OPTN/UNOS Liver and Intestinal Organ Transplantation Committee

National Liver Review Board

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National Liver Review Board

Executive Summary

A liver candidate receives a MELD[1] or, if less than 12 years old, a PELD[2] score that is used for liver allocation. The score is intended to reflect the severity of the candidate's disease. When the calculated score does not reflect disease severity, a liver transplant program may request an exception score. Currently there is not a national system that provides equitable access to transplant for liver candidates whose calculated MELD or PELD score does not accurately reflect the severity of their disease. Instead, each region has its own review board that evaluates exception requests submitted by the liver transplant programs in its region. Most regions have adopted independent criteria used to request and approve exceptions, commonly referred to as "regional agreements." Some have theorized that regional agreements may contribute to regional differences in exception submission and award practices, even among regions with similar organ availability and candidate demographics.[3,4,5] In November 2013, the OPTN/UNOS Board of Directors charged the Liver and Intestinal Organ Transplantation Committee with developing a conceptual plan and timeline for the implementation of a national liver review board.

Through policy and revised operational guidelines, this proposal establishes a national structure for review of MELD and PELD exception cases in which all liver transplant programs have an equal opportunity for representation. The National Liver Review Board seeks to mitigate regional differences in award practices by establishing new voting procedures and giving the Committee the ability to develop national guidance for assessing common requests, which supports Goal 2 of the OPTN Strategic Plan.[6] This proposal also improves the efficiency of the review board system by reducing the overall workload for reviewers and eliminating unnecessary delays in awarding exception points when appropriate.

Is the sponsoring Committee requesting specific feedback or input about the proposal?

The Committee is considering changes to the number of points assigned to exception candidates. To assist them in further developing this proposal for a second round of public comment, the Committee would like feedback on whether it is appropriate to:

- Award exception candidates one or two MELD points below the median allocation MELD at transplant for the candidate's Donor Service Area (DSA).
- Remove the automatic three-month increases in standardized exception scores, also referred to as the "MELD elevator."

See "Continued Policy Development" under "How was this proposal developed?" for more information.

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[1] Model for End-Stage Liver Disease
[2] Pediatric End-Stage Liver Disease
[3] Argo, C. K., G. J. Stukenborg, T. M. Schmitt, et al. "Regional Variability in Symptom-Based MELD Exceptions: A Response to Organ Shortage?" American Journal of Transplantation, 11(2011), 2353-2361.
[4] Massie, A. B., B. Caffo, S. E. Gentry, et al. "MELD exceptions and rates of waiting list outcomes." American Journal of Transplantation, 11(2011), 2362-2371.
[5] Rodriguez-Luna, H., H. E. Vargas, A. Moss, et al. "Regional variations in peer reviewed liver allocation under the MELD system." American Journal of Transplantation, 5(2005), 2244-2247.
[6] http://optn.transplant.hrsa.gov/governance/strategic-plan/

National Liver Review Board

Affected Policies: Policy 9.3: Status and MELD/PELD Score Exceptions, Policy 9.3.A: MELD/PELD Exception Applications, Policy 9.3.B: Review of Exceptions by the RRB and Committees, Policy 9.3.C: Specific MELD/PELD Exceptions, Policy 9.3.D: Pediatric Liver Candidates with Metabolic Diseases, Policy 9.3.E: Candidates with Cholangiocarcinoma, Policy 9.3.F: Candidates with Hepatocellular Carcinoma (HCC), Policy 9.3.G: MELD/PELD Score Exception Extension

Sponsoring Committee: Liver and Intestinal Organ Transplantation Committee

Public Comment Period: January 25, 2016 – March 25, 2016

What problem will this proposal solve?

A liver candidate receives a MELD[7] or, if less than 12 years old, a PELD[8] score that is used for liver allocation. The score is intended to reflect the severity of the candidate's disease. When the calculated score does not reflect disease severity, a liver transplant program may request an exception score. Currently there is not a national system that provides similar access to transplant for liver candidates whose calculated MELD or PELD score does not accurately reflect the severity of their disease. Each region has its own review board that evaluates exception requests submitted by the liver programs in its region. Chaired by the Regional Representatives who are appointed to serve on the Liver and Intestinal Organ Transplantation Committee (hereafter, "the Committee"), these Regional Review Boards (RRBs) have different rules regarding representation, including program eligibility, length of service terms, and member rotation. Most regions have adopted independent criteria used to request and approve exceptions for specific diagnoses, commonly referred to as "regional agreements." Some have theorized that regional agreements may contribute to regional differences in exception submission and award practices, even among regions with similar organ availability and candidate demographics.[9,10,11] This has led some to suggest that a national board replace the current RRB system.[12,13] On average, 88.4% of initial, appeal, and extension requests submitted between July 1, 2014 and June 30, 2015 were approved; however, the regions approved as few as 75.8% and as many as 93.5% of requests during this timeframe. Excluding recipients transplanted in a status, the proportion of recipients transplanted with an exception score ranged from 29% to 61% among the regions.[14]

The current system also has some inefficiencies that can lead to delays in candidates being awarded exception points, as well as excess work for review board members. The RRB Chairs review over 1,000 standardized exception requests each year (including initial applications and extensions), which they approve because candidates meet criteria in policy.[15] Chair review has been used as an alternative to

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[7] Model for End-Stage Liver Disease

[8] Pediatric End-Stage Liver Disease

[9] Argo, C. K., G. J. Stukenborg, T. M. Schmitt, et al. "Regional Variability in Symptom-Based MELD Exceptions: A Response to Organ Shortage?" American Journal of Transplantation, 11(2011), 2353-2361.

[10] Massie, A. B., B. Caffo, S. E. Gentry, et al. "MELD exceptions and rates of waiting list outcomes." American Journal of Transplantation, 11(2011), 2362-2371.

