

Briefing to the OPTN Board of Directors on

Guidance Addressing the Use of Pediatric Heart Exceptions

OPTN Heart Transplantation Committee

*Prepared by: Sarah Konigsburg and Eric Messick
UNOS Policy and Community Relations Department*

Contents

Executive Summary	2
Background	3
Purpose	4
Sentiment from Public Comment	5
Guidance for Board Consideration	7
NOTA and Final Rule Analysis	11
Alignment with OPTN Strategic Plan	11
Implementation Considerations	12
Post-implementation Monitoring	12
Conclusion	13
Guidance for Pediatric Heart Exception Requests	14

Guidance Addressing the Use of Pediatric Heart Exceptions

Sponsoring Committee: Heart Transplantation
Public Comment Period: August 4, 2020 – October 1, 2020
Board of Directors Date: December 7, 2020

Executive Summary

In June 2020, the Organ Procurement and Transplantation Network (OPTN) Board of Directors (Board) approved the creation of a National Heart Review Board (NHRB) for pediatric candidates.¹ The NHRB for pediatric candidates was established to ensure pediatric heart exceptions are reviewed by pediatric heart experts and to reduce regional variance in determinations. To assist future NHRB members in making consistent decisions during their review of exception requests and to improve the information submitted by transplant programs drafting exception requests, the Pediatric Heart Workgroup (Workgroup) developed this proposed guidance document.

The Workgroup determined a guidance document was more appropriate than policy changes since exceptions arise because the candidate's condition cannot be easily aligned with the criteria established in policy. A guidance document allows reviewers to consider the specific clinical circumstances of each candidate on a case by case basis to determine whether the exception criteria set forth by OPTN Policy are met. Similar guidance documents that further define clinical criteria to assist with the review of exception requests are implemented for other organ review boards such as the National Liver Review Board.

In alignment with the strategic plan to improve equity in access to transplants, this guidance promotes that pediatric candidates are listed at a status most appropriate to their medical urgency. In addition, the guidance increases consistency in how exception requests are reviewed as well as the information included in the request to reduce inter-transplant program variance as authorized by the National Organ Transplantation Act of 1984 (NOTA) and the Final Rule.²

Receiving strong support through the regional meetings and public comments submitted through the OPTN website, the Workgroup chose to only make minor changes to the guidance. These edits came as recommendations from the transplant community and are intended to strengthen the guidance by providing more clarity.

¹This policy notice is available at https://optn.transplant.hrsa.gov/media/3841/2020_06_thoracic_nhrb_for_pediatrics_policy_notice.pdf

² 42 C.F.R. §121.8(b)(4)

Background

The National Organ Transplantation Act of 1984 (NOTA), as amended, provides special status to pediatric transplant candidates. Under NOTA, the OPTN is required to “adopt criteria, policies, and procedures that address the unique health care needs of children” under the age of 18.³ As part of its ongoing commitment to this population, the Board approved changes to pediatric heart allocation policy that were implemented in 2016. The Board’s primary goal was improving waiting list mortality rates for pediatric candidates. The Board sought to achieve this, in part, by redefining the criteria associated with pediatric heart Statuses 1A and 1B to ensure that candidates of comparable levels of medical urgency are in the same statuses.

However, initial findings suggested little change in waiting list mortality rates. In October 2017, members of both the Thoracic and Pediatric committees reviewed a monitoring report analyzing the first 12 months after implementation of the new policy.⁴ According to a subsequent report, analysis of the first 12 months of data following implementation found that pediatric death rates on the heart waiting list did not change after policy implementation.⁵ At the time, Committee members noted a marked increase in the use of exceptions at transplant for candidates in Status 1A, particularly among those diagnosed with cardiomyopathy.⁶ Following the policy modifications, candidates diagnosed with cardiomyopathy were less likely to be placed in Status 1A at transplant based on qualifying criteria and more likely to be placed in Status 1A through exception. Evaluation of the monitoring data also revealed that the candidates being listed at Status 1A by exception following implementation saw an increase in their access to transplantation as evidenced by increase transplant rates, which was not found among other diagnoses.⁷

³ 42 USC §274(b)(2)(M), (O).

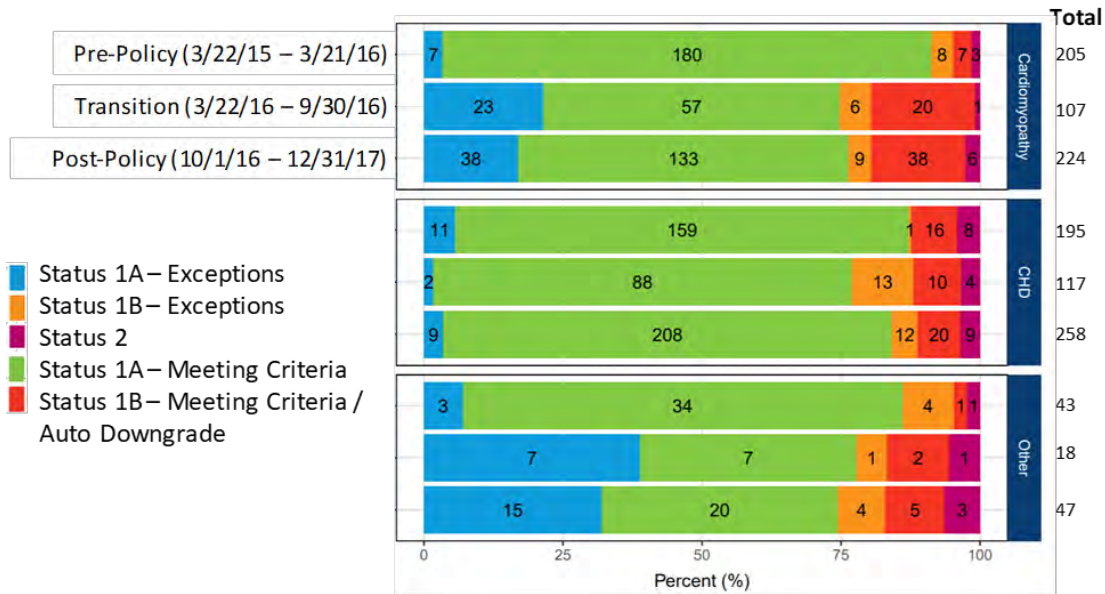
⁴ OPTN, Final Report: Changes to Pediatric Heart Allocation Policy Evaluation, October 12, 2017.

