OPTN

Public Comment Proposal

Update Post-Transplant Histocompatibility Data Collection

OPTN Histocompatibility Committee

Prepared by: Courtney Jett
UNOS Policy Department

Contents

OPTN

Update Post-Transplant Histocompatibility Data Collection

Sponsoring Committee:	*Histocompatibility*
Data Collection Affected:	*Donor Histocompatibility Form* *Recipient Histocompatibility Form*
Public Comment Period:	*January 23, 2024 – March 19, 2024*

Executive Summary

Post-transplant histocompatibility data collection in the OPTN Computer System requires updating to accommodate current laboratory practices. Much of the current data collection incorporates testing methods which are no longer common practice, such as serologic human leukocyte antigen (HLA) typing. By 2013, 99.9% of all deceased donors were typed via molecular methods,[1] and in 2016 use of molecular methods for all deceased donor HLA typing became a requirement in OPTN policy.[2] In addition, while there is post-transplant data collection on physical crossmatching, there is no current data collection on virtual crossmatching. Crossmatching is a test performed by histocompatibility laboratories. It is used to determine the immunologic compatibility of a potential transplant recipient with a donor organ. Physical crossmatching involves the mixing of patient serum with donor cells, and virtual crossmatching involves assessment of immunologic compatibility based on candidate HLA antibody and donor HLA typing data. Previously, physical crossmatching was the primary way laboratories assessed immunologic compatibility, but studies have shown an increasing trend of virtual crossmatching use.[3]

The Committee reviewed all of the post-transplant histocompatibility data collection in the OPTN Computer System and identified the following areas of change:

- Update post-transplant histocompatibility data collection forms to be consistent with current histocompatibility testing methods
- Add data collection for virtual crossmatching to inform recipient treatment and evaluate impacts of the practice on recipient outcomes, graft outcomes, and cold ischemic time
- Generate Discrepant HLA Typings reports for all potential HLA critical discrepancies which will increase awareness of, allow for a system-wide perspective of, and better inform future policy updates related to critical HLA discrepancies

The Committee is seeking the following feedback from the community:

- Would the proposed changes to the Donor and Recipient Histocompatibility Forms be collected within discrete fields within a Laboratory Information System (LIS)? Please specify which data elements may not be collected discretely by all labs if relevant.

[1] OPTN Histocompatibility Committee, *Expanding Candidate and Deceased Donor HLA Typing Requirements to Provide Greater Consistency Across Organ Types Board Briefing Paper*. (Richmond: Organ Procurement and Transplantation Network, 2014).
[2] "Expanding Candidate and Deceased Donor HLA Typing Requirements to Provide Greater Consistency Across Organ Types" was implemented on January 21, 2016.
[3] Puttarajappa CM, et al. *Trends and impact on cold ischemia time and clinical outcomes using virtual crossmatch for deceased donor kidney transplantation in the United States*. Kidney Int. 2021 Sep;100(3):660-671. doi: 10.1016/j.kint.2021.04.020. 2021.

- Is the proposed list of discrepancy reasons comprehensive and clear? Are there any additional reasons you would recommend adding, or any you would recommend clarifying or taking away?
- Do you have usability recommendations for any of the post-transplant histocompatibility data collection instruments?

Purpose

The Committee reviewed the post-transplant histocompatibility data collection within the OPTN Computer System and identified the following areas they are proposing to change:

- Update post-transplant histocompatibility data collection forms to be consistent with current histocompatibility testing methods
- Add data collection for virtual crossmatching to inform recipient treatment and evaluate impacts of the practice on recipient outcomes, graft outcomes, and cold ischemic time
- Generate Discrepant HLA Typings reports for all potential HLA critical discrepancies which will increase awareness of, allow for a system-wide perspective of, and better inform future policy updates related to critical HLA discrepancies

Background

There are three post-transplant histocompatibility data collection instruments in the OPTN Computer System that are required to be completed by histocompatibility laboratories within 60 days post-transplant. These instruments collect data on donor and recipient HLA typings, recipient antibody testing, crossmatching, and donor and recipient discrepant HLA typings. These instruments currently include data collection on outdated testing methods, and do not collect information on virtual crossmatching. Data collection on virtual crossmatching practices could be used to evaluate impacts of the practice on recipient and graft outcomes as well as cold ischemic time (and therefore allocation efficiency). In addition, this information is important to inform recipient treatment. The existing data collection related to serologic HLA typing may no longer be informative, as by 2013, 99.9% of all deceased donors were typed via molecular methods,[4] and as of 2016 all deceased donor HLA typing was required by OPTN policy to be performed via molecular methods.[5]

The Committee formed a subcommittee that met six times and performed a comprehensive review of the data elements within the Donor Histocompatibility Form (DHF), Recipient Histocompatibility Form (RHF), and Discrepant HLA Typings report, as well as the generation and branching logic included. These proposed data collection changes were presented to the Data Advisory Committee (DAC) prior to[6] and after the completion of the comprehensive review[7] and received endorsement from the DAC.