[11] Rodriguez-Luna, H., H. E. Vargas, A. Moss, et al. "Regional variations in peer reviewed liver allocation under the MELD system." American Journal of Transplantation, 5(2005), 2244-2247.

[12] Gish, R. G., R. J. Wong, G. Honerkamp-Smith, et al. "UNOS Regional Variations in Appeal Denial Rates with Non-Standard MELD/PELD Exceptions: Support for a National Review Board." *Clinical transplantation* (2015).

[13] Rodriguez-Luna, H., H. E. Vargas, A. Moss, et al. "Regional variations in peer reviewed liver allocation under the MELD system." American journal of transplantation, *5*(2005), 2244-2247.

[14] Based on OPTN data presented to the Committee on 10/20/2015

[15] Policy 9.3.C: Specific MELD/PELD Exceptions, Organ Procurement and Transplantation Network Policies.

programming these exceptions for auto-approval in UNet[SM] as is done for hepatocellular carcinoma (HCC) candidates that meet criteria. According to policy, some candidates meeting standardized criteria automatically receive exception extensions, as well. However, if the transplant program ever submits an exception request after the extension due date, the full review board must evaluate all subsequent extension requests despite meeting all other criteria in policy for approval. This has led to the RRBs reviewing an estimated 800 additional requests each year.

In November 2013, the OPTN/UNOS Board of Directors (hereafter, "the Board") charged the Committee with developing a conceptual plan and timeline for the implementation of a national liver review board.

Why should you support this proposal?

The Committee proposes establishing a National Liver Review Board (NLRB) to provide fair, equitable, and prompt peer review of exceptional candidates. This proposal contains changes to OPTN/UNOS policy and updated operational guidelines (**Exhibit A**), which govern the review boards. The NLRB will be comprised of three specialty boards including Adult HCC, Adult Other Diagnosis, and Pediatrics. Assigning requests to the appropriate specialty board, rather than by geographic location, allows for reviewers with appropriate policy and clinical expertise to evaluate the request.

Every liver transplant program has the opportunity to be represented on the NLRB. An active liver transplant program may appoint a representative and alternate to each of the adult specialty boards. A liver transplant program with an active pediatric component may appoint a representative and alternate to the pediatric specialty board.[16] Representatives and alternates serve one-year terms, which may be renewed annually as long as the representative continues to fulfill obligations to the NLRB. Individuals may serve on more than one specialty board at the same time. All NLRB members must complete orientation prior to each term of service, which will include training on exception policy, operational guidelines, and guidance for evaluating common types of exceptions.

The NLRB will mitigate regional differences in award practices by establishing new voting procedures and guidance for assessing requests. Exception requests will be randomly assigned to five reviewers of the appropriate specialty board. A request must achieve four of five affirmative votes in order to be approved. If denied, the program has the opportunity to appeal to another random group of five reviewers. If denied on appeal, the program may request a conference call with the second group of reviewers. Ultimately, the program may appeal to the Committee if the outcome of the call is not favorable.

This proposal eliminates the regional agreements and instead tasks the Committee with developing or maintaining existing guidance to assess the most common types of exceptions. The Committee periodically reviews exception requests for opportunities to revise the MELD score or provide guidance for review board members. For example, the Board recently passed guidance to evaluate requests for candidates with neuroendocrine tumors, polycystic liver disease, primary sclerosing cholangitis, and portopulmonary hypertension.[17] Unlike the Thoracic Organ Transplantation Committee, the Liver and Intestinal Organ Transplantation Committee must present review board guidance to the Board for approval. Consistent with thoracic policy, this proposal includes policy language that allows the Committee to provide specific recommendations to NLRB members without Board approval.

The Committee also proposes improvements to the efficiency of the review board system to reduce the workload for reviewers and eliminate unnecessary delays in awarding exception points when appropriate. This proposal automates all standardized MELD/PELD exceptions in policy, an estimated 1,000 initial and

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[16] Appendix F.7: Liver Transplant Programs that Register Candidates Less than 18 Years Old, Organ Procurement and Transplantation Network Policies (pending implementation)

[17] Organ Procurement and Transplantation Network. *Guidance on MELD/PELD Exception Review*. Richmond, VA, 2015, available at http://optn.transplant.hrsa.gov/resources/by-organ/liver-intestine/guidance-on-meld-peld-exception-review/.

extension requests each year. Proposed changes to standardized exception policy language are limited to those necessary to program UNet^{SM} to automatically award exception points to those meeting criteria and are not intended to change the criteria for approval. This proposal also allows a candidate that meets standardized criteria to be eligible for automatic approval of a subsequent extension request after the liver transplant program misses a submission deadline, so long as the late request was reviewed by the NLRB. Currently the RRBs review an estimated 800 additional requests each year because of a missed extension deadline. With these improvements, the overall caseload will decrease by nearly 2,000 requests each year, which will be distributed equally among all reviewers nationally.

How was this proposal developed?

In response to the Board's directive, the MELD Enhancements and Exceptions Subcommittee (hereafter, "the Subcommittee") investigated various concepts for implementing a national review board. The Board most recently reaffirmed their support for this effort at its June 2015 meeting. In September 2015, the Vice Chair reconvened the Subcommittee to further develop this proposal. The Subcommittee considered three broad structures:

1. A single, national liver review board
2. Four, super-regional review boards
3. National, specialty review boards

In 2014, the Subcommittee explored the option of a single, national liver review board and identified the need for pediatric transplant specialists to review pediatric exception requests. The Committee questioned whether a national system would be effective unless regional differences in MELD score at transplant are mitigated. Otherwise, the exception scores would still have to be calibrated to the MELD score at transplant for the geographic area where the candidate is registered. Efforts were directed to redistricting as a potential solution to improving geographic disparities in access to liver transplantation.

