OPTN

Briefing to the OPTN Board of Directors on

Require Reporting of HLA Critical Discrepancies and Crossmatching Events to the OPTN

OPTN Histocompatibility Committee

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Require Reporting of HLA Critical Discrepancies and Crossmatching Events to the OPTN

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Sponsoring Committee:	*Histocompatibility Committee*
Public Comment Period:	*July 31, 2024 – September 24, 2024*
Board of Directors Meeting:	*December 2-3, 2024*

Executive Summary

Human Leukocyte Antigen (HLA) typing is a vital step for ensuring donor-recipient compatibility leading to successful organ transplantation. Current OPTN Policy defines a critical HLA discrepancy as a "difference among non-equivalent values, according to OPTN *Policy 4.11: 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." Currently, histocompatibility laboratories must report critical discrepancies to the transplant hospital, as well as the organ procurement organization (OPO). However, they are not currently required to report these events to the OPTN. HLA critical discrepancies reflect instances of potential incompatibility between the potential recipient and donor wherein a severe, potentially fatal, immunologic reaction is possible if the organ were to be transplanted. Due to patient safety concerns, as well as increasing transparency through data collection, the OPTN Histocompatibility Committee (Committee) proposes required reporting of these events to the OPTN within 72 hours of discovery through the OPTN Patient Safety Reporting Portal. This was changed from the original proposal language of 24 hours due to public comment feedback. Furthermore, this proposal modifies the definition of a critical discrepancy to no longer encompass discrepancies within the same split antigen group if the HLA typing is reported at low resolution. The proposal would also require reports to the OPTN Patient Safety Reporting Portal when an incorrect sample is used for a physical crossmatch, or when an incorrect donor HLA typing or incorrect candidate HLA antibody test is analyzed for a virtual crossmatch.

Purpose

This proposal is intended to require reporting of critical discrepancies in HLA typing to the OPTN to gain insight into the root cause and use the gained information to reduce the total number of HLA critical discrepancies. When identified before transplant, these discrepancies may require re-allocation, which can impact system efficiency and impact organ quality through increased cold ischemic time. When identified after transplant, they may be a patient safety concern due to their potential to cause an immunologic reaction in the recipient(s). Reducing HLA critical discrepancies would increase patient safety and increase system efficiency.

Background

There are two main sources of HLA critical discrepancy data that the OPTN Histocompatibility Committee reviewed for this proposal. The first is a quarterly report the Committee receives, which compares HLA typings from the OPTN Donor Data and Matching System, the Recipient Histocompatibility Form donor retyping section, and the Donor Histocompatibility Form.

The OPTN Histocompatibility Committee (Committee) reviews retrospective, aggregate donor and recipient HLA critical discrepancies through a report utilizing data entered in the OPTN Computer System. This data is reviewed quarterly, with about 60-70 total cases of HLA critical discrepancies identified every year.[1] This report is a deidentified report without root cause data or information on recipient outcomes.

The second source of HLA critical discrepancy data reviewed is based on cases from the OPTN Patient Safety Portal, which have been voluntarily submitted by OPTN members. This data is less complete, as submission is voluntary, but does have information on root causes and recipient outcomes. Since OPTN policy does not require reporting critical discrepancies to the OPTN Patient Safety Reporting Portal for compliance and medical peer review, and the Committee reviews them in a deidentified manner, there is a lack of meaningful root cause data on recipient outcomes and no avenue for targeted OPTN intervention for recurrences.

While current OPTN policy requires reporting of HLA critical discrepancies to organ procurement organizations (OPOs) and transplant hospitals, reporting of critical discrepancies to the OPTN is voluntary. Between January 1, 2015, and March 1, 2023, there were a total of 91 OPTN Patient Safety Portal cases for HLA related events, see **Figure 1**. This is an average of approximately 13 submissions per 12-month period.

[1] Based on OPTN Critical HLA Discrepancy Data as of June 24, 2024.

Table 1: HLA-Related OPTN Patient Safety Portal Reports

Error Type	Number of OPTN Patient Safety Portal HLA-related cases
Data Entry	35
Verification	23
Interpretation	14
Sample Switches	11
Equipment Malfunctions	10
Laboratory/IT Technical Issues	8
Typing Method	7
Pending	1
Total	91[2,3]

During the Winter 2023 OPTN Public Comment cycle, the Committee sought feedback on their proposal *Requiring HLA Confirmatory Typing for Deceased Donors*.[4] While the Committee ultimately did not submit this proposal for consideration to the OPTN Board of Directors, the feedback obtained was instrumental in gaining a better understanding of community concerns and determining the appropriate avenue to address HLA critical discrepancies. The ultimate goals of the committee and community are aligned in preventing HLA critical discrepancies that could lead to graft loss, morbidity, and mortality. Many in the community supported reporting these HLA critical discrepancies to the OPTN, with commenters noting the scarcity of data on HLA critical discrepancies and subsequent recipient outcomes due to the current voluntary reporting process. The Committee heard the community's concerns and agreed that additional data was needed on critical HLA discrepancies and their causes. [5,6]

The Committee evaluated additional data to understand critical discrepancies. In a report provided to the OPTN Board of Directors regarding the *Requiring HLA Confirmatory Typing for Deceased Donors* proposal, alternative solutions were identified, including revision of the OPTN Computer System existing discrepancy reports and collection of additional data on discrepancies.[7]

The Committee noted that it would be premature to make a final decision on the method used for reducing HLA critical discrepancies before evaluating additional data related to the root causes of the discrepancies. The Committee reviewed aforementioned OPTN Patient Safety Reporting Portal submissions.

