Interim Report of the
OPTN/UNOS Liver and Intestinal Organ Transplantation Committee
July 15, 2009

1. Orientation and Committee Goals. The Committee received several brief orientations to OPTN policy-making, UNOS research support, and support provided by the Scientific Registry of Transplant Recipients (SRTR) contractor. The Committee was reminded of its charge, as well as the annual goals set for 2009-2010:

    - Continue to study and address geographic/regional variation and disparities in access to liver transplantation. Identify areas that can be addressed by the OPTN, and recommend appropriate approaches to addressing them;
    - Update the HCC exception criteria based on recommendations from the consensus conference held in November 2008;
    - Conduct evidence-based policy development for liver allocation to determine whether incorporating net benefit into liver allocation policy, at some point in the future, would further the long-range strategic goals and priorities of the OPTN; and
    - Re-examine the feasibility of a national review board for MELD/PELD exceptions.

2. OPTN/UNOS Board of Directors Meeting, June 2009. Elizabeth Pomfret, M.D., immediate past chair, reviewed the actions taken during the Board of Directors Meeting in June 2009. The Board approved the proposal for regional distribution for Status 1 candidates. The Committee did not bring the proposal for regional distribution for all candidates listed with a MELD/PELD score to the Board because the proposal had created significant controversy. The Committee requested that the Board approve a public forum on liver distribution to be held in the Spring of 2010, which was approved.

    The Board also approved the proposal for standardized MELD/PELD exception criteria for six diagnoses, but the proposal was modified at the Board meeting. This was due primarily to concerns about the requirement for uniform MELD/PELD score assignments across all regions, as candidates in some Regions may need higher scores in order to receive an offer. Board members also expressed concern over the projected costs of programming the policy to allow 'automatic' exceptions (i.e., not requiring RRB review but calculated in UNet^{SM}, similar to the programming for candidates with hepatocellular carcinoma (HCC)). As a result, the policy approved by the Board states that:

    > "Candidates meeting the criteria listed in 3.6.4.5.1 – 3.6.4.5.6 are eligible for additional MELD/PELD exception points, provided that the criteria are included in the clinical narrative. Unless the applicable RRB has a pre-existing agreement regarding point assignment for these diagnoses, an initial MELD score of 22/PELD score of 28 shall be assigned. For candidates with Primary Hyperoxaluria meeting the criteria in 3.6.4.5.5, an initial MELD score of 28/PELD score of 41 shall be assigned."

Under the approved language, the Regional Review Boards (RRBs) would review these cases, instead of allowing automatic approval by the UNet^{SM} application as originally proposed. The Committee reviewed a list of questions compiled by UNOS staff members regarding how the policy would be implemented, such as:

- How to reconcile the words "eligible" versus "shall" in the approved language?
- What if a Region has additional criteria?
- What if the RRB doesn't follow policy? Can this be enforced?
- What if an RRB wants a new agreement or wants to change their existing agreement?
- When should the cholangiocarcinoma (CCA) protocol get submitted and when will it get reviewed?
- How will the data collection for CCA work?
- Are there other 'costs' of this non-programming solution?

The MELD/PELD Exceptions Subcommittee will address these questions and provide guidance to the transplant programs and RRB members. The subcommittee will also discuss alternate methods to collect data for candidates with these diagnoses, which was one of the goals of the original proposal.

The Committee discussed whether an approved MELD/PELD exception for a standardized diagnosis should transfer if a candidate moves to another Region (i.e., should the candidate's approved score be maintained?). This question had been referred to the Committee after a candidate with an approved HCC exception moved to another Region and the physician had petitioned the new RRB for a score equivalent to that of an HCC exception with two extensions. Committee members felt that these scores should transfer. In many cases, candidates may have no control over where they are transferred due to their insurance coverage. The Committee felt that this should only apply to diagnoses with standardized criteria, such as HCC (meeting criteria) and the six newly-approved diagnoses. The Subcommittee will develop guidance for the review boards. The Committee approved the following:

Motion: When a candidate receives a MELD/PELD exception for a standardized diagnosis, the score should transfer if the candidate transfers to another center. Committee vote: 19 in favor, 0 opposed, 0 abstentions.

These cases could be managed in a similar fashion to the waiting time reinstatement process used for kidney candidates who transfer to another center. This will require a policy change that will follow the usual policy development process.