In 2015, the Subcommittee considered an alternative structure for the review boards, which would combine regions with dissimilar award practices into four super-regional review boards. Ultimately, the Subcommittee decided that any incremental improvement in geographic variability in award practices using this structure would be enhanced with a national board.

Finally, the Subcommittee proposed establishing national, specialty boards to ensure that requests are assigned to reviewers with appropriate expertise. The Vice Chair met with liver representatives from the Pediatric Transplantation Committee and received their support for establishing a separate pediatric specialty board. The Committees will collaborate to develop a guidance document for assessing pediatric exception requests, which will be an interim measure to promote equity until pediatric liver allocation can be revised to lessen the number of transplants that occur under exception.

On October 20, 2015, the Subcommittee presented its recommendations on the structure and operation of the NLRB to the full Liver and Intestinal Organ Transplantation Committee. Initial recommendations were well received, and the Subcommittee worked over the next month to draft policy language and operational guidelines to establish the NLRB. On December 18, 2015, the Committee approved the proposal for public comment (16-Yes, 0-No, 0-Abstentions).

The Committee anticipates a second round of public comment as it further develops this proposal to address concerns raised by the Subcommittee in 2014 about how to assign appropriate exception scores (see "Continued policy development" below).

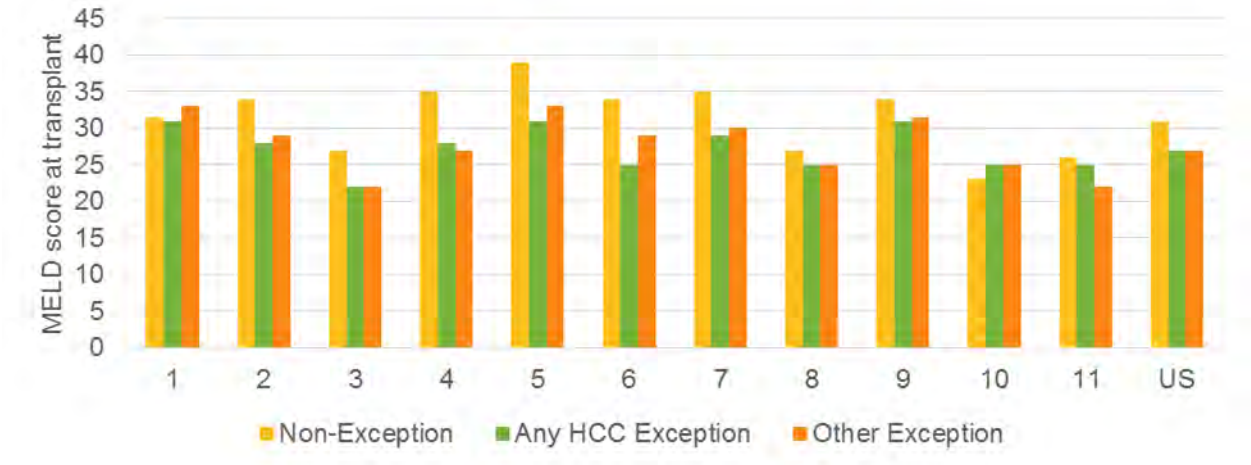
Continued Policy Development

The Committee is requesting feedback from the community on the optimal method of assigning MELD score exception points. Currently, the MELD exception score for many standardized exception diagnoses begins at 22 points and automatically increases every three months to reflect a 10% increase in waitlist

mortality, so long as the candidate continues to meet criteria in policy.[18] This automatic three-month increase in standardized exception score is also referred to as the "MELD elevator."

The MELD elevator is problematic for several reasons. The waitlist mortality for non-exception candidates actually exceeds the mortality for exception candidates.[19] Non-exception candidates are also transplanted at higher MELD scores than those with approved exceptions (see **Figure 1**). Some have suggested that the MELD elevator has contributed to the escalation in MELD score at transplant that has occurred over the past decade.[20]

Figure 1. Adult deceased donor liver transplant recipients transplanted from July 1, 2014 – June 30, 2015, by OPTN region and MELD score at transplant



For candidates with certain standardized exception diagnoses, the Committee is considering whether it is appropriate to assign a fixed exception score that is 1 to 2 points below the median allocation MELD for the Direct Service Area (DSA) of the candidate's transplant program. The Committee would recommend the same for non-standardized exceptions. The Committee is also seeking feedback from the community on whether to eliminate automatic increases in MELD score for the candidates upon extension.

In December 2015, the Board approved a new project to revise the standard exception eligibility criteria for HCC candidates. Currently only candidates within Milan criteria automatically receive exception scores.[21] However, nearly all RRBs have developed agreements in which candidates meeting certain downstaging criteria may also receive exception scores. The Committee is considering expanding standard HCC exception eligibility criteria to include candidates meeting specific downstaging criteria. The Committee is also considering whether the following candidates should not be eligible for exceptions scores:

- Those with a single, small, well-treated tumor, until evidence of recurrence
- Those who have an A-fetoprotein (AFP) greater than 1,000, until AFP is below 500

The Committee anticipates submitting an HCC policy proposal for public comment in August 2016.

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[18] Policy 9.3.C: Specific MELD/PELD Exceptions, Organ Procurement and Transplantation Network Policies.
[19] Massie, A. B., B. Caffo, S. E. Gentry, et al. "MELD exceptions and rates of waiting list outcomes." American Journal of Transplantation, 11(2011), 2362-2371.
[20] Northup, P. G., N. M. Intagliata, N. L. Shah, et al. "Excess mortality on the liver transplant waiting list: Unintended policy consequences and model for End-Stage Liver Disease (MELD) inflation." Hepatology, 61(2015), 285-291.
[21] Policy 9.3.F: Candidates with Hepatocellular Carcinoma (HCC), Organ Procurement and Transplantation Network Policies.

How well does this proposal address the problem statement?

