  - Kelley Hitchman
  - Lenore Hicks
  - Julie Houp
  - Helene McMurray
  - Omar Moussa
  - Hemant Parekh
  - Marcelo Pando
  - Jerome Saltarrelli
  - Crystal Usenko
  - Manu Varma
  - Qingyong Xu
  - Hua Zhu
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
- **SRTR Staff**
  - Katherine Audette
  - Rajalingam Raja
- **UNOS Staff**
  - Courtney Jett
  - Isaac Hager
  - Thomas Dolan
  - Krissy Laurie
  - Susan Tlusty
  - Debra Vicars