3. Public Forum. Two subcommittees were created to direct this work: a Public Forum Subcommittee and a Broader Distribution Subcommittee. The Committee will likely issue a Request for Information (RFI), which will help frame the questions and concepts that will be considered at the forum. All public comments received from the MELD/PELD regional distribution proposal will be reviewed for ideas that should be considered. In addition to potential changes to the current local-regional-national distribution system, the forum may also include the concept of net benefit. The Committee considered a question as to whether the forum should be restricted to liver distribution only, or whether it should be broadened to include other organ types as well, perhaps with emphasis on liver. Committee members felt that broadening the scope of

the forum would make the discussion too diffuse, and that it would make it difficult to come to any conclusions. However, this forum could be used as a springboard for other discussions.

4. Review of Net Benefit Analyses. Doug Schaubel, Ph.D., presented an overview of net benefit modeling and a summary of the SRTR's work on the use of net benefit for liver allocation. Transplant benefit is currently being used for lung allocation, and is also being considered for heart and kidney allocation. The Committee is looking at net benefit as one possible way to improve liver allocation. Transplant benefit combines the concepts of future wait-list lifetime with post-transplant lifetime, and reflects the number of life years gained through liver transplantation. The post-transplant model includes both recipient and donor factors. A "benefit score" is calculated for each MELD score. This benefit score increases as MELD increases, and is positive above a MELD score of 9. Dr. Schaubel noted that two patients with equal MELD scores could have different benefit scores because MELD is not the only factor that predicts waiting list and post transplant mortality. There is also overlap in benefit between ranges of MELD scores. The index of concordance (IOC), which conveys the predictive ability of a model, is 0.75 for the waiting list model and 0.65 for the post-transplant model. In comparison, the MELD score has an IOC of 0.64.

   Some Committee members felt that this concept will be difficult for patients to understand. Other comments and questions included:

   - Should there be delisting criteria for those who are too sick?
   - What is the impact on older candidates?
   - These models do not account for long-term survival; and
   - The model does not include cold ischemia time (CIT).

   Dr. Schaubel noted that ischemia time is not known until time of transplant, so it would be difficult to include in the score; further, ischemia time does not add much to the model when adjusted for other factors. Age plays a much less significant role for liver transplant survival than it does for kidney transplants.

   The impact of transplant benefit was modeled using the LSAM simulation model and compared to the current liver allocation algorithm and to regional sharing for all candidates using MELD/PELD. Transplant benefit was projected to reduce total deaths by 102 and increase life-years saved over 5 years by 2,223 when compared to the current system. Transplant benefit did not appear to negatively impact any group of patients. In general, pediatric candidates have lower benefit scores, but due to age and size-matching for donors and the preference given to pediatric candidates for pediatric donors, these candidates do not appear to be disadvantaged by a net benefit system. As a next step, the concept could be applied to the allocation system in a similar fashion to "Share 15," with some threshold of benefit score used for broader distribution of livers.

5. SRTR LSAM Modeling Results for Multiple Distribution Algorithms. During the May 2009 conference call, the SRTR was asked to model several liver allocation algorithms using MELD/PELD threshold values of 22, 25, 29 and 35, for local followed by regional distribution (similar to "Share 15" but with different MELD/PELD thresholds). Several scenarios included full regional distribution for the highest scores, while others incorporated 500-mile concentric circles as distribution units. The SRTR provided the number of projected pre- and post-transplant and total deaths and changes in distance travelled for each scenario. Committee members expressed the following concerns:

   - An area of 500 nautical miles is too large for the "local" unit;

- Distance could be based on driving versus flying as a logical cut-point;
- The models do not include effect of increased CIT on morbidity and survival;
- The Committee will need to assess costs as increased distance leads to increased travel time/costs, and ischemia time;
- Will this system lead to higher quality donors leaving the local area DSA and poorer donors staying?

While these are valid criticisms, it was noted that the Committee is just beginning the discussion, and such concerns will need to be considered as the committee looks at alternatives. As a starting point, the Committee must frame the question: is the goal to minimize waiting list death? What about the impact on post-transplant outcomes/survival benefit? Each option considered by the Committee will have consequences and trade-offs. One Committee member suggested that a starting point would be to minimize waiting list mortality without a significant increase in costs/distance and post-transplant mortality.

