

Concept Paper

Clarification of OPO and Living Donor Recovery Hospital Requirements for Donors with Positive HIV Test Results

OPTN Ad Hoc Disease Transmission Advisory Committee

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Clarification of OPO and Living Donor Recovery Hospital Requirements for Donors with Positive HIV Test Results

Sponsoring Committee: Ad Hoc Disease Transmission Advisory
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Executive Summary

The Ad Hoc Disease Transmission Advisory Committee (the Committee) aims to gather relevant data to consider the creation of an algorithm that would account for situations where a donor may have a positive Human Immunodeficiency Virus (HIV) test but does not have HIV infection. The Committee hopes to identify:

1. What (if any) test results could be used to classify a deceased donor as not infected with HIV although the donor has at least one positive HIV test result?
2. What (if any) test results could be used to classify a living donor as not infected with HIV although the donor has at least one positive HIV test result?
3. What (if any) clinical judgment or individual protocols would be appropriate and consistent with requirements to assess situations where the donor is not thought to be infected although there is a positive HIV result?

The exact number of times a donor has a positive HIV test but is later found to be HIV uninfected and is therefore allocated to a recipient without HIV is unknown. Therefore, the Committee has little data to support the creation of the algorithm. The purpose of this concept paper is to request feedback from the community to inform a future policy proposal.

Background

The HIV Organ Policy Equity (HOPE) Act amended the Public Health Service Act to repeal the requirement that the OPTN adopt and use standards of quality for the acquisition and transportation of donated organs that include standards for preventing the acquisition of organs infected with the etiologic agent for acquired immune deficiency syndrome (AIDS).¹ The HOPE Act was passed by the U.S. Congress and signed into law in 2013. OPTN Policy 15.7 *Open Variance for the Recovery and Transplantation of Organs from HIV Positive Donors*² allows organ transplants from donors with positive HIV test results to recipients living with HIV under approved research studies in the U.S. to assess the safety and success of this form of transplantation.³ This applies to living and deceased donors.

Prior to the enactment of the HOPE Act, federal law prohibited the use of organs from donors with HIV, even though there were candidates living with HIV awaiting, and receiving transplants. People living with HIV (PLWH) are more likely than those not living with HIV to develop end-stage kidney and liver disease and may need transplantation. The HOPE Act-authorized research protocols allow PLWH with a need for an organ transplant to potentially experience decreased waiting time for transplantation if an organ from a donor with a HIV positive test is available. The protocols also mean that PLWH may sign up to become organ donors.⁴

The OPTN has been made aware of fewer than ten donors where the donor had a positive HIV result, but was considered as not infected with HIV and the donor organ was used in regular allocation. The OPTN contractor evaluates the data in the OPTN Computer System to identify cases where an OPO reported a positive HIV result but considered the donor as not infected with HIV. These cases are then referred to the OPTN Membership and Professional Standards Committee (MPSC), but the OPTN is not made aware every time this occurs. None of the donors were later determined to be HIV infected.

The Committee was asked by the MPSC to clarify the OPTN policies surrounding the allocation of donors with a HIV positive test. Clinical situations have arisen where some deceased donors with at least one positive HIV test were treated as if not infected with HIV and allocated to candidates without HIV. The MPSC has requested the Committee provide clinical guidance or policy consistent with all applicable laws and regulations to consider whether HOPE Act requirements apply to any donor with at least one positive HIV test result, or a clinical determination based on all available tests.⁵

OPTN Policy 5.5.C *OPO Requirements for Positive HIV Results* currently uses the terminology, "If a donor is found to be *positive* for HIV..."⁶ whereas the OPTN Final Rule (42 C.F.R. §121.6(b)(1)) and the HOPE Act refer to organs from individuals "*infected* with human immunodeficiency virus..."⁷ Historically, the

¹ Congress.gov. "S.330 - 113th Congress (2013-2014): HIV Organ Policy Equity Act." November 21, 2013. <https://www.congress.gov/bill/113th-congress/senate-bill/330>.

² OPTN Policy 15.7: Open Variance for the Recovery and Transplantation of Organs from HIV Positive Donors (Accessed May 15, 2023) https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf

³ HIV.gov. "HHS Advisory Committee to Discuss Results of Hope Act Research on Organ Transplants between People with HIV." HIV.gov, November 9, 2022. <https://www.hiv.gov/blog/hhs-advisory-committee-to-discuss-results-of-hope-act-research-on-organ-transplants-between-people-with-hiv/>.