⁵ OPTN, Final Report: Changes to Pediatric Heart Allocation Policy Evaluation, April 9, 2018.

⁶ *ibid.*

⁷ *ibid.*

Figure 1: Pediatric Heart Transplants by Exception Status, Era and Diagnosis⁸



Source: OPTN, Final Report, *Changes to Pediatric Heart Allocation Policy Evaluation*, Figure 14, pg. 18

The Workgroup members considered these findings and other information during their 2019 and 2020 work on the NHRB for pediatric candidates. Based on the information, the Workgroup also identified the need to clarify the use of exception requests for pediatric heart Status 1A candidates. They also decided that a guidance document, similar to guidance created for the National Liver Review Board, was a more appropriate tool than a policy change because exceptions fall outside of established policy by their nature, and involve the discretion of those submitting and reviewing them. A guidance document also allows them to clarify the intent of existing policy, without rising to the level of policy requirement.

Purpose

The purpose of this proposal is to create a guidance document for the NHRB for pediatric candidates to make access more equitable to candidates with comparable medical urgency. The guidance document is intended to assist the members of the NHRB for pediatric candidates standardize decision-making when reviewing exception requests for certain Status 1A and Status 1B candidates. This guidance document does not create or change OPTN policy.

The document provides guidance on the following pediatric heart diagnoses:

- Dilated cardiomyopathy
- Hypertrophic or restrictive cardiomyopathy
- Single ventricle heart disease
- Coronary allograft vasculopathy and retransplantation

The Committee submits the following proposal for Board consideration under the authority of the OPTN Final Rule, to support “reducing inter-transplant program variance.”⁹

⁸ OPTN, *Briefing Paper, National Heart Review Board for Pediatrics*, June 2020, p. 4. Accessed 07/08/2020. https://optn.transplant.hrsa.gov/media/3808/202006_thoracic_natl_heart_reviewboard_for_peds_bp.pdf

⁹ 42 C.F.R. §121.8(b)(4)

Sentiment from Public Comment

This proposal was available for public comment from August 4, 2020 through October 1, 2020. During that time, 29 comments were submitted to the OPTN website. The entries included summaries of the 11 regional meetings as well as the OPTN Pediatric Transplantation Committee and the OPTN Transplant Coordinators Committee where the proposal was discussed. The remaining 16 entries were submitted by individuals, and on behalf of transplant programs, professional organizations, and a patient advocacy organization. When combined with the sentiment scoring conducted at the regional meetings, the proposal received nearly 300 responses.

The proposal received support in all 11 regional meetings, and from members of both OPTN Committees that reviewed the proposal. Of the 297 sentiment scores submitted, 208 or 70 percent, indicated support for the proposal, with 21 percent strongly supportive. Twenty-nine percent of scores submitted were neutral or abstentions, and only 3 scores, or approximately one percent, were submitted in opposition.

As shown in **Figure 2**, a total of 258 sentiment scores were submitted as part of the 11 regional meetings. All meetings were changed to virtual meetings due to the COVID-19 pandemic.

Figure 2: Sentiment Support for the Proposal, by Region¹⁰

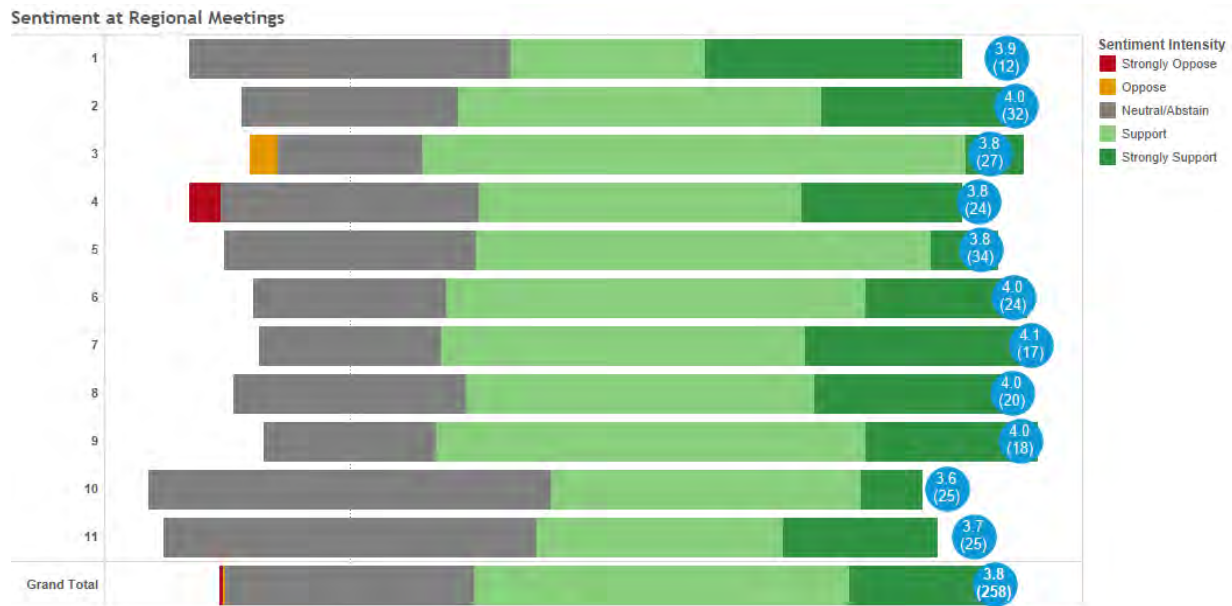
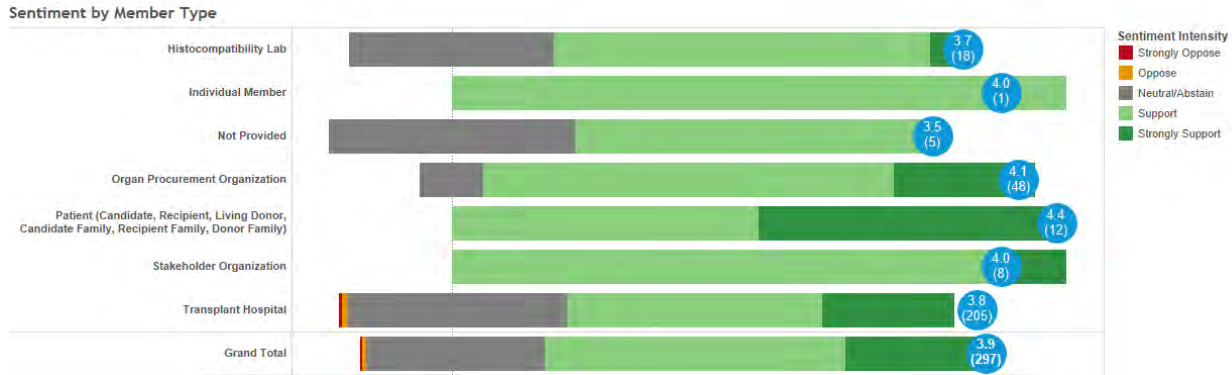