6. Proposed Listing Requirements for Simultaneous Liver-kidney (SLK) Transplant Candidates. A proposal for listing requirements for candidates awaiting an SLK transplant was circulated for public comment in February 2009, but has not been forwarded to the Board due to questions about implementation. The proposal included specific criteria for those candidates needing an SLK, plus a "safety net" for those not meeting the criteria who subsequently need a kidney transplant following a liver-alone transplant. These two aspects of the policy would have to be programmed at the same time. However, the number of kidney alternative allocation system (AASs) makes changes to the kidney algorithm very complicated. Further, it is likely that this may not be programmed until the new kidney allocation system (KAS) is implemented. If the policy were to be put forward without the safety net, it would require another round of public comment. A joint subcommittee with the Kidney Committee will address these issues.

7. HCC Consensus Conference. The meeting report from the conference held on November 2009 was submitted for publication in early July. Some of the recommendations may be incorporated into the liver allocation policy. The HCC policy also needs to be updated and revised/reorganized. A subcommittee was formed to review the conference recommendations and the current policy. Dr. Pomfret reported that the members of the imaging working group received funding from the American College of Radiology Imaging Network (ACRIN), which is part of the National Cancer Institute (NCI), for a multi-center trial that will compare pre-transplant imaging studies with post-transplant pathology. The OPTN/UNOS Board voted to endorse the ACRIN project in June 2009. The subcommittee will be asked to assist with developing the RFI for this trial.

8. Criteria for Intestinal Transplant Surgeons and Physicians. Several years ago, the Committee developed criteria for intestine transplant surgeons and physicians that were circulated for public comment. The proposal was criticized by many as being "too restrictive," and some felt it would impair development of intestinal transplant programs and the field of intestine transplantation in general. The proposal was not forwarded to the Board. Subsequently, the ASTS developed criteria for intestinal transplant fellowship training programs for surgeons. The ASTS requires that a surgeon perform 10 transplants and 5 procurements, either through volume during the fellowship or through experience over 2-5 years. A subcommittee was formed to review these criteria for possible inclusion in the Bylaws.

Heung Bae Kim, M.D., subcommittee chair, reviewed the requirements for every organ to determine whether the intestine criteria seemed reasonable, based on the numbers of transplants performed annually in the US. Currently, six intestine transplant programs would meet the ASTS requirements for a fellowship training program based on their transplant volume, but none are listed on the ASTS website as being approved. The subcommittee felt that 10 transplants and 5 procurements would be an appropriate number for UNOS to set for the surgical director of an intestine transplant program. As there is currently no equivalent of a hepatology fellowship, the subcommittee recommended that the requirements for intestine physicians would be obtained via the experience pathway. For the physician, the subcommittee proposed a requirement for 10 patients followed for 3 months post-transplant, either during a hepatology or GI fellowship or as an attending physician on a transplant service, with some combination of isolated intestine and combined liver-intestine transplant recipients. The individual would also be required to view at least one isolated and one combined liver-intestine transplant and to be involved in the evaluation of one multi-organ donor. Some Committee members felt that limiting the surgeon experience pathway to 10 per year may be too few, while others felt it may be difficult to obtain that volume. The subcommittee will continue to refine the proposal.

9. Request to Change the Liver-Intestine Allocation Policy. The Committee received a letter from a member asking for a change to the adult intestine allocation system in a similar fashion to the pediatric intestine allocation system, to reduce the adult mortality rate for these candidates. The Intestine Subcommittee will review this request and make a recommendation to the full committee.

10. Split Liver Allocation Policy. A joint-pediatric subcommittee will be revisiting the split liver policy, which was put into place several years ago. The intent of the policy was to incentivize splitting, but it does not seem to be enhancing the use of split livers.

11. Status 1A/1B Review. All Status 1A/1B cases that do not meet the criteria in policy are reviewed by a subcommittee, which then makes recommendations to the full committee. If a center is referred for the first time, typically the committee will send a letter of education or warning, while repeat offenders are referred to the Membership and Professional Studies Committee (MPSC). In the past, the subcommittee considered only repeat violations of the same criteria (e.g., PNF outside the time limit in policy), but did not consider infractions for different criteria as repeat offenses. The subcommittee will now review a center's history of cases as a whole. The subcommittee was asked to develop more specific criteria for how cases are reviewed and referred to MPSC (i.e., how many infractions within some period of time).