[2] Some HLA Critical Discrepancies had multiple root causes reported.
[3] There were 95 total submissions to the OPTN Patient Safety Portal during the time period. Four of these were duplicate submissions, for a total of 91 unique cases submitted.
[4] OPTN Histocompatibility Committee. Public Comment Proposal. https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/require-human-leukocyte-antigen-hla-confirmatory-typing-for-deceased-donors/https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/require-human-leukocyte-antigen-hla-confirmatory-typing-for-deceaseddonors/.
[5] OPTN Histocompatibility Committee. Meeting Summary, April 11, 2023. Available at https://optn.transplant.hrsa.gov/.
[6] OPTN Histocompatibility Committee, Meeting Summary, September 27, 2023. Available at https://optn.transplant.hrsa.gov/.
[7] OPTN Histocompatibility Committee. Public Comment Proposal. https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/require-human-leukocyte-antigen-hla-confirmatory-typing-for-deceased-donors/https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/require-human-leukocyte-antigen-hla-confirmatory-typing-for-deceaseddonors/.

The Subcommittee reviewed data from labs with discrepant typings in 2022 from their quarterly reports obtained from data within the Data System for the OPTN. This includes discrepancies and HLA typings for donors entered pre- and post-transplant, but does not include OPTN Patient Safety Reporting Portal reports.

In 2022, there were 84 histocompatibility laboratories that performed at least one of the 14,763 deceased donor typings completed that year, and out of that number there were 37 laboratories who had one or more donor HLA critical discrepancies. Due to the deidentified nature of the data utilized, it was not possible to tell which laboratory identified the discrepancies. This review and data demonstrate a spread of HLA discrepancies across the nation. This data indicates that the majority of histocompatibility laboratories should experience little to no impact with additional required reporting to the OPTN. See **Table 2** for a breakdown of the number of discrepancies for each of the 37 OPTN Histocompatibility laboratories with at least one donor HLA critical discrepancy in 2022.

Table 2: OPTN Histocompatibility Laboratories with Donor HLA Critical Discrepancies, 2022

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

Proposal for Board Consideration

This proposal has multiple components, focusing on reporting critical HLA discrepancies to the OPTN, modifying the definition of an HLA critical discrepancy, and reporting incorrect specimens or reports used for crossmatching. All of these proposed changes are integral for increasing transplant recipient safety.

Reporting Critical HLA Discrepancies to the OPTN

Currently, the OPTN only requires submission for certain safety events to the OPTN Patient Safety Reporting Portal, none of which are reported by histocompatibility labs. The Committee is aware that not all HLA critical discrepancies are reported to the OPTN Patient Safety Reporting Portal, as their deidentified review process pulls more discrepancies from data submitted in the OPTN Computer System than are reported through the OPTN Patient Safety Reporting Portal. These are all critical discrepancies as currently defined in *OPTN Policy 4.11 Reference Tables of HLA Antigen Values and Split Equivalences.*

When any safety event is reported through the OPTN Patient Safety Reporting Portal, members often provide a Root Cause Analysis (RCA) to better understand what went wrong for this issue to occur. Members are not required to submit an RCA with their initial report, but oftentimes will be asked for one in the ensuing investigation. If the member identifies a gap in their training, process, or a misunderstanding of policy requirements through the RCA; often members will submit a Corrective Action Plan (CAP) which details how they will prevent this error from recurring. Subsequently, the OPTN Membership and Professional Standards Committee (MPSC) will review each case and its supporting

documentation, as part of a medical peer review, and determine if any further actions or interventions are appropriate to ensure patient safety per the OPTN Bylaws.[8]

Current OPTN policy requires laboratories to notify the host organ procurement organizations (OPOs) of critical discrepancies as soon as possible, but no later than one hour following determination of the correct HLA typing.

Currently, upon independent discovery or receipt of documentation of the discrepancy, the OPO is requested to notify and provide supporting documentation to all accepting transplant programs no later than 12 hours (if the discrepancy is discovered prior to procurements) or 24 hours (if the discrepancy is discovered post-procurement).[9] In review of policy, the Committee reasoned that since action and review from the OPTN takes place later in the process, a 24-hour reporting window would be appropriate.[10] Following public comment, the Committee is proposing a perspective based on community feedback, which generally aligned with lengthening the critical discrepancy reporting time from the discovering lab to the OPTN Patient Safety Reporting Portal to 72-hours rather than the originally proposed 24-hours. The community generally agreed that 24-hours is not enough time to report the critical discrepancy. The change to a 72-hour reporting window addresses community feedback and also aligns with the remaining required reporting events outlined in OPTN *Policy 18.5: Reporting of Patient Safety Events* reporting norm of 72-hours.