As discussed above, regional differences in MELD/PELD score exception submission and approval rates have been well documented in the literature. These have been confirmed by recent OPTN data provided to the Committee (**Exhibit B**). The Committee believes that a national structure for exceptional case review will lead to more equitable review outcomes. It will achieve this by:

- Creating specialty boards that allow for reviewers with appropriate policy and clinical expertise to evaluate the request.
- Giving every liver transplant program the opportunity to be represented on the NLRB.
- Requiring orientation for all reviewers at the beginning of each term of service, which will include training on exception policy, operational guidelines, and guidance for evaluating common types of exceptions.
- Instituting new voting procedures that assign requests randomly to reviewers and require a super majority vote.

This proposal also improves the efficiency of the exception process. The RRB Chairs review over 1,000 standardized exception requests each year (including initial requests and extensions), which they approve since the requests meet criteria in policy. Their review of these cases is an inappropriate use of the peer review system, since their medical judgment is not critical to evaluate these cases. Automatically awarding exception points to candidates meeting criteria in policy will reduce the workload for reviewers and eliminate unnecessary delays in awarding exception points. Based on OPTN data, the Committee estimates that automating the standardized exceptions will reduce the overall workload of the NLRB by nearly 2,000 requests each year.

Which populations are impacted by this proposal?

This proposal promotes equitable access to transplant for liver candidates whose calculated MELD or PELD score does not accurately reflect the severity of their disease. This includes pediatric candidates, who have a disproportionately high rate of transplant under exception.[22] This proposal also benefits approximately 500 candidates each year who meet the criteria for standardized MELD exceptions in policy by automatically approving their exception score upon submission of their requests.

In addition, these changes will improve access to transplant for adult candidates without exception points, who are transplanted at higher MELD scores than those with approved exceptions (see **Figure 1**).

This proposal also affects current RRB members and prospective NLRB members (see "How will members implement this proposal?").

How does this proposal support the OPTN Strategic Plan?

1. *Increase the number of transplants:* There is no impact to this goal.

2. *Improve equity in access to transplants:* The primary goal for this proposal is to improve equity in access to transplant by establishing a national structure for exceptional case review in which all liver transplant programs have an equal opportunity for representation. The NLRB seeks to mitigate regional differences in award practices by establishing new voting procedures and giving the Committee the ability to develop national guidance for assessing common requests.

3. *Improve waitlisted patient, living donor, and transplant recipient outcomes:* The NLRB promotes fair and equitable assignment of exception points to appropriate candidates, which contributes to

[22] From July 1, 2014-June 30, 2015, 32% of all deceased donor liver transplants in 0-11 year old recipients were performed under a PELD exception.

better waitlist outcomes for both exceptional candidates and those who will be transplanted on the basis of the calculated MELD/PELD score.

4. *Promote living donor and transplant recipient safety:* There is no impact to this goal.

5. *Promote the efficient management of the OPTN:* This proposal improves the efficiency of the review board system by reducing the workload for reviewers by approximately 2,000 requests each year and eliminating unnecessary delays in awarding exception points when appropriate.

How will the sponsoring Committee evaluate whether this proposal was successful post implementation?

To assess the efficacy of the NLRB, the UNOS Research Department will analyze a number of relevant outputs in a pre vs. post analysis. Such analyses will be performed at 6-month intervals up to 24 months post-implementation (or longer if requested by the Committee). Both national results and results by region of the program requesting the exception (where feasible) will be compared. Some analyses will also be performed by specialty board type (i.e., Adult HCC, Adult Other Diagnosis, and Pediatric). Note that many exception requests for diagnoses that currently require review by the RRB chair will be automated under the NLRB system. For this reason, some of the post-implementation results will not be directly comparable to those from the pre-implementation era.

Relevant analyses:

- Total number of exception cases automatically approved and those reviewed by the NLRB, overall and by diagnosis (note: exceptions with “Other Specify” diagnoses will be reclassified into diagnostic categories as feasible)
- Number and percent Approved/Denied/Appealed, overall and by diagnosis
- Number and percent of cases that required NLRB review that were returned to the auto-approval track
- Number of cases not closed within time required by policy
- Distribution of MELD/PELD scores approved/denied by the NRLB, by initial/extension/appeal and diagnosis
- Distribution of time to close cases
- Distribution of annual number of cases reviewed per NLRB member
- Waiting list drop-out rates (death or too sick) for candidates with initial exceptions versus those without exceptions and, if possible, the drop-out rates for candidates who were denied exception points

How will the OPTN implement this proposal?

This proposal will require programming in UNet^{SM}, estimated at an enterprise level. However, this programming will eliminate several manual processes for UNOS Review Board staff, which will result in long-term cost-savings. Review Board staff will still be responsible for facilitating conference calls for programs that choose to appeal a case to the NLRB after a second randomized review results in a denial.

The OPTN will work with the Committee to develop the orientation training all NLRB representatives and alternates must complete before beginning their term of service. This proposal also requires an instructional program for members to educate them on changes to policy and how it will affect their work, especially the submission of exception requests. The proposal will be monitored for specific educational needs throughout the public comment and approval process. Communication and education efforts will provide members with resources to prepare for implementation and compliance.

Specific communication and educational efforts associated with this proposal may include:

- Policy notice outlining policy changes
- System notice outlining UNet[SM] system changes and updates to Help Documentation
- UNet[SM] system training with system changes
- Articles on the OPTN and Transplant Pro websites
- Presentations at regional meetings

How will members implement this proposal?

Every active liver transplant program may appoint a representative and alternate to each of the adult specialty boards. A liver transplant program with an active pediatric component may appoint a representative and an alternate to the pediatric specialty board.[23] Transplant programs are encouraged to appoint representatives from both hepatology and surgery who have active transplant experience. Liver transplant programs are not required to provide a representative to the NLRB.