⁴ Ibid.

⁵ Membership and Professional Standards Committee, OPTN, meeting summary for July 13-14, 2022, accessed June 1, 2023, https://optn.transplant.hrsa.gov/media/zxsctdoz/20220713_mpsc_meeting_minutes_public.pdf

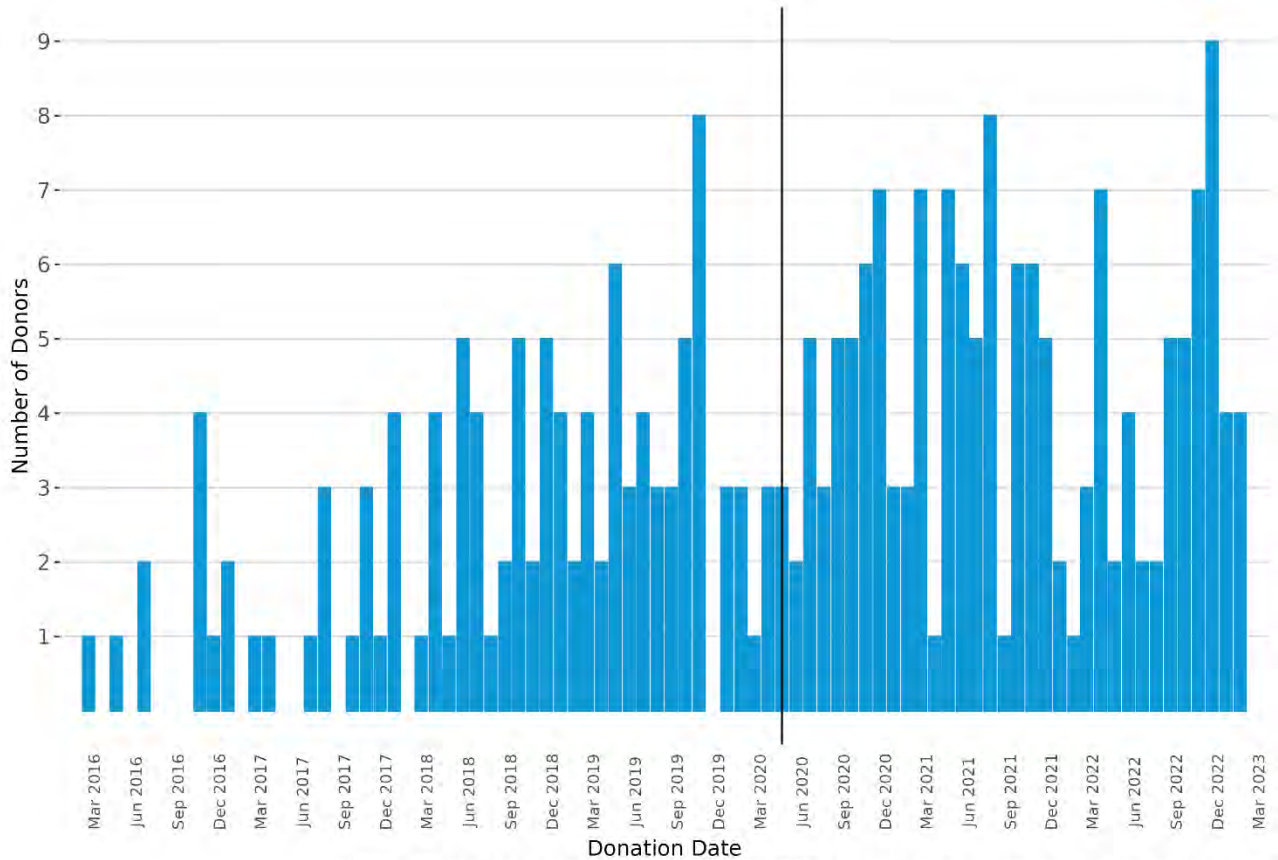
⁶ OPTN Policy 5.5.C: OPO Requirements for Positive HIV Results (Accessed May 15, 2023) https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf.

⁷ 42 CFR §121.6(b)(1)

OPTN has treated any donor with a positive HIV test result as HIV infected, and thus the donor organ is only allowed to be allocated to candidates living with HIV under the HOPE Act variance. OPTN Policy has not attempted to account for or clarify false positive results of HIV testing.