With this update, the proposal would require that histocompatibility laboratories report an HLA critical discrepancy to the OPTN via the OPTN Patient Safety Reporting Portal within 72 hours of discovery.[11] This initial report to the OPTN Patient Safety Reporting Portal does not require an RCA or CAP, nor does it require the correct typing to be identified. While any information the member has available at that time is helpful, the initial report only requires that a discrepancy has been discovered and reported. Reports can be updated as more information becomes available. RCAs and CAPs may be requested as part of the inquiry into the event and the Committee believes that engaging in these quality improvement efforts will improve the overall processes and safety standards for histocompatibility laboratories.

In line with protections of medical peer review, these events will only be reviewed in an identified and individualistic manner by the MPSC and the MPSC Histocompatibility Subcommittee in closed session. Through systematic monitoring, the MPSC will be able to identify and refer any recurring themes or issues to the Histocompatibility Committee to pursue a policy or guidance project as appropriate. The Histocompatibility Committee will also review the deidentified, aggregate information on a regular cadence. This aggregate information will be used to inform community-wide education and ongoing updates to policy and guidance.

Modifying the Definition of a Critical HLA Discrepancy

Currently, the definition of a critical HLA discrepancy is “a difference among non-equivalent values, according to *OPTN Policy 4.11 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” as listed in *OPTN Policy 4.4: 4 Critical HLA*

[8] OPTN Bylaws, Appendix L: Reviews and Actions. https://optn.transplant.hrsa.gov/media/lgbbmahi/optn_bylaws.pdf.
[9] OPTN Policy 4.4.A.i: Donor HLA Critical Discrepancies as of July 24, 2023.
[10] OPTN Histocompatibility Committee, Meeting Summary, September 27, 2023. Available at https://optn.transplant.hrsa.gov/.
[11] OPTN Histocompatibility Committee, Meeting Summary, October 1, 2024 . Available at https://optn.transplant.hrsa.gov/.

Discrepancies in Candidate, Donor, and Recipient HLA Typing Results. The Committee had originally proposed the following:

> " a human leukocyte antigen (HLA) critical discrepancy is a difference among non-equivalent values, at one or more loci in a candidate's, donor's, or recipient's HLA typing. Values within the same serologic split antigen group or provided as equivalent for the purposes of unacceptable antigen screening within *Policy 4.11 Reference Tables of HLA Antigen Values and Split Equivalences* are considered equivalent."

By this definition, a donor typed as HLA-A*01:02 would not be critically discrepant if retyped as HLA-A*01:01. The committee disagreed with this definition upon further examination because there is the potential for an unrecognized immunological reaction.

Following public comment, the Committee made adjustments to the proposed critical discrepancy definition to align with community feedback that necessitated p-group inclusion for loci that do not have Immunogenetics Information System/Human Leucocyte Antigen (IMGT)/HLA) assigned serology, such as DPB1, DPA1, and DQA1.[12] IMGT/HLA is used as an international reference guide for assigned serology.

The Committee is proposing changing the definition of a critical HLA discrepancy to:

> " a human leukocyte antigen (HLA) critical discrepancy is a difference among non-equivalent values, at one or more loci in a candidate's, donor's, or recipient's HLA typing. For typing reported from a low-resolution method by serologic nomenclature, values within the same serologic split antigen group or within the same P group according to IMGT/HLA are considered equivalent. For typing reported at the two-field resolution, values within the same P group according to IMGT/HLA are considered equivalent."

By this definition, a donor typed as HLA-A*01:02 would not be critically discrepant if retyped as HLA-A*01 but would be critically discrepant if typed as HLA-A*01:01.

This new definition was chosen to focus required reporting on what is most immunologically significant and align with the required HLA typing resolution. This means that certain antigen pairs with no immunologic significance will not be required to be reported with the revised definition. The addition of p-groups helps align equivalencies for values that do not have assigned serology.

Reporting Incorrect Specimens or Typings Used for Crossmatching

When receiving a presentation on the histocompatibility-related reports submitted through the OPTN Patient Safety Reporting Portal, the Committee discussed the potential for incorrect donor or recipient samples to be used in a physical crossmatch.[13] The Committee agreed that this is a patient safety concern and should be a required report to the OPTN because it could cause a potential immunologic reaction between the recipient and potential donor to go undetected. The Committee also felt that analyzing the incorrect donor HLA typing or incorrect candidate HLA antibody test for a virtual crossmatch should be a required report to the OPTN for the same reasons. Therefore, the Committee is proposing that both of these events be included in the required reports to the OPTN. This required

[12] OPTN Histocompatibility Committee. Meeting Summary, October 1, 2024. Available at https://optn.transplant.hrsa.gov/.
[13] OPTN Histocompatibility Committee. Meeting Summary, May 14, 2024. Available at https://optn.transplant.hrsa.gov/.

reporting would need to happen within 72-hours of discovery of the critical discrepancy, changed from the original 24-hour proposal.