Overview of Proposal

The Committee is proposing changes to all of the histocompatibility post-transplant data collection instruments within the OPTN Computer System. The majority of these changes are to update the data collection to reflect current testing methods. There is also proposed added data collection on virtual

[4] OPTN Histocompatibility Committee, *Expanding Candidate and Deceased Donor HLA Typing Requirements to Provide Greater Consistency Across Organ Types Board Briefing Paper*. (Richmond: Organ Procurement and Transplantation Network, 2014), 6.
[5] "Expanding Candidate and Deceased Donor HLA Typing Requirements to Provide Greater Consistency Across Organ Types" was implemented on January 21, 2016.
[6] https://optn.transplant.hrsa.gov/media/uj4auklx/20230202_data-advisory-committee_meeting-summary.pdf.
[7] Data Advisory Committee Meeting, December 11, 2023.

crossmatching, as well as a proposed update to how the Discrepant HLA Typings report is generated. The proposed changes are outlined below grouped by each individual instrument.

Donor Histocompatibility Form

The Donor Histocompatibility Form is filled out within 60 days post-transplant by the laboratory that performed the original living or deceased donor HLA typing. All of the data collection on this form is related to the donor HLA typing. Proposed updates to this form are to remove a net of four data collection fields related to previous laboratory practices or testing methods.

The Committee is proposing to remove separate data collection fields for the date HLA typing is completed and the target cell source for Class I and Class II typing. Currently, these dates are separated, even though almost all labs are performing Class I and Class II typing simultaneously on samples processed together. They are replacing the date HLA typing was completed and target cell source with singular data collection fields , as both are still important and relevant data collection.

The Committee is also proposing to remove the data collection fields for typing method for Class I and Class II typing entirely. Currently the response options are “DNA” and “Serology”. Since all donor HLA typings are required by OPTN policy to be via molecular, or DNA-based, methods, the Committee felt that asking which typing method was performed is no longer necessary.

Recipient Histocompatibility Form

The Recipient Histocompatibility Form is filled out within 60 days post-transplant by the laboratory for each organ recipient. The data collection on this form is currently broken into five sections: test information, recipient HLA typing, HLA antibody screening, crossmatching, and donor retyping. The data collection changes being proposed to this form include removal of unnecessary data collection related to previously used test methods, clarification of existing data elements, and the addition of data collection on virtual crossmatching.

Test Information and Virtual Crossmatching

The “Test Information” section of the Recipient Histocompatibility Form drives which other sections are generated. All data collection fields within this section are required. The form is able to be marked complete if this section is completed and no HLA testing was completed for the recipient. The Committee is not proposing changes to this logic, as they feel the current logic reduces data collection burden on users, as they are only required to fill out data collection for the testing that was actually completed.

The Committee is recommending adding virtual crossmatching data to this section in order to measure the impacts of virtual crossmatching on recipient outcomes and cold ischemic time. In addition, this information is important to inform recipient treatment. The Committee is proposing one data collection field asking if a prospective virtual crossmatch was performed. The Committee felt that knowing prospective virtual crossmatching information was more important for measuring impact on allocation efficiency. If a lab reports that a prospective virtual crossmatch was performed, they are then asked the result, with the response options of “Positive”, “Negative”, and “Indeterminate”. The Committee felt that “Indeterminate” was an important option to include, as not every result will be clearly positive or

negative, and some candidates may still require physical crossmatches to fully determine the level of immunologic risk a donor organ poses.

While there is existing data collection on current donor-specific antibodies, this does not capture the necessary data on virtual crossmatching. While an assessment for pre-transplant donor-specific HLA antibodies is a part of a virtual crossmatch, a virtual crossmatch is an assessment of overall compatibility of the candidate and the donor organ. This includes additional factors, such as an analysis of the patient's sensitization history, and levels of burden of the donor-specific antibodies and their epitopes or cross-reactive groups. In addition, a candidate may have low-level donor specific antibodies and may be positive for donor-specific antibodies, but negative for a virtual crossmatch as there may be a low immunologic risk for those antibodies. Therefore, the Committee felt it important to have both a question on donor-specific antibodies as well as a question on virtual crossmatching.