The following graphic shows the number of deceased donors with a positive HIV result recovered for transplant by month. The graph shows the greatest number of deceased donors with a positive HIV test recovered in a month as of February 28, 2023, was nine. Further studies indicate that some of these donors may have had false positive HIV test results.

Figure 1: Number of Deceased Donors with a Positive HIV Result Recovered for Transplant by Month⁸

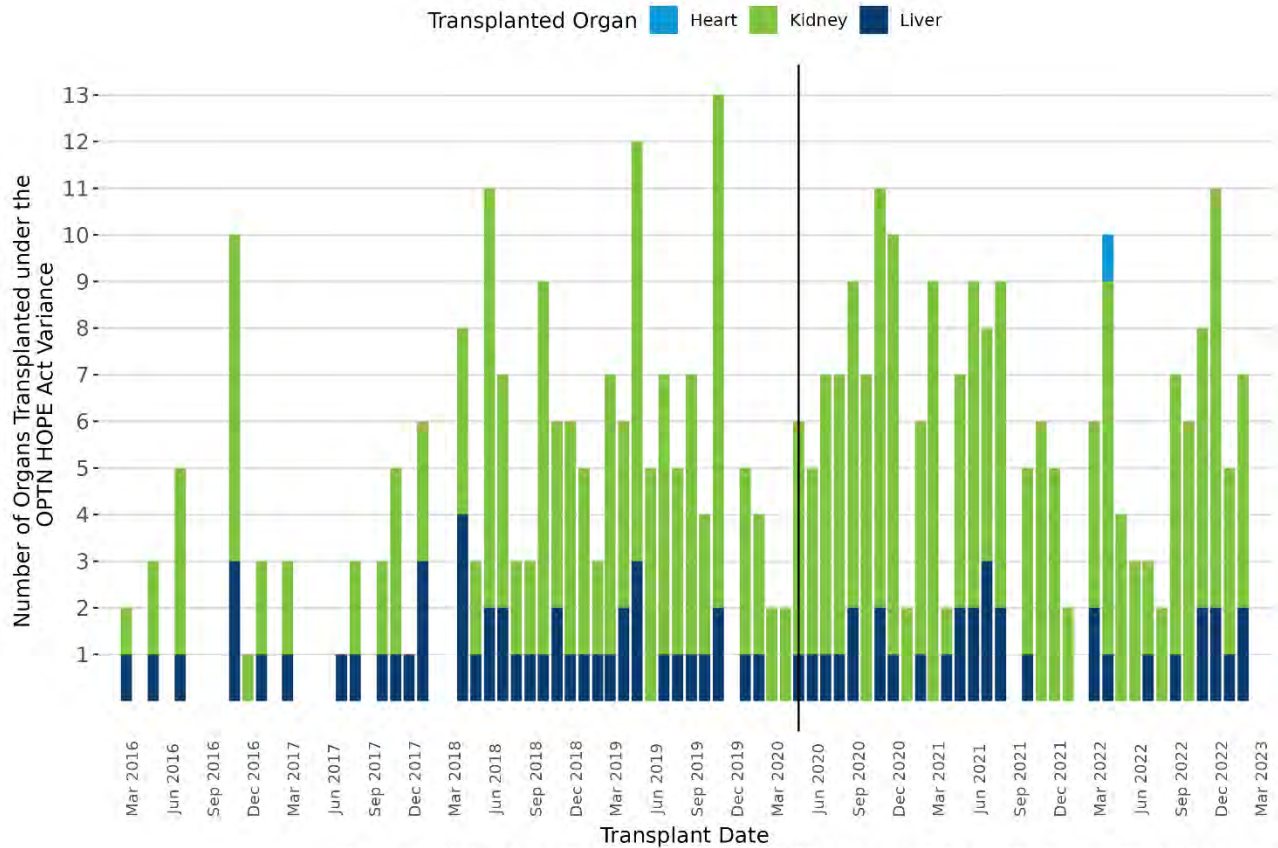


Note: vertical black line indicates when the OPTN HOPE Act variance was modified to include all solid organs

⁸ OPTN, Data request prepared for the Ad Hoc Disease Transmission Advisory Committee, June 19, 2023, pp. 1.

The following graphic shows the number of transplants completed under the HOPE Act by month and organ. As of February 28, 2023, the most transplants performed in one month was 13. The majority of HOPE Act transplants are kidneys and livers.