Overall Sentiment from Public Comment

Sentiment is collected on public comment proposals and is measured on a 5-point Likert scale from strongly oppose to strongly support (1-5). These reports are helpful to spot high-level trends but they are not meant as public opinion polls. Generally, public comment sentiment has been supportive of this proposal, as indicated by the overall sentiment score of 4.1, with some small pockets of concern. Below are graphics that illustrate the sentiment received through public comment.

Figure 3 shows sentiment received from all respondents (regional meeting, online, and email) by their stated member type. Again, there was overall support for the concept, demonstrated by a sentiment score of 4.1. However, data showed some concerns about the proposal from certain organizations.

Figure 3: Sentiment by Member Type

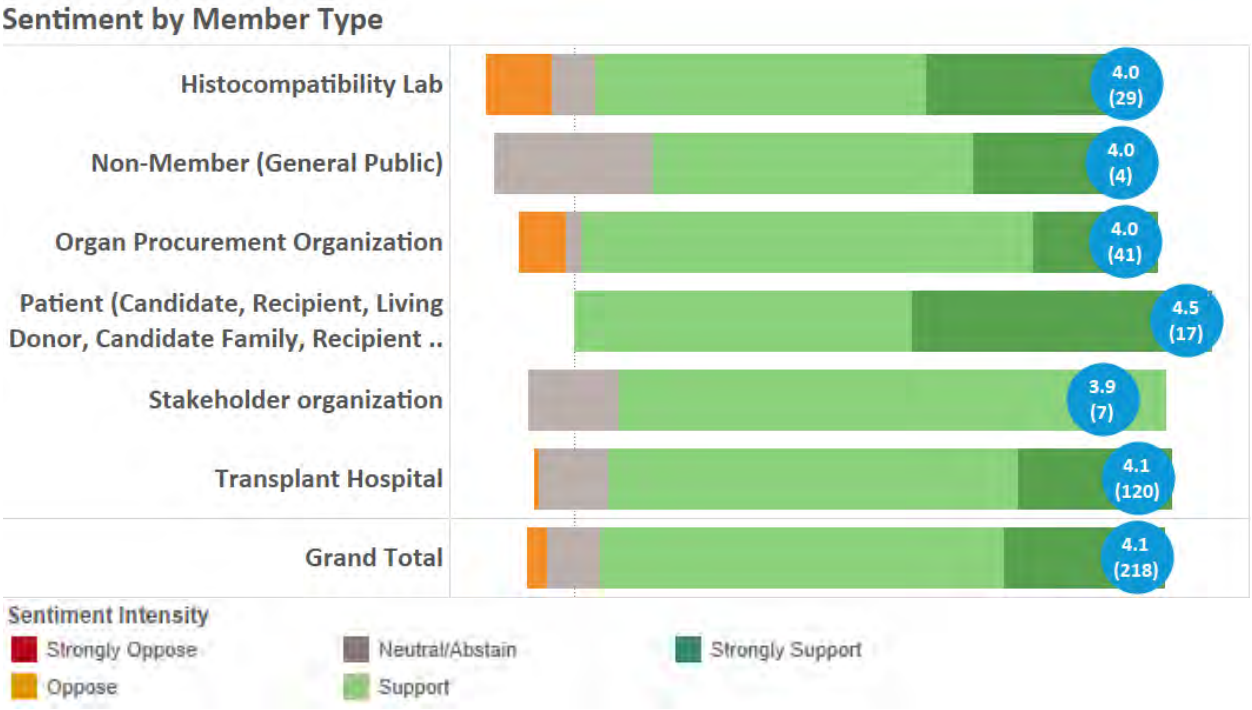
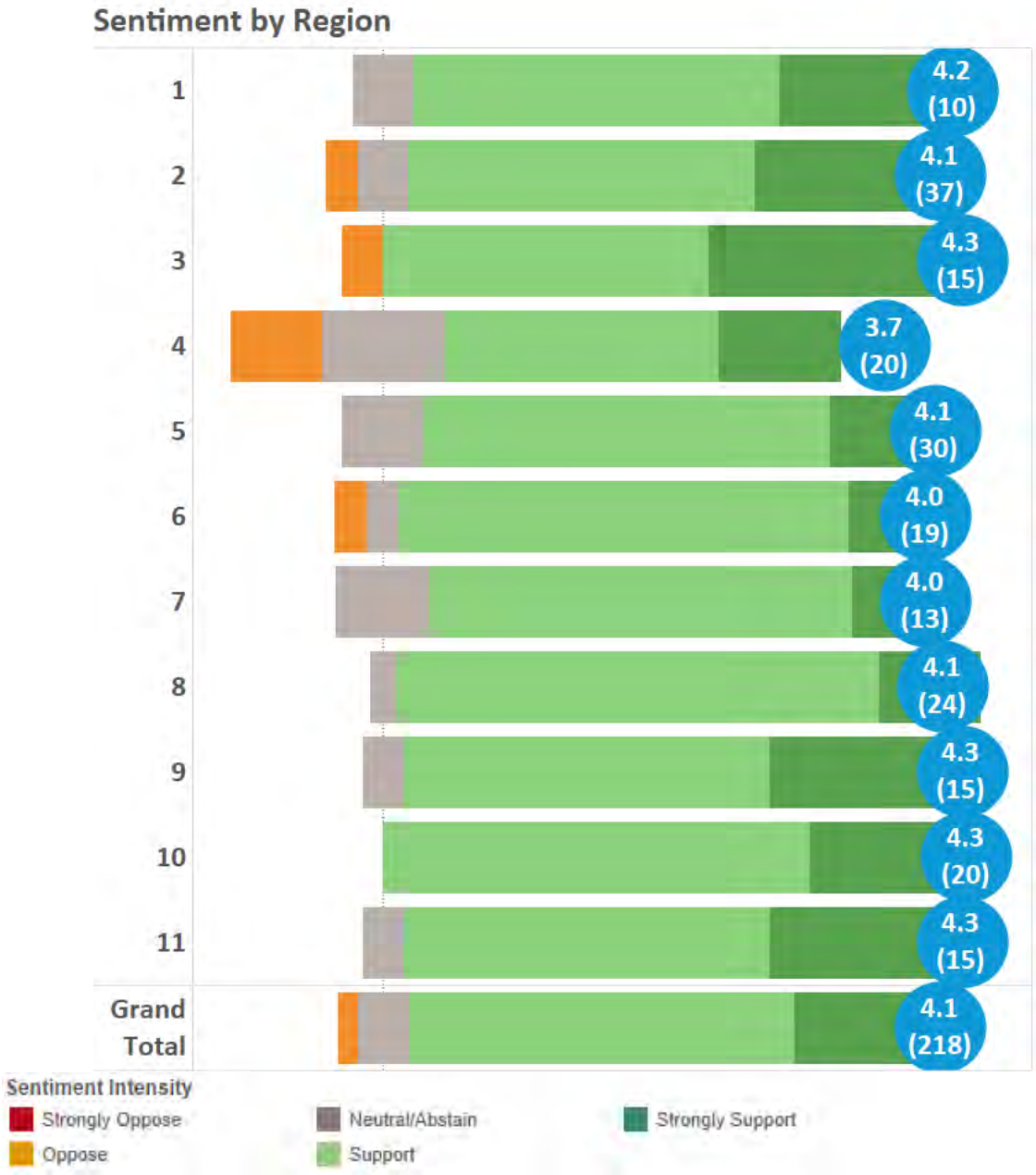