Recipient HLA Typing and Donor Retyping

The "Recipient HLA Typing" section of the form generates if the user selects that a recipient HLA typing was performed, and the "Donor Retyping" section generates if the user selects that the donor was retyped at the recipient's transplant program's request. These sections do not generate if the user selects that the respective testing was not completed.

For both the recipient HLA typing and the donor retyping sections of the form, the Committee is proposing the same data collection changes as those on the Donor Histocompatibility Form. The Committee is proposing removal of separate data collection fields for Class I and Class II typing date and target cell source, replaced with singular data collection fields for each. In addition, the Committee is removing the data collection fields for whether Class I and Class II typing methods were DNA-based or serologic-based entirely.

HLA Antibody Screening

The "HLA Antibody Screening" section of the form generates if a user selects that HLA antibody screening was completed in the "Test Information" section of the form. If the user selects that HLA antibody screening was not completed, this section does not generate.

General HLA antibody detection relates to any HLA antibodies a recipient may have, not just HLA antibodies to a donor's HLA typing. Currently, there are two data collection fields for general HLA antibody detection, one for cytotoxicity and one for solid-phase testing. The Committee discussed whether they would like to just remove cytotoxicity as a response option, since it is no longer a common form of testing. However, they ultimately felt that the type of HLA antibody testing was less important than whether HLA antibodies were present. In addition, they wanted to clarify the timing of the HLA antibodies being detected. So ultimately, they determined that the data collection field would be "Were any HLA antibodies detected pre-transplant?", with the response options of "Yes", "No", and "Not Done".

There is currently a data collection field "Were there current donor specific HLA antibodies". The Committee felt that the timing of "current" is unclear and are proposing this data collection be rephrased to "Were there pre-transplant donor-specific HLA antibodies" for clarity.

The Committee is proposing removing a data collection field related to historical donor specific antibodies, as they felt these are not relevant to graft outcomes if not present at the time of transplantation.

There are two data collection fields related to a recipient's Calculated Panel Reactive Antibody (CPRA) on the form for heart and lung recipients, one for the most recent CPRA and one for the peak CPRA. The most recent CPRA and peak CPRA is displayed for kidney and pancreas recipients as read-only and calculated from unacceptable antigens in the OPTN Waiting List. The Committee felt that displaying the calculated CPRA as read-only from the OPTN Waiting List for the most recent CPRA would be most helpful option and is proposing to do so for all organ recipients. This will be displayed in the "Recipient Information" section of the form. In addition, the Committee is proposing that the recipient's peak CPRA data collection should be removed, as well as the read-only peak CPRA field for kidney and pancreas recipients. They felt that it was unclear on the necessary timing and may be difficult to find for candidates who have been waiting for many years, as it is not a discrete field in most laboratory information systems (LISs). In addition, they felt that this is likely not clinically relevant to graft outcomes if this is not the recipient's sensitization level at the time of transplantation.

Crossmatching

The "Crossmatch" section of the Recipient Histocompatibility Form generates if a user selects that a physical crossmatch was completed in the "Test Information" section of the form. If the user selects that a physical crossmatch was not completed, this section does not generate.

The Committee is proposing that the "Crossmatching" section of the form be renamed to "Physical Crossmatch", so that it is not confused with virtual crossmatching.

Current response options for T-cell and B-cell crossmatches being performed are reported as multi-select options and include "Cytotoxicity no AHG", "Cytotoxicity AHG", "Flow Cytometry", "Solid Phase", and "Not tested". Each option selection generates a single-select sub-response for "Positive" or "Negative". The Committee is proposing to remove both response options that include cytotoxicity, as that testing is no longer in common use. In addition, they are proposing to add "Indeterminate" for the sub-response options, as some physical crossmatches can provide indeterminate results that are neither positive nor negative.