Representative and alternate responsibilities are detailed in the National Liver Review Board Operational Guidelines (**Exhibit A**). Prior to each term of service, representatives and alternates are required to sign the *UNOS Confidentiality and Conflict of Interest Statement* and complete orientation training. Representatives must vote within 7 days on all exception requests, extension requests, and appeals. The representative must notify UNOS in UNet[SM] of an absence, during which the alternate will fulfill the responsibilities of the representative.

If after 7 days the representative has not voted on an open request, then it will be randomly reassigned to another representative. If a representative or alternate does not vote on an open request within 7 days on three separate instances within a 12-month period, the Chair will remove the individual from the NLRB. A representative or alternate who has been removed for failure to perform the duties required is not eligible to serve again for 3 years.

A liver program may appeal a denied request to the NLRB. All reviewer comments are available in UNet[SM]. The NLRB advises programs to respond to the comments of dissenting reviewers in the appeal. The appeal is randomly assigned to five members of the appropriate specialty board. The appeal must achieve four out of five affirmative votes in order to be approved. If the appeal does not achieve the necessary four affirmative votes, it is denied. If the appeal is denied by the second review team, the liver program may request a conference call with the second review team. A representative at the petitioning program will serve as the candidate's advocate. If the outcome of the conference call is to uphold the denial, the program may initiate a final appeal to the Committee or register the candidate at the requested score. However, if the program chooses to register the candidate at the requested score and the Committee upholds the NLRB's decision to deny the request, the Committee may refer the program to the Membership and Professional Standards Committee (MPSC). The MPSC will determine whether the program's action was in violation of OPTN obligations and will result in punitive action.

Will this proposal require members to submit additional data?

The proposal does not require additional data collection. However, in order to automate approval of the standardized exceptions, liver programs will have to submit required information in discrete data fields in

[23] Appendix F.7: Liver Transplant Programs that Register Candidates Less than 18 Years Old, Organ Procurement and Transplantation Network Policies (pending implementation)

UNet[SM] instead of in narrative form as they do currently. The principles of data collection used to support this change are:

1. *Develop transplant, donation and allocation policies:* The Committee will periodically review the data to determine if revisions to the standardized exception criteria or to the MELD score calculation are needed.
2. *Determine if Institutional Members are complying with policy:* The OPTN requires that this data is submitted to demonstrate that the candidate meets criteria for automatic assignment of additional MELD or PELD points.

How will members be evaluated for compliance with this proposal?

The proposed language will not change the current routine monitoring of OPTN members. Any data submitted to the OPTN Contractor may be subject to OPTN review, and members are required to provide documentation as requested.

Policy or Bylaw Language

Proposed new language is underlined and (example) and language that is proposed for removal is struck through (~~example~~).

9.3 Status and MELD/PELD Score ~~and Status~~ Exceptions

The Liver and Intestinal Organ Transplantation Committee establishes guidelines for review of status and MELD/PELD score exception requests.

If a candidate's transplant program believes that a candidate's status does not appropriately reflect the candidate's medical urgency, the transplant physician may register a candidate at the exceptional status. However, the Liver and Intestinal Organ Transplantation Committee will retrospectively review candidates registered as status 1A or 1B. The Liver and Intestinal Organ Transplantation Committee may refer these cases to the Membership and Professional Standards Committee (MPSC) for review according to *Appendix L* of the OPTN Bylaws.

If a candidate's transplant program believes that a candidate's MELD or PELD score does not appropriately reflect the candidate's medical urgency, the transplant physician may ~~apply~~ submit a MELD/PELD score exception request to the ~~Regional Review Board (RRB)~~ National Liver Review Board (NLRB) ~~for a MELD or PELD score exception~~.

9.3.A MELD/PELD Score Exception ~~Applications~~ Requests

~~A~~n MELD/PELD score exception ~~application~~ request must include *all* of the following:

1. A request for a specific MELD or PELD score~~.~~
~~2. Justify why accepted medical criteria supports that the candidate has a higher MELD or PELD score and explain how the patient's current condition and potential for benefit would be comparable to that of other candidates with that MELD or PELD score.~~
2. A justification of how the medical criteria supports that the candidate has a higher MELD or PELD score
3. An explanation of how the candidate's current condition and potential for benefit would be comparable to that of other candidates with that MELD or PELD score

9.3.B ~~Review of Exceptions by the RRB and Committees~~ NLRB and Committee Review of Status Exceptions

~~Each RRB must review requests within 21 days of the date the application is submitted to the OPTN Contractor. If the RRB does not approve the application within 21 days, then the candidate's transplant physician may *either*:~~

- ~~Appeal the decision.~~
- ~~Register the candidate at the requested MELD or PELD score following a conference call with the RRB. However, these cases will be automatically referred to the Liver and Intestinal Organ Transplantation Committee. The Liver and Intestinal Organ Transplantation Committee may refer these cases to the MPSC for appropriate action according to *Appendix L* of the OPTN Bylaws.~~

~~The RRB will report its decisions and justifications to the Liver and Intestinal Organ Transplantation Committee and the MPSC. The Committees determine whether the MELD or PELD score exceptions are consistently evaluated and applied within OPTN regions and across the country. Additionally, the Committees evaluate whether existing MELD or PELD score criteria continue to be appropriate.~~

The NLRB must review initial or extension exception requests within 21 days of the date the request is submitted to the OPTN Contractor. If the NLRB fails to make a decision on the initial request within the 21 day review period, the candidate will be assigned the requested MELD or PELD exception score.

9.3.B.i: NLRB Appeals

If the NLRB denies a request, the candidate's transplant program may appeal to the NLRB within 14 days of receiving the denial. If the NLRB denies the appeal, the candidate's transplant program may request a conference with the NLRB. If the NLRB upholds its denial of the appeal, then the candidate's transplant program may appeal to the Liver and Intestinal Organ Transplantation Committee. The Committee will review the NLRB's decisions and rationale and approve or deny the request.

