Interim Report
OPTN/UNOS HISTOCOMPATABILITY COMMITTEE

Chicago, IL
July 11, 9:00am CDT-5:00pm CDT
July12, 8:00am CDT-3:00PM CDT

Nancy Reinsmoen, Ph.D. opened the meeting by introducing herself as the chair of the Committee and Lee Ann Baxter-Lowe, Ph.D. as the vice chair. Lori Gore, Committee Liaison, and Anna. Kucheryavaya, Committee Research Liaison, then gave brief orientations on the Committee roles and responsibilities, and the effective use of data by the Committee respectively.

Orientation from the Scientific Registry of Transplant Recipients (SRTR): Dr. Howard Gebel, the SRTR representative for the Committee, gave an overview of the SRTR. Committee members asked how can they could ensure elements of histocompatibility are incorporated into the models used to simulate kidney allocation; Dr. Gebel replied," You just did." He reassured the Committee that he would bring their requests back to the SRTR. The Committee said they are especially interested in a sliding scale for CPRA sensitivity points and how they would work within the proposed kidney allocation system.

Review of the New Kidney Allocation Proposal: Ciara Samara, UNOS liaison to the Kidney Transplantation Committee gave a review of the proposed kidney allocation system to the Committee as it exists currently. First, she emphasized that this was not a full proposal but a high-level overview of what the Kidney Committee had developed so far. She cautioned the Committee that this overview did not include the intricacies that may interest the Committee such as sensitization points. She said those decisions have yet to be made and will be partially based on the recommendations from the Committee.

James Selby, at large member of the Committee, asked about the place of "wait time" within the system. Ms. Samara replied that candidates would be ranked within their categories by waiting time as well as and other considerations such as s sensitization points that have yet to be determined.

CPRA.Ms. Kucheryavaya gave the Committee a report about the second phase of CPRA implemented in UNetSM on October 1, 2009 (18 months after implementation). A summary of her report follows:

- There was an increase in the number of unacceptable antigens that were reported on the waiting list and a substantial decrease in the number of kidney refusals due to the positive crossmatch.
- The percentage of non-sensitized registrations (0%/Not reported PRA/CPRA) increased and the percentage of low sensitized registrations (1-20% PRA/CPRA) decreased. The percentage of very broadly sensitized registrations (>95% PRA/CPRA) also increased.
- Only 30% of primary transplant registrations are sensitized to any degree (>0% CPRA) compared to 77% for registrations with a previous graft failure.
- There is a variation in CPRA distribution by center. There has been some criticism within the transplant community of CPRA because a given candidate may have a different CPRA at different centers. Ms. Kucheryavaya reported that for adult kidney alone patients actively waiting at two or more centers on 03/31/2011 60% of patients have the same CPRA value at all centers and 19% of those listed with 0% CPRA at one center had >20% CPRA at a different center. She also compared CPRA values at removal from the first center and at listing at the second center for adult kidney alone registrations transferred to a different center; 61% of registrations had the

same CPRA value at both centers. Committee members opined that the difference in the reporting of unacceptables was center driven not technique.

- After initial decline for non sensitized and increase for broadly sensitized patients, transplant rates for these groups seem to return to pre policy implementation level.

- For all ethnicity groups, the percentage of very broadly sensitized registrations (PRA/CPRA > 95%) increased. She also illustrated that only 49% of female registrations are non-sensitized (0% CPRA) compared to 72% for males. In addition, that 25% of females are broadly sensitized (80%+ CPRA) compared to 11% males. After CPRA implementation the percentage of very broadly sensitized registrations (>95% CPRA) increased for both genders.

- Only 30% of primary transplant registrations are sensitized to any degree (>0% CPRA) compared to 77% for registrations with a previous graft failure.

- 18 months after CPRA implementation the percentage of very broadly sensitized registrations (>95% CPRA) increased by 16 percentage points for those waiting for a re-transplants compared to 18 months prior.

- Transplant rates for low sensitized group (1-20% PRA/CPRA) significantly decreased after the policy implementation. Even after the decrease transplant rate for this group was not significantly different from rates for other groups post policy implementation.

