OPTN Histocompatibility Committee
Meeting Summary
April 5, 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 04/05/2022 to discuss the following agenda items:

1. Public Comment Feedback: *Change Calculated Panel Reactive Antibody (CPRA) Calculation* proposal
2. Kidney Paired Donation (KPD) Update
3. Policy Oversight Committee (POC) Update
4. Review of Current Histocompatibility Policies and Guidance

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

1. Public Comment Feedback: *Change Calculated Panel Reactive Antibody (CPRA) Calculation* proposal

The Committee received an overview of the feedback that was received during public comment on the *Change Calculated Panel Reactive Antibody (CPRA) Calculation* proposal. The proposal received general support during public comment.

Responses to Feedback Questions

- Transition plan
  - General consensus that 1 week was not enough time to transition all patients
  - Recommendations ranges from two weeks to two months
  - Recommendation to include additional information for waitlist management such as kidney allocation system (KAS) points
  - Staff working on a report to provide to programs, and the earliest feasible timeframe for the report and an update
- CPRA viewable for all organs
  - General consensus that it would be beneficial for many programs and organ types, and would not hurt those that did not use it

Concerns

- Potential reduction in matching efficiency by adding additional loci and allele specificities to calculations
- One member unsure about the clinical relevance of DP antibodies
- There is potential for abuse with allele-level antibodies in calculation

Recommendations for Future Improvement

- Inclusion of human leukocyte antigen (HLA) DQA1-DQB1 heterodimers in calculation and deceased donor screening
- Easier interface for entry of unacceptable antigens
    - There is an application programming interface (API) available for unacceptable antigen entry

The Committee also reviewed further validation that is being done with CPRA data.

Summary of discussion:

Public Comment Feedback

A member mentioned that changing the transition time frame from two/three weeks to a month would seem reasonable.

The Chair inquired about a practical time frame for the transition. Staff stated that the goal is to provide as long of a time frame as possible without delaying implementation. There is a quality assurance period when the Information Technology (IT) department is making sure that nothing in UNet will break once the CPRA calculator is implemented. Staff is still determining how long that time frame can be.

The Chair inquired if it would be reasonable to give centers a minimum of two weeks to transition. Staff stated that two weeks is realistic, at the least. Staff also mentioned that a report will also be provided to centers that include all of the changes and the changes to Kidney Allocation System (KAS).

The Chair inquired if any of the feedback leads Committee members to believe there's a need to adjust the calculator or policy language. A member stated that they thought the proposal was well received. The Chair mentioned that one particular response should be considered – the original KAS policy proposal included modeling of the effect of using CPRA on offer rates and the Committee didn't have the opportunity to do modeling to that extent using this calculator. The Chair inquired if any members have concerns about this and stated that staff had mentioned trying to put more data together, at least using a more recent iteration of the calculator. Staff mentioned that they were planning on updating the wait list analysis based on the updates the Committee had talked about previously – staff would have to check which updates the Committee had talked about doing between public comment and the Board of Directors meeting.

An OPTN contractor noted that they believe they have re-run the entire wait list unacceptable antigen data set with the latest version of the calculator, so the wait list analysis could be regenerated based on that.

The Chair stated that another point the public comment response had noted was in regards to the resolution typing data from National Marrow Donor Program (NMDP) and looking at differences between antigen recognition domain (ARD) and primary sequence differences. The Chair mentioned that the Committee had looked into this and has done a fair amount to address this, they just imagine the commenter couldn't get into all of the details that were presented in the public comment proposal. Staff stated the Committee reviewed which typings were equivalent with the ARD last June and the genotype data set has been updated since then, removing ARD equivalencies for everything except the typings that couldn't be distinguished between exons, outside of exons 2 and 3.

An OPTN contractor agreed and stated that this dataset is a divergence from the way the NMDP match algorithm works and the data underlying it, which will continue to be the case for some time. The OPTN Contractor mentioned that the Committee could include a paragraph or two in the proposal to make it clearer.

The Chair stated the last point brought up in the public comment response was regarding the availability of the calculator itself to programs for HistoTrac. The Chair mentioned that they imagine all of that will work the way it currently does and will provide the same information between the applications. The Chair wasn't concerned about this point.