9.3.B.ii: NLRB Overrides

If a request is not approved by the NLRB, the candidate's transplant program may override the decision and register the candidate at the requested status or MELD/PELD score, subject to automatic review by the Liver and Intestinal Organ Transplantation Committee. The Committee will review the NLRB's decisions and rationale and may refer the case to the Membership and Professional Standards Committee (MPSC) for further review.

9.3.C Specific Standardized MELD/PELD Score Exceptions

Candidates meeting the criteria in *Table 9-2: Specific Standardized MELD/PELD Score Exceptions* are eligible for MELD or PELD score exceptions that do not require evaluation by the ~~full RRB~~ NLRB. ~~The transplant program must submit a for a specific MELD or PELD score exception with a written narrative that supports the requested score. Additionally, a candidate may receive a higher MELD or PELD score if the RRB has an existing agreement for the diagnosis. These agreements must be renewed on an annual basis.~~

Table 9-2: Specific Standardized MELD/PELD Score Exceptions

If the candidate has:	And submits to the OPTN Contractor evidence that includes:	Then the candidate:
Cholangiocarcinoma	The information required according to *Policy 9.3.E: Candidates with Cholangiocarcinoma.*	Will receive a MELD score of 22 or PELD score of 28; then will receive a MELD or PELD score equivalent to a 10 percentage point increase in the risk of three-month mortality every three months.
Cystic Fibrosis	The candidate's diagnosis has been confirmed by genetic analysis, and the candidate has ~~signs of reduced pulmonary function with~~ a forced expiratory volume at one second (FEV_1) ~~that falls~~ below 40 percent of predicted FEV_1 within 30 days prior to submission of the initial exception request.	Will receive a MELD score of 22 or PELD score of 28; then will receive a MELD or PELD score equivalent to a 10 percentage point increase in the risk of three-month mortality every three months.

If the candidate has:	And submits to the OPTN Contractor evidence that includes:	Then the candidate:
Familial Amyloid Polyneuropathy (FAP)	*All* of the following: ~~1. Clear diagnosis of FAP.~~ ~~2.~~ 1. Either that the candidate is also registered for a heart transplant or has an echocardiogram ~~Echocardiogram~~ showing the candidate has an ejection fraction greater than 40 percent within 30 days prior to submission of the initial exception request. ~~3.~~ 2. The candidate can walk without assistance ~~Ambulatory status~~. ~~4.~~ 3. Identification of transthyretin (TTR ~~gene~~) gene mutation ~~(Val30Met vs. non-Val30Met)~~. ~~5.~~ 4. Biopsy-proven amyloid.	Will receive a MELD score of 22 or PELD score of 28; then will receive a MELD or PELD score equivalent to a 10 percentage point increase in the risk of three-month mortality every three months if an echocardiogram shows that the candidate has an ejection fraction greater than 40 percent every six months. The echocardiogram must have been performed within 30 days prior to submission of the extension.
Hepatic Artery Thrombosis (HAT)	Candidate has HAT within 14 days of transplant but does not meet criteria for status 1A in Policy 9.1.A: Adult Status 1A Requirements.	Will receive a MELD score of 40.
Hepatocellular Carcinoma (HCC)	The information required according to *Policy 9.3.F: Candidates with Hepatocellular Carcinoma (HCC)*.	*See Policy 9.3.F: Candidates with Hepatocellular Carcinoma (HCC)*.
Hepatopulmonary Syndrome (HPS)	*All* of the following: 1. Ascites, varices, splenomegaly, or thrombocytopenia. 2. Evidence of a shunt by either contrast echocardiogram or lung scan. 3. PaO_2 less than 60 mmHg on room air within 30 days prior to submission of the initial exception request. 4. No ~~significant clinical~~ clinically significant evidence of underlying primary pulmonary disease.	Will receive a MELD score of 22 or PELD score of 28; then will receive a MELD or PELD score equivalent to a 10 percentage point increase in the risk of three-month mortality every three months ~~that~~ as long as the candidate~~'s~~ has a PaO_2 ~~remains~~ under 60 mmHg within 30 days prior to submission of the extension.
Metabolic Disease	The information required according to *Policy 9.3.D Pediatric Liver Candidates with Metabolic Disease.*	See *Policy 9.3.D Pediatric Liver Candidates with Metabolic Disease.*

If the candidate has:	And submits to the OPTN Contractor evidence that includes:	Then the candidate:
Portopulmonary Hypertension	~~The candidate has a mean pulmonary arterial pressure (MPAP) below 35 mmHg following intervention.~~ ~~The diagnosis must also include~~ ~~*a*~~*All* of the following: 1. Initial mean pulmonary arterial pressure (MPAP) level greater than or equal to 35 mmHg. 2. Initial pulmonary vascular resistance (PVR) level. 3. ~~Initial transpulmonary gradient to correct for volume overload.~~ 4. Documentation of treatment. 5. Post-treatment MPAP less than 35 mmHg within 90 days prior to submission of the initial exception. 6. Post treatment PVR less than 400 dynes/sec/cm^{-5}, or less than 5.1 Wood units (WU), on the same test date as post-treatment MPAP less than 35 mmHg.	Will receive a MELD score of 22 or PELD score of 28; then will receive a MELD or PELD score equivalent to a 10 percentage point increase in the risk of three-month mortality every three months if a repeat heart catheterization confirms that the mean pulmonary arterial pressure (MPAP) remains below 35 mmHg.
Primary Hyperoxaluria	*All* of the following: 1. Is registered for a combined liver-kidney transplant. 2. Alanine glyoxylate aminotransferase (AGT) deficiency proven by liver biopsy using sample analysis or genetic analysis. 3. ~~Glomerular filtration rate (GFR)~~ Estimated glomerular filtration rate (eGFR) ~~less than or equal to 25 mL/min,~~ by six variable Modification of Diet in Renal Disease formula (MDRD6) or glomerular filtration rate (GFR), ~~direct measurement of~~ measured by iothalamate or iohexol, less than or equal to 25 mL/min ~~for 42 or more days~~ on two occasions at least 42 days apart.	Will receive a MELD score of 28 or PELD score of 41; then will receive a MELD or PELD score equivalent to a 10 percentage point increase in the risk of three-month mortality every three months.