- Transplant rate for moderately sensitized candidates (21-79%) did not change significantly following the policy implementation.

Dr. Reinsmoen said it was essential that the Committee make note of the type of transplant sensitized candidates were getting (0MM vs. Non0MM). And when reviewing the data, it must be noted that as of January 2009 the 0MM offer was only made to candidates that have a 20% CPRA and higher. Dr, Reinsmoen said it is important that the Kidney Committee be made aware that a large amount of the transplants that took place for the higher CPRA candidates were 0MM.

The Committee then discussed how a sliding scale for sensitization points would work within the new kidney allocation system. Members opined that sensitized candidates should be removed from the system because it would limit their donor pool. They said all of the data we have reviewed so far was based on exposure to 100% of the donor pool. So then the question becomes at what point is a candidate "sensitized "enough to be removed from the system and when they should get just points within a category. Members of the Committee also opined that these changes must be on a local level to adjust for geographical variation in the donor pool size.

Dr. Reinsmoen reminded members the goal of such a policy would be to have sensitized candidates to be transplanted at the same rate as unsensitized.

Ms. Kucheryavaya went on to say the data presented on the transplant rates is expressed by transplants per 1,000 active patient-years. This is calculated by dividing the number of all deceased donor kidney transplants within an interval by the number of active year's patients spent waiting, and then multiplying by 1,000. The Committee members took issue with this method of displaying the data because it did not take into account how long a given candidate had waited. Many feared this unfairly skewed the data for the sensitized candidate, making it appear that the sensitized candidate was being transplanted at a higher rate than unsensitized.

To ensure that the impact of sensitization is not underestimated in the analyses the Committee requested the data on the median waiting and dialysis time and percent transplanted within several years of listing by sensitization group. Since it often takes kidney candidates years after listing to receive a deceased donor transplant and CPRA is not available for older data, the Committee requested to use PRA values for median waiting and dialysis time for pre policy implementation data.

Report from Pediatric committee: The Pediatric Committee asked for guidance from the Histocompatibility Committee in a memo dated April 26, 2011, because pediatric kidney transplantation candidates experience substantial long-term side effects due to dialysis, including growth and development delays. These effects are more pronounced for pediatric candidates who experience barriers to transplant (e.g., due to sensitization).

This memo said that since the implementation of Share 35 in September 2005, there has been an increase in the absolute number of all kidney transplants in children; a general increase in the transplant rate per 1,000 active patient years for all blood groups and sensitivity cohorts; and a decrease in the total amount of time spent on the waiting list. Although these results are encouraging, those highly sensitized pediatric candidates (especially teens and adolescents) have realized significantly less benefit when compared to all other pediatric candidates. To improve highly sensitized pediatric kidney candidates' access to transplant, the Pediatric and Kidney Committees have recently discussed the possibilities of regionally sharing kidneys for highly sensitized pediatric candidates. Modeling regional kidney sharing for this group within the current kidney allocation algorithm indicates improved access for these pediatric candidates with minimal impact on adult kidney candidates.

The Pediatric Committee asked for volunteers from the Histocompatibility Committee to join a working group to discuss further the Histocompatibility Committee's opinions and recommendations.

Dr. Reinsmoen thought the Pediatric Committee needed some guidance because some of the suggestions contained in the memo seemed too stringent. She suggested that we could provide some guidelines, maybe based on the guidelines from the KPD program. Dr. Cathi Murphy, Dr. Dolly Tyan, Dr. Dimitri Monos, and Dr. Reinsmoen volunteered to take part in this work group.

Proposal to Update CPRA**:** The Committee reviewed the proposal from the Committee to Update CPRA. This proposal is scheduled to go out for public comment in the fall of 2011 and to the Board in June 2012.

The purpose of this proposal is to update CPRA so it can better reflect current laboratory practices as well as the current donor pool. These revisions include updating the HLA frequencies used to calculate CPRA, the addition of the antigen C to the calculation and the addition of a question to the waiting list to better interpret 0% default CPRA value.