The Chair highlighted that the most important/relevant point out of that response was the modeling that the Committee is going to be doing prior to the briefing paper to the Board of Directors being put together.

A member inquired if the CPRA calculation API is going to be updated at the same time this is being implemented or if there will be a lag. Staff explained that it will be a part of the project so it will be updated at the same time.

An OPTN contractor stated they plan on releasing the calculation as an open source in a paper, so labs can run it and make their own versions. A member mentioned that they don't think the Committee should be able to control how a member emulates the CPRA calculation because that is something they are doing on their own rather than taking it directly from the source data. Staff mentioned they are planning to provide any of the materials upon request and will have it on the OPTN website as well, along with CPRA calculation. The calculation will be available in Waitlist as well as the API.

The Chair inquired if the Committee needed to vote on the proposal. Staff explained that the final policy language vote will occur during the May committee meeting.

CPRA Data Validation

Looking at the Typing Resolution Scores, the OPTN contractor stated that for class 2, some of this reflects that there are sets of alleles within the same G group that aren't distinguished and the expectation-maximization (EM) algorithm is spreading out the weight evenly on those alleles, unless there's some typings on the same haplotype where the allele is distinguished. Some of the Typing Resolution Scores are due to a lack of resolution beyond exons 2 and 3 for class 2. Also reflecting missing typing. Some of the class 2 haplotypes haven't been typed at the DPA1 loci and the EM doesn't have enough information to infer the result. The OPTN contractor stated that that is where this validation is limited and they believe a few more of the DPA1s should be in red. The OPTN contractor also highlighted that, for Caucasian, the EM algorithm is able to incur the missing data pretty well and resolve the ambiguity. Some of this would be resolved by just accumulating more data over time. Otherwise, this is reflecting that the EM algorithm is able to resolve a lot of ambiguity.

Staff stated that the concern with restricting the data set to what is available in HLA-DPA and HLA-DQA is that it would restrict the number of typings and it would potentially provide less inclusiveness at other loci. Staff mentioned that that may be something the Committee can update in the future as NMDP does their registry typing. The OPTN contractor agreed and mentioned it's something the Committee could consider.

The Committee agreed this is the accuracy that they're able to obtain at this time and that they can be updated once there is more available data.

There was no further discussion.

2. Kidney Paired Donation (KPD) Update

The Committee received an overview of the Kidney Paired Donation (KPD) project.

The KPD Workgroup has recommended the following updates to OPTN Histocompatibility policy:

- Policy 13.5.A: *HLA Typing Requirements for OPTN KPD Candidates* and 13.5.B: HLA Typing Requirements for OPTN KPD Donors
    - Implementation of updates to the HLA Equivalency tables proposed by the Committee will update these policies to include HLA-DPA1
- Policy 13.5.D: *Responding to OPTN KPD Match Offers*
    - Workgroup recommended the review of existing data on explanation of declines for unacceptable antigens to determine if this requirement is still needed
- Policy 13.7.B: *Blood Type A, non-A1 and Blood Type AB, non-A1B*
    - Focus group recommended updating antibody titer requirement to align with Kidney Policy 8.5.D
    - Workgroup determined this update will need to be a separate project
- Policy 13.10: *OPTN KPD Crossmatching Requirements*
    - The Committee recommended maintaining the requirement for physical crossmatch
    - High resolution typing discussion

Summary of discussion:

A member inquired if the KPD Workgroup recommended keeping physical crossmatching and not transitioning to virtual crossmatching. A member explained that the KPD Workgroup is recommending performing a physical crossmatch pre-transplant. The member stated that if labs have both a physical and virtual crossmatch, then they can provide more information.

A member mentioned that it seems surprising that a lot of labs are pushing for virtual crossmatches and the histocompatibility field is trying to get Centers for Medicare and Medicaid Services (CMS) approval for virtual crossmatches, yet the KPD Workgroup is recommending the opposite. The member explained that the KPD Workgroup wants to avoid a patient being incompatible since that could destroy the whole KPD chain.