9.3.D Pediatric Liver Candidates with Metabolic Disease

A pediatric liver transplant candidate with a urea cycle disorder or organic acidemia will receive a MELD/PELD score of 30. If the candidate does not receive a transplant within 30 days of being registered with a MELD/PELD of 30, then the candidate's transplant physician may register the candidate as a status 1B.

If a candidate has a ~~different~~ metabolic disease other than urea cycle disorder or organic academia, and the candidate's transplant program believes that a candidate's MELD/PELD score does not appropriately reflect the candidate's medical urgency, then the transplant physician may request an exception according to ~~*Policy 9.3: Score and Status Exceptions*~~ *Policy 9.3.A: MELD/PELD Score Exception Requests*. ~~However, the RRB will review these applications based on standards jointly developed by the Liver and Intestinal Organ Transplantation Committee and the Pediatric Transplantation Committee.~~

9.3.E Candidates with Cholangiocarcinoma

A candidate will receive the MELD/PELD exception in *Table 9-2: Specific MELD/PELD Score Exceptions* for cholangiocarcinoma, if the candidate's transplant hospital meets *all* the following qualifications:

1. Submit a written protocol for patient care to the Liver and Intestinal Organ Transplantation Committee that must include *all* of the following:
   a. Candidate selection criteria
   b. Administration of neoadjuvant therapy before transplantation
   c. Operative staging to exclude any patient with regional hepatic lymph node metastases, intrahepatic metastases, or extrahepatic disease
   d. Any data requested by the Liver and Intestinal Organ Transplantation Committee

2. Document that the candidate meets the diagnostic criteria for hilar CCA with a malignant appearing stricture on cholangiography and *one* of the following:
   a. Biopsy or cytology results demonstrating malignancy
   b. Carbohydrate antigen 19-9 greater than 100 U/mL in absence of cholangitis
   c. Aneuploidy

   The tumor must be considered un-resectable because of technical considerations or underlying liver disease.

3. Cross-sectional imaging studies are required. If cross-sectional imaging studies demonstrate a mass, the mass must be single and less than three cm.
4. Intrahepatic and extrahepatic metastases must be excluded by cross-sectional imaging studies of the chest and abdomen ~~at the time of the initial application for the MELD/PELD exception~~ within 90 days prior to submission of the initial exception request and ~~every three months before the MELD/PELD score increases~~ within 30 days prior to submission of every exception extension request.
5. Regional hepatic lymph node involvement and peritoneal metastases must be assessed by operative staging after completion of neoadjuvant therapy and before liver transplantation. Endoscopic ultrasound-guided aspiration of regional hepatic lymph nodes may be advisable to exclude patients with obvious metastases before neo-adjuvant therapy is initiated.
6. Transperitoneal aspiration or biopsy of the primary tumor (either by endoscopic ultrasound, operative or percutaneous approaches) must be avoided because of the high risk of tumor seeding associated with these procedures.

9.3.F.vi Extensions of HCC Exceptions

In order for a candidate to maintain an HCC approved exception, the transplant program must submit a~~n updated~~ MELD/PELD exception ~~application~~ extension request every three months. The candidate will receive the additional priority until transplanted or is found unsuitable for transplantation based on the HCC progression. Upon submission of the first extension, the candidate will be listed at the calculated MELD/PELD score. Upon submission of the second extension, the candidate will be assigned a MELD/PELD score equivalent to a 35 percent risk of 3-month mortality (MELD 28/PELD 41). For each subsequent extension, the candidate

will receive additional MELD or PELD points equivalent to a 10 percentage point increase in the candidate's mortality risk every three months.

The HCC exception score will be capped at 34. Upon implementation, candidates with HCC exception scores greater than 34 will receive a score of 34 for their remaining HCC exception extensions. Candidates with scores greater than 34 at the time of implementation may be referred to the ~~RRB~~ NLRB if they demonstrate the need for higher priority.

To receive the extension, the transplant program must submit a~~n updated~~ MELD exception extension request that contains all of the following:

1. ~~Submit an~~ A Hepatocellular Carcinoma (HCC) MELD/PELD score exception ~~application~~ request with an updated narrative
2. ~~Document~~ Documentation of the tumor using a CT or MRI
3. ~~Specify the~~ The type of treatment if the number of tumors decreased since the last ~~application~~ request.

Invasive studies such as biopsies or ablative procedures and repeated chest CT scans are not required after the initial ~~application~~ exception request is approved. If a candidate's tumors have been resected since the previous ~~application~~ request, then the transplant program must submit the extension ~~application~~ request to ~~its RRB~~ the NLRB for prospective review.

Candidates with Class 5T lesions will receive a MELD or PELD equivalent to a 10 percentage point increase in the candidate's mortality risk every three months, without ~~RRB~~ NLRB review, even if the estimated size of residual viable tumors falls below stage T2 criteria due to ablative therapy.

9.3.F.vii Candidates Not Meeting Criteria (Class 5X)

A candidate not meeting the above criteria may continue to be considered a liver transplant candidate according to each transplant hospital's own specific policy, but the candidate must be registered at the calculated MELD or PELD score with no additional priority given because of the HCC diagnosis. All such candidates with HCC, including those with downsized tumors whose original or presenting tumor was greater than a stage T2, must be referred to the applicable ~~RRB~~ NLRB for prospective review in order to receive additional priority.