Figure 3 identifies sentiment support by OPTN member type. Sentiment scores submitted on behalf of transplant hospitals comprised approximately 70 percent of the total. Of the 205 sentiment scores submitted by transplant hospital members, about 21.5 percent were strongly supportive of the proposal, another 41.5 percent were supportive, 35.6 percent were neutral or abstentions, two

¹⁰ This chart shows the sentiment for the public comment proposal. Sentiment is reported by the participant using a 5-point Likert scale (1-5 representing Strongly Oppose to Strongly Support). Sentiment for regional meetings only includes attendees at that regional meeting. Region 6 uses the average score for each institution. The circles after each bar indicate the average sentiment score and the number of participants is in the parentheses

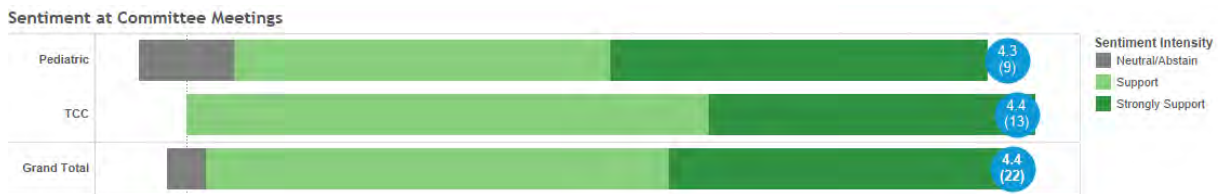
sentiment scores were submitted in opposition, and one sentiment score was submitted in strong opposition. OPOs accounted for the second largest number of sentiment scores submitted by member type, and sentiment scores submitted on behalf of those organizations were around 90 percent in support of the proposal with the remaining scores submitted as neutral or abstentions.

Figure 3: Sentiment Support for the Proposal, by Member Type



The Heart Transplantation Committee requested the feedback of the OPTN Pediatric Transplantation Committee and the OPTN Transplant Coordinator Committee. As shown in **Figure 4**, the proposal was supported by both Committees with 89 percent support and 100 percent support scores submitted respectively.

Figure 4: Sentiment Support for the Proposal, by Committee



The proposal received support from the American Society of Transplantation (AST), Association of Organ Procurement Organizations (AOPO), Society of Pediatric Liver Transplantation, The Organization for Donation and Transplant Professionals (NATCO), Transplant Families, and the strong support of American Society of Transplant Surgeons (ASTS).

Many comments were received in support of creating a guidance document, rather than policy, to promote an efficient and consistent exception request evaluation process by reviewers with pediatric expertise. AOPO commented in support of the appropriate utilization of exceptions to maximize the gift of donation. The community made several comments that this guidance is a great start and can remain flexible to address additional cases in the future when deemed appropriate. Several commenters praised the Workgroup’s effort in standardizing the eligibility criteria as well as the information programs should include in their exception requests while one commenter stated that information included in the clinical narrative submitted should be at the program’s discretion.

Transplant Families and several commenters raised concern about addressing the root cause of exception requests. Other recommendations included conducting retrospective analysis of approved and denied exception requests at predetermined intervals. As proposed in the *Post-Implementation Monitoring* section, the NHRB for pediatric candidates will be formally evaluated approximately six

months, one year, and two years post-implementation. Key variables regarding transplant rates, listing rates, outcomes, and waiting list mortality by status as well as status by exception will be assessed as part of the monitoring plan. In addition, exception request approvals and denials will be reviewed. Significant findings will be used to enhance NHRB operational processes including modification to this guidance document. Any changes identified that would strengthen the guidance, including the addition of other diagnoses, may be included on an updated version that is reviewed during a future public comment period.

Guidance for Board Consideration

The Committee is proposing a guidance document to assist the members of the NHRB for pediatric candidates by providing further clarification of eligibility criteria for exception requests submitted on the behalf of patients with the diagnoses of dilated cardiomyopathy (DCM), hypertrophic or restrictive cardiomyopathy (HCM/RCM), coronary allograft vasculopathy (CAV) and retransplantation, and single ventricle congenital heart disease. Guidance is also provided to the transplant program submitting exception requests. Both components of the guidance are intended to increase consistency, equity, and efficiency of the exception request review process.