A member noted that they recommend doing auto-crossmatches to control autoantibody activity. The member explained that the KPD Workgroup is recommending that too.

A member emphasized that they wouldn't want to get just before transplant and then the crossmatch is positive – physical crossmatches have potential false positives which can cause delays. The member explained that if they perform an auto-crossmatch and it's positive, then they can say that it's auto-active and move forward. Staff inquired if the member would suggest guidance or education, in addition to the crossmatch requirements. The member stated that that should be something for the KPD Workgroup or the Committee to consider.

A member mentioned that they will relay this feedback to the KPD Workgroup and suggest adding guidance or education to the crossmatch requirements.

There was no further discussion.

3. Policy Oversight Committee (POC) Update

The Committee reviewed the role of the Policy Oversight Committee (POC), the Strategic Plan, and the Strategic Policy Priorities. It was explained that the POC has a renewed focus on portfolio management, which aims to maximize benefit given the available resources.

Summary of discussion:

There was no discussion.

4. Review of Current Histocompatibility Policies and Guidance

The Committee reviewed current OPTN Histocompatibility Policy with the following goals:

- Determine if policy requirements/guidance are in line with current practice or require updating
    - The most recent update to some sections was 5 years ago
- Start refining potential changes after determining needed areas of focus

The following requirements/guidance were reviewed:

- Review of HLA typing and crossmatching reports
- Review of sensitization history
- Deceased donor HLA typing
- Candidate HLA typing
- Candidate antibody screening
- Physical crossmatching
- Preservation of excess specimens
- Virtual crossmatching

Summary of discussion:

Review of HLA typing and crossmatching reports

A member stated they didn't think there were any specific concerns with OPTN Policy 4.1. The member was curious about how other labs handle the secondary review of typing, antibody, and crossmatch results – do lab professionals review them while they are on call or the next business day? The member emphasized that they want to leave this requirement open for variability across labs.

A member mentioned that they believe the next business day requirement is more for signing the official report and most lab professionals are reviewing results as they become available.

A member inquired if the current standard states the results should be reviewed on the next business day.

A member stated that they think most labs release a preliminary report, which is usually done verbally, and then the actual sign out happens the next morning. The member thought that seemed reasonable.

A member inquired about how much data labs are responsible for since some programs want to manage their own data. The member explained that their lab manages all data except for heart transplant and they can't be held accountable for what the heart program does with their waitlist.

A member thought the term "histocompatibility data" was very vague. A member recommended clarifying what is in scope for histocompatibility data and clarifying when documentation is required, without being too prescriptive. The member emphasized the Committee wants to accommodate variability across labs, while still meeting the need to have documentation about who has reviewed what.

A member inquired about what data is already captured in UNet. For example, when somebody logs in to UNet, makes changes to unacceptable antigens, then logs out, the member inquired if that is tracked. Staff inquired if this data should be tracked for members that don't make any changes to unacceptable antigens. A member explained that the audit log should track everyone as long as you click save at the end.

A member stated that often times a program will enter what they think is accurate typing and unacceptable antigens, then the programs sends their lab emails for the lab to go in and verify. The

member mentioned that that's the only time coordinators are entering data, so the member feels like that should be tracked and documented.

A member inquired if the audit log is for tracking or for true verification. The member noted that they would think it would be spelled out who does the verification in a transplant agreement.

A member stated that as long as a reference lab, that's not managing patients or waitlist, has this spelled out in the transplant agreement then the member believes that would meet the spirit of what the Committee is trying to accomplish.

A member stated that they agree, but the difference here is that there is no double entry of unacceptable antigens. When updating unacceptable antigens with a new sample, it's clearly documented but there's no second check on any changes made. The member emphasized that they don't want to go down the road of requiring double checking for every entry.

A member stated that it would be ideal if a patient's unacceptable antigens were being uploaded through the upload file or through an API once that becomes available, and then a periodic verification could be instituted. It could then be verified for a group of patients that the process is working. The member stated that they believe that would satisfy the verification.