Figure 2: HOPE Act Transplants by Month and Organ⁹



Note: vertical black line indicates when the OPTN HOPE Act variance was modified to include all solid organs

In 2020, 30,635 people received an HIV diagnosis in the U.S and dependent areas. From 2016 to 2019, HIV diagnoses decreased by 8% overall in the US and dependent areas.¹⁰ Between November 23, 2015 and December 31, 2018, the kidney nonuse rate for HOPE Act donors was 27%, the majority was after the OPTN Waiting List was exhausted, while the liver nonuse rate was 3% due to biopsy findings.¹¹

There were 133 registrations that were indicated as willing to accept an HIV positive organ as of April 13, 2023, with 130 registrations waiting for a kidney, two registrations waiting for a liver, and one

⁹ Ibid.

¹⁰ CDC. "HIV in the US." Centers for Disease Control and Prevention, September 2, 2022.

<https://www.cdc.gov/hiv/statistics/overview/ataglance.html>.

¹¹ Amber R. Wilk, Robert A. Hunter, Maureen A. McBride, David K. Klassen, National landscape of HIV+ to HIV+ kidney and liver transplantation in the United States, American Journal of Transplantation, Volume 19, Issue 9, 2019, Pages 2594-2605, ISSN 1600-6135, <https://doi.org/10.1111/ajt.15494>.

registration waiting for a heart.¹² From March 15, 2021 to March 14, 2023, five kidneys were not utilized from deceased donors due to a positive HIV test.¹³

A National Institutes of Health (NIH) "HOPE in Action" clinical trial participant has provided an algorithm to identify potential donors with false positive HIV results after transplantation.¹⁴ This includes confirmatory testing with either Western blot, fourth-generation antigen/antibody assay, or quantitative NAT, depending on whether the initial positive HIV test result was an antibody or a NAT test. The clinical trial participant estimates 50-100 HIV false-positive donors per year given the false-positivity rates of currently approved assays used to screen more than 20,000 donors annually.¹⁵ There are multiple IRB-approved research studies in which OPTN members can participate that would allow candidates living with HIV to receive transplants from donors with a positive HIV test, and not all have studied or reported rates of HIV false positivity in donors. The "HOPE in Action" trial has reported a rate of HIV false positivity, as defined by their algorithm, in donors whose organs were transplanted as HIV positive in their clinical trial to be 46% for the 56 donors with organs recovered for transplant under the HOPE Act between March 2016 and December 2018.¹⁶

The HOPE in Action trial reported confirmatory testing to take between 24 hours and five days,¹⁷ so the determination of whether a donor has a false positive result for HIV may not be feasible in all situations. However, an HIV testing algorithm may help increase organ utilization in test-positive, but uninfected donors by allowing allocation to candidates without HIV. It is also important to clarify OPTN policy, even if a method for determining donors to be HIV uninfected with at least one positive HIV result is not incorporated, to increase patient safety by preventing donor-derived HIV transmissions if an organ is incorrectly allocated.

A study that examined the clinical utility of HIV confirmatory testing in the deceased donor organ transplant setting analyzed 577 specimen HIV results and found 196 (33.97%) yielded a positive result, 329 (57.02%) yielded a negative result, and 52 (9.01%) instances yielded an indeterminate result. After confirmatory testing was used to verify the positive results, this study found serology-only reactive results were confirmed 25% of the time by confirmatory testing whereas 75% of samples were negative by confirmatory. In cases in which samples were HIV serology Reactive/NAT screen Reactive and not discriminated for HIV/HBC/HCV, 80% of samples had a confirmatory positive result.¹⁸

A survey of organ procurement organizations (OPOs) collected the number of donors and ruled-out potential donors who had a positive result on a HIV test from January 1, 2006, to October 31, 2008. Participation included 62% of U.S. OPOs. There was an examination of 12,397 donor/nondonor cases. There were 56 donor/nondonor cases (0.45%) who had an initial positive result on an HIV antibody or

¹² OPTN, Data request prepared for Health Resources and Service Administration, April 7, 2023, pp. 5.

¹³ OPTN, Data request prepared for the Kidney Transplantation Committee, June 22, 2023, pp. 1.

¹⁴ Durand et al, 2018, "Organs from deceased donors with false-positive HIV screening tests: An unexpected benefit of the HOPE act", <https://onlinelibrary.wiley.com/doi/full/10.1111/ajt.14993>.

