

Briefing to the OPTN Board of Directors on

Pediatric Candidate Pre-Transplant HIV, HBV, and HCV Testing

OPTN Ad Hoc Disease Transmission Advisory; Pediatric Transplantation Committees

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Pediatric Candidate Pre-Transplant HIV, HBV, and HCV Testing

<i>Affected Policies:</i>	<i>Policy 15.2: Candidate Pre-Transplant Infectious Disease Reporting and Testing Requirements</i>
<i>Sponsoring Committees:</i>	Ad Hoc Disease Transmission Advisory; Pediatric Transplantation
<i>Public Comment Period:</i>	January 27, 2022 – March 23, 2022
<i>Board of Directors Date:</i>	June 27, 2022

Executive Summary

OPTN Policy 15.2: *Candidate Pre-Transplant Infectious Disease Reporting and Testing Requirements* specifies that all candidate human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) testing must occur during hospital admission for transplant but prior to anastomosis.¹ This purpose of this timing requirement is to minimize inadvertent disease transmission through organ transplantation. For pediatric candidates younger than 12 years of age, incidence of HIV, HBV, and HCV is very low and unlikely to change from baseline testing,² while the risk of adverse medical outcomes from overdrawing blood directly prior to transplant is greater.³

The OPTN Ad Hoc Disease Transmission and Pediatric Transplantation Committees (the Committees) propose modifying policy so that all candidates less than 12 years of age are not required to receive HIV, HBV, and HCV testing during hospital admission for transplant. Those candidates must still have baseline testing that occurs prior to transplantation and is documented. This proposal does not change which tests must be performed; it only removes a requirement for *when* the testing must occur.

The proposal was widely supported during public comment and had one modification post-public comment, changing the threshold age from 11 to 12. The change promotes an inclusive threshold of candidates potentially impacted by blood overdraw concerns. Available data do not demonstrate additional risk associated with 11 versus 12 years of age.⁴ The Committees considered that an age threshold of 12 would align with existing liver and lung allocation policies for pediatric children under 12, while still limiting the likelihood of HIV, HBV and HCV transmission due to risk behavior associated with adolescents. This policy change aligns with the OPTN strategic goal to improve transplant recipient safety by removing an unnecessary timing requirement that could incur the need for a blood transfusion for certain pediatric candidates, while still ensuring all necessary testing is performed to avoid infectious disease transmission.

¹ OPTN Policy 15.2: *Candidate Pre-Transplant Infectious Disease Reporting and Testing Requirements* (Accessed November 7, 2021).

² Jones JM, Kralalik I, Levi ME, et al. Assessing Solid Organ Donors and Monitoring Transplant Recipients for Human Immunodeficiency Virus, Hepatitis B Virus, and Hepatitis C Virus Infection — U.S. Public Health Service Guideline, 2020. *MMWR Recomm Rep* 2020; 69(No. RR-4):1–16. DOI: <http://dx.doi.org/10.15585/mmwr.rr6904a1>

³ Stephen. (2011). *Blood sample volumes in child health research: Review of safe limits*. ResearchGate; World Health Organization. DOI:[10.2471/BLT.10.080010](https://doi.org/10.2471/BLT.10.080010)

⁴ Centers for Disease Control and Prevention. HIV Surveillance Report, 2019; vol. 32. <http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html>. Published May 2021. Accessed May 10, 2022.

Purpose

The requirement for pediatric candidates less than 12 to receive HIV, HBV, and HCV testing directly prior to transplant is not necessary from a patient safety perspective. Incidence of HIV, HBV, and HCV with this population is very low and unlikely to change from baseline testing,⁵ while the risk of adverse medical outcomes from overdrawing blood directly prior to transplant is greater.⁶

Background

In December 2020, the OPTN Board of Directors (the Board) approved modifications that aligned OPTN policy with the 2020 U.S. Public Health Service (PHS) Guideline issued by the Centers for Disease Control and Prevention (CDC). One change included requiring all HIV, HBV, and HCV testing to occur during hospital admission for transplant but prior to anastomosis of the first organ. The OPTN Pediatric Transplantation Committee, American Society of Transplantation (AST), Transplant Families, and Society for Pediatric Liver Transplantation expressed concern about this requirement for pediatric candidates, given concerns about the amount of blood drawn directly prior to transplant.⁷ However, the proposed changes were passed by the Board without modification to ensure alignment with the 2020 PHS Guideline and to mitigate risk of HIV, HBV, and HCV transmission through transplantation, which was a primary objective of the Guideline.^{8,9}