The Committee reviewed the data needed to support the proposal. Calculated PRA (CPRA) is used for allocation of deceased donor kidneys since October 1, 2009. HLA frequencies currently used for CPRA calculation (HLA-A, -B, -DR and -DQ) are based on the HLA phenotypes of deceased kidney donors recovered from January 1, 2003 through December 31, 2004. Ethnic frequencies are based on deceased kidney donors recovered from January 1, 2006 through June 30, 2007. The Committee opined these frequencies must be updated to a more recent time frame so that the CPRA truly reflects the probability of an incompatible match with the current donor pool.

The Histocompatibility Committee reviewed data to access whether using HLA frequencies based on a more recent cohort of donors would improve CPRA accuracy. CPRA was recalculated based on HLA and ethnic frequencies derived from a more recent cohort of deceased kidney donors (2007-2008). It should be noted that the reporting of HLA-DQ 4, 5, 6, 7, 8, and 9 antigens increased in the past decade that would lead to a substantial CPRA increase for some kidney registrations if the current HLA frequencies were used. It was shown that if the recalculated CPRA were used for allocation of deceased donor kidneys, almost 500 kidney registrations with current CPRA of less than 80 would become eligible for 4 sensitization points. Committee members noted a large portion of this increase is due directly to the increased reporting of split DQ antigens in donors and more frequent reporting of subtypes rather than broad antigens.

At the July 13-14, 2010 meeting, the Histocompatibility Committee voted to propose the inclusion of HLA-C frequencies into CPRA calculation. The committee reviewed data that compared Current CPRA values to recalculated CPRA for all kidney registrations on the kidney waiting list with antibodies to HLA-C antigens and 0% CPRA or 50-79% CPRA.

On February 28, 2011, there were 93,711 kidney registrations on the waiting list. Eleven percent (10,569) of these registrations had at least one unacceptable HLA-C antigen reported on the waiting list. As of June 2010 it is required that all standard criteria donors be typed for C. Therefore, candidates with C marked as an unacceptable are currently screened from match runs but they do not receive a fair priority because their CPRA value is lower than it should be. Among all kidney registrations with unacceptable HLA-C antigens, 7% (728) only had antibodies to HLA-C antigens. These candidates are also being screened from match runs and have a CPRA of 0.

Also of the kidney candidates on the waiting list that have antibodies to HLA-C antigens, only 63% have a CPRA of 80% or higher and are eligible for 4 additional sensitization points during allocation of deceased donor kidneys. Inclusion of HLA-C frequencies into CPRA calculation would result in a higher CPRA value for most registrations. For those listed with C antibodies, almost 644 registrations had a recalculated CPRA value increased to 80%. The Committee said that 644 out of 93,711 represented a small change but it would be very important to those 644 registrations. Members of the Committee pointed out that it is likely that the incidence of HLA-C antibodies is underestimated because some programs do not currently list C as an unacceptable because it is not part of the CPRA calculation and it has only recently been added to the requirements for deceased donors. They said it should be expected that the number of reported instances of C antibody would soon increase.

Based on these observations the inclusion of HLA-C frequencies into CPRA calculation would benefit a relatively large number of kidney registrations who have antibodies to HLA-C.

Zero (0) default of CPRA. The main problem with the CPRA value of 0 is that it could mean many different things. It could be that the candidate had not been tested yet. It could be that the candidate is truly unsensitized and has no HLA antibodies. Alternatively, it could mean that the candidate does have some HLA antibodies, but none that the in the judgment of the center warrants the listing as an unacceptable. Or it could mean the candidate has antibody to C and/or DP HLA antigens, which are not part of the CPRA algorithm, and would therefore registrar a CPRA of 0 but truly is a sensitized candidate. On the other hand, it could be that the unacceptables listed are so rare that the CPRA is less than .5%, which would show as a CPRA of 0. Each one of the above scenarios describes a very different candidate but all would be shown to have a CPRA as 0.

On 03/31/2011 56,669 of adult kidney alone registrations had 0% CPRA. Out of these registrations:

- 974 had antibodies to HLA-C antigens
- 1,490 had antibodies to non HLA-C antigens
- 226 had antibodies to both HLA-C and non HLA-C antigens

The Committee has requested that there to be a way to distinguish these candidates on the waitlist. UNOS IT informed the Committee that the field on waitlist could not remain blank if untested, and must be filled with a numeric value. (00 is also not an option).