The Committee agreed that the following updates are needed for OPTN Policy 4.2:

- Clarification on documentation needed for verification versus (vs.) eliminating verification altogether
- Clarification on what an acceptable level of verification is and what would be required

The Committee agreed that the following updates are needed for OPTN Policy 4.1:

- Clarification on timing for initial and final report review
    - It was noted that labs don't create "reports" and charts aren't available until the next business day.
- Clarification on how to document the review and verification in terms of typing
    - A member suspected that documentation of the review must be kept for three years, which was instituted back when everything was paper-driven. Staff explained that this hasn't been changed since at least 2009, before there was an audit log for HLA data.

Review of sensitization history

A member stated that this guidance seemed to be up to date and accurate. Another member mentioned that they didn't have any suggestions to change this guidance at all.

The Committee agreed that there were no updates needed for this guidance.

Deceased Donor HLA typing

The Chair stated that the Committee has extensively discussed this and this is coming up in the new changes. The Committee wants all loci for all donors, with the caveat for livers, to be included.

Members suggested considering addressing HLA typing for thoracic donors. A member inquired if CPRA should be incorporated into the continuous distribution algorithms for the assignment of points for hearts and lungs, and now for kidneys as well. The member noted that the only way patients are going to be excluded based on some of those aspects is if they're prospectively screened off of match runs.

Staff suggested having the Committee receive an update on continuous distribution efforts in order to guide discussions surrounding these requirements.

Candidate HLA typing

The Chair inquired if candidates were included in the enhanced typing. Staff explained that the Committee didn't change any HLA typing for candidate requirements and when the typing changed to molecular requirements for donors, the Committee didn't specify candidate requirements either.

The Chair inquired if any members do less than full typing on kidney recipients.

A member stated that, currently, they don't do full typing; however, their lab is bringing in Next Generation Sequencing (NGS) and will perform full typing when NGS is up and running. A member mentioned that their lab doesn't perform C or DB typing on recipients.

The Chair inquired if members do full typing on thoracic candidates. A member stated no, but they wish they did. The Chair stated their lab is the same way. The Chair inquired if there's any reason to change this, since the information is really only to help labs and to identify 0-ABDR mismatches, or is this sufficient.

A member mentioned that their center only did ABDRs on kidneys until they changed policy, which occurred when allocation moved to concentric circles and their center was getting donors from outside of the 250 nautical mile (NM) circle. The member stated that, even for 0-ABDR kidneys that hadn't been screen in a while, not having DQ typing was terrible because using associations will only go so far. The member explained that there could be allocation efficiency arguments to support either getting full typing or at least DQ typing in order for those ABDR offers to be interpretable. It was noted that if this is common practice, then it makes sense to put it in policy because it's probably better for the patients.

A member stated that, with all the new data coming out, the Committee should include DQ in the mix if they're not going to require full typing.

The Chair emphasized the distinction between requirements and best practices. Aside from speeding up allocation a bit by having more typing, the Chair stated that candidate HLA typing doesn't really affect other people like donor typing, which is going to be provided to anyone else. If we have the minimum typings required for allocation, then the rest would be suggested.

A member stated that they agree this would be a best practice; however, it would be a transplant center's decision.

Staff inquired if there would be any potential for incorporating DQ matching in the future because, if so, the Committee would need data to justify that. The Chair stated it depends on how many labs currently don't have DQ typing, especially for current patients. It was noted that if the Committee were to look at survival data, it may look significantly different from current wait list data.

The Chair stated that staff would have to be able to answer whether current data is sufficient to make analyses like that and, if it is, then that is when we can decide whether or not to change policy to include DQ matching.

Staff summarized that the Committee would want to look at the data before discussing including DQ further.

A member inquired if best practices are allowed in guidance documents. Staff stated that it depends – the Committee can put out information on best practices, but they must be cautious how they phrase it. There must be a distinction made between what members are required to do vs. what is beneficial for patients. The member stated that that might be a good stepwise approach – include DQ matching in guidance before changing policy with the better data. Staff mentioned that the Committee can always add in a section for candidates when updating their current guidance.

Candidate antibody screening

A member stated that the guidance says initial serial screening could include cytotoxicity or more sensitive tests. The member stated that probably all labs are using Luminex or Flow-PRA, but they're not sure who is still using antihuman globulin (AHG) screens to do their antibody screening. The member suggested that this guidance should be updated.

