

**OPTN/UNOS Histocompatibility Committee  
Report to the Board of Directors  
June 1-2, 2015  
Atlanta, Georgia**

**Dolly Tyan, Ph.D., Chair  
Robert Bray, Ph.D., Vice Chair**

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*This report reflects the work of the OPTN/UNOS Histocompatibility Committee between the November 2014 and March 2015 period.*

**Action Items**

1. Histocompatibility Bylaws Rewrite Phase II

*Public Comment:* [September 29 – December 5, 2014](#)

*Board Consideration:* June 2015

Many of the Bylaws governing laboratories are ambiguous, fail to reflect advances in technology and current clinical practice, or are more appropriately monitored by the histocompatibility accrediting agencies (ASHI and CAP). As a result, the Committee conducted a comprehensive review of the Bylaws governing histocompatibility laboratories. The Committee determined that rewriting the Bylaws was a large project and decided to split the rewrite into two phases. In November 2013, the Committee completed and the Board of Directors approved the first phase of changes in the Bylaws. This phase included changes that required all laboratories to comply with the requirements in the documents issued by ASHI and CAP (as of a certain date), expanded the definition of changes in key personnel, and required laboratories to submit a coverage plan to the OPTN/UNOS. Those changes became effective February 1, 2014. The Committee is now proposing the following additional changes:

- Adding the general supervisor to the list of laboratory key personnel.
- Creating two pathways for approval of histocompatibility laboratory directors--M.D./D.O. or earned doctoral degree. Each pathway specifies particular education, experience, and certification requirements. The Committee also proposes the addition of a foreign equivalent qualifier for both pathways (current Bylaws are silent on foreign equivalent education and experience for laboratory directors).
- Simplifying requirements for the technical supervisor, general supervisor, and clinical consultant by only requiring that these individuals meet the requirements in the federal Clinical Laboratory Improvement Amendments (CLIA).
- Eliminating references to the histocompatibility technologist, since no requirements for this position are included in the Bylaws.
- Adding criteria for performance review of a histocompatibility laboratory, including HLA typing errors that result in an incompatible transplant or the reallocation of an organ.
- Removing sections that are out of date or more appropriately monitored by the histocompatibility accrediting agencies.

The second phase of the Bylaws rewrite contains changes dealing with education, certification, and experience requirements for laboratory key personnel and performance indicators that will trigger a mandatory performance review of a laboratory.

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The Committee agreed there should be a pathway for laboratory directors who were approved and served as directors prior to the 2003 requirement for their board certification to have that requirement waived. This is a CLIA based clause and requires waiving board certification for individuals already operating as a laboratory director prior to 2003. The Committee approved an amendment to include this group of individuals as qualified laboratory directors.

Some commenters were concerned that the requirement that laboratory directors have publications in (greater than one) peer-reviewed journal was too stringent. The Committee came to a compromise on this language. The amendment allows for either demonstrated participation in laboratory professional conferences or publications in peer-reviewed journals.

In addition, there was concern that the proficiency testing performance review criteria was too excessive since the words “satisfactory” and “unsatisfactory” apply to individual send-outs. The Committee was divided on this issue and came to a compromise on the following amendment:

1. For programs other than ABO, a less than 80% successful satisfactory performance on more than one in an external histocompatibility proficiency testing program within a year the previous twelve months.

Notably, the Committee also agreed to delete *C. Submission Requirements for Laboratories Using New Techniques*. The Committee reasoned that this section was more appropriate for the histocompatibility laboratory accrediting agencies to monitor.

The Committee voted unanimously to send this proposal with the post-public comment amendments to the Board of Directors for consideration.

**RESOLVED, that additions and modifications to Bylaws Appendix C and Policies 4.2 (Requirements for Laboratory Review of Reports) and 4.3 (Requirements for Waiting List Data Verification) are modified as set forth below, effective September 1, 2015. The addition of general supervisor as key personnel is effective pending programming and notice to membership.**

### Committee Projects

2. Histocompatibility Guidance Document

*Public Comment: N/A*

*Board Consideration: December 2015 (Estimated)*

The OPTN/UNOS Histocompatibility committee continuously reviews and monitors bylaws and policies that govern histocompatibility testing for solid organ transplantation. New requirements and changes to OPTN/UNOS policy are sponsored by an OPTN/UNOS committee, submitted for public comment, and revised accordingly before being submitted to the OPTN/UNOS Board of Directors for a vote. In many instances, a bylaw or policy may have several different interpretations depending upon the situation or may require additional information for interpretation. To address this issue, a guidance document is being developed to address aspects of the bylaws and policies that need additional clarification. Laboratories may also use this document to assist in ensuring they are compliant with all OPTN/UNOS bylaws and policies. This guidance document is designed to provide additional information or clarification, where needed, to both the bylaws and policies of the OPTN/UNOS.