In April 2021, after the proposed changes were enacted, the OPTN received a letter expressing renewed concerns about unnecessary pre-transplant blood draws for pediatric candidates.¹⁰ The OPTN Ad Hoc Disease Transmission Advisory Committee (DTAC) collaborated with the Pediatric Transplantation Committee and members from the Centers for Disease Control (CDC) on a DTAC-Pediatric Workgroup (the Workgroup) to address the concerns. The Workgroup agreed that the timing requirement for pediatric candidates was not necessary to protect pediatric candidates from disease transmission and that the blood draw could be risky for low weight pediatric candidates, indicating that the policy should be modified.¹¹ In November 2021, the Advisory Committee on Blood and Tissue Safety and Availability (ACBTSA) of the HHS Office of Infectious Disease and HIV/AIDS Policy (OIDP) reviewed and unanimously supported the proposed changes described in this briefing paper.¹²

⁵ Jones JM, Kracalik I, Levi ME, et al. Assessing Solid Organ Donors and Monitoring Transplant Recipients for Human Immunodeficiency Virus, Hepatitis B Virus, and Hepatitis C Virus Infection — U.S. Public Health Service Guideline, 2020. *MMWR Recomm Rep* 2020; 69(No. RR-4):1–16. DOI: <http://dx.doi.org/10.15585/mmwr.rr6904a1>

⁶ Stephen. (2011). *Blood sample volumes in child health research: Review of safe limits*. ResearchGate; World Health Organization. DOI: [10.2471/BLT.10.080010](https://doi.org/10.2471/BLT.10.080010).

⁷ *Align OPTN Policy with U.S. Public Health Service Guideline, 2020* Public Comment Feedback. August – September 2020. Available at <https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/align-optn-policy-with-us-public-health-service-guideline-2020/>

⁸ Jones JM, Kracalik I, Levi ME, et al. Assessing Solid Organ Donors and Monitoring Transplant Recipients for Human Immunodeficiency Virus, Hepatitis B Virus, and Hepatitis C Virus Infection — U.S. Public Health Service Guideline, 2020. *MMWR Recomm Rep* 2020; 69(No. RR-4):1–16. DOI: <http://dx.doi.org/10.15585/mmwr.rr6904a1>

⁹ *Align OPTN Policy with U.S. Public Health Service Guideline, 2020*. Available at https://optn.transplant.hrsa.gov/media/3933/align_policy_with_phs_guideline_2020_pc.pdf

¹⁰ Letter on behalf of Pediatric Transplant Program at Indiana University (INIM) and the Indiana Transplant Quality Committee. May 14, 2021.

¹¹ OPTN DTAC-Pediatric Workgroup Meeting Summary. June 22, 2021. Available at https://optn.transplant.hrsa.gov/media/4764/dtac-pediatric_wg_summary_62221.pdf

¹² HHS OIPD Advisory Committee on Blood and Tissue Safety and Availability (ACBTSA) Meeting, December 1, 2021.

The OPTN is coordinating with the CDC so that the PHS Guideline and the OPTN policy continue to be aligned. From February 4 to March 7, 2022, a Federal Register Notice solicited public comment feedback for a proposed change to exempt pediatric candidates less than 11 years of age from the timing requirement for HIV, HBV, and HCV testing during hospital admission for transplant but prior to anastomosis of the first organ. The CDC participated in post public comment discussions with the OPTN Committees regarding the appropriateness of modifying the age criteria for the exemption from 11 to 12 (see “Overall Sentiment from Public Comment” section below); given this alignment, the PHS Guideline and OPTN policy are anticipated to both reflect an age threshold of less than 12 years of age.¹³

Proposal for Board Consideration

The DTAC and Pediatric Committees (the Committees) propose modifying policy so that all candidates less than 12 years of age are not required to receive HIV, HBV, and HCV testing during hospital admission for transplant. Those candidates must still have baseline testing that occurs prior to transplantation and is documented. This proposal does not change which tests must be performed; it only removes a requirement for *when* the testing must occur.