Figure 4 shows sentiment received by the OPTN Region of the commenter including regional meeting participants. Again, overall sentiment was supportive, as indicated by a total sentiment score of 4.1. Concerns were raised in a few regions, mostly under the theme of time burdens; see below in “Themes in Public Comment” for additional discussion. The most concern was seen in Region 4, who shared concern for the original 24-hour reporting time requirement.

Figure 4: Sentiment by OPTN Region



Themes in Public Comment

In addition to the sentiment score, items out for public comment also provide the opportunity for respondents to submit a substantive written comment. Of the responses submitted, 224 also contained a substantive, written comment. Responses are submitted by members of the public at large, as well as on behalf of regions and committees. Commenters covered many different topics, including the themes outlined below. Each theme is described based on the feedback provided.

Support for Reporting Critical Discrepancies

Regarding the overall topic of the proposal, commenters were supportive of reporting critical discrepancies to the OPTN. Their support highlighted the importance of matching recipients to the best donor, as well as support for tracking and documenting critical discrepancies.

Overall, commenters touched on the following themes:

- Timeframe for reporting
- Critical discrepancy definition
- Virtual crossmatching
- Patient safety

Timeframe for Reporting

The proposal asked for feedback on a potential 24-hour reporting time to OPTN when critical discrepancies are discovered. The community had mixed feedback regarding this topic. Many commenters stated that 24-hours was not reasonable for the discovering lab to report the critical discrepancy. Comments regarding specific time frame included suggestions with a wide range, but 72-hours was a recurring timeframe. The Committee agreed with commenters suggesting that 72-hours would be reasonable, thereby aligning with the 72-hour reporting requirement for all other OPTN members as outlined in OPTN *Policy 18.5: Reporting of Patient Safety Events*.

Critical Discrepancy Definition

The proposal asked for feedback on a potential critical discrepancy definition modification. The community had mixed feedback regarding this topic. Support was found for the modified definition, stating that it reduces false discrepancies and is more precise. Suggestions and concerns included wanting further clarification around the p-group level OPTN Computer System transition. Commenters also specifically mentioned clarification of discrepancies in DP and DQ and request for high resolution typing entry. The Committee modified the critical discrepancy definition to alleviate concerns about the resolution of typings reported with p-groups. The modified definition ensures that the discrepancies are evaluated at the resolution they are reported, and that the definition is applicable to all reportable HLA loci, as DPA1, DPB1, DQA1, and DQB1 loci do not have IMGT/HLA assigned serologies.