~~9.3.F.viii Appeal for Candidates not Meeting Criteria~~

~~If the RRB denies the initial HCC exception application, the transplant program may appeal with the RRB but the candidate will not receive the additional MELD or PELD priority until approved by the RRB. The RRB will may refer the matter to the Liver and Intestinal Organ Transplantation Committee for further review and possible action if the RRB finds the transplant program to be noncompliant with these Policies.~~

~~Applications and appeals not resolved by the RRB within 21 days will be referred to the Liver and Intestinal Organ Transplantation Committee for review. The Liver and Intestinal Organ Transplantation Committee may refer these matters to the MPSC for appropriate action according to *Appendix L* of the OPTN Bylaws.~~

[*Subsequent headings affected by the re-numbering of this policy will also be changed as necessary.*]

9.3.G MELD/PELD Score Exception Extensions

Transplant hospitals may ~~apply for~~ submit a ~~MELD or PELD~~ MELD/PELD score exception extension request to the NLRB ~~to receive the equivalent of a 10 percentage point increase in candidate mortality~~ every three months ~~as long as the candidate continues to meet the exception criteria. Extensions must be prospectively reviewed by the RRB.~~

A candidate's approved exception score will be maintained if the transplant hospital enters the extension ~~application~~ request ~~more than~~ between three and 30 days before the due date according to *Table 9-1: Liver Status and Score Update Schedule,* even if the ~~RRB~~ NLRB does not act before the due date. If the extension ~~application~~ request is later denied then the candidate will be assigned the calculated MELD or PELD score based on the most recent reported laboratory values.

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National Liver Review Board Operational Guidelines

1. Overview

The purpose of the National Liver Review Board (NLRB) is to provide fair, equitable, and prompt peer review of exceptional candidates whose medical urgency is not accurately reflected by the calculated MELD/PELD score.

The NLRB is comprised of specialty boards, including:

- Adult Hepatocellular Carcinoma (HCC)
- Adult Other Diagnosis
- Pediatrics, which reviews requests made on behalf of any candidate registered prior to turning 18 years old and adults with certain pediatric diagnoses

The immediate past-Chair of the Liver and Intestinal Organ Transplantation Committee serves as the Chair of the NLRB for a two year term.

2. Representation

Every active liver transplant program may appoint a representative and alternate to each of the adult specialty boards. A liver transplant program with an active pediatric component may appoint a representative and alternate to the pediatric specialty board. Individuals may serve on more than one specialty board at the same time. Transplant programs are encouraged to appoint representatives from both hepatology and surgery who have active transplant experience. Liver transplant programs are not required to provide a representative to the NLRB.

Representatives and alternates serve a one year term. A liver transplant program may appoint the same representative or alternate to serve consecutive terms.

If a transplant hospital withdraws or inactivates its liver program, it may not participate in the NLRB. However, the transplant hosptial's participation may resume once it has reactivated its liver program.

3. Representative and Alternate Responsibilities

Prior to each term of service, representatives and alternates are required to sign the *UNOS Confidentiality and Conflict of Interest Statement* and complete orientation training.

Representatives must vote within 7 days on all exception requests, exception extension requests, and appeals. A representative will receive an e-mail reminder after day 3 if the representative has an outstanding vote that must be completed. On the eighth day, if the vote has not been completed, then the request will be randomly reassigned to another representative. The original reviewer will receive a notification that the request has been reassigned.

The representative must notify UNOS in UNet^{SM} of an absence, during which the alternate will fulfill the responsibilities of the representative.

If a representative or alternate does not vote on an open request within 7 days on three separate instances within a 12 month period, the Chair will remove the individual from the NLRB. If a representative or alternate does not vote because a case is approved and closed before the 7

day timeframe expires, it is not considered a failure to vote. A representative or alternate who has been removed for failure to perform the duties required is not eligible to serve again for 3 years.

If a transplant program exhibits a pattern of non-responsiveness, as evidenced by the removal of two members from the NLRB, the Chair may suspend the program's participation for a period of three months after notifying the program director. Further non-compliance with the review board process may result in cessation of the program's representation on the NLRB until such a time as the transplant hospital can satisfactorily assure the Chair that it has addressed the causes of non-compliance.

4. Voting Procedure

An exception request is randomly assigned to five representatives of the appropriate specialty board. A representative may vote to approve or deny the request, or ask that the request be reassigned. The request must achieve four out of five affirmative votes in order to be approved. If the request does not achieve the necessary four affirmative votes, it is denied.

As part of the MELD/PELD Exception program in UNet^{SM}, NLRB members are notified of new cases by email. To access the exception request, click on the emailed link or go to https://www.unet.unos.org/. Log-in using your UNet^{SM} username and password and click on "Waitlist," then "NLRB."

Voting on an exception request is closed when no additional votes will change the outcome of the vote. Members no longer have the ability to vote once a request is closed.

5. Appeal Process

A liver program may appeal the NLRB's decision to deny an exception request. Patients are not eligible to appeal exception requests. All reviewer comments are available in UNet^{SM}. The NLRB advises programs to respond to the comments of dissenting reviewers in the appeal.

The appeal is then randomly assigned to five members of the appropriate specialty board. The appeal must achieve four out of five affirmative votes in order to be approved. If the appeal does not achieve the necessary four affirmative votes, it is denied.

If the appeal is denied by the second review team, the liver program may request a conference call with the second review team. A representative at the petitioning program will serve as the candidate's advocate. The review team will work with UNOS staff to document the content of the discussion and final decision in UNet^{SM}.

The liver program may initiate a final appeal to the Liver and Intestinal Organ Transplantation Committee if the final outcome of the appeal is negative. Referral of cases to the Liver and Intestinal Organ Transplantation Committee will include information about the number of previous referrals from that program and the outcome of those referrals.

RRB Decisions (All Cases)

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