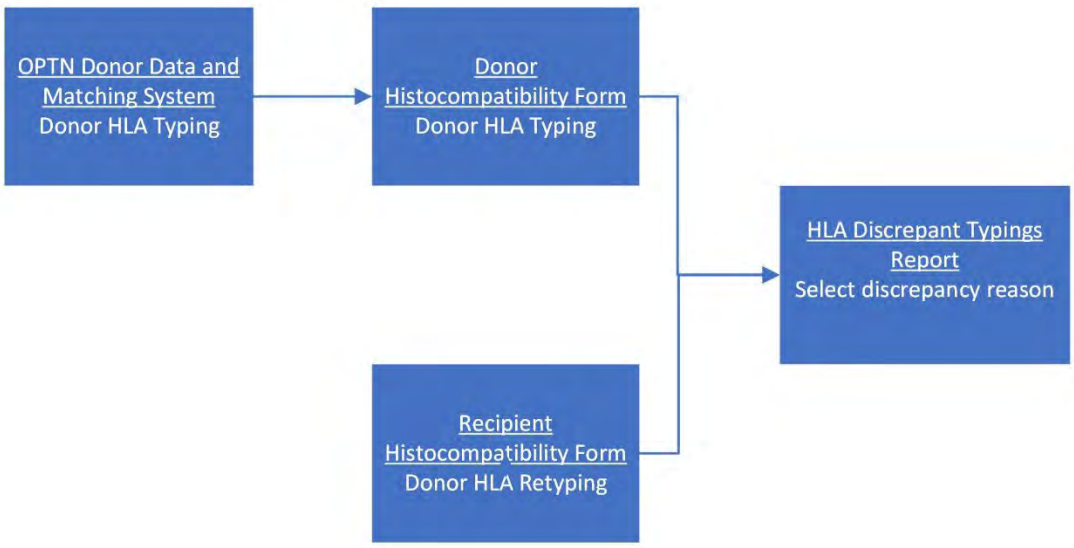
The Committee is also proposing to remove the data collection field for historical crossmatch results, as they felt that it is not clinically relevant to graft outcomes and the timing around how old historical results should be reported is unclear. Candidates who had been waiting for multiple years may have multiple historical crossmatches, and since they were performed for other donors they are likely not impactful for clinical decision making and patient care.

The Committee is proposing to add one data element in this section, "If virtual crossmatch done, was physical crossmatch considered concordant with virtual crossmatch?", with the response options of "Yes", "No", and "Not Done". The Committee discussed at length whether there needed to be a definition of mean fluorescence intensity (MFI) cutoffs or other thresholds for concordance. They ultimately felt that the determination of concordance would be best left to the clinical judgment of the lab directors performing the testing, as these are not standardized values.

Discrepant HLA Typings Report

The Discrepant HLA Typings Report compares HLA typings for donors and recipients from the OPTN Donor Data and Matching System, OPTN Waiting List, and the Donor and Recipient Histocompatibility Forms. When HLA typings provided by one or more labs are not equivalent by the HLA equivalency tables provided within OPTN *Policy 4.11.B: HLA Unacceptable Antigen Equivalences*, a report is generated for every lab which reported an HLA typing for that donor or recipient. For example, if the original donor HLA typing lab reported A*01:02 and a recipient typing lab re-typed the donor and reported A*01:01, a Discrepant HLA Typings Report would be generated as these values are not equivalent. However, if the original donor lab reported A1 and the recipient typing lab reported A*01:01, a report would not be generated, as these values are equivalent, even though they are at two different resolutions of HLA typing. See **Figure 1** for the current data flow for the HLA Discrepant Typings report. OPTN *Policy 4.4.B: Requirement to Resolve Critical Discrepant Donor and Recipient HLA Typing Results* requires labs to identify the correct HLA typing and report the reason for the discrepancy. Labs routinely review attached source documentation and contact other involved labs in order to resolve discrepancies.

Figure 1: Current Data Flow for HLA Discrepant Typings Report



Currently, the Discrepant HLA Typings Report generates for discrepancies in the HLA-A, B, and DRB1 loci for kidney, pancreas, and kidney-pancreas donors and recipients. The Committee felt that it was important for providers to be aware of discrepancies regardless of the organ transplanted and regardless of the locus, as all organ types and all loci have the potential for patient safety implications. In addition, they felt it important for labs to resolve and report the reason for every discrepancy. The Committee is proposing that this report be generated for discrepancies at all loci for all organ types.