Dilated Cardiomyopathy (DCM)

DCM candidates have generally had lower waiting list mortality after the 2016 changes, regardless whether they had a Status 1A exception or not.¹¹ DCM candidates had a higher frequency of using exceptions than hypertrophic or restrictive cardiomyopathy (HCM/RCM) candidates.¹² Accordingly, the intent by including this population in the guidance is to limit the use of exceptions among DCM candidates to those who are at particularly high risk based on clinical conditions in order to maximize the number of all candidates who get a transplant within an appropriate amount of time.¹³ This includes candidates under five kilograms (kg) in weight who carry a higher risk for use of mechanical support, as well as candidates that weigh between five and ten kg and likely carry a similar risk.¹⁴

Candidates under five kilograms and under ten kilograms

The proposed guidance states that candidates under five kg should be considered for a Status 1A exception if they are on at least one high-dose inotrope or a continuous infusion of at least two intravenous inotropes. Candidates under ten kg may be eligible for a Status 1A exception if they are supported by inotropes and demonstrate some evidence of poor systemic perfusion that distinguish a candidate's relative health. Evidence includes feeding intolerance requiring total parenteral nutrition or the need for noninvasive respiratory support like high flow nasal cannula, continuous positive airway pressure (CPAP) device, or a bilevel positive airway pressure (BiPAP) device.

¹¹ Magnetta, DA, Godown, J, West, S, et al. Impact of the 2016 revision of US Pediatric Heart Allocation Policy on waitlist characteristics and outcomes. *Am J Transplant*. 2019;19: 3276–3283. p. 3281. <https://doi.org.proxy.library.vcu.edu/10.1111/ajt.15567>

¹² Robinson, Mahle, Davies, "Increasing Use of Exceptions After Changes to Pediatric Heart Allocation," presentation to the American Transplant Conference, June 4, 2018, slide 26.

¹³ OPTN, Thoracic Organ Transplantation Committee, meeting summary, January 28, 2020.

¹⁴ Conway J, St Louis J, Morales DL, Law S, Tjossem C, Humpl T. Delineating survival outcomes in children <10 kg bridged to transplant or recovery with the Berlin Heart EXCOR Ventricular Assist Device. *JACC Heart Fail*. 2015;3(1):70-77. doi:10.1016/j.jchf.2014.07.011

Patients who are eligible for 1A status under standard criteria with a ventricular assist device (VAD) may be more stable than similarly medically urgent candidates without a VAD. The exception pathway provided in the guidance for this population allows programs to use their discretion in choosing to manage their patients medically, rather than mechanically, to avoid potential complications and risks associated with VAD placement in smaller patients when deemed appropriate.

Candidates ten kilograms and more

For this population, the primary reason to provide a 1A exception is the presence of contraindications to mechanical circulatory support. The proposed guidance document lists criteria that would demonstrate to a review board that a candidate has either contraindications to a VAD or indications that inserting a VAD would be very high-risk.

In cases where a candidate is listed at a transplant program where staff may be uncomfortable inserting VADs, the guidance does not prohibit a transplant program from requesting an exception for a candidate receiving inotropes with evidence of poor systemic perfusion, and that such requests could be reviewed on a case-by-case basis. Transplant programs may provide hemodynamic criteria justifying the use of a second inotrope to ensure the second inotrope was not used solely to make a candidate eligible for an exception. Additionally, the transplant program is also requested to submit information describing the escalation from lower inotrope dosage or a candidate's failure to wean.

High dose inotropes for candidates with cardiomyopathy

The guidance provides criteria for inotrope administration to assist in determining eligibility for status exceptions for candidates diagnosed with dilated, hypertrophic, or restrictive cardiomyopathy. This inotrope criteria is consistent with the standard status eligibility criteria as defined in OPTN *Policy 6.1.C.ii Multiple Inotropes or a Single High Dose Inotrope and Hemodynamic Monitoring* for adult candidates.

Several comments were received by individuals as well as AST and NATCO expressing concern that a continuous infusion of milrinone greater than or equal to 0.50 mcg/kg/min should not be considered a single high dose and thereby is not indicative of increased medical urgency, but rather a standard dose used for therapeutic purposes. Comments were also received that supported the dosage criteria as written, as it does indicate that the patient is inotrope dependent. This feedback was considered by the Workgroup and, as a result, they chose to adjust the guidance language that helps clarify the eligibility criteria by suggesting the candidate is eligible for the increased status if they are exhibiting either an escalation from lower dosage or a failure to wean from listed doses. The dosing information remains consistent with existing policy. Information describing inotrope escalation and/or failure to wean adds value to the clinical narrative and a request for these details is included in the guidance's *Standard Information for Inclusion with Pediatric Heart Exception Requests* section.

Hypertrophic/Restrictive (HCM/RCM) Cardiomyopathy

Among cardiomyopathy candidates, there were no significant differences in the cumulative incidences of waitlist mortality for DCM, RCM, and HCM candidates between pre and post policy implementation eras.¹⁵ However, "RCM and HCM candidates not utilizing a status 1A exception had increased cumulative

¹⁵ Magnosta, DA, Godown, J, West, S, et al. Impact of the 2016 revision of US Pediatric Heart Allocation Policy on waitlist characteristics and outcomes. *Am J Transplant*. 2019; 19:3276–3283. <https://doi-org.proxy.library.vcu.edu/10.1111/ajt.15567>.

incidence of death on the waitlist following criteria revision, whereas DCM candidates without status 1A exception fared no worse after criteria revision” included in the 2016 changes in allocation policy.¹⁶ The proposed guidance for this population aims to decrease the high degree of variability in approval for cardiomyopathy under Status 1A exceptions by recommending an exception for HCM/RCM candidates and by better defining the population of DCM patients that qualify for 1A exception.¹⁷

This category combines guidance for HCM and RCM candidates and identifies the following criteria as supporting the need for approving a Status 1A exception request: candidate is on inotropes, at risk for premature death, particularly unexpected sudden death, experiencing syncopal episodes, or showing evidence of increased pulmonary vascular resistance. The existing guidance document for adult HCM/RCM cardiomyopathy exception requests was used as a starting template and amended to address the specifics of pediatric heart candidates.¹⁸

Guidance addressing this candidate population should help pediatric heart transplant programs as well as the NHRB for pediatric candidates members in two ways. First, by clarifying that such candidates likely qualify for an exception to the clinical requirements established in policy. Second, HCM/RCM candidates would benefit by better defining and limiting the population of DCM patients who qualify for a Status 1A exception.