12. Memoranda from MPSC Regarding Status 1 Criteria. Policy 3.6 states that a candidate must be located in an Intensive Care Unit (ICU) to meet Status 1A/B criteria. The Committee reviewed a memorandum from the MPSC stating that some liver transplant programs list candidates as Status 1A or 1B while they are admitted to telemetry or step down units. The MPSC expressed concern location is used as a surrogate for severity of illness, and "may encourage costly and inefficient behavior patterns by some transplant centers that admit candidates to an ICU exclusively to achieve adult 1A(i) and pediatric 1A or 1B status on the Waitlist." The MPSC requested that the Pediatric Transplantation and Liver and Intestinal Organ Transplantation

Committees "reevaluate the current listing criteria that require candidates to be admitted to the ICU to achieve status 1A/1B and determine whether the use of candidate location (ICU) as a surrogate for severity of illness remains appropriate and advisable." Committee members discussed the valid reasons why a critically ill patient may not be admitted to the ICU (e.g., no ICU beds, patient not intubated or on vasopressors). Step-down and telemetry units were not felt to be equivalent to an ICU. The Committee felt that there is currently a mechanism for a center to justify why a candidate was not in the ICU via the narrative, and that the policy should not be changed.

13. Bylaws Pertaining to Liver Transplant Physicians. The MPSC asked that the Committee provide input regarding the bylaws pertaining to liver transplant physicians. The current bylaw is problematic because there are individuals who may be well-trained but do not meet the specifics of the bylaws. Centers who are recruiting a primary liver transplant physician may not know whether a candidate will be approved by the MPSC prior to hiring, and the MPSC does not have the ability to grant waivers for individuals who may have experience but lack the appropriate boards. Further, it is hard to document "foreign equivalent" training. The MPSC asked for feedback on the following:

    - Should the bylaws be expanded to include a pathway for individuals who have completed a transplant hepatology fellowship but did not complete a GI fellowship?
    - Should the board certification requirements be amended to allow Transplant Hepatology as an alternative to Gastroenterology Boards?

    A subcommittee has begun to review these issues, which are complicated because several related factors are still in flux: the certificate of added qualification (CAQ) in transplant hepatology that was approved in 2008, as well as the movement for a separate board in transplant hepatology to obtain subspecialty training during a gastroenterology fellowship, which may be 5-7 years away. Committee members recommended that feedback should obtained from the American Association for the Study of Liver Disease (AASLD), American Society for Transplantation (AST), American Gastroenterology Association (AGA), and American College of Gastroenterology (ACG). This may also be a topic for the program directors meeting at Digestive Disease Week (DDW) this year.

14. Analysis of ABO-incompatible Liver Transplants. Policy 3.6.2.2 (Liver Allocation to Candidates Willing to Accept an Incompatible Blood Type) states that "For Status 1A or 1B candidates or candidates with a match MELD or PELD score of 30 and greater, centers may specify on the Waiting List those candidates who will accept a liver from a donor of any blood type." During the November 2008 meeting, the Committee reviewed a request to revise the existing liver allocation policy requirements regarding incompatible ABO transplants to be similar to that used in thoracic organ allocation. The thoracic organ allocation policy states that "Following allocation for all born transplant candidates who have blood types that are compatible with donors, hearts will be allocated locally first and then within zones in the sequence described in 3.7.10, by heart status category to born Status 1A or 1B pediatric heart candidates who are eligible to receive a heart from any blood type donor." The policy also lists specific criteria regarding which candidates are eligible to accept a heart from any blood type donor.

The Committee asked for current data on ABO incompatible liver transplants in order to evaluate this request. OPTN data for deceased donor liver transplants between January 1, 2003 and October 31, 2008 were included in the analysis. Graft and patient outcomes were computed using standard Kaplan-Meier survival rates for deceased donor liver transplants between March 1, 2003 and December 31, 2006. Cases where blood type A_2 donors were transplanted into O recipients were considered compatible and excluded from the analyses. There were 118 transplants with incompatible blood type matches, or 0.3% of the transplant cohort. Approximately 50% of cases were adults, and 80% in were listed in Status 1/1A/1B at the time of transplant. The age distribution was normal in adults, but was concentrated among the youngest pediatric recipients. ABO incompatible transplants had the lowest graft/patient survival, although these were also the sickest candidates. The lowest graft survival for ABO incompatible transplants was for those with a calculated MELD/PELD score of 30 or higher, while patient survival was similar for MELD/PELD scores less than 30 as compared to 30 or higher. The survival rates were better for pediatric patients than for adults. The Committee asked that the Joint Liver-Pediatric subcommittee review the data and the policy and make a recommendation to the Committee.

15. Proposals Circulated for Public Comment, June 2009. The Committee discussed six proposals that had been circulated for public comment.