Virtual Crossmatching

The proposal specified which types of virtual crossmatch discrepancies should be reported. The public supported the committee's proposal to require reporting of incorrect donor HLA typings or incorrect candidate HLA antibody test, as well as incorrect samples. The Committee addressed concerns with virtual crossmatching discrepancies by clarifying the critical discrepancy definitions for low-resolution and two-field typing. The new definition would highlight that for typing at low-resolution, values within the same serologic split antigen group or within the same P-group according to IMGT/HLA are considered equivalent. For typing reported at the two-field resolution, values within the same P group according to IMGT/HLA are considered equivalent.

Patient Feedback

The proposal asked if the patient, living donor, and donor family community agreed that this proposal adequately addresses the issue. Patients were supportive of the proposal and its projected contributions towards patient safety. Commenters agreed that patient safety should be a priority of the proposal. One recipient stated that reporting is a necessary measure to identify where and how critical discrepancy errors were made, and to develop internal controls to avoid future errors and to protect future

recipients. Patient feedback was largely supportive of the proposal both in sentiment and public comments.

Compliance Analysis

NOTA and OPTN Final Rule

This project is authorized under the authority of the National Organ Transplant Act of 1984 (NOTA), which states, "The Organ Procurement and Transplantation Network Shall… (A) establish… (ii) a national system… to match organs and individuals included in the list, especially individuals whose immune system makes it difficult for them to receive organs…"[14] HLA discrepant typings may disproportionately negatively impact highly sensitized recipients, as they are more likely to have developed antibodies towards the HLA typing and are at higher risk for rejection events. In addition, the Committee submits the proposal for consideration under the authority of NOTA, which requires the OPTN to "adopt and use standards of quality for the acquisition and transportation of donated organs"[15] and the OPTN Final Rule, which states that "An OPTN member procuring an organ shall assure that laboratory tests and clinical examinations of potential organ donors are performed to determine any contraindications for donor acceptance."[16] This proposal is intended to increase the quality standard for laboratory testing that is used to evaluate the immunologic risk of deceased donor organs for a given candidate by increasing laboratory accountability and oversight.

OPTN Strategic Plan[17]

- Aligns with other important initiative

This project fits into the strategic plan under "aligns with other important initiatives" because it works to require reporting of discrepancies in Human Leukocyte Antigen (HLA) to reduce the number of critical discrepancies over time through identifying and gaining insight into root causes. It also works to increase patient safety through critical discrepancy reduction.

Implementation Considerations

Histocompatibility Laboratories

Operational Considerations

This proposal would require histocompatibility laboratories to report HLA critical discrepancies and crossmatching events to the OPTN within 72 hours of discovery. Upon review of the reported incident, this may involve performing root cause analyses to determine the cause of the HLA critical discrepancy and implementing corrective action plans as needed. This would total about 40-50 additional reports per year[18] spread across all 138 active histocompatibility laboratories nationally.[19]

[14] 42 USC §274 (b).
[15] 42 USC §274(b)(2)(E).
[16] 42 CFR §121.6(a).
[17] OPTN Executive Committee. *Briefing to the OPTN Board of Directors on Strategic Plan 2024-2027*. June 2024. Available at: https://optn.transplant.hrsa.gov/media/h51awrli/exec-strategic-plan-briefing-paper.pdf.
[18] Based on OPTN Critical HLA Discrepancy Data as of June 24, 2024, assuming the current rate of 20 cases per year reported through the OPTN Improving Patient Safety Portal.
[19] Based on OPTN Membership Data as of October 23, 2024.

Organ Procurement Organizations

Operational Considerations

No anticipated impact.

Transplant Programs

Operational Considerations

No anticipated impact.

OPTN

Operational Considerations

The OPTN is expected to receive approximately 40-50 additional reports to the OPTN Patient Safety Reporting Portal per year, increasing the quantity of patient safety cases the OPTN and MPSC reviews. The OPTN will use the information submitted in the OPTN Patient Safety Reporting Portal as the basis for their inquiry to the member. Based on historical information, it is possible that additional MPSC engagement and monitoring could arise from the findings of the review. This includes any component of monitoring or member action outlined in the *OPTN Bylaws Appendix L: Reviews and Actions.*[20]

Potential Impact on Select Patient Populations

HLA critical discrepancies can impact any recipient of any organ if the recipient is unknowingly transplanted with an organ they have preexisting donor-specific antibodies towards. However, these scenarios may most greatly impact highly sensitized candidates, as they have more pre-formed antibodies and would be more likely to have pre-formed antibodies toward the donor as well. If a recipient is unknowingly transplanted with an organ they have a high level of preexisting donor-specific antibodies toward, they are at risk for hyperacute rejection and graft failure. Since highly sensitized patients, certain minority groups, and women are more likely to have pre-formed antibodies, HLA critical discrepancies may disproportionately impact them. As previously stated, this proposal will provide information related to the root causes of the discrepancies that will assist the Committee in assessing how to reduce HLA critical discrepancies and increase patient safety.