Formerly, requiring one or more inotropes could qualify a candidate for Status 1A. However, the 2016 changes eliminated inotrope usage as qualifying criteria for this population, reducing this access point to a higher status.¹⁹ The guidance provides a status exception pathway for HCM/RCM patients by suggesting multiple criteria in addition to inotrope use to avoid encouraging clinicians to give inotropes to patients unnecessarily.

Pediatric RCM candidates with syncopal events, refractory ventricular arrhythmias/implantable cardioverter defibrillator firing, elevated pulmonary vascular resistance, and/or inotrope treatment should be considered for listing at Status 1A. For HCM candidates, increasing frequency of arrhythmia is an indication that a candidate should be elevated to Status 1A. To further assist in the determination of these exception requests, a timeline of changes in symptoms are requested in the guidance’s *Standard Information for Inclusion with Pediatric Heart Exception Requests* section.

Single Ventricle Heart Disease

Single ventricle heart disease is included in the guidance although it is a relatively small population of candidates. As a result, waiting list mortality information for this category of candidates is limited. The decision to include this population in the guidance was based in part on questions from the pediatric community regarding a perceived incongruity in current policy for single ventricle candidates. A Fontan candidate who is listed at 17 years old, without being on inotropes in the hospital, is assigned to pediatric Status 2, but if the candidate is 18 years old at the time of listing, the candidate is assigned to adult Status 4, which is broadly equivalent to pediatric Status 1B.

¹⁶ *ibid.*

¹⁷ OPTN Thoracic Organ Transplantation Committee, meeting summary, September 24, 2019.

¹⁸ OPTN, *Review Board Guidance for Hypertrophic/Restrictive (HCM/RCM) Cardiomyopathy Exception Requests*, October 2018, https://optn.transplant.hrsa.gov/media/2637/thoracic_guidance_review_board_hcm_rcm_201806.pdf (accessed June 5, 2020).

¹⁹ OPTN, Thoracic Organ Transplantation Committee, meeting summary, February 25, 2020.

Most Fontan candidates, who would typically qualify for Status 2, either get approved for pediatric Status 1B by exception, or the candidates receive an exception for pediatric Status 1A after being admitted to the hospital and administered inotropes. In light of this, the guidance is written broadly so that if a candidate is admitted and experiencing complications, like protein-losing enteropathy (PLE) or plastic bronchitis, then pediatric Status 1A is appropriate. If they are experiencing complications but are not admitted, a Status 1B exception is appropriate.

The guidance document for adult congenital heart disease states that single ventricle candidates admitted to the hospital with complications like PLE can be upgraded to Status 3 by exception.²⁰ Status 3 shares many of the same clinical criteria as pediatric Status 1A including the qualifying condition of being supported by multiple intravenous inotropes or a high dose of a single intravenous inotrope. Based on the comparison of the two statuses, pediatric Status 1A is the appropriate classification for admitted Fontan candidates experiencing complications. Many of these patients would already be in the hospital and qualify for a higher status by meeting other criteria.

While the population of Fontan candidates admitted to the hospital but not on inotropes is small, they are addressed in the proposed guidance based on several considerations. There are particular challenges associated with transplanting sick Fontan patients including a window of frailty in which they quickly become unsuitable candidates from a surgical standpoint.²¹ If such candidates are not assigned a higher status before being admitted to the hospital with inotropes, then their post-transplant survival may be low. In addition, acceptable donors for these candidates are more difficult to find due to the complexity of their anatomy from previous surgeries and reconstruction, and many of these candidates are sensitized from their exposure to blood products.²²

The proposed guidance that all Fontan patients would be eligible for Status 1B exception received mixed support. The Workgroup determined that if the candidate is not admitted but is a Fontan with complications, then pediatric Status 1B by exception is appropriate due to the considerations of difficulty in finding a donor and the increased likelihood of sensitization discussed prior. The guidance supports exception pathways to promote that these more medically urgent candidates receive a transplant sooner rather than waiting for them to decline to the point that they need to be hospitalized and /or put on inotropes.

Coronary Allograft Vasculopathy (CAV) and Retransplant

CAV and retransplant patients do not have any particular prioritization under the current allocation system.²³ These candidates are generally assigned to Status 2. However, transplant programs ask for exceptions when they believe it is merited. Although this population is small and their conditions vary,

²⁰ OPTN, *Review Board Guidance for Adult Congenital Heart Disease (CHD) Exception Requests*, December 2017, https://optn.transplant.hrsa.gov/media/2349/thoracic_guidance_201712.pdf (accessed July 7, 2020).

²¹ Griffiths, Eric R, Kaza, Aditya K, Wyler Von Ballmoos, Moritz C, Loyola, Hugo, Valente, Anne Marie, Blume, Elizabeth D, and Nido, Pedro Del. "Evaluating Failing Fontans for Heart Transplantation: Predictors of Mortality." *The Annals of Thoracic Surgery* 88, no. 2 (2009): 558-64.

²² Kanter, Kirk R., MD, Mahle, William T., MD, Vincent, Robert N., MD, Berg, Alexandria M., MSN, Kogon, Brian E., MD, and Kirshbom, Paul M., MD. "Heart Transplantation in Children With a Fontan Procedure." *Annals of Thoracic Surgery* 91, no. 3 (2011): 823-30.

²³ OPTN, Thoracic Organ Transplantation Committee, meeting summary, February 25, 2020.

CAV and retransplant candidates are included in the guidance document because such candidates are a high-risk population who tend to have higher waiting list mortality.