The Committees considered proposed modifications to modify the age threshold, to include a weight threshold, and to add a time limit for when pre-transplant testing must occur. The Committees concurred with feedback that the age threshold should be 12, not 11, given that the available data do not show an elevated risk for those candidates aged 10 versus aged 11 (reflecting a threshold of less than 11 or less than 12, respectively) – the Committees also considered that a threshold age of less than 12 years would avoid confusion for those liver and lung candidates since liver and lung allocation uses a threshold of 12 years of age as the young pediatric age bracket. The Committees considered this change to enhance the inclusivity of the exception without adding to the risk. The Committees identified that adding a weight threshold or timeframe for when pre-transplant testing must occur would not substantively improve the proposal in terms of patient safety concerns due to blood overdraws, and could potentially elevate patient safety concerns related to risk of infectious diseases. The Committees therefore did not modify the proposal based on the feedback for weight or timing thresholds. The themes and Committee responses are reviewed in the subsequent section: Overall Sentiment from Public Comment.

Overall Sentiment from Public Comment

The proposed changes received widespread support across member type and region during public comment. NATCO, American Society of Transplantation (AST), American Society of Transplant Surgeons (ASTS), American Nephrology Nurses Association (ANNA), Society of Pediatric Liver Transplantation (SPLIT), American Society of Pediatric Nephrology, and the OPTN Transplant Administrators Committee (TAC) and OPTN Transplant Coordinators Committee (TCC) indicated support; some stakeholders also suggested changes that will be reviewed below. Commenters noted the proposal swiftly addressed an important issue and improved safety while increasing program flexibility. Figures 1 and 2 show sentiment by region and member type. Figure 1 shows that all regions supported the proposal, with very

¹³ A Notice by the Health and Human Services Department, “Request for Information: Regarding a Revision to U.S. Public Health Service Guideline: Assessing Solid Organ Donors and Monitoring Transplant Recipients for Human Immunodeficiency Virus, Hepatitis B Virus, and Hepatitis C Virus Infection.” *Federal Register*. Accessed April 27, 2022. Available at <https://www.federalregister.gov/documents/2022/02/04/2022-02389/request-for-information-regarding-a-revision-to-us-public-health-service-guideline-assessing-solid>

few individuals within the regions indicating opposition. Similarly, Figure 2 demonstrates strong support across the different member organizations.

Figure 1: Sentiment by Region

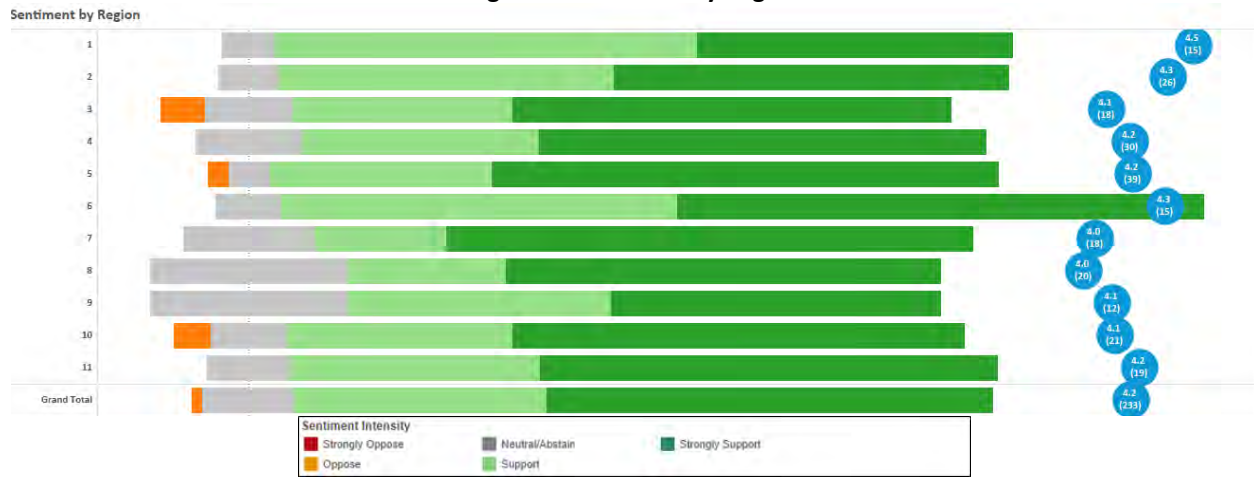
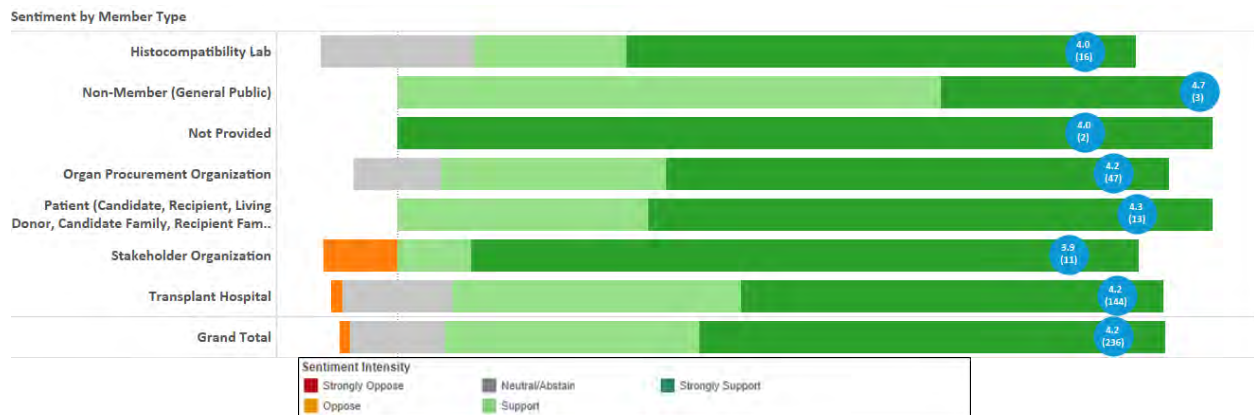