Projected Fiscal Impact

Overall Projected Fiscal Impact

The Fiscal Impact Advisory Group, comprised of representatives from histocompatibility laboratories, organ procurement organizations, and transplant hospitals, reviewed this proposal and completed a survey to estimate anticipated costs. They rated this project as low, medium, or high based on the estimated staffing and/or training, overtime, equipment, or IT support needed in the implementation of this proposal. This proposal was determined to have low impact on histocompatibility labs. No fiscal impact was recorded for transplant hospitals and organ procurement organizations.

[20] OPTN Bylaws, Appendix L: Reviews and Actions. https://optn.transplant.hrsa.gov/media/lgbbmahi/optn_bylaws.pdf.

Projected Impact on Histocompatibility Laboratories

This proposal is anticipated to have a low fiscal impact on histocompatibility laboratories as staff will be required to submit reports of HLA discrepancies to the OPTN in addition to the submissions already being made to transplant centers and organ procurement organizations. Though there will be an increase in submission requirements, the burden on staff is estimated to be low as it does not deviate significantly from standard operating procedures.

Projected Impact on Organ Procurement Organizations

This proposal is not anticipated to have any impact on OPOs.

Projected Impact on Transplant Hospitals

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

Projected Fiscal Impact on the OPTN

It is estimated that $24,207 would be needed to implement this proposal. Implementation would involve review of all current processes, documents, templates, and guidance to account for new types of required cases and updates to all reporting templates and processes. In addition, implementation would include reviewing and preparing implementation communications and educational materials and creation of new education courses. It is estimated that $46,606 will be needed for ongoing support annually. Ongoing support includes investigation of critical discrepancy cases, compiling case documentation, posting of cases for MPSC review, and monthly reporting. In addition, ongoing hours will include consulting on member questions, evaluation and monitoring of data, and any necessary follow-up. The total for implementation and ongoing support is estimated to be $70,813.[21]

Post-implementation Monitoring

Member Compliance

OPTN Contractor staff will continue to send inquiries on behalf of the MPSC to OPTN members who report these patient safety events and will request information about the laboratory and safety event, such as:

- Procedures and protocols
- Quality review processes
- Plans for improvement

The MPSC will continue to review the information submitted by the histocompatibility laboratory and may request that the member submit additional information about certain aspects of the program or submit a plan for quality improvement. The MPSC may also request that a member participate in additional engagement with the MPSC, such as an informal discussion or a peer visit. In rare circumstances where the MPSC identifies a potential ongoing risk to patient health or public safety, the MPSC may request that a member inactivate the histocompatibility laboratory to mitigate the risk.

[21] Resource estimates are calculated by the current contractor for that contractor to perform the work. Estimates are subject to change depending on a number of factors, including which OPTN contractor(s) will be performing the work, if the project is ultimately approved.

Policy Evaluation

The Final Rule requires that allocation policies "be reviewed periodically and revised as appropriate."[22] The Committee actively monitors the prevalence of HLA discrepancies per their charge through HLA quarterly discrepancy reports. For this policy, the Committee will continue to monitor the prevalence of HLA discrepancies through these quarterly HLA discrepancy reports with the included metric of the number of discrepancies that were reported to the OPTN Patient Safety Reporting Portal.

Conclusion

This proposal, which has an overarching goal of increasing patient safety, is multifaceted. Post-public comment changes from the original proposal including a change to the reporting window time limit and an improved definition of discrepancies. The proposal will require reporting of HLA critical discrepancies to the OPTN within 72 hours of discovery, modify the definition of an HLA critical discrepancy, and require reporting incorrect specimens or reports used for crossmatching. By reporting critical discrepancies to the OPTN, labs can benefit from the evaluation of HLA critical discrepancy events which can increase patient safety, improve efficiency, and positively impact the transplant system as a whole. Modifying the definition of an HLA critical discrepancy is intended to reduce required reports to only the most immunologically significant and align with the required HLA typing resolution. Through the information and knowledge gained by reporting and quality improvement reviews, such as RCAs and CAPs, more systemic data can be used to help identify where education or policy may be needed to prevent future occurrences of critical discrepancies. Finally, requiring the reporting of incorrect specimens or typings used for crossmatching is intended to increase patient safety by mitigating potential future immunologic reactions between the recipient and potential donor. The required reporting and subsequent examination of the event will yield information to improve patient safety and maintain system integrity. This new qualitative information on the causes of HLA critical discrepancies could be utilized to refine policies further and create guidance to reduce future discrepancies and increase overall system efficiency.

[22] 42 CFR §121.8(a)(6).

OPTN Policy Language

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~). Heading numbers, table and figure captions, and cross-references affected by the numbering of these policies will be updated as necessary.

4.4: Critical HLA Discrepancies in Candidate, Donor, and Recipient HLA Typing Results

~~For the purposes of this policy, a~~ A human leukocyte antigen (HLA) critical discrepancy is a difference among non-equivalent values, ~~according to Policy 4.10: Reference Tables of HLA Antigen Values and Split 4 Equivalences,~~ at one or more loci in a candidate's, donor's, or recipient's HLA typing.

- For typing reported from a low-resolution method by serologic nomenclature, values within the same serologic split antigen group or within the same P group according to IMGT/HLA are considered equivalent.
- For typing reported at the two-field resolution, values within the same P group according to IMGT/HLA are considered equivalent.