3. CPRA and Priority for Kidney Candidates Undergoing Desensitization

*Public Comment: January 2016 (Estimated)*

*Board Consideration: June 2016 (Estimated)*

The Committee continues to discuss CPRA prioritization points for kidney candidates undergoing desensitization. Under the kidney allocation system, highly sensitized kidney candidates who undergo desensitization lose allocation points associated with their CPRA score, reducing their opportunity for kidney offers. Previously, a workgroup comprised of members of the Histocompatibility, Kidney Transplantation, and Minority Affairs Committees held an introductory call on this project and discussed barriers to getting data on how many patients would benefit from a policy change.

The workgroup decided that the most effective step for moving forward was to conduct a survey of kidney transplant programs to learn whether more programs would utilize desensitization for highly sensitized candidates if these candidates could keep the prioritization associated with their CPRA score for a period of time.

At the Committee's August 11-12, 2014, in-person meeting, an update on the survey's design was presented to the Committee. A series of draft survey questions were presented and reviewed by the Committee. The Committee recommended the KAS Desensitization Workgroup refine the survey questions for eventual distribution.

4. Annual Update to HLA Equivalency Tables

*Public Comment: August 2015*

*Board Consideration: December 2015*

OPTN/UNOS policy requires the Committee to review and recommend any changes needed to the equivalency tables on an annual basis. In February, the HLA Equivalency Table Update Subcommittee provided a status report on updating the equivalency tables. The Committee directed the subcommittee to review the tables and provide recommendations during the Committee's in-person meeting. The Committee believes there will need to be a corresponding educational effort with any update to the tables. The Committee discussed updating the equivalency tables for DPB/DQA reporting and future equivalencies. The Committee reviewed the subcommittee's draft of the equivalency tables and directed the subcommittee to continue its update of the tables.

5. CPRA Manuscript

*Public Comment: N/A*

*Board Consideration: N/A*

The goal of this manuscript is to describe the changes in CPRA distribution that have occurred since the CPRA replaced PRA for kidney allocation based on analysis performed for the Committee. This manuscript is the final step in CPRA monitoring done by the Histocompatibility Committee.

6. Evaluating Priority for DR Matching in Kidney Allocation

*Public Comment: August 2016 (Estimated)*

*Board Consideration: December 2016 (Estimated)*

In fall 2013, the DR Mismatch Subcommittee met to review data aimed at addressing two issues:

- To assess the impact of lower level of HLA-DR mismatch on kidney graft survival;
- To test the hypothesis that lower levels of HLA-DR and –DQB mismatch is superior to lower DR mismatch alone with a secondary goal of assessing whether HLA-DQB matching should be considered as an additional element in organ allocation

During the Committee's August 11-12, 2014 meeting, a summary of results and conclusions drawn from the data were presented. The Committee agreed with the subcommittee's conclusion that based on data shown to date, there is no added value to adding priority points for DQB matching in addition to those already assigned for HLA-DR matching in kidney allocation. The Committee members also agreed the DR Matching Subcommittee should focus on whether the current priority for lower levels of DR mismatch is appropriate or whether additional priority should be given to those patients.

The Committee directed the DR Matching Subcommittee to request at their next meeting multivariable analysis to determine if lower DR mismatch levels are associated with better deceased donor kidney graft survival after adjusting for other facts that affect survival (different donor, recipient and transplant characteristics including CPRA value, induction, cold ischemia time). The DR Matching Subcommittee will specify several factors to be included in the model and will consult SRTR in suggesting additional variables.

The Committee discussed a request for simulation modeling to analyze the outcome if an increased number of points was given for a lower level of DR mismatch during deceased donor kidney allocation. The Committee ultimately decided to wait until they review the results of multivariable analysis and then revisit this request. The Committee is aware that they will need to involve the Kidney Committee prior to requesting simulation modeling.

7. Programming Allele Level Typing In UNet<sup>SM</sup>

*Public Comment: August 2016 (Estimated)*

*Board Consideration: December 2016 (Estimated)*

Current histocompatibility testing allows for the identification of allele level types of HLA and unacceptable antigens. These allele level types are a more exact indication of a patient's HLA and antibody level. However, there is no structure in UNet<sup>SM</sup> for laboratories to enter allele level typing. Instead, the laboratory staff must convert the allele level type into one of the existing antigens listed. This increases the likelihood for mistakes, especially since conversion of an allele level type to an antigen is not possible for all alleles. In addition, the inability to list allele level antibodies disadvantages candidates in the screening process because, when only antigens can be entered, candidates are screened from donors from whom they could safely accept an organ.