Figure 2: Sentiment by Member Type



Age

Some commenters, while indicating support for the proposal, questioned the age threshold of less than 11 and suggested that an age of 12 would align better with lung and liver allocation. Prior to public comment, the Workgroup had considered 12 as an age threshold, for similar reasons of efficiency, ease of implementation, and alignment with allocation systems.¹⁴ A Workgroup member noted post-public comment that the data presented by the CDC on HIV prevalence compared children less than 13 to those older. Therefore, regardless of age 10 or 11, children under 13 are among the lowest HIV risk group in the U.S.¹⁵ Given that the available data indicated those under 12 would still be extremely low risk of potential HIV, HBV, and HCV exposure, the Committees considered it appropriate to enhance the inclusivity of the proposal to extend to candidates aged less than 12 instead of less than 11. The

¹⁴ OPTN DTAC-Pediatric Workgroup. Meeting Summary. July 30, 2021. Available at https://optn.transplant.hrsa.gov/media/3qeb2r5t/2021_07_30_dtac-peds-wg_mtg-summary.pdf

¹⁵ Centers for Disease Control and Prevention. HIV Surveillance Report, 2019; vol. 32. <http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html>. Published May 2021. Accessed May 10, 2022.

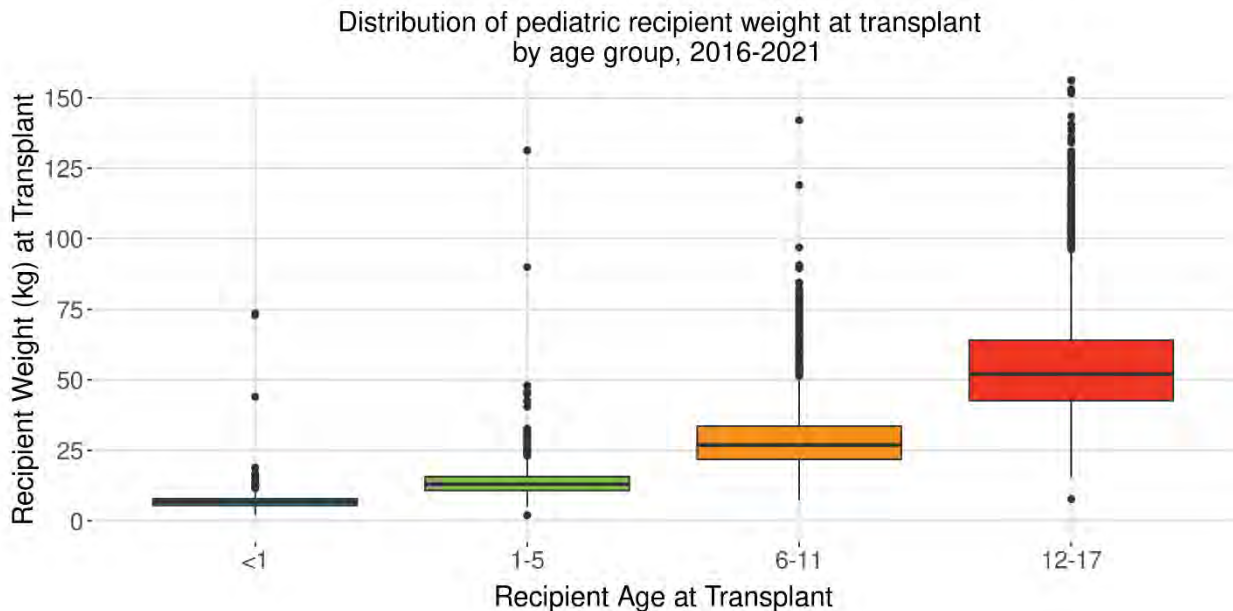
Committees agreed to change the age threshold to less than 12 and voted to send modified policy language to the Board for approval.

Weight Threshold

While there was widespread support for the proposed changes during public comment, a number of public comments suggested adding a weight threshold either instead of or in addition to the age threshold. The weight thresholds suggested were below 20 or 30 kg. The reasoning expressed by some members noted that the cause of renal failure may be associated with syndromes that impact growth and weight, and may impact children older than the age of 10.

Prior to public comment the Workgroup reviewed pediatric recipient weight by age, showing that average weight increased with age from a median of 6.9 kilograms for age group < 1 to median weight 50.8 kilograms for age group 11-17.¹⁶ Over a six year period, there were nine transplants of candidates aged 12 to 17 who weighed less than 20 kilograms.¹⁷ In Workgroup discussions, it was noted that weight could potentially include very low weight adults or adolescents with social behavior such as drug use that increases their risk for HIV, HBV and HCV transmission.¹⁸ Figure 3 shows an updated summary of the weight distribution, based on the proposed age threshold of less than 12 instead of less than 11; it indicates there would be very few (but more than zero) outlier adolescent underweight recipients that could potentially be impacted by being so underweight so as to incur patient safety risk.