[…]

4.4.B: Requirement to Resolve and Report to the OPTN Critical Discrepant Donor and Recipient HLA Typing Results

The laboratory director of each laboratory involved in ~~the~~ a candidate, donor, or recipient critical HLA typing discrepancy, or their designee, must identify the correct HLA typing. The laboratory director of the laboratory who discovers the critical HLA typing discrepancy, or their designee, must report the critical HLA typing discrepancy to the OPTN via the OPTN Improving Patient Safety Portal within 72 hours of discovery of the discrepancy. Each laboratory director involved in the critical HLA typing discrepancy, or their designee, must ~~and~~ report the reason for the discrepancy to the OPTN within 60 days of ~~discovery of the discrepancy~~ the initial report.

4.11.B: HLA Unacceptable Antigen Equivalences

At the time of the match run, if an antigen or epitope is entered as unacceptable for a candidate, then the candidate will not appear on the match run for donors reported with any of the equivalent antigens described in Tables 4-7, 4-8, 4-9, 4-10, 4-11, 4-12, 4-13, 4-14, 4-15, 4-16, 4-17, and 4-18 below. CPRA calculations include all donor alleles equivalent to a candidate's reported unacceptable antigens, alleles, and epitopes. ~~HLA values listed below as equivalent for the purposes of unacceptable antigen screening are also equivalent for the purposes of reporting HLA typing, with the exception of epitope-based unacceptable antigen assignments in the Table 4-18.~~

18.5.D: Required Reporting by Histocompatibility Laboratories

Histocompatibility laboratories must report the following events to the OPTN according to *Table 18-6* below.

Table 18-6: Required Reporting by Histocompatibility Laboratories

Discovering Laboratories must report if:	To the:	Within 72 hours after:
A donor, candidate, or recipient HLA typing critical discrepancy occurs, as defined by OPTN *Policy 4.4: Critical HLA Discrepancies in Candidate, Donor, and Recipient HLA Typing Results*	OPTN Patient Safety Reporting Portal	The laboratory becomes aware
An incorrect donor or candidate sample was used for a physical crossmatch	OPTN Patient Safety Reporting Portal	The laboratory becomes aware
An incorrect candidate HLA antibody sample was analyzed for a virtual crossmatch per program testing agreement	OPTN Patient Safety Reporting Portal	The laboratory becomes aware

#

Post-Public Comment Changes

New language that was proposed following public comment is underlined and highlighted (example); language that is proposed for removal following public comment is struck through and highlighted (~~example~~).

4.4: Critical HLA Discrepancies in Candidate, Donor, and Recipient HLA Typing Results

~~For the purposes of this policy, a~~ A human leukocyte antigen (HLA) critical discrepancy is a difference among non-equivalent values, ~~according to Policy 4.10: Reference Tables of HLA Antigen Values and Split 4 Equivalences,~~ at one or more loci in a candidate's, donor's, or recipient's HLA typing. ~~Values within the same serologic split antigen group or provided as equivalent for the purposes of unacceptable antigen screening within Policy 4.11: Reference Tables of HLA Antigen Values and Split Equivalences are considered equivalent.~~

- For typing reported from a low-resolution method by serologic nomenclature, values within the same serologic split antigen group or within the same P group according to IMGT/HLA are considered equivalent.
- For typing reported at the two-field resolution, values within the same P group according to IMGT/HLA are considered equivalent.

[…]

4.4.B: Requirement to Resolve and Report to the OPTN Critical Discrepant Donor and Recipient HLA Typing Results

The laboratory director of each laboratory involved in ~~the~~ a candidate, donor, or recipient critical HLA typing discrepancy, or their designee, must identify the correct HLA typing. The laboratory director of the laboratory who discovers the critical HLA typing discrepancy, or their designee, must report the critical HLA typing discrepancy to the OPTN via the OPTN Improving Patient Safety Portal within ~~24~~ 72 hours of discovery of the discrepancy. Each laboratory director involved in the critical HLA typing discrepancy, or their designee, must ~~and~~ report the reason for the discrepancy to the OPTN within 60 days of ~~discovery of the discrepancy~~ the initial report.

18.5.D: Required Reporting by Histocompatibility Laboratories
Histocompatibility laboratories must report the following events to the OPTN according to *Table 18-6* below.

Table 18-6: Required Reporting by Histocompatibility Laboratories

Discovering Laboratories must report if:	To the:	Within ~~24~~ 72 hours after:
A donor, candidate, or recipient HLA typing critical discrepancy occurs, as defined by OPTN *Policy 4.4: Critical HLA Discrepancies in Candidate, Donor, and Recipient HLA Typing Results*	OPTN Patient Safety Reporting Portal	The laboratory becomes aware
An incorrect donor or candidate sample was used for a physical crossmatch	OPTN Patient Safety Reporting Portal	The laboratory becomes aware
An ~~incorrect donor HLA typing or~~ incorrect candidate HLA antibody ~~test~~ sample was analyzed for a virtual crossmatch per program testing agreement	OPTN Patient Safety Reporting Portal	The laboratory becomes aware