These proposed changes will increase required data collection for labs. However, in 2022 there were only 66 deceased donor critical HLA discrepancies in the country[8] that the form would have been

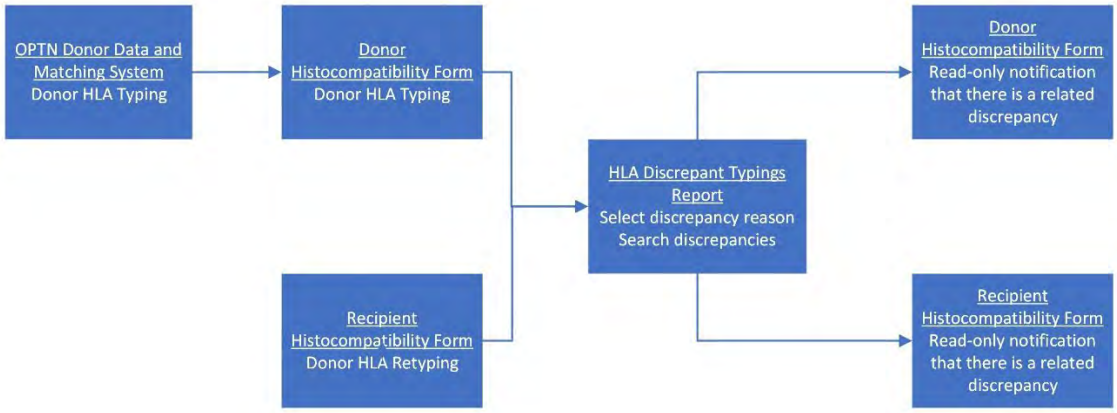
[8] https://optn.transplant.hrsa.gov/media/xxpdbnrr/06132023_histo-committee-meeting-summary.pdf.

generated for with the proposed logic, with a median of one discrepancy across all labs with critical HLA discrepancies.[9] These reports generate for all labs involved in the discrepancy, which means there may be less than 150 reports in total across the entire country per year, as there are on average 1.05 retypings per donor.[10] These reports would then be spread across 139 total HLA lab members in the country.[11] In addition, some of these reports are already being generated based on the existing logic. Overall, most labs should not have a significantly increased number of Discrepant HLA Typings reports to fill out.

In addition, the Committee heard multiple concerns about insufficient data collection on critical HLA discrepancies during public comment for a previous proposal. During the proposal to "Require Confirmatory Human Leukocyte Antigen (HLA) Typing for Deceased Donors", multiple community members gave feedback during regional meetings and through individual written comments that there is insufficient information about the causes of critical HLA discrepancies. In addition, community members provided feedback the current data collection on critical HLA discrepancies is incomplete.[12] The Committee agreed that more robust data collection was needed to better understand the reasons behind these critical discrepancies and ensure they are being resolved as required by OPTN policy.

The Discrepant HLA Typings Reports are not currently viewable or searchable by the user once the resolved reason for the discrepancy is provided. The Committee is proposing that the data remain searchable to labs, and that a read-only notification is added on both the Donor and Recipient Histocompatibility Forms, as applicable if there is a discrepancy, so that labs are aware of all relevant information for recipient care when reviewing records. The proposed data flow for discrepant HLA typings is outlined in **Figure 2**. The Committee is interested in hearing any other usability recommendations from the community to include in this effort.

Figure 2: Proposed HLA Discrepant Typings Data Flow



[9] https://optn.transplant.hrsa.gov/media/pywl00xm/07112023_histo-committee-meeting.pdf.
[10] Based on OPTN data for all organs between September 1, 2021 and August 31, 2022.
[11] Based on OPTN Membership data as of December 8, 2023.
[12] https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/require-human-leukocyte-antigen-hla-confirmatory-typing-for-deceased-donors/.

The Committee is also proposing to update the list of discrepancy reasons labs can provide, as many of the discrepancy reasons were related to serologic testing and are no longer applicable. The Committee is proposing revising the list to the reasons provided in **Table 1**.

Table 1: Proposed Discrepancy Reasons and Definitions

Discrepancy Reason	Definition
Ambiguous Assignment (with required free text box)	The HLA typing results were ambiguous. Requires additional explanation as to how the results were ambiguous.
Reagent/Assay Issue	There was a reagent or assay malfunction that caused the discrepancy. For example, a well in an assay did not react.
Parent Vs. Split	The HLA typing results are equivalent, as one HLA typing result is a parent antigen and the other is a split antigen of that parent.
Null Allele	A null allele was reported as non-null in the HLA typing.
P-group Equivalency	The HLA typing results are equivalent, as one HLA typing result is a P-group and the other is an allele within that P-group.
Incorrect Specimen	The specimen or HLA typing was for a different patient than it was reported for.
Transcription Error	There was an error in manual transcription of the HLA typing data.
Incorrect Split	The incorrect serologic split was reported from a broader parent allele.
Incorrect Allele Assignment	The incorrect allele was reported from a list of multiple potential alleles.
Original Typing Confirmed Correct	This HLA typing result has been confirmed to be the correct HLA typing for the patient.
Other, Specify (with required free text box)	The reason for the discrepancy does not fit into any of the other reasons. Requires additional explanation as to the reason for the discrepancy.