Compared to the other projects requested from this Committee, this project is on the lower end of the Committee's prioritization list. This project will require a re-evaluation after current projects advance through the policy process. Members indicated interest in programming the most common alleles before programming all of the alleles.

### Committee Projects Pending Implementation

8. Require HLA-C and HLA DQB for Decased Kidney, Kidney Pancreas, and Pancreas Donors

*Public Comment:* [March 19, 2010 – July 16, 2010](#)

*Board Approval:* [November 2010](#)

*Project Implementation:* First Quarter 2015

This proposal requires that OPOs and their associated laboratories perform HLA typing of all deceased donors by DNA methods and identify the HLA-A, -B, -Bw4, Bw6, -C, -DR, -DR51, -DR52, -DR53, and –DQ antigens before making any kidney, kidney-pancreas, pancreas, or pancreas islet offers.

9. Expanding Candidate and Decased Donor HLA Typing Requirements to Provide Great Consistency Across Organ Types (DQA and DPB)

*Public Comment:* [March 14 – June 13, 2014](#)

*Board Approval:* [November 2014](#)

*Project Implementation:* Fourth Quarter 2015 (Estimated)

In November 2014, the OPTN/UNOS Board of Directors approved new policies for histocompatibility testing required for solid organ transplantation. These new policies are not yet in effect but will become effective with IT programming, likely by the end of 2015. The changes include the following:

- Typing for HLA-DQA and –DPB will be mandatory for deceased kidney, kidney-pancreas, and pancreas donors. OPOs will be required to report this information in DonorNet® in order to make kidney, kidney-pancreas, or pancreas offers.
- Upon implementation, DonorNet® will contain fields to report these types. Waitlist<sup>SM</sup> will also contain unacceptable antigens for these types. The system will be programmed to automatically avoid donors with the unacceptable –DQA or –DPB antigens listed for the candidate.
- When performing HLA typing on deceased donors (whether the typing is required by OPTN policy or requested by the transplant program), all of the following types will be required to be reported:
  - A, B, Bw4, Bw6, C, DR, DR51, DR52, DR53, DQA, DQB, and DPB
  - OPTN policy will require HLA typing for deceased kidney, kidney-pancreas, and pancreas donors. It will only be required on deceased heart, lung, and liver donors if it is requested by a candidate's transplant program.
  - HLA typing will be required for deceased pancreas islet donors and candidates.
  - Upon implementation, HLA typing for all deceased donors, whether required or requested, must be performed by molecular methods.

## Implemented Committee Projects

### 10. Update to the HLA Equivalency Tables

*Public Comment:* [March 3, 2013 – June 6, 2013](#)

*Board Approval:* [November 2013](#)

*Project Implementation:* First Quarter 2015

Current Policy requires the Histocompatibility Committee to recommend updates, on an annual basis, to the HLA Equivalency tables. This project will implement the following changes to the HLA Equivalency tables:

- 8 broad antigens will be eliminated in the Matching Antigen Equivalences tables.
- 4 equivalences will be added and 57 deleted in the Unacceptable Antigen Equivalences tables.
- The Cw13 antigen will be removed from the system completely.

## Review of Public Comment Proposals

The Committee didn't comment on any of the proposals recently released for public comment.

## Other Committee Work

### 11. Quarterly Review of HLA Typing Discrepancies

OPTN/UNOS Policy requires the Committee to review, at least every three months, any outstanding discrepant typing in Discrepant Donor and Recipient HLA Typing reports in UNetSM. This past fall, the subcommittee reviewed the first quarter report. Following that call, the subcommittee chair created a list categorizing discrepancies which was agreed upon by the other subcommittee members. Afterwards, the Committee directed the subcommittee to perform two tasks: (1) prioritize the categories by seriousness of their implications and provide examples for each; (2) determine how many discrepancies fall into each category. The subcommittee chair explained that members began to form the following problem statement: "Donor match-runs in quarterly reports contain donor HLA discrepancies that could affect organ allocation or safety in transplantation." It was noted that members believe most of these errors are at the local level and not on the match-run. Members are unsure as to how and where these errors are occurring; therefore, the subcommittee will work to track the source of these errors. The next step is to audit the quarterly report data to determine which individuals actually entered the data. The Committee requested that UNOS staff audit the quarterly reports for the subcommittee to review.

## Meeting Summaries

The Committee held meetings on the following dates:

- March, 2015
- February, 2015
- January, 2015
- December, 2014
- November, 2014
- August, 2014

Meetings summaries for this Committee are available on the OPTN website at: <http://optn.transplant.hrsa.gov/converge/members/committeesDetail.asp?ID=7>.