Therefore, the Committee proposes that a mandatory field be added to the waitlist form for all kidney, kidney/pancreas and pancreas candidates. They also requested that this field be added to other organ allocation systems, such as the Thoracic waitlist form, if that group decides to utilize CPRA within their system. This field would ask, "Was this candidate tested for anti HLA antibodies?" with the drop down box that gave the following options; yes, antibodies detected, yes, no antibodies detected, or no, not tested. This information would distinguish between the various circumstances underlying a CPRA equal to zero.

Revision of the UNOS bylaws, the OPTN Bylaws and the OPTN Policies that govern HLA laboratories:
UNOS staff has begun the process of consolidating, reorganizing, and simplifying the language of the OPTN Policies and OPTN and UNOS Bylaws. (These updates are not substantive in nature; they are not intended to change the meaning of the policies and bylaws.) These changes to the language are scheduled to go out for public comment; the Bylaws in the winter of 2012 and the Policies in the summer of 2012.

The Histocompatibility Committee reviewed the documents from the Rewrite Project pertaining to histocompatibility (HLA) laboratories at their July 2011 meeting and identified several challenges. The Committee defined these areas as major defects that are not in line with current practice. The Committees voted to make these updates within the current UNOS bylaws, the OPTN Bylaws and the OPTN Policies in an effort to improve the review process that will happen later next year within the Rewrite Project.

The Committee voted to make amendments to the existing requirements in an effort to improve the review process that will happen later next year within the Rewrite Project. They are as follows:

Current Language

UNOS BYLAWS ATTACHMENT II TO APPENDIX B OF THE UNOS BYLAWS
I. Key Personnel Qualifications
A.1. Director Credentials
(i) The Director must be an MD, DO, or PhD in science, and must meet the qualifications of director of high complexity testing according to Federal CLIA requirements defined in 42CFR 493.1441.
(ii) In addition to A1 (i), at least two of the years of the Director's training and/or experience must be in histocompatibility testing in a OPTN/UNOS approved training program or three years experience under a qualified OPTN/UNOS Histocompatibility Director.

Proposed Revision

UNOS BYLAWS ATTACHMENT II TO APPENDIX B OF THE UNOS BYLAWS

I. Key Personnel Qualifications
(i) The Director must be an MD, DO, or PhD in science, and must meet the qualifications of director of high complexity testing according to Federal CLIA requirements defined in 42CFR 493.1441. An M.D. or D.O. must also have a license to practice medicine in the state where the laboratory is located.
(ii) In addition to A1 (i), ~~at least two of the years of the Director's training and/or experience must be in histocompatibility testing in a OPTN/UNOS an approved training program or~~ ~~Three years experience~~ if the candidate is also the technical supervisor of the laboratory, they must have completed two years general immunology plus two years histocompatibility experience under a qualified OPTN/UNOS Histocompatibility Director doing histocompatibility testing for solid organ transplantation.

Committee Rational for Revision

These corrections must be made to be compliant with Federal CLIA requirements. It is also important to note that the OPTN/UNOS does not approve training programs.

Current Language

A2. Director Candidates
(ii) The director candidate must provide documentation of appropriate training and experience through submission of a portfolio of cases (see iii and iv, below) covered during the training in a OPTN/UNOS approved transplant center or must have certification by the American Board of Histocompatibility and Immunogenetics. Evidence of active laboratory involvement and interaction with transplant groups must also be documented and submitted.

Proposed Revision

(ii) The director candidate must provide documentation of appropriate training andexperience through submission of a portfolio of cases (see iii and iv, below) covered during the training in a OPTN/UNOS approved transplant center or must have certification by the American Board of Histocompatibility and Immunogenetics or other CMS approved board certification.…

Committee Rational for Revision

This correction is important because it is now possible for a lab director to be qualified using other CMS approved certifications and there are currently several directors that do.