A member believes that we should be matching what the Centers for Disease Control (CDC) is requiring. Staff explained that that requirement is only for labs that are performing antibody screening upon request. A member stated that if a lab wants to use AHG screens then they should be able to do it.

A member suggested that OPTN Policy 4.5 is good as it is and it's just the guidance that needs to be updated to get rid of all the old techniques that labs no longer use.

A member inquired if the Committee should make a recommendation for labs to use a method that addresses prozones, like EDTA plasma, or is that not necessary. A member mentioned that something like that should be addressed within the College of American Pathologists (CAP) or American Society for Histocompatibility and Immunogenetics (ASHI) laboratory standards. The member highlighted that it's not the Committee's job to mandate practice. Staff mentioned that the Committee could include that this is something that centers perform and reference the CAP and ASHI standards in guidance.

A member mentioned that the Committee is assuming the antibody screening results are accurately reported here, so, as long as the Committee can clean up the assays, this guidance is probably alright. A member expressed concern that the Committee is not mandating the antibody screening in policy and, instead, suggesting that the screening should only be done if requested by a physician. However, antibody screening is mandated for donor typing. The member stated that they believe the candidate antibody screening should be required.

A member stated that it is surprising that antibody screening isn't required; however, they assume all centers do antibody screening because, otherwise, they would just be relying on a crossmatch. The member mentioned that if the Committee were to mandate antibody screening, then the Committee would have to review the options that document the results in UNet, which are (1) Yes, antibodies detected, (2) Yes, no antibodies detected, or (3) No, not tested. Staff explained that there are a few options in the recipient histocompatibility form. Staff also mentioned that labs only have to enter unacceptable antigens based on clinical criteria, although labs can have antibodies that they don't enter as antigens. The Chair confirmed that in UNet there are only three options.

Staff inquired if the Committee would want to see how often labs are not testing before they evaluate requiring antibody screening.

Staff inquired if members think policy/guidance needs to include antibody screening for patient safety or if it should be a clinical decision, so then programs can either do an antibody screening or institute other policies like physical crossmatching. The Chair stated that they would prefer the second option because they can't imagine a governing body would give accreditation to a lab that isn't doing any antibody testing.

A member argued that requiring labs to do antibody testing is essential for efficient allocation, however, the Committee has no control over reporting so it nullifies that issue. A member noted that the ASHI standard is antibody screening of all patients at the time of evaluation and often enough.

Staff inquired, with antibody screening being regulated elsewhere, whether the Committee want to change the requirements or leave it up to clinical practice – programs can either require a physical crossmatch or not if they don't do antibody screening.

A member mentioned that they think that would be ok, but this could be something that comes up in the future. The Chair stated that there's a difference between what the Committee can mandate and what members would want to occur if they were getting transplanted at that center. Staff mentioned that that can be something the Committee discusses in their guidance too.

The Chair mentioned the way policy is written is fine as it is and members agreed.

Physical crossmatching

Staff inquired if the Committee needs to clarify the guidance in terms of what should be done with a physical crossmatch. A member stated that the physical and virtual crossmatching guidance had a lot of overlap and they suggested combining the guidance in some way. The member stated that they mainly want to make sure that the use of virtual crossmatching in lieu of physical crossmatching is a common practice and that concurrent retrospective physical crossmatches may be performed but are not required in policy.

A member explained that the intent with the policy language of physical crossmatching was to leave it open potentially for virtual crossmatching to be incorporated – explicitly why policy states "if a lab performs a physical crossmatch". The Chair explained that a letter was just sent to ASHI and that the concerns about the CMS regulations revolving around virtual crossmatching have not been resolved yet. The Chair stated that they had hoped that more certainty would have been available to write these policies regarding the usability of virtual crossmatches or the delineation between using physical crossmatches vs. virtual crossmatches.

Staff explained that this policy was updated in 2017 to intentionally be vaguer to allow for virtual crossmatches.