"Original Typing Confirmed Correct" is provided in the list of reasons because all labs involved in a discrepancy must provide a response, and at least one of the typing labs will likely have submitted the correct HLA typing information when originally entering HLA typing information into the OPTN Computer System. It is important for clinical care that the correct HLA typing information be known and clearly marked in order to allow for proper monitoring of donor-specific antibody development. "Confirmed Correct" is included in the reason, as the Committee wanted to ensure it was clear to labs that they must resolve the discrepancy and confirm that the typing was correct in some way, as required by OPTN *Policy 4.4.B*.

"P-group Equivalency" is provided in the list of reasons as there is not currently an equivalency table in OPTN Policy or the OPTN Computer System for P-groups that would separate them out as a difference in typing resolution instead of as a potential critical discrepancy. The Committee has discussed modifying the definition of critical HLA discrepancies for a future public comment,[13] so their inclusion within the definition and report is potentially subject to change in the future.

[13] https://optn.transplant.hrsa.gov/media/rx5ozmtz/09272023_histo-meeting-summary.pdf.

"Null Allele" is provided in the list of reasons as these results will appear discrepant in the OPTN Computer System, even if a null allele originally reported as non-null will not cause an immunologic reaction in a recipient. Many of the common null alleles are at the third-field, with other third-field alleles in the same two-field allele or serologic antigen that are non-null. There is no way to distinguish from a serologic antigen or two-field allele HLA typing if the original result was reported incorrectly for another reason or because a null allele was present that was not distinguished at the time of reporting the HLA typing to the OPTN.

The Committee is proposing removing the data element on the report for "Discrepancy not resolvable". The Committee felt that every discrepancy should have a known resolution or cause. OPTN *Policy 4.4.B: Requirement to Resolve Critical Discrepant Donor and Recipient HLA Typing Results* requires labs to identify the correct HLA typing and report the reason for the discrepancy. Labs routinely review attached source documentation and contact other involved labs in order to resolve discrepancies.

The Committee would appreciate input on whether the proposed list of discrepancy reasons and their definitions is comprehensive or if there are additional reasons that should be included. In addition, the Committee would appreciate input on the clarity of the reasons, to ensure consistency in data collection between labs.

NOTA and OPTN Final Rule Analysis

The Committee submits this data collection proposal under the authority of the National Organ Transplant Act of 1984 (NOTA) and the OPTN Final Rule. NOTA requires the Organ Procurement and Transplantation Network (OPTN) to "collect, analyze, and publish data concerning organ donation and transplants,"[14] and the Final Rule requires the OPTN to "receive and maintain records.[15] This proposal will update the collection of data concerning post-transplant histocompatibility of organ recipients as well as add data collection for virtual crossmatching to inform recipient treatment and evaluate impacts of the practice on recipient outcomes, graft outcomes, and cold ischemic time.

Implementation Considerations

Member and OPTN Operations

Operations affecting Histocompatibility Laboratories

This proposal alters the post-transplant data collection required by histocompatibility laboratories. Labs will need to become familiar with the revised data collection requirements, including new data collection for virtual crossmatching. This proposal overall reduces the number of data collection elements required to be submitted for the Donor and Recipient Histocompatibility Forms by removing a net four data elements from the DHF and eight from the RHF, but does increase the number of projected occurrences that the Discrepant HLA Typings Report will be generated for labs. However, in 2022 there were only 66 donor critical HLA discrepancies in the country[16] that the form would have been generated for with the proposed logic, with a median of one donor discrepancy across all labs with

[14] 42 USC. §274(b)(2)(I).
[15] 42 CFR § 121.11(a)(1)(i-iii).
[16] https://optn.transplant.hrsa.gov/media/xxpdbnrr/06132023_histo-committee-meeting-summary.pdf.

critical HLA discrepancies.[17] While these reports generate for all labs involved in the discrepancy, some of these reports are already being generated and most labs should not have a significantly increased number of Discrepant HLA Typings reports to fill out.

Operations affecting Organ Procurement Organizations

This proposal is not expected to impact Organ Procurement Organization operations.

Operations affecting Transplant Hospitals

This proposal is not expected to impact transplant hospital operations.