Current Language

B.1. Responsibilities of a Director of a Histocompatibility Laboratory
(i) Ensure that the laboratory facilities are adequate and safe from physical, chemical, and biological hazards.
(ii) Provide consultation to clients on test results.
(iii) Must be accessible to the laboratory to provide onsite, telephone or electronic consultation, as needed.
(iv) Ensure that an approved procedure manual is available to all technical personnel.
(v) Ensure and monitor that all delegated duties are properly performed.
(vi) Determine that a laboratory has a qualified general supervisor. is on-site for all routine testing.
(vii) Ensure…….

Proposed Revision

B.1. Responsibilities of a Director of a Histocompatibility Laboratory
(i) Ensure that the laboratory facilities are adequate and safe from physical, chemical, and biological hazards.
(ii) Provide consultation to clients on test results.
(iii) Must be accessible to the laboratory to provide onsite, telephone or electronic consultation, as needed.
(iv) Ensure that an approved procedure manual is available to all technical personnel.
(v) Ensure and monitor that all delegated duties are properly performed.
(vi) Determine that a laboratory has a qualified general supervisor. ~~is on-site for all routine testing.~~
(vii) Ensure…

Committee Rational for Revision

The Committee said this bylaw was unrealistic and that no laboratory requires that the general lab supervisor be on site 24 hours a day, seven days a week.

Current Language

UNOS Bylaws Appendix B Attachment IIA - Standards for Histocompatibility Testing
C. Quality Assurance
C5.000 Proficiency Testing and Competency Evaluation
C5.300 The laboratory must test proficiency samples in a manner comparable to that for testing clinical samples.

Proposed Revision

UNOS Bylaws Appendix B Attachment IIA - Standards for Histocompatibility Testing
C. Quality Assurance
C5.000 Proficiency Testing and Competency Evaluation
C5.300 The laboratory must test proficiency samples in the same manner ~~comparable~~ to that for testing clinical samples.

Committee Rational for Revision

It is important that this bylaw be changed because this is a CLIA standard and must be adhered to by law.

Current Language

C9.000 Subcontracting
C9.100 A UNOS approved laboratory may engage another laboratory to perform testing by subcontracting the work to that laboratory. In that event, if histocompatibility and/or transplantation immunology testing is referred, the subcontracting laboratory must be CLIA certified/exempt and either UNOS approved or ASHI accredited for that testing…

Proposed Revision

C9.000 Subcontracting
C9.100 A UNOS approved laboratory may engage another laboratory to perform testing by subcontracting the work to that laboratory. In that event, if histocompatibility and/or transplantation

immunology testing is referred, the subcontracting laboratory must be CLIA certified/exempt and either UNOS approved or ASHI / CAP accredited for that testing…

Committee Rational for Revision

CAP also has deemed status with UNOS and currently there are several HLA laboratories that are CAP certified.

Current Language

F. Renal and Pancreas Organ Transplantation
F2.000 HLA Typing
F2.100 Prospective typing of donors and recipients for HLA-A, B, Bw4, Bw6, and DR antigens is mandatory.
F2.200 Prospective typing of donors and recipients for HLA-C, and DQ antigens and for DR51, DR52, DR53, is highly recommended.

Proposed Revision

~~F2.100 Prospective typing of donors and recipients for HLA-A, B, Bw4, Bw6, and DR antigens is mandatory.~~
~~F2.200 Prospective typing of donors and recipients for HLA-C, and DQ antigens and for DR51, DR52, DR53, is highly recommended~~
F.2.100 Prospective typing of deceased donors for HLA-A, B, C, Bw4, and Bw6, and DR, DR51, DR52, DR53 and DQ antigens is mandatory.
F2.200 Prospective typing of candidates of A, B, Bw4, Bw6 and DR is mandatory, and the typing of C, DR51, DR52, DR53, and DQ is highly recommended.

Committee Rational for Revision

This correction is important because OPTN policy requires that this level of typing be done. Prospective typing of deceased donors for these antigens is required by OPTN policies 3.5.9.1 (Essential Information for Kidney Offers) and 3.8.2.2 (Essential information for Pancreas Offers).

For kidney and pancreas candidates HLA antigen information (at lease 1A, 1B, and 1DR antigen) is required by OPTN policies 3.2.1.5 (Renal and Renal Pancreas Combination Candidate Listing) and 3.8.2.1 (Inclusion of HLA Data). This requirement does not apply to candidates listed for combined kidney-nonrenal transplantation, with the exception of kidney-pancreas transplantation.