Of individuals listed for retransplant more than a year after pediatric primary heart transplant between October 1, 1987 and October 14, 2012, 63% (395 of 632) were due to CAV.²⁴ Waiting list mortality for these retransplant candidates was 25.2%, 6.6% higher than candidates receiving their first heart transplant with the average wait time for retransplant being 3 months.²⁵

As with all 1A status assignments by exception, hospitalization is required by policy.²⁶ Hospitalized CAV retransplant patients who are most medically urgent are those who have suffered an arrest event, warranting the approval for listing at Status 1A by exception. Candidates who are experiencing other symptoms suggesting that they are close to cardiac arrest are also included for Status 1A consideration in the guidance. Such symptoms might include non-sustained ventricular arrhythmias or unexplained syncope. Candidates with a history of revascularization for CAV may be eligible for consideration at Status 1B by exception as these candidates are also at higher risk for sudden death.

NOTA and Final Rule Analysis

The OPTN issues this guidance for the operation of the OPTN.²⁷ This guidance will support the operation of the NHRB by assisting the reviewers with evaluating exception requests. The OPTN Final Rule requires the Board to establish performance goals for allocation policies, including “reducing inter-transplant program variance.”²⁸ This guidance document will assist in reducing inter-transplant program variance in the performance indicators initially adopted by the Board when it established the NHRB. These performance indicators include: changes in the number and percent of pediatric candidates and transplant recipients by status, exception, age group, OPTN region, and diagnosis; changes in waiting list mortality rate for pediatric candidates by status and exception; changes in transplant rate for pediatric candidates by status and exception; the percent of approvals and denials for exception requests by status; and changes in post-transplant patient survival rates overall and stratified by status.²⁹

Alignment with OPTN Strategic Plan³⁰

Improve equity in access to transplants:

The proposal intends to improve equity in access to transplant by promoting that pediatric candidates are listed at a status most appropriate for their medical urgency. The proposed guidance also increases the consistency in how specific candidates are reviewed by the NHRB by providing suggested criteria for

²⁴ Bock, Matthew J., Khanh Nguyen, Stefano Malerba, Kimberly Harrison, Emilia Bagiella, Bruce D. Gelb, Sean P. Pinney, and Irene D. Lytrivi. "Pediatric cardiac retransplantation: Waitlist mortality stratified by age and era." *The Journal of Heart and Lung Transplantation* 34, no. 4 (2015): 530-537.

²⁵ *ibid.*

²⁶ OPTN, 6.2.A Pediatric Heart Status 1A Requirements. Accessed October 27, 2020.

https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf

²⁷ 2019 OPTN Contract Task 3.2.4: Development, revision, maintenance, of OPTN Bylaws, policies, standards and guidelines for the operation of the OPTN.

²⁸ 42 C.F.R. §121.8(b)(4)

²⁹ OPTN Briefing Paper: National Heart Review Board for Pediatrics. June 8, 2020.

https://optn.transplant.hrsa.gov/media/3808/202006_thoracic_natl_heart_reviewboard_for_peds_bp.pdf (accessed on June 24, 2020).

³⁰ For more information on the goals of the OPTN Strategic Plan, visit <https://optn.transplant.hrsa.gov/governance/strategic-plan/>.

evaluation. In addition, guidance is provided to assist transplant programs who are submitting exception requests a framework for what data is most pertinent to ensure their patient receives as comprehensive of a review as a candidate listed at another program.

Implementation Considerations

The proposed guidance will require additional communication from the OPTN to both transplant programs and NHRB for pediatric candidate members.

Fiscal Impact

Minimal or no member impact.

OPTN Actions

The OPTN will need to communicate the proposed guidance to all pediatric heart transplant programs and NHRB for pediatric candidate members.

Member Actions

Pediatric heart transplant programs will need to ensure that staff responsible for submitting exception requests are familiar with the proposed guidance document.

Projected Impact on the OPTN

The implementation of the guidance should be low effort but will require communication and clarifications between the cross committee collaborators and potentially members of the Heart Transplantation Committee and Pediatric Heart Workgroup. Ongoing work related to monitoring has already been planned, scoped, and assigned resourcing as part of the National Heart Review Board for pediatric candidates effort.

Post-implementation Monitoring

The Final Rule requires allocation policies to be “reviewed periodically and revised as appropriate.”³¹ Although this proposal is not policy, it provides guidance to enhance the implementation of the National Heart Review Board for pediatric candidates. The following evaluation plan will provide the Committee with information on a periodic basis about whether the NHRB for pediatric candidates is achieving its goals, and whether any revisions are warranted.

The NHRB will be formally evaluated approximately 6 months, 1 year, and 2 years post-implementation. The following metrics, and any subsequently requested by the Committee, will be evaluated as data become available (Appropriate lags will be applied, per typical OPTN conventions, to account for time delay in institutions reporting data to UNetSM) and compared to an appropriate pre-policy cohort to assess performance before and after implementation of the NHRB.

³¹ 42 C.F.R. §121.8(a)(6).

- Examine changes in the number and percent of pediatric candidates by status, exception, age group, OPTN region, and diagnosis
- Examine changes in the number and percent of pediatric transplant recipients by status, exception, age group, OPTN region, and diagnosis
- Evaluate changes in waiting list mortality rate for pediatric candidates by status and exception
- Evaluate changes in transplant rate for pediatric candidates by status and exception
- Report the percent of approvals and denials for exception requests by status
- Examine changes in post-transplant patient survival rates overall and stratified by status

Conclusion

This guidance document aims to assist future NHRB for pediatric candidate members in their decision making when they receive exception requests for pediatric candidates with the diagnoses of dilated cardiomyopathy, hypertrophic or restrictive cardiomyopathy, single ventricle heart disease, and coronary allograft vasculopathy and retransplantation. This document also provides guidance to the transplant program submitting a request on their candidate's behalf to improve the efficiency of the review process. The ultimate goal is to ensure that these medically urgent, unique candidates are reviewed consistently by NHRB for pediatric candidates members and that the information provided by the transplant program provides enough appropriate detail for the NHRB for pediatric candidates members to make an informed determination.

Several minor clarifications and additions to the guidance were added following the analysis of the feedback received during public comment. These edits do not significantly alter the criteria included in the guidance and are intended to strengthen the usability of the document when submitting and reviewing status exception requests.