Operations affecting the OPTN

This proposal will require technical implementation within the OPTN Computer System, for the Donor Histocompatibility Form, Recipient Histocompatibility Form, and Discrepant HLA Typings Report. This proposal requires the addition and removal of multiple data elements, as well as changes to field labels for clarity. It also requires changes to when the Discrepant HLA Typings Report generates and how the entered data is viewed after resolution and associated with donor and recipient records.

This proposal requires the submission of official OPTN data that are not presently collected by the OPTN. The OPTN Contractor has agreed that data collected pursuant to the OPTN's regulatory requirements in §121.11 of the OPTN Final Rule will be collected through OMB approved data collection forms. Therefore, after OPTN Board approval, the forms will be submitted for OMB approval under the Paperwork Reduction Act of 1995. This will require a revision of the OMB-approved data collection instruments, which may impact the implementation timeline.

Projected Fiscal Impact

Projected Impact on Histocompatibility Laboratories

There is a low expected fiscal impact on Histocompatibility Laboratories. Minor changes to staff training are anticipated.

Projected Impact on Organ Procurement Organizations

This proposal is not anticipated to have any fiscal impact on Organ Procurement Organizations.

Projected Impact on Transplant Hospitals

This proposal is not anticipated to have any fiscal impact on transplant hospitals.

Projected Impact on the OPTN

The OPTN contractor estimates that 4,095 hours would be needed to implement this proposal. Implementation would involve updates within the OPTN Computer System for the Donor Histocompatibility Form, Recipient Histocompatibility Form, and Discrepant HLA Typings Report. In addition, implementation would include educating histocompatibility laboratories on the revised data

[17] https://optn.transplant.hrsa.gov/media/pywl00xm/07112023_histo-committee-meeting.pdf.

collection requirements. The OPTN contractor estimates 70 hours for ongoing support. Ongoing support will involve the evaluation of incoming data to assess post-implementation performance and answering member questions.

Post-implementation Monitoring

Member Compliance

The proposal will not change the current routine monitoring of OPTN members. Any data entered in the OPTN Computer System may be reviewed by the OPTN, and members are required to provide documentation as requested.

Policy Evaluation

The following metrics, and any others subsequently requested by the Committee, will be evaluated as data become available to assess performance after the implementation of this policy:

Crossmatch Practices

1. Count and percent of transplants with a prospective virtual crossmatch performed
2. Count and percent of transplants with a prospective virtual crossmatch by results of virtual crossmatch
3. Count and percent of transplants where physical crossmatch was considered concordant with virtual crossmatch/antibody analysis
4. Count and percent of transplants with a physical crossmatch performed
5. Count and percent of transplants with a physical crossmatch performed by whether it was prospective to transplant

Outcomes

1. Distribution of cold ischemic time
2. Count and Percent of transplants with delayed graft function
3. Post-transplant graft and patient survival rates

The above outcomes metrics will be stratified by virtual crossmatch status, as well as physical crossmatch results. Graft and patient survival will be reserved for the 1- and 2-year reports as enough data becomes available.

These metrics will be evaluated at approximately 6-months, 1-year and 2-years post-implementation.

Conclusion

After a comprehensive review of post-transplant histocompatibility data collection in the OPTN Computer System, the Committee is proposing the following changes:

- Update post-transplant histocompatibility data collection forms to be consistent with current histocompatibility testing methods
- Add data collection for virtual crossmatching to inform recipient treatment and evaluate impacts of the practice on recipient outcomes, graft outcomes, and cold ischemic time

- Generate Discrepant HLA Typings reports for all potential HLA critical discrepancies which will increase awareness of, allow for a system-wide perspective of, and better inform future policy updates related to critical HLA discrepancies

The Committee is seeking the following feedback from the community:

- Would the proposed changes to the Donor and Recipient Histocompatibility Forms be collected within discrete fields within a Laboratory Information System (LIS)? Please specify which data elements may not be collected discretely by all labs if relevant.
- Is the proposed list of discrepancy reasons comprehensive and clear? Are there any additional reasons you would recommend adding, or any you would recommend clarifying or taking away?
- Do you have usability recommendations for any of the post-transplant histocompatibility data collection instruments?