Figure 3: Distribution of pediatric recipient weight at transplant by age group, 2016-2021



¹⁶ OPTN DTAC-Pediatric Workgroup. Meeting Summary. July 30, 2021. Available at https://optn.transplant.hrsa.gov/media/3qeb2r5t/2021_07_30_dtac-peds-wg_mtg-summary.pdf

¹⁷ 2022 OPTN data. Six year period of 2016 through 2021.

¹⁸ OPTN DTAC-Pediatric Workgroup. Meeting Summary. June 22, 2021. https://optn.transplant.hrsa.gov/media/4764/dtac-pediatric_wg_summary_62221.pdf

Review of OPTN data shows there could be several candidates a year aged 12 to 17 that weigh less than 20 kilograms.¹⁹ However, the Committees still considered post-public comment that increased likelihood of adolescent engagement in risk behavior such as intravenous drug use would indicate that access to the exemption should be identified based on age and not weight, since the goal of this policy is to avoid any increase in risk of HIV, HBV and HCV transmission while ensuring patient safety.²⁰ The Committees therefore did not change the proposal based on this feedback.

Timing of Testing

The Committees received several comments suggesting that a timing threshold be added for the pediatric candidates who are exempted from the timing requirement of testing during hospital admission for transplant but prior to anastomosis of the first organ. A commenter noted that pediatric candidates could be highly sensitized and be on the list for multiple years. Prior to public comment, the Committees had considered that inclusion of a timeframe (e.g. 3 or 6 months from transplant) could be too prescriptive and add complexity to policy without addressing a meaningful patient safety risk.²¹ The Committees did reconsider in the post public comment period whether a timing threshold should be included, but affirmed that for candidates less than 12 the baseline testing would be sufficient, given the extremely low risk of HIV, HBV and HCV prevalence and associated risk behaviors.^{22,23} This decision was reviewed with CDC members on a joint call in which Workgroup members discussed the post public comment changes considered in this section.²⁴