Guidance for Pediatric Heart Exception Requests

Diagnoses addressed in this Guidance

The guidance document was drafted with the goal of helping the members of the National Heart Review Board for Pediatrics standardize decision-making when reviewing exceptions requests for certain Status 1A and Status 1B candidates. The document provides guidance on the following pediatric heart diagnoses:

- Dilated cardiomyopathy
- Restrictive or hypertrophic cardiomyopathy
- Single ventricle heart disease
- Coronary vasculopathy allograft and retransplant

Standard Information for Inclusion with Pediatric Heart Exception Requests

The following information provides useful guidance for transplant program staff responsible for completing the clinical narrative portion of an initial exception request or an extension exception request on behalf of a pediatric heart candidate. Transplant programs are expected to demonstrate that a candidate has both the medical urgency and potential for benefit comparable to that of other candidates at this status.³²

Transplant programs are strongly encouraged to submit the following information as part of each exception request:

- Contain specific description of the candidate's current diagnoses and methods of support, inclusive of inotropes and mechanical circulatory support;
 - Describe inotrope escalation and/or failure to wean
- Specifically describe how:
 - The candidate meets the exception criteria, or
 - Why standard therapies may not be ideal for the candidate and why the candidate's condition is not addressed by the pre-specified exception criteria
 - Describe why the current policy does not adequately account for the candidate's particular situation and high risk of waitlist mortality
 - Provide timing of symptom changes in relation to exception request

This resource is not OPTN Policy, so it does not carry the monitoring or enforcement implications of policy. It is not an official guideline for clinical practice, nor is it intended to be clinically prescriptive or to define a standard of care. This resource is intended to provide guidance to transplant programs and the National Heart Review Board.

Category 1: Dilated Cardiomyopathy Patients

Most candidates with dilated cardiomyopathy, in the absence of specific criteria below, are appropriately categorized based on the need for inotropes as Status 1B or for mechanical circulatory

³² OPTN, Adult heart status 2 exception criteria justification form. Accessed in UNetSM October 29, 2019.

41 support as Status 1A. Table 1 provides useful guidance for the review board asked to approve upgraded
 42 listing urgency by exception for children with dilated cardiomyopathy.

43
 44

Table 1: Recommended criteria for status exceptions

If the candidate has dilated cardiomyopathy and meets this criteria:	Then the candidate may be eligible for:
<p><u>Is admitted to the transplant hospital that registered the candidate on the waiting list and meets <i>all</i> of the following criteria:</u></p> <ul style="list-style-type: none"> • <u>Weighs less than 5kg</u> • <u>Supported by <i>one</i> of the following with either an escalation from lower dosage or a failure to wean from listed dose:</u> <ul style="list-style-type: none"> ○ <u>A continuous infusion of at least one high-dose intravenous inotrope:</u> <ul style="list-style-type: none"> ▪ <u>Dobutamine greater than or equal to 7.5 mcg/kg/min</u> ▪ <u>Milrinone greater than or equal to 0.50 mcg/kg/min</u> ▪ <u>Epinephrine greater than or equal to 0.02 mcg/kg/min</u> ○ <u>A continuous infusion of at least two intravenous inotropes:</u> <ul style="list-style-type: none"> ▪ <u>Dobutamine greater than or equal to 3 mcg/kg/min</u> ▪ <u>Milrinone greater than or equal to 0.25 mcg/kg/min</u> ▪ <u>Epinephrine greater than or equal to 0.01 mcg/kg/min</u> ▪ <u>Dopamine greater than or equal to 3 mcg/kg/min</u> 	<p><u>Status 1A exception</u></p>
<p><u>Is admitted to the transplant hospital that registered the candidate on the waiting list and meets <i>all</i> of the following criteria:</u></p> <ul style="list-style-type: none"> • <u>Weighs less than 10kg</u> • <u>Supported by <i>one</i> of the following with either an escalation from lower dosage or a failure to wean from listed dose:</u> <ul style="list-style-type: none"> ○ <u>A continuous infusion of at least one high-dose intravenous inotrope:</u> <ul style="list-style-type: none"> ▪ <u>Dobutamine greater than or equal to 7.5 mcg/kg/min</u> ▪ <u>Milrinone greater than or equal to 0.50 mcg/kg/min</u> ▪ <u>Epinephrine greater than or equal to 0.02 mcg/kg/min</u> ○ <u>A continuous infusion of at least two intravenous inotropes:</u> <ul style="list-style-type: none"> ▪ <u>Dobutamine greater than or equal to 3 mcg/kg/min</u> ▪ <u>Milrinone greater than or equal to 0.25 mcg/kg/min</u> ▪ <u>Epinephrine greater than or equal to 0.01 mcg/kg/min</u> ▪ <u>Dopamine greater than or equal to 3 mcg/kg/min</u> • <u>Has poor systemic perfusion as evidenced by <i>any</i> of the following:</u> <ul style="list-style-type: none"> ○ <u>Need for non-invasive positive pressure ventilation</u> ○ <u>Feeding intolerance requiring total parenteral nutrition</u> ○ <u>A decline in end-organ function (e.g. Acute kidney injury)</u> 	<p><u>Status 1A exception</u></p>

45
 46 Among older and larger patients, the primary reason to provide a 1A exception should be the presence
 47 of contraindications to mechanical circulatory support. Such contraindications are often subjective and
 48 based on center experience. However, among the relevant considerations (even in the adolescent
 49 population who are overall likely to do well with a VAD) are: recurrent or severe gastrointestinal
 50 bleeding, recent or recurrent embolic or hemorrhagic stroke, dialysis-dependent patients requiring
 51 simultaneous heart-kidney transplant, hypercoagulable disorder, or the presence of a mechanical
 52 prosthetic valve.

53
54 Of note, given that there are no reliable predictors of RV failure after LVAD placement in pediatric
55 patients, the concern for the need for biventricular support would not generally be deemed a
56 contraindication to VAD placement.