    A. Proposal to Improve the ABO Verification Process for Living Donors. This proposal brings the policy for double ABO verification of living donors in line with the policy for deceased donors. The Committee was unanimously in support of this proposal.

    B. Proposed Guidance for the Medical Evaluation of Living Liver Donors. These guidelines were modeled after the Living Kidney Donor Guidelines that have been approved by the Board. Some members expressed concerns that these types of guidelines should be developed by the professional societies and not UNOS. Committee members requested more time to review the document, and voted to defer comments until it has time for more review and discussion. Committee Vote: 15 in favor, 3 opposed, and 0 abstentions.

    C. Proposal to Add Language to the OPTN/UNOS Bylaws Requiring Transplant Center and OPO Members to Follow State Law Regarding Anatomical Gifts. The Committee was in support of this proposal that requires centers to follow their own state laws regarding end of life care and organ recovery. A reference showing where the state laws can be found would be helpful. Committee vote: 18 in favor, 0 opposed, and 0 abstentions.

    D. Proposal to Change the UNOS Bylaws to Reconcile Discrepancies in Patient Volume Requirements for Full and Conditional Program Approval When Qualifying Kidney, Liver and Pancreas Primary Transplant Physicians. This proposal would make the bylaws regarding patient volume requirements internally consistent. The Committee was in support by a vote of 18 in favor, 0 opposed, and 0 abstentions.

E. OPTN Notification Requirements for OPOs, Transplant Hospitals, and Histocompatibility Labs When Faced with an Adverse Action Taken by Regulatory Agencies. The MPSC is proposing a change in the number of days by which a member must notify the MPSC when faced with an adverse action by a regulatory agency. One Committee member asked whether the proposed change would diminish the performance-monitoring function of the MPSC. One approach would be to separate the notification from the submission of required materials. No vote was taken as the proposal does not specifically apply to liver/intestine transplantation.

F. Proposal to Change Requirements for Labeling and Packaging Organs Procured by Visiting Transplant Center Teams and for OPO Labeling of Tissue Typing Materials. This proposal would transfer the responsibility of packaging and labeling of organs from the OPO to the transplant center when its recovery team elects to recover an organ and transport it directly to their transplant center for transplant. Sometimes the recovery teams opt to forgo the required labeling procedure, which leaves the OPO out of compliance with policy. Committee members felt that the labeling requirements should be enforced, and that OPOs should be required to report these centers to the MPSC, rather than simply transfer the responsibility to the center. The Committee did not support this proposal by a vote of 1 in favor, 18 opposed, and 1 abstention.

Committee Attendance at the
July 15 Committee Meeting
Chicago, IL

NAME	COMMITTEE POSITION	In Attendance
W. Kenneth Washburn, M.D.	Chair	X
Kim Olthoff, M.D.	Vice Chair	
Michael Curry, M.D.	Regional Rep.	X
Stephen Dunn, M.D.	Regional Rep.	X
Nigel Girgrah, M.D., Ph.D.	Regional Rep.	X
Goran Klintmalm, M.D., Ph.D.	Regional Rep.	X
Scott Biggins, M.D.	Regional Rep.	X
John Ham, M.D.	Regional Rep.	X
Anthony D'Alessandro, M.D.	Regional Rep.	X
Harvey Solomon, M.D.	Regional Rep.	X
Thomas Schiano M.D.	Regional Rep.	X
Shawn Pelletier, M.D.	Regional Rep.	X
James Eason, M.D.	Regional Rep.	by telephone
Maureen Burke-Davis, RN, NP-C, CCTC	At Large	by telephone
Patricia Carroll PA-C, CPTC	At Large	X
Julie Heimbach, M.D.	At Large	X
Heung Bae Kim, M.D.	At Large	X
Timothy McCashland, M.D.	At Large	X
Lisa McMurdo, RN, MPH	At Large	X
Kenyon Murphy	At Large	X
John Roberts, M.D.	At Large	X
Debra Sudan, M.D.	At Large	X
Kerri Wahl, M.D.	At Large	
Elizabeth Pomfret, M.D., Ph.D.	Ex Officio	X
Bernard Kozlovsky, M.D., MS	HRSA	X
Monica Lin, Ph.D.	HRSA	X
Mary Guidinger, MS	SRTR Liaison	X
Robert Merion, M.D.	SRTR Liaison	X
Douglas Schaubel, Ph.D.	SRTR Liaison	X
Ann Harper	Committee Liaison	X
Erick Edwards, Ph.D.	Research Support Staff	X