NOTA and Final Rule Analysis

The Committees submit the following proposal under the authority of 42 U.S.C. 274(b)(2)(M), which requires the OPTN to "recognize the differences in health and in organ transplantation issues between children and adults throughout the system and adopt criteria, polices, and procedures that address the unique health care needs of children..." This proposal would impact the timing requirement for pre-transplant testing of pediatric candidates in recognition of the differences in health and organ transplantation issues between children and adults, and the policy would be addressing the unique health care needs of children in terms of their lesser risk of HIV, HBV, and HCV, and their greater risk of adverse medical outcomes from the overdraw of blood directly prior to transplant.

The proposal is also submitted under the authority of the OPTN Final Rule, which states "The OPTN Board of Directors shall be responsible for developing...policies, consistent with recommendation of the Centers for Disease Control and Prevention, for the testing of organ donors and follow-up of transplant recipients to prevent the spread of infectious diseases."²⁵ Pre-transplant candidate testing helps prevent the spread of infectious diseases by providing a baseline for comparison with post-transplant testing results to identify whether transmission occurred through transplantation and to limit the spread

¹⁹ 2022 OPTN data.

²⁰ OPTN DTAC Meeting Summary. April 25, 2022. OPTN Pediatric Committee Meeting Summary. April 27, 2022.

²¹ OPTN DTAC-Pediatric Workgroup Meeting Summary. September 14, 2021. Available at https://optn.transplant.hrsa.gov/media/hgyfhqy3/2021_09_14_dtac-peds-wg_meeting-summary.pdf

²² 2019 Viral Hepatitis Surveillance Report, CDC:

<https://www.cdc.gov/hepatitis/statistics/2019surveillance/pdfs/2019HepSurveillanceRpt.pdf>

²³ OPTN DTAC Meeting Summary. April 25, 2022. OPTN Pediatric Committee Meeting Summary. April 27, 2022.

²⁴ Ibid.

²⁵ 42 CFR §121.4(a)(ii).

of infectious diseases. The PHS Guideline is due to change to reflect the same age requirements as are proposed here, and therefore the OPTN policy will remain consistent with the CDC's recommendations.

Implementation Considerations

Member and OPTN Operations

Operations affecting Transplant Hospitals

Members will not have to perform HIV, HBV, and HCV testing directly prior to transplant for candidates under 12 years of age. Instead, those candidates may receive testing at any time prior to transplant.

Operations affecting the OPTN

OPTN policy will be updated and a policy notice sent out to members.

Operations affecting Histocompatibility Laboratories

This proposal is not anticipated to affect the operations of histocompatibility laboratories.

Operations affecting Organ Procurement Organizations

This proposal is not anticipated to affect the operations of organ procurement organizations.

Potential Impact on Select Patient Populations

This proposed policy change would positively impact pediatric candidates younger than 12 by eliminating the risk of depleting their overall blood volume directly prior to transplant from testing and avoidance of the subsequent medical issues caused by an unnecessary timeframe for infectious disease testing of a low risk population.

Project Fiscal Impact

This proposal is projected to have a minimal fiscal impact on the OPTN, minimal fiscal impact on organ procurement organizations and transplant hospitals, and no impact on histocompatibility laboratories.

Projected Impact on Organ Procurement Organizations

There is minimal impact to organ procurement organizations.

Projected Impact on Transplant Hospitals

This proposal is not anticipated to have a large fiscal impact. Testing still needs to be performed, but allowing a larger time for testing to be completed for patient safety and clinical appropriateness may make it easier and eliminate the need for additional testing.

There are no major resources required to implement. The approximate time to implement this proposal is less than one month and will consist of staff education and training.

There are no additional ongoing staffing requirements or staffing costs associated with this proposal for transplant hospitals.

There will be no changes to the ongoing cost, just a change in the timing of the required testing. However, it should be noted that if testing occurs prior to admission, as compared to during inpatient stay, reimbursement for costs may vary.

Candidate pre-transplant testing is reimbursable via the Centers for Medicare and Medicaid Services (CMS) cost report for organ acquisition costs, or by payer per pre-transplant testing rates. This proposal may also eliminate re-testing if the institution is unable to obtain testing during inpatient admission. As such, there may be a cost savings.

