Interim Report
November 15, 2011 Conference Call
OPTN/UNOS HISTOCOMPATABILITY COMMITTEE

Draft of Board report for current November 2011 meeting: The Committee reviewed the Histocompatibility Report that went to the Board in November 2011 with no comment.

Review of the Public Comment Proposals: The Committee chose not to comment on any of the proposals that are currently out for public comment because they said the proposals did not contain any issues that are pertinent to HLA laboratories.

Update on Proposals out for public comment from the Histocompatibility Committee: Most of the Committee members who presented the proposals from the Histocompatibility at their respective regional meetings reported all went well and had nothing to report.

Dr. David Maurer, the Committee's region 7 representative reported his region questioned the addition of C to the CPRA algorithm because the relevance of C antibody has not been established. Committee members opined that it did not matter. It is up to each individual center if they choose to list C antigens as an unacceptable or not. Currently, over 10,000 candidates have a C antigen listed as an unacceptable. Because the reporting of C is now mandatory for all deceased donors, these candidates are screened from match runs but receive no CPRA value. If a center does not believe the C antibody is relevant they should not list it as unacceptable. This will not disadvantage candidates from their center because candidates who do have C listed as an unacceptable are screened from match runs.

Report from the Policy Oversight Committee (POC): Dr. Baxter-Lowe, vice chair of the Committee, reported that the POC is providing oversight of all OPTN committee projects and helping with the prioritization of the implementation of those projects.

She also said the POC has set up a task force to decide how to allocate organs to candidates that need multi-organs transplants.(not including kidney/pancreas). Dr. Baxter-Lowe said maybe the HLA requirements should be more stringent in these cases to avoid the possibility of an unexpected positive cross match. She added currently UNOS provides little direction in this area of allocation. Dr. Baxter-Lowe asked for volunteers from the Committee to help develop some guidelines. Ms. Laine Krisiunas, and Dr. Reinsmoen said they would help.

Forming plan for moving forward with the rewrite project: The Committee again asked for an explanation as to why UNOS must have its own independent Histocompatibility standards. "Why couldn't we just say labs must be accredited by an agency which has deemed status with UNOS?" Ms. Gore explained that because these agencies could change their standards without the change going out for public comment and without UNOS approval, we must have our own standards. MS. Gore went on to say these standard could be more stringent then those of the deemed agency, but not less. The Committee was not satisfied with that answer and asked to speak again with Brian Sheppard, the Director of Policy, at the earliest convenience.

Update from the Kidney Committee: The Kidney Transplantation Committee met on March 21, 2011. Darren Stewart, UNOS research support for the Kidney Committee, gave a presentation to the Histocompatibility Committee to update them on the continued discussion of the details of a potential new kidney allocation system. He said much of the current discussion

within the Kidney Committee focused on ensuring equitable access to transplantation for HLA sensitized candidates, either through giving regional or national priority to ultra-highly sensitized candidates (e.g., 95%+ CPRA) and/or using a "sliding scale" that would assign rank-ordering points on a graduated scale based on CPRA. The Kidney Committee recently asked for data to help answer specific questions, such as what threshold(s) should be used to start/end the CPRA "sliding scale."

Mr. Stewart reported that nearly two-thirds of kidney registrations had CPRA of 0 at the end of 2009 and 2010. He said at the other end of the spectrum, about 11% of candidates had a CPRA of 95% or greater. Of those very highly sensitized candidates (>=95%), nearly half of them had CPRA=100%. He went on to say these distribution percentages did not vary remarkably from 12/31/09 to 12/31/10. His data showed that although candidates with a CPRA of 100% represented about 5% of the waitlist, less than 1% were actually ever transplanted.

He then reported on the demographics for the highly sensitized candidate; he said females were more likely than males to be very highly sensitized, or sensitized at all. However, the relationship of gender and CPRA appeared to be nonlinear. The ratio of percent female (68.6%) to percent male (31.4%) increased as CPRA increased, peaking around CPRA=95%. But as CPRA increased from 95% to 100%, the ratio gradually decreased, to 58.3% to 41.7%.

He also reported Blacks tended to disproportionately have very high CPRAs (>=95%), whereas Hispanics and Asians tended not to be as highly sensitized. He said the relationship between sensitization and ethnicity was fairly weak, however.

Offer and transplant rates were also evaluated as a function of CPRA. These results were similar to reports previously produced for the Histocompatibility Committee, except he reported on the very highly sensitized group (>=95%) as broken out into single-integer groups.