58 Category 2: Restrictive or Hypertrophic Cardiomyopathy Patients

59 Patients with restrictive and hypertrophic cardiomyopathy may have higher mortality on the waitlist
60 when not receiving Status 1A exceptions. The following table (Table 2) provides useful guidance for the
61 review board when evaluating exception requests for candidates with these diagnoses.

62
63 **Table 2: Recommended criteria for status exceptions**

<u>If the candidate has restrictive or hypertrophic cardiomyopathy and meets this criteria:</u>	<u>Then the candidate may be eligible for:</u>
<p><u>Is admitted to the transplant hospital that registered the candidate on the waiting list and meets <i>any</i> of the following criteria:</u></p> <ul style="list-style-type: none"> • <u>Supported by <i>one</i> of the following with either an escalation from lower dosage or a failure to wean from listed dose:</u> <ul style="list-style-type: none"> ○ <u>A continuous infusion of at least one high-dose intravenous inotrope:</u> <ul style="list-style-type: none"> ▪ <u>Dobutamine greater than or equal to 7.5 mcg/kg/min</u> ▪ <u>Milrinone greater than or equal to 0.50 mcg/kg/min</u> ▪ <u>Epinephrine greater than or equal to 0.02 mcg/kg/min</u> ○ <u>A continuous infusion of at least two intravenous inotropes:</u> <ul style="list-style-type: none"> ▪ <u>Dobutamine greater than or equal to 3 mcg/kg/min</u> ▪ <u>Milrinone greater than or equal to 0.25 mcg/kg/min</u> ▪ <u>Epinephrine greater than or equal to 0.01 mcg/kg/min</u> ▪ <u>Dopamine greater than or equal to 3 mcg/kg/min</u> • <u>Has had an episode of sudden death or recurrent prolonged runs of hemodynamically significant arrhythmia that are not controlled by medical therapy</u> • <u>Has had syncopal episodes felt to be related to restricted ventricular filling</u> • <u>Has evidence of increased pulmonary vascular resistance (exceeding 6 WU*m²)</u> 	<p><u>Status 1A exception</u></p>

64 65 Category 3: Single Ventricle Heart Disease

66 Patients with congenital heart disease are not generally disadvantaged by the current allocation system,
67 where they receive 1A status as long as they are admitted and supported on continuous inotrope
68 infusions. However, because certain single ventricle adult transplant candidates have had an increase in
69 status (adult Status 4 [equivalent to pediatric 1B] for all congenital patients, with increased status
70 assignments under specific circumstances), this has resulted in the incongruous circumstance where the
71 same patient will have lower listing status as a child (< 18 years old) than as an adult (≥ 18 years).
72 Accordingly, it appears appropriate to consider more urgent listing for many patients with single
73 ventricle congenital heart disease, even where not supported by inotropes as an inpatient.
74

75 To provide more congruity between adult and pediatric listings, the following table should assist the
 76 National Heart Review Board members with evaluating exception requests for single ventricle congenital
 77 heart disease patients:

78 **Table 3: Recommended criteria for status exceptions**

<u>If the candidate has single ventricle congenital heart disease and meets this criteria:</u>	<u>Then the candidate may be eligible for:</u>
<u>Is admitted to the transplant hospital that registered the candidate on the waiting list and is experiencing complications related to their congenital heart disease (including but not limited to: protein-losing enteropathy, plastic bronchitis, or Fontan circuit thrombosis), and is actively receiving therapy for said complication, without regard for change in the candidate’s cardiac support</u>	<u>Status 1A exception</u>
<u>Has been palliated through a Fontan procedure, is listed for heart transplantation, and has ongoing complications of the Fontan (including, but not limited to: protein-losing enteropathy, plastic bronchitis, or Fontan circuit thrombosis) and is actively receiving therapy for said complication but does not require hospital admission.</u>	<u>Status 1B exception</u>

80

81 **Category 4: Coronary Allograft Vasculopathy and Retransplantation**

82 Patients with a prior transplant do not have specific criteria within policy for qualifying for an urgency
 83 status higher than Status 2. However, many patients with coronary allograft vasculopathy develop a
 84 significant component of restrictive physiology and may not benefit from inotropes. Many patients with
 85 coronary allograft vasculopathy may have poor outcomes and a high-risk for sudden cardiac death
 86 without significant systolic dysfunction.

87

88 Per policy, all patients must be admitted to the hospital where registered to be eligible for Status 1A
 89 exception.³³

33 OPTN, 6.4 Adult and Pediatric Status Exceptions. Accessed October 27, 2020.
https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf

91

Table 4: Recommended criteria for status exceptions

<u>If the candidate has a prior heart transplant and evidence of chronic rejection or significant coronary allograft vasculopathy and meets this criteria:</u>	<u>Then the candidate may be eligible for:</u>
<p><u>A history of recent cardiac arrest, or signs or symptoms placing patients at high-risk for sudden cardiac death, including any of the following:</u></p> <ul style="list-style-type: none"> • <u>A diagnosis of severe CAV similar to ISHLT CAV 3³⁴</u> • <u>Significant restrictive hemodynamics</u> • <u>Non-sustained ventricular tachycardia</u> • <u>Unexplained syncope</u> • <u>Inotrope dependence</u> 	<p><u>Status 1A exception</u></p>
<p><u>A history of revascularization (either surgical or transcatheter) for coronary allograft vasculopathy</u></p>	<p><u>Status 1B exception</u></p>

92

93

#

³⁴ Mehra, Mandeep R, Crespo-Leiro, Maria G, Dipchand, Anne, Ensminger, Stephan M, Hiemann, Nicola E, Kobashigawa, Jon A, Madsen, Joren, Parameshwar, Jayan, Starling, Randall C, and Uber, Patricia A. "International Society for Heart and Lung Transplantation Working Formulation of a Standardized Nomenclature for Cardiac Allograft Vasculopathy—2010." *The Journal of Heart and Lung Transplantation* 29, no. 7 (2010): 717-27.