Projected Impact on the OPTN

The OPTN Contractor estimates 175 hours to implement. This includes time associated with communication and education to members, as well as updating policy. The OPTN Contractor estimates 50 hours for ongoing support, including post-implementation monitoring.

Post-implementation Monitoring

Member Compliance

At transplant hospitals, site surveyors will continue to review a sample of medical records, and any material incorporated into the medical record by reference, for documentation of either:

- Results of required HIV, HBV, and HCV tests
- Evidence that the candidate was already known to be infected with HIV, HBV, or HCV, if required tests for one or more of these infections were not performed prior to transplant

Site surveyors will also continue to verify that required HIV, HBV, and HCV tests were performed using blood samples collected during hospital admission for transplant and prior to first anastomosis for recipients who were at least 12 years old at the time of anastomosis of the first organ. Site surveyors will begin verifying that required HIV, HBV, and HCV tests were performed using blood samples collected prior to first anastomosis for recipients who were less than 12 years old at the time of anastomosis of the first organ. Note that whether pediatric candidates are required to receive testing during hospital admission for transplant and prior to first anastomosis reflects age at time of transplant, not age at time of listing. If the pediatric candidate turns 12 while on the wait list, then the testing would need to be done during hospital admission for transplant, even if it would be repeat testing.

Policy Evaluation

This policy will be formally evaluated at approximately one and two years post-implementation. The following metrics, and any others subsequently requested by the Committee, will be evaluated as data are available and sample size allows. Comparisons will be made pre/post policy when applicable, and metrics will be evaluated across all organs:

- Volume of proven/probable pediatric (0-17 years of age) specific potential donor derived disease transmission events (PDDTE) recipient cases reviewed by the DTAC that were submitted through the Improving Patient Safety Portal

- Number/Percent of pediatric waiting list registrations by age (yr) group and weight (kg) group
- Number/Percent of deceased donor pediatric recipients with a positive HIV, HCV, or HBV result reported on the TRR, and the associated overall distribution of HBV, HCV, and HIV infectious disease test results for deceased donor pediatric recipients (positive, negative, indeterminate not done, unknown)

Conclusion

This proposal removes an unnecessary timeframe from policy while still supporting safe transplant of young pediatric candidates. Even with the removal of the time requirement, pediatric candidates who are 12 years and less will still have baseline HIV, HBV, and HCV test results. Within this cohort of pediatric candidates, the risk of HIV, HBV, and HCV transmission is significantly low while the risk of adverse medical outcomes from overdrawing blood is high; thus, this proposal aims to limit infectious disease transmission while addressing patient safety concerns.

Policy Language

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~). Heading numbers, table and figure captions, and cross-references affected by the numbering of these policies will be updated as necessary.

1 **15.2 Candidate Pre-Transplant Infectious Disease Reporting and Testing** 2 **Requirements**

3 ~~To be eligible for an organ transplant,~~ transplant candidates must be tested for:

- 4 1. HIV using a CDC recommended laboratory HIV testing algorithm
- 5 2. Hepatitis B surface antigen (HBsAg)
- 6 3. Hepatitis B core antibody (total anti-HBc)
- 7 4. Hepatitis B surface antibody (HBsAb)
- 8 5. Hepatitis C antibody (anti-HCV)
- 9 6. Hepatitis C ribonucleic acid (RNA) by nucleic acid test (NAT)

10 unless the testing would violate state or federal laws.

11

12 Infectious disease testing must be performed in a CLIA-certified laboratory or in a laboratory meeting
13 equivalent requirements as determined by CMS using FDA-licensed, approved, or cleared tests.

14

15 For all candidates 12 years or older, ~~C~~andidate samples must be drawn during the hospital admission
16 for transplant but prior to anastomosis of the first organ.

17

18 If the candidate is known to be infected with HIV, HBV, or HCV, then testing for the known viral infection
19 or infections is not required, however the other tests required according to this policy must still be
20 performed.

21

22 Candidates who test positive for HIV, hepatitis B, or hepatitis C must be offered appropriate counseling.

23

24 The OPTN permits HIV test positive individuals as organ candidates if permitted by the transplant
25 hospital. Care of HIV test positive organ candidate and recipients must not deviate from general medical
26 practice.

27

28