Current Language

F3.000 Antibody Screening
F3.100 Laboratories must have a policy in place to evaluate the extent of sensitization of each patient at the time of initial evaluation and following potentially sensitizing events, based on the antibody characteristics that are clinically relevant to each transplant center's protocols.

Proposed Revision

F3.000 Antibody Screening
F3.100 Laboratories must have a policy in place to evaluate the extent of sensitization of each patient at the time of initial evaluation and following potentially sensitizing events, based on the antibody

characteristics that are clinically relevant to each transplant center's protocols. This information is provided to the laboratory by the transplant program.

Committee Rational for Revision

This correction is important because OPTN Policy 3 Appendix D requires a contract between the laboratory and the transplant center and requires that this information be provided.

Current Language

F3.200 Laboratories must have a program to periodically screen serum samples from each patient for antibody to HLA antigens. The laboratory must have a documented policy establishing the frequency of screening serum samples and must have data to support this policy. It is recommended that samples be collected monthly.

Proposed Revision

F3.200 Laboratories must have a program to periodically screen serum samples from each patient for antibody to HLA antigens. The laboratory must have a documented policy establishing the frequency of screening serum samples and must have data to support this policy. ~~It is recommended that samples be collected monthly~~. Samples will be collected at time intervals outlined in the joint agreement between the laboratory and the transplant program.

Committee Rational for Revision

This correction is important because OPTN Policy 3 Appendix D requires a contract between the laboratory and the transplant center and requires that the schedule of collection times be specified within that document. It is also important that each transplant center may define that time period depending on their needs.

Current Language

ABO Blood Group Determination
I1.000 Laboratories performing ABO blood group determination, must use be performed by techniques compliant with Federal regulations.

Proposed Revision

I. ABO Blood Group Determination
I1.000 Laboratories performing ABO blood group determination, must use ~~be performed by~~ techniques compliant with Federal regulations.

Committee Rational for Revision

This change is important because not all HLA laboratories do ABO blood group determination.

Current Language

J Chimerism Analysis
J1.000 Laboratories performing engraftment and chimerism testing using nucleic acid analysis must conform to all pertinent standards in Section K- Nucleic Acid Analysis.

J2.000 The specificity and sequence of primers must be defined. The genetic designation (e.g., locus) of the target amplified by each set of primers must be defined and documented. For each locus analyzed, the laboratory must have documentation that includes the chromosome location, the approximate number of known alleles, and the distinguishing characteristics (e.g., sizes, sequences) of the alleles that are amplified.
J3.000 If sample processing involves the isolation of cell subsets or specific hematopoietic cell lineages, the laboratory should document the purity obtained whenever possible. If purity is not documented for a given sample, then this information must be provided on the patient report.
J4.000 For each locus tested, patient and donor samples collected pre-transplant, and/or control samples demonstrated to have similar performance characteristics (e.g., sensitivity, competition in PCR) must be amplified and analyzed concurrently with patient samples collected post-transplant.
J5.000 Analysis and Reports
J5.100 Potential for preferential amplification of different sized alleles must be assessed and considered in the analysis.
J5.200 If more than one locus is amplified in a single amplification (multiplex), the effects of such amplification on each system must be assessed and considered in the analysis.
J5.300 Reports must identify the genetic loci analyzed according to standard nomenclature or published reference. For RFLP testing, the restriction endonuclease used and the fragment size must be identified.
J5.400 If results are reported in a quantitative or semi-quantitative manner, criteria for evaluating the relative amounts of recipient and donor in a mixed chimeric sample must be established.
J5.500 When mixed chimerism is not detected, reports must state the sensitivity level of the assay.

Proposed Revision

~~**J Chimerism Analysis**~~
~~J1.000 Laboratories performing engraftment and chimerism testing using nucleic acid analysis must conform to all pertinent standards in Section K- Nucleic Acid Analysis.~~
~~J2.000 The specificity and sequence of primers must be defined. The genetic designation (e.g., locus) of the target amplified by each set of primers must be defined and documented. For each locus analyzed, the laboratory must have documentation that includes the chromosome location, the approximate number of known alleles, and the distinguishing characteristics (e.g., sizes, sequences) of the alleles that are amplified.~~
~~J3.000 If sample processing involves the isolation of cell subsets or specific hematopoietic cell lineages, the laboratory should document the purity obtained whenever possible. If purity is not documented for a given sample, then this information must be provided on the patient report.~~
~~J4.000 For each locus tested, patient and donor samples collected pre-transplant, and/or control samples demonstrated to have similar performance characteristics (e.g., sensitivity, competition in PCR) must be amplified and analyzed concurrently with patient samples collected post-transplant.~~
~~**J5.000 Analysis and Reports**~~
~~J5.100 Potential for preferential amplification of different sized alleles must be assessed and considered in the analysis.~~
~~J5.200 If more than one locus is amplified in a single amplification (multiplex), the effects of such amplification on each system must be assessed and considered in the analysis.~~
~~J5.300 Reports must identify the genetic loci analyzed according to standard nomenclature or published reference. For RFLP testing, the restriction endonuclease used and the fragment size must be identified.~~
~~J5.400 If results are reported in a quantitative or semi-quantitative manner, criteria for evaluating the relative amounts of recipient and donor in a mixed chimeric sample must be established.~~
~~J5.500 When mixed chimerism is not detected, reports must state the sensitivity level of the assay.~~

Committee Rational for Revision

Chimerism testing is routinely used for blood and marrow transplantation. It is rarely used in solid organ transplantation (predominantly for suspected graft-versus-host disease, which is rare). Since it has never been routinely used for solid organ transplant, the subcommittee suggested removing it.

Current Language

Attachment IIB – UNOS Test Data Criteria for New HLA Laboratories and for the Addition of New Techniques

Data Submission

New Laboratories are required to submit procedures and test validation data for all categories and methods of testing unless such work is performed, without exception, by another approved laboratory…

These materials are required to be submitted to an Agency with deemed status for the Accreditation of UNOS Laboratories, with a copy to the UNOS Histocompatibility committee.

Proposed Revision

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New Laboratories are required to submit procedures and test validation data for all categories and methods of testing unless such work is performed, without exception, by another approved laboratory…
These materials are required to be submitted to an Agency with deemed status for the Accreditation of UNOS Laboratories~~, with a copy to the UNOS Histocompatibility committee~~.

Committee Rational for Revision

This material is not shared with the committee at this time nor has it been in at least 5 years.

The Committee said this would only be the first step in rewriting the existing UNOS Histo standards. The UNOS bylaws, the OPTN Bylaws and the OPTN Policies that govern HLA laboratories are antiquated. Many of the required tests and methods are out of date and are no longer useful. These requirements should become more succinct and must reflect current lab practices.

The Committee said this would be a huge undertaking. The only way to do it would be to divide the standards into sections, and assign them to members of the Committee. In addition, because HLA laboratories are not accredited or monitored directly by UNOS, but through agencies that have deemed status with UNOS (American Society of Histocompatibility and Immunogenetics-ASHI and College of American Pathologists -CAP) a cross walk must be initiated between UNOS, CAP, and ASHI. The contracts with these agencies must also be brought up to date.

Dr. Dimitri Monos and Dr. Lee Ann Baxter-Lowe agreed to do the initial work of dividing the standards. Committee members also said that when the time came to fine tune and consolidate what had been done, it would be best if that work were done in a face-to-face meeting.

Committee Answered Questions from Members**:**

1. In the next revision, is it possible to include another column to list the actual CPRA for each antigen or groups of antigens relative to the current equivalences? We know this new set of equivalences went into effect 3/16/2011, however, there are significant changes to other antigens, including DQ1 and DQ3. It would be helpful to have a side-by-side listing of the CPRAs (old and new) for each antigen for comparison.

   The Committee felt that this would not be worth the cost of implementation. A member could get the same answer through the CPRA calculator.

2. Can you please give us an update on the UNOS Histo Committee recommendations and your lab's molecular testing to rule out DRB4*0103n?

   When a DR7 and DQ9 are reported most assume it represents a DR53 null and therefore report DQ53 negative.