Proposed Changes to Data Elements

1 Donor Histocompatibility Form

Data Element	Proposed Modification
Date Typing Completed	Add
Date Typing Completed Class I	Remove
Date Typing Completed Class II	Remove
Target Source Response: Peripheral Blood, Lymph Nodes, Spleen, Buccal Swab or Other (Multi-select)	Add
Target Source for Class I Response: Peripheral Blood, Lymph Nodes, Spleen, Buccal Swab or Other (Multi-select)	Remove
Target Source for Class II Response: Peripheral Blood, Lymph Nodes, Spleen, Buccal Swab or Other (Multi-select)	Remove
Typing Method Class I Response: Serology, DNA (Multi-select)	Remove
Typing Method Class II Response: Serology, DNA (Multi-select)	Remove

2
3

4 Recipient Histocompatibility Form

Section: Test Information	
Data Element	**Proposed Modification**
Prospective Virtual Crossmatch Performed Response: Yes, No If yes, What was the result? Response: Positive, Negative, Indeterminate	Add
Section I: Recipient HLA Typing	
Data Element	**Proposed Modification**
Date Typing Completed	Add

Date Typing Completed Class I	Remove
Date Typing Completed Class II	Remove
Typing Method Class I Response: Serology, DNA (Multi-select)	Remove
Typing Method Class II Response: Serology, DNA (Multi-select)	Remove
Section II: HLA Antibody Screening	
Data Element	**Proposed Modification**
Were any HLA antibodies detected by: Cytotoxicity? Response options: Yes, No, Not Done Solid-phase? Response options: Yes, No, Not Done	Remove separate response options, change to "Were any HLA antibodies detected pre-transplant?" Response options: Yes, No, Not Done
Were there current donor specific HLA antibodies? Response options: Yes, No, Unknown	Change wording to: "Were there pre-transplant donor specific HLA antibodies?" Response options: Yes, No, Unknown
Were there historical donor specific HLA antibodies? Response options: Yes, No, Unknown	Remove
CPRA (%) – Most Recent	Display calculated CPRA from Waitlist, no free text response option • This will be moved to the "Recipient Information" section
CPRA (%) – Peak	Remove
Section III: Change to: Physical Crossmatch	
Data Element	**Proposed Modification**
Which T-cell crossmatch tests were performed? Response options: Cytotoxicity no AHG, Cytotoxicity AHG, Flow Cytometry, Solid Phase, Not tested (multi-select, each one generates a sub-response for negative or positive single select)	Remove response options Cytotoxicity no AHG and Cytotoxicity AHG, add sub-response for "Indeterminate"
Which B-cell crossmatch tests were performed? Response options: Cytotoxicity no AHG, Cytotoxicity AHG, Flow Cytometry, Solid Phase, Not tested (multi-select, each one generates a sub-response for negative or positive single select)	Remove response options Cytotoxicity no AHG and Cytotoxicity AHG, add sub-response for "Indeterminate"

Which historical crossmatch tests were performed? Response options: Cytotoxicity no AHG, Cytotoxicity AHG, Flow Cytometry, Solid Phase, Not tested (multi-select, each one generates a sub-response for negative or positive single select)	Remove
If virtual crossmatch done, was physical crossmatch considered concordant with virtual crossmatch? Response Options: Yes, No, Not Done	Add
Section IV: Donor Retyping	
Data Element	**Proposed Modification**
Donor Retyped Class I Response options: Yes, No, Unknown	Remove
Donor Retyped Class II Response options: Yes, No, Unknown	Remove
Date HLA Typing Completed	Add
Date Typing Completed Class I	Remove
Date HLA Typing Completed Class II	Remove
Typing Method Class I Response: Serology, DNA (Multi-select)	Remove
Typing Method Class II Response: Serology, DNA (Multi-select)	Remove

5

6 Discrepant HLA Typings Report

Data Element	Proposed Modification
Resolved Reason for Discrepancy Response options: Low Cell Numbers Poor Cell Viability Low Antigen Expression PBL Vs LN/Spleen Serology Vs Molecular Typing Incorrect Assignment Parent Vs Split(s) Incorrect Split Crossreactive Antigen Blank Antigen Unable to Type/Identify Antigens Incorrect Specimen Transcription Error Correct Typing Other	Remove: Low Cell Numbers Poor Cell Viability Low Antigen Expression PBL Vs LN/Spleen Serology Vs Molecular Typing Crossreactive Antigen Blank Antigen Unable to Type/Identify Antigens Correct Typing Incorrect Split Incorrect Assignment Add: Null Allele Original Typing Confirmed Correct Reagent/Assay Issue Incorrect Allele Assignment P-group Equivalency Ambiguous Assignment, add free text box Change: “Other” into “Other, specify” and add free text box
Discrepancy Not Resolvable Response Options: Check box	Remove

#