¹⁵ Ibid.

¹⁶ Durand et al, 2020, "Clarifying the HOPE Act landscape: The challenge of donors with false-positive HIV results", <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7132607/>.

¹⁷ Durand CM, Halpern SE, Bowring MG, Bismut GA, Kusemiju OT, Doby B, Fernandez RE, Kirby CS, Ostrander D, Stock PG, Mehta S, Turgeon NA, Wojciechowski D, Huprikar S, Florman S, Ottmann S, Desai NM, Cameron A, Massie AB, Tobian AAR, Redd AD, Segev DL. Organs from deceased donors with false-positive HIV screening tests: An unexpected benefit of the HOPE act. *Am J Transplant*. 2018 Oct;18(10):2579-2586. doi: 10.1111/ajt.14993. Epub 2018 Jul 23. PMID: 29947471; PMCID: PMC6160348.

¹⁸ M. Gooch, M. Hansen, and S. Dionne, "Clinical Utility of HIV Confirmatory Testing in the Deceased Donor Organ Transplant Setting." (Poster, American Transplant Congress (ATC), San Diego, CA, June 2023), <https://epro01.ativ.me/web/page.php?page=IntHtml&project=ATC23&id=1229>.

HIV nucleic acid test, and only 8 (14.3%) of those were confirmed positive. It was determined that half of false positive results were from HIV antibody tests and half were from HIV NAT tests.¹⁹

Table 3-3 shows false positivity rates as identified by the FDA. OPTN Policy 2.9: *Required Deceased Donor Infectious Disease Testing* requires HIV antibody (anti-HIV) donor screening test or HIV antigen/antibody (Ag/Ab) combination test and HIV ribonucleic acid (RNA) by donor screening or diagnostic NAT be completed for all deceased donors using FDA licensed, approved, or cleared tests.²⁰

Table 3-3: Sensitivity and specificity rates of FDA-Approved, Licensed, or Cleared HIV Screening Tests for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products for HIV²¹

| Assay Name | Assay Types | Manufacturer | Sensitivity | Specificity | False Positivity Rate |
|------------------------------------|-------------|-------------------------|-------------|-------------|-----------------------|
| A. Antibody assays | | | | | |
| GS HIV-1/HIV-2 Plus O EIA | EIA | Bio-Rad Laboratories | 100% | 99.89% | 0.11% |
| ABBOTT PRISM HIV O Plus | ChLIA | Abbott Laboratories | 100% | 99.94% | 0.06% |
| HIVAB HIV-1/HIV-2 (rDNA) EIA | EIA | Abbott Laboratories | 100% | 99.90% | 0.1% |
| B. Nucleic acid tests | | | | | |
| COBAS AmpliScreen HIV-1 Test, v1.5 | PCR | Roche Molecular Systems | 99.1% | 99.7% | 0.3% |
| Procleix HIV-1/HCV | TMA | Gen-Probe, Inc. | 99.8% | 99.87% | 0.13% |
| Procleix Ultrio | TMA | Gen-Probe, Inc. | 99.6% | 99.8% | 0.2% |
| COBAS TaqScreen MPX | PCR | Roche Molecular Systems | 100% | 99.98% | 0.02% |
| Procleix Ultrio Plus | TMA | Gen-Probe, Inc. | 99.72% | 100% | 0% |

^aEIA: enzyme immunoassay; ChLIA: chemiluminescent immunoassay; PCR: polymerase chain reaction; TMA: transcription-mediated amplification.

OPTN Policy 14.4.A *Living Donor Medical Evaluation Requirements* requires an HIV antibody (anti-HIV) testing or HIV antigen/antibody (Ag/Ab) combination test as close as possible, but within 28 days prior to organ recovery and an HIV ribonucleic acid (RNA) by NAT as close as possible, but within 28 days prior to organ recovery be completed for all living donors using FDA licensed, approved, or cleared tests.²²

¹⁹ Shafer TJ, Schkade D, Schkade L, Geier SS, Orlowski JP, Klintmalm G. Zero Risk Tolerance Costs Lives: Loss of Transplantable Organs Due to Human Immunodeficiency Virus Nucleic Acid Testing of Potential Donors. *Progress in Transplantation*. 2011;21(3):236-247. doi:10.1177/152692481102100309

²⁰ OPTN Policy 2.9: *Required Deceased Donor Infectious Disease Testing* (Accessