Interim Report
OPTN/UNOS HISTOCOMPATABILITY COMMITTEE

Teleconference
January 19, 2011
1:00-3:00 (EDT)

I. **Review of the Public Comment Proposals.** The Committee voted unanimously to strongly endorse the proposal requiring HLA typing for thoracic offers. They did not comment on any of the other proposals because they did not deal with Histocompatibility issues.

II. **Appendix 3A**.At the November 2010 BOD meeting, the Board of Directors (BOD) approved the Committee's Proposal to update the HLA Equivalency tables in Policy Appendix 3A. Lori Gore, liaison to the Committee, told the Committee that all the proposed changes to the Appendix could not be implemented before a deadline of January 31, 2011 imposed by the UNOS IT department. After this date, all new programming at UNOS will be delayed because the IT Department must concentrate all their efforts into the Chrysalis Project. (The Chrysalis Project is the rewrite of the entire waitlist of UNet.) Ms. Gore said only the data driven changes (table updates) could be made before the closing date. She went on to say that the revisions that require special programming such as the addition of screening for BW4, BW6, DR51, DR52 and DR53 could not be done till after the Chrysalis Project. This would mean, most likely, that full implementation of the updated tables in Appendix 3A would not happen till after June 2012.

    Ms. Gore asked the Committee if they would approve this partial implementation plan or if they would prefer the tables stay as is, till all the changes could be made. The Committee reluctantly voted to go ahead with the phased implementation plan.

III. **The Committee answered 2 Questions from members.**

- "I have a concern about a current UNOS HLA policy. We received a lung shipped to us from xxxx last week. In retyping the donor here, we found that we identified a DQ5 and DQB1*0301/19/22/22/24 by SSOP. The xxxx reported a DQ5, (blank second allele). I spoke with xxxxx, who said they identified DQB1*0319 which has no serologic equivalent. I understand not reporting DQ7, 8, or 9, (although the HLA Dictionary reports a neural net, expert, and UCLA assignment of DQ7), but I would think that a DQ3 would be more appropriate than nothing. If this had been my donor, I would have reported the donor having a DQ3, would this be correct? The Committee said yes, the lab should have reported a DQ7; if they were uncomfortable with that they should report a DQ3.
- What is the correct way to enter DNA tissue typing of a recipient (or donor) when the antigen is a null one, such as DR7 DQ9 DR53N. Prior to transplant, the recipient is listed as DR7 DR53 negative DQ9 to denote the null DR53. Technically that does not seem to be the correct way to enter the DNA typing; however, there is no DR53N to indicate "positive". Shall we leave the recipient typing as is, after transplant? The Committee said leave the typing as is; there is no other way to do it.

IV Review of CPRA data. The Histocompatibility Committee has been charged by the BOD to monitor the use of CPRA which was fully implemented in UNet[SM] on October 1, 2009. At the July 13-14, 2010 meeting the Committee reviewed waiting list and transplant data 6 months before and after policy implementation. Preliminary data showed an increase in the number of unacceptable antigens reported on the waiting list and a dramatic drop in the number of positive crossmatches reported as a reason for organ refusal. Transplant rates decreased for non sensitized patients (0% CPRA) and stayed about the same moderately sensitized registrations (21-79%). Transplant rate increased for broadly sensitized registrations (80 %+), but this increase wasn't statistically significant.

During the October 13, 2010 conference call the Committee requested an update of these analyses comparing data one year before and after policy implementation to be presented during this call. Anna Y. Kucheryavaya, UNOS research liaison, presented the data to the committee. A summary the results are as follows:

- There was an increase in the number of unacceptable antigens that were reported on the waiting list and a decrease in the number of kidney refusals due to positive crossmatch.
- The percentage of non sensitized registrations increased and the percentage of low sensitized registrations decreased. The percentage of very broadly sensitized registrations (>95% PRA/CPRA) also increased.
- After initial decline transplant rates for none and low sensitized patients seem to return to pre policy implementation level. Transplant rates for broadly sensitized patients significantly increased.

The Committee was pleased with the results. Several members asked for a further analysis to be presented at the July meeting in Chicago. They thought it would be important to monitor the way different centers list unacceptable antigens for their candidates. The concern being that some centers may be in essence "delisting "their candidates by over assigning unacceptables listed for their candidates.

A. Eisenbrey, M.D., Ph.D. said that in the state of Michigan, they looked at this issue by two different methods. First, through sera exchanges between the centers; they examined how different labs characterized the antibodies for the same individual. This analysis was made available to all that precipitated and it included the specific cut offs used to make those decisions. The second way they monitored listing of unacceptables within the state, was to evaluate the unexpected positive crossmatch frequencies between the centers. Dr. Eisenbrey reported sharing this data between the involved centers has lead to more common cut offs used to define unacceptable antigens and the frequency of the unexpected crossmatch between the centers was becoming more uniform.

J. Michael Cecka Ph.D. said we should try to do something like this for the national histocompatibility community because he believed that if the community could review the data, the same thing would happen for the nation at large.