Report from the Membership and Professional Standards Committee (MPSC):
The Committee approved the ballot of new laboratory and new laboratory directors for the membership ballot in February 2009. This ballot is prepared by Sally Aungier, Administrator from the UNOS Membership Department. In it, she summarizes the progress made in the approval process for applicant HLA laboratories and laboratory personnel. This summary is provided to her by the two agencies that have deemed status with UNOS to accredit laboratories: the American Society of Histocompatibility and Immunogenetics (ASHI) and the College of American Pathologists (CAP). The Committee reviews this document periodically and then makes recommendations to the MPSC as to whether these changes should be approved for UNOS membership.

The Committee reviewed key personnel changes within histocompatibility laboratories and made recommendations to be presented to the Membership and Professional Standards Committee.

The Committee then discussed the problem created when one individual directs many laboratories. The Committee is troubled by the lack of standards in both the accrediting agencies and UNOS. They discussed what matrix could be used to form a standard, but soon concluded that the problem was too complex to solve at this meeting. A subcommittee was formed to discuss the matter further, with the hope they could make recommendations to the full Committee soon. Drs. Tyan and Eisenbrey agreed to co chair the effort with Drs. Baxter-Lowe, Campos, Dionne, Ms. Laine Krisiunas, and Mr. David Kiger offered to help.

Dr. Tyan suggested that the members of the subcommittee look at the results of a survey the Committee made several years ago to try to tackle the question how many laboratories one individual could safely direct. They suggested the first order of business would be to have UNOS staff compile a spreadsheet that would list all the laboratory directors with the labs they direct. The members of the subcommittee said they could validate the results of the data by checking their personal information.

Discrepant typing report**:** The Histocompatibility Committee annually reviews the data from the Discrepant HLA Typings Reports in UNet^{SM}, as referenced in Appendix C to Policy 3. The Committee also receives annual updates on how often donor HLA (A, B and DR) on kidney match runs is different from donor HLA reported on donor and recipient histocompatibility forms. These data is used for reviewing and evaluating discrepancies and determining if any actions should be taken.

At the July 2011 meeting, the Committee reviewed the data and asked to provide an annual update at their July 2012 meeting. The Committee felt that it was important to continue to monitor discrepancies within the transplant community given the increased use of a prospective virtual crossmatch. The Committee was also concerned that there were still many laboratories that were not aware of the existence Appendix C to Policy 3 and of the report. In an effort to assure compliance with the policy, they asked Ms. Gore to send letters to member laboratories informing them of the number of their unresolved discrepancies and compare their numbers to the national average. Mr. David Kiger volunteered to help Ms. Gore craft this letter. The Committee also asked that the discrepant typing report be added to the ASHI/Cap checklist when they do lab inspections.

OPTN/UNOS Histocompatibility Committee Meeting
July 11-12, 2011
Chicago, Illinois

NAME	COMMITTEE POSITION	07/11-12/2011
Nancy Reinsmoen, PhD	Chair	x
Lee Ann Baxter-Lowe, PhD	Vice chair	x
Massimo Mangiola, PhD	Region 1 Rep.	x
Dimitri Monos, PhD	Region 2 Rep.	x
Robert Bray, PhD	Region 3 Rep.	
Cathi Murphy, PhD	Region 4 Rep.	x
Dolly Tyan, PhD	Region 5 Rep.	x
Paul Warner, PhD	Region 6 Rep.	x
David Maurer, PhD	Region 7 Rep.	x
Sara Dionne, PhD	Region 8 Rep.	x
Rex Friedlander,	Region 9 Rep.	x
A. Bradley Eisenbrey MD, PhD	Region 10 Rep.	x
David Kiger,	Region 11 Rep.	x
Laine Krisiunas, BS,MBA	At Large	x
Luis Campos, MD	At Large	x
James Selby	At Large	x
Howard Gebel	SRTR Liaison	x
Bryn Thompson	SRTR Liaison	x
Lori Gore	Committee Liaison	x
Anna Kucheryavaya	Support Staff	x
Jory Parker	Support Staff	x
James Bowman	Ex officio (HRSA)	x