A member stated that they have recently found this language confusing; however, they think it is great if it was the intent of the Committee to leave it vague. A member explained that it was left vague because, at the time, the Committee didn't have the definitive ruling on the utility and the usability of virtual crossmatches as a substitute for physical crossmatches. It was highlighted that this policy still adheres with the language that is in Clinical Laboratory Improvement Amendments (CLIA) regulations; however, they don't define exactly what a crossmatch is.

Staff mentioned that there are a fair number of questions regarding this policy, so the intentional vagueness does confuse a lot of people.

A member inquired about the use of lymph node and spleen as the preferable source for deceased donor crossmatching, given that peripheral blood is more often used. A member referenced a paper from Johns Hopkins stating that peripheral blood can have reduced expression of HLA, but it is a common practice to use peripheral blood.

A member noted that the term "preferable" does not mean that labs have to use it. The member explained that it probably is preferable to use spleen, but that doesn't mean that all labs are going to use it. A member agreed that it helps to leave it this way, since it is not mandating the use of lymph nodes and spleens.

Preservation of excess specimens

A member stated that this policy was very vague and mentioned that their lab stores everything that comes to them. The member explained that the main reasons labs will be using cells after transplant is for either deoxyribonucleic acid (DNA) or retrospective crossmatches. The member inquired whether the Committee should clarify the language to state which conditions labs need to save material and how much labs need to save. The member stated that their lab saves material specifically for themselves and

will save a vial for the organ procurement organization (OPO) in case they need to extract DNA for testing post-transplant.

A member also emphasized that every lab has different instructions and limitations. For example, in the member's previous lab they couldn't save materials for more than 5 years because they didn't have the space. The member stated that not all labs would be able to follow policy if the Committee includes more specifications into policy surrounding preservation of specimen.

A member mentioned that their lab only saves DNA and not cells.

A member suggested leaving the policy as it is and allow labs to do what is necessary in order to have a good agreement with the OPO. A member noted that there are storage requirements for OPOs, which is mainly plasma and serum, so the real question is whose responsibility is it to save material for additional testing.

A member stated that that would be dependent on the agreement that the lab has with the transplant center. For example, it used to be useful to have Luminex and antibody assays on hand for crossmatches; however, that is becoming less and less useful.

Staff inquired if there are different instances in which labs would not need to save specimen, like a lab had high resolution typing at all loci and it wasn't necessary to save specimen. A member stated that high resolution isn't needed for typing unless DNA is needed for testing, other than histocompatibility testing. A member mentioned that a lab can have other polymorphic regions that they found as a potential cause of rejection and they need donor and recipient typing, so being able to have DNA available would allow a lab to do testing of additional genes of interest for transplant.

A member agreed and stated that having the DNA is important for patient care.

The Chair stated that it's important for labs to preserve excess specimen and suggested that the current requirements in policy are sufficient and vague to allow for labs to do what works best for them.

A member mentioned that, when reviewing the guidance, it did satisfy a number of questions that they've received on this policy and really spells out what expectations there are to be compliant with policy.

Virtual crossmatching

The Chair stated that virtual crossmatching does not exist in policy, so the only source of guidance is in the Committee's guidance document. Basically, the guidance suggests that the written agreement should outline the following: (1) how labs manage virtual crossmatching with the transplant program, (2) what criteria to use, and (3) how to determine the criteria. The Chair mentioned that, outside of the agreement, it's also a good idea to determine what the donors DPA1 antibody is if a candidate has DPA1 antibodies.

The Chair mentioned that the Committee had discussed how common performing virtual crossmatches was, under what circumstances they should be performed, and how qualified someone has to be to perform a virtual crossmatch. When writing the guidance, the Committee determined that it should be someone with experience in a technical supervisory, clinical consultant, or equivalent experience type of role.

A member noted that it's probably time to make this policy and not guidance and suggested that the Committee needs to define a virtual crossmatch since there are different implications for how labs use it – are virtual crossmatches used as a sanity check, a way to prescreen the match run, or a determination that the organ is ready for transplant with the offered candidate?

A member also mentioned the importance of having guidance regarding what data is required and what level of review is required for virtual crossmatches.