Nancy Reinsmoen Ph.D. said we must be cognizant that there may be other reasons for differences between centers listing practices. An example may be that there are centers that may not list all the antibodies for an individual but were willing to transplant across a positive cross match. She said we must also keep in the fore front, the importance of listing unacceptables to make the 0mm offer available for the sensitized candidate. (Current policy says candidates will only come up for a 0MM offer if their CPRA is 20% or higher.) She said the 0MM offer may be the only real chance a very sensitized candidate may have for a transplant. Therefore, centers that

do not list unacceptables for their candidates may be doing the highly sensitized candidates a grave injustice.

The Committee requested an update of the analyses of CPRA with several additional analyses to be presented during their July 2011 meeting.

The Committee requested data on:

- The use of unacceptable antigens (UAs)
- CPRA distribution for kidney registrations listed on 03/31/2011 compared to the PRA distributions for kidney alone registrations listed on 03/31/2008 and 09/30/2009, stratified by ethnicity.
- CPRA distribution of kidney alone registrations on 03/31/2011 by center stratified by gender and ethnicity.
- CPRA distribution of kidney alone registrations waiting for retransplant on 03/31/2011 by center.
- Compare the CPRA values for kidney patients who are multiply listed
- Compare the CPRA values for kidney patients transferred to a different center
- The numbers of positive crossmatches reported as a reason for organ refusal for kidney matches during 04/01/2008-09/30/2009 and 10/01/2009-3/31/2011. They want this further stratified by the candidate's sensitization level (0, 1-20, 21-79, 80+).
- The numbers of deceased donor kidney transplants performed for adult recipients during 04/01/2008-12/31/2008, 01/01/2009-09/30/2009, 10/01/2009-06/30/2010 and 07/01/2010-03/31/2011, stratified by recipient's sensitization level (0, 1-20, 21-79, 80+) and HLA-ABDR mismatch level (0ABDR mismatch vs. non 0ABDR mismatch).
- Transplant rates per 1,000 patient years for adult kidney alone registrations on the waiting list during 04/01/2008-12/31/2008, 01/01/2009-09/30/2009, 10/01/2009-06/30/2010 and 07/01/2010-03/31/2011, stratified by allocation PRA/CPRA (0, 1-20, 21-79, 80+).

The Committee said it might also be time to look at the graft survival rates for the sensitized candidate. The feeling of the Committee was that these rates have improved given the use of solid phase testing. They ,therefore, also asked for the graft survival for kidney deceased donor transplants performed in 2001-2003, 2004-2006, 2007-9/30/2009, 10/01/2009-03/31/2010 stratified by recipient's sensitization level (0, 1-20, 21-79, 80+).

Ms. Gore had told the Committee that there would be no programming of new policy during the Chrysalis Project. She said this would include the Committee's desire to update the HLA frequencies used to calculate CPRA and the incorporation of the antigen C into the CPRA algorithm. This concerned the Committee greatly. They said this could greatly disadvantage a number of candidates. The Committee asked for the following data points to try to get a handle on how many candidates will be disadvantaged.

- Provide the number and percentage of adult kidney alone registrations with 0% CPRA and at least one unacceptable antigen (excluding C locus) entered on the waiting list on 03/31/2011.
- Provide the number and percentage of adult kidney alone registrations with 0% CPRA and at least one C locus unacceptable antigen entered on the waiting list on 03/31/2011.

At the November 2010 BOD meeting, BOD also approved the requirement that deceased donor HLA typing be performed by DNA methods and that the additional antigens C and DQ be used for kidney, kidney-pancreas, pancreas, and pancreas islet offers. This Policy will become effective on June 1, 2011. Ms. Gore said she would send a reminder to the transplant community about the implementation date because there seemed to be some confusion about it.

The Committee reviewed donor HLA and typing methods reported on the donor histocompatibility forms (DHFs) for deceased donors recovered in 2007-2008 while writing the public comment document for this policy. The Committee also requested updated data to be presented at the July 2011 meeting to monitor changes in typing practices and reporting of broad antigens. This data will also be used to monitor and evaluate the DNA typing requirement once it has becomes effective.

New Business-

The Committee set the date for their face to face meeting in Chicago as July 13-14, 2011. This was later amended to July 11-12, 2011.

Several members of the Committee thought it might be a good idea have both a CAP and an ASHI representative on the Committee to help with educational efforts for policy changes. Ms. Gore said she would look into this.

Members who were present:

Nancy Reinsmoen, Ph.D.	Chair
Lee Ann Baxter-Lowe, Ph.D	Vice Chair
Massimo Mangiola Ph.D.	Region 1
Dimitri S Monos Ph.D.	Region 2
Karen Sullivan, Ph.D.	Region 3
Jerry Morrisey, Ph.D.	Region 4
Dolly Tyan, Ph.D.	Region 5
Paul Warner Ph.D.	Region 6
David Maurer, Ph.D.	Region 7
Sara Dionne Ph.D.	Region 8
Char Hubbell, M.T.	Region 9
A. Bradley Eisenbrey, M.D.	Region 10
John Schmitz, Ph.D.	Region 11
Dawn Brims, B.S.N., RN	At Large
Douglas Keith, M.D.	At Large
Brad Kornfeld	At large
Jim Bowman, M.D.	Ex-Officio
J. Michael Cecka, Ph.D.	Past chair

UNOS Staff

Lori Gore	Committee Liaison
Anna Kucheryavaya	Data Liaison
Jory Parker	IT Liaison

SRTR

Howard M. Gebel Ph.D.