The transplant rate – the number of transplants per 1,000 person-years – varied between 160 and 215 as CPRA increased from 0 to 69%. For the CPRA=70-79 group, the transplant rate dropped to 128.3. However, the transplant rate jumped to over 500 for the 80-84 group, then decreased as CPRA increased further, falling below 150 once CPRA reached 98%. The Committee was not surprised by the spike starting at CPRA=80-84, since candidates are currently defined as "highly sensitized" are awarded four additional allocation points if CPRA is at or above 80%. The decrease in transplant rates for the highly sensitized candidates was more pronounced by excluding zero-mismatches.

The Committee reviewed data which showed that unlike transplant rates, which showed very little trend before CPRA<70, offer rates decreased steadily as CPRA increased from 0% to 79%. As with transplant rates, offer rates showed an increase once CPRA reached 80%, then steadily decreased again, falling to 0.09 offers per patient year for 100% sensitized candidates. Though the offer rate jumped up when CPRA went from 75-79% to 80-84%, this 54% increase (3.88 to 5.99) was substantially lower than the 416% increase in transplant rates (128.3 to 534.4). Comparing non-sensitized candidates with the opposite extreme, the offer rate for CPRA=0% candidates was 187 times greater than for CPRA=100% candidates; excluding zero-mismatches, this offer rate ratio exceeded 300.

The Committee thought an explanation for large disparity between offer rates – which showed a smooth, steady trend as a function of CPRA with an expected but moderate spike at 80% – and transplant rates, which revealed a more erratic pattern, may lie in transplant programs' offer acceptance practices. As CPRA increases, transplant programs may become less selective and

more willing to accept a lower quality kidney, being concerned that their sensitized candidate may not receive another suitable offer due to positive (virtual or prospective) crossmatch. The Committee opined that maybe this concern is even greater for candidates with CPRA>=80%, since this threshold has been traditionally considered as defining "highly sensitized" and thus may be a label perceived as indicating very little chance of another suitable offer being received.

The Committee was pleased to hear that the Kidney Committee would be asking for modeling that would start a sliding scale at a CPRA of 20% with a mandatory national share at 98%. The Kidney Committee will discuss the results of this model run in the near future.

Update on Pediatric/Histo subcommittee: Dr. Reinsmoen, in the interest of time, gave a brief summary of a conference call that took place between a subcommittee made up of Pediatric, Kidney and Histocompatibility Committee members whose charge is to design a system to allocate Pediatric Kidney transplants, and in particular the sensitized pediatric candidate.

She reported the subcommittee developed a trial kidney allocation system which would prioritize all highly-sensitized, pediatric, kidney candidates that are located within the same region after the local prior living organ donors. (See below)

This would add one new classification to the kidney allocation algorithm, and the general sequence would be as follows, with the new classification underlined:

All Current Zero ABDR Mismatch Classifications

OPO KI, Prior Living Organ Donors

<u>OPO and Regional KI, Highly Sensitized Pediatric</u>

OPO KI, Highest Scoring High CPRA

OPO KI, Pediatric

[no further changes]

This allocation system would define "highly-sensitized" as candidates with a Calculated Panel Reactive Antibody (CPRA) of 80% or greater, and "pediatric" as any candidate who is placed on the waiting list prior to their 18th birthday.

She reported that the subcommittee asked for modeling of the above sequence, and would review the results sometime in the near future.

Question-Now that DP typing can be requested for thoracic donors, does there need to be a place on DonorNet to report the results? Ms. Gore reported to the Committee that she has received several calls from members because they were not able to post the DP typing that is now required for thoracic donors (if requested) on DonorNet. She said there is a process that must be followed if the Committee thought it was time to add the fields to Donor Net; she asked if it was time to start the process. The Committee answered with a resounding yes, not only should members be able to report DP but also DQ alpha. Ms. Gore said the first step in the process was to write a problem statement that would be reviewed by the Executive Committee; she would look do this. Drs. Bray, Reinsmoen and Tyan offered to help.

NAME	COMMITTEE POSITION	11/15/2011
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.	x
Cathi Murphy, PhD	Region 4 Rep.	
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, CHS, CHT	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	
Lori Gore	Committee Liaison	x
Anna Kucheryavaya	Support Staff	x
Jory Parker	Support Staff	x
James Bowman	Ex officio (HRSA)	x