A member stated that they thought the guidance was well inclusive, but couldn't find something equivalent in policy. The member mentioned that policy needs a requirement for labs to create an agreement with the transplant program, including how to handle virtual crossmatches, since many transplant programs are going to transplant simply on a virtual crossmatch.

A member mentioned that the language "notifications should be documented in the patient's results" implies that labs are providing virtual crossmatch results in the patient results. A member explained that that's not necessarily true. If a lab is running a physical and virtual crossmatch, then they are going to have a physical report which would be the results. A member pointed out that, if it's retrospective and after time of transplant, that's when a lab is going to find discrepancy.

A member inquired if a lab should document that the virtual crossmatch was negative in the circumstance where they perform a virtual crossmatch, the patient receives the transplant, and then they perform a physical crossmatch and it doesn't match. The member also inquired if there should be documentation of the review of the antibodies if a transplant program is going to perform a transplant with only a virtual crossmatch. The Chair mentioned that they don't understand how a transplant program could perform a transplant at all without documenting the review of the antibodies, mainly just to cover themselves.

A member noted that labs would have to perform a crossmatch before transplant programs can perform a transplant, so, from a regulatory perspective, that makes sense and it would be helpful to clarify that in policy/guidance. The member also inquired if it's a best practice to make a note in the chart when the virtual crossmatch is discrepant, especially because that note may not always make it into their chart. A member mentioned that that may be a sentinel result that needs a notification to be sent when it's documented – the crossmatch is now positive, so there should be an alert since it is something different than what was expected.

A member noted that a critical result notification isn't the same as a report where a lab reconciles the two discrepant crossmatches. Staff explained that the critical HLA discrepancy right now only refers to HLA typing, not antibody or crossmatching results. A member mentioned that sometimes it's expected to have discrepant results between a physical and virtual crossmatch, but suggested adding some type of guidance regarding that. Members stated that is seems the Committee needs to update policy and it should include the following elements: virtual crossmatching definition, who should be able to perform virtual crossmatching, and what should be included in the agreement that labs have with transplant programs.

The Chair mentioned that the above elements are the least under the Committee's control. The Chair suggested that the Committee wait to see what type of response CMS provides because they can't make policy that is against the law. The Chair explained that that should drive what the Committee's next steps will be. Secondly, the Chair mentioned that a workgroup is being organized by ASHI, including all relevant stakeholders, to focus on all these questions. The Chair mentioned that the workgroup has initially planned to discuss the following: (1) define virtual crossmatch, (2) define antibody assessment, and (3) determine other definitions or changes in terminology needed within the histocompatibility field. Lastly, that workgroup plans to decide how these definitions will be implemented and proposes that they are included in a consensus paper in American Society of Transplantation (AST). The Chair agrees that this is essential, but these are a few steps that need to be taken before the Committee can include definitions in policy.

Members agreed that it's reasonable to take those steps before updating policy; however, they suggested updating the guidance document. A member mentioned that the guidance document should be updated to include mandating molecular DPA typing. Another member also suggested that the guidance document could be updated to include all of the considerations that the Committee discussed today. A member emphasized that updating the guidance document will re-establish it as a document in the histocompatibility community and will refresh labs on guidance for virtual crossmatching.

There was no further discussion.

The meeting was adjourned.

Upcoming Meetings

- May 10, 2022 (teleconference)

Attendance

- **Committee Members**
  - Peter Lalli
  - John Lunz
  - Bill Goggins
  - Caroline Alquist
  - Eric Weimer
  - Evan Kransdorf
  - Gerald Morris
  - Idoia Gimferrer
  - Jennifer Schiller
  - Karl Schillinger
  - Manu Varma
  - Marcelo Pando
  - Reut Hod Dvorai
  - Valia Bravo-Egana
  - Vikram Pattanayak
- **HRSA Representatives**
  - Jim Bowman
- **SRTR Staff**
  - Katherine Audette
- **UNOS Staff**
  - Courtney Jett
  - Rebecca Brookman
  - Amelia Devereaux
  - Betsy Gans
  - Kayla Temple
  - Kelsi Lindblad
  - Lauren Mauk
  - Sarah Scott
- **Other Attendees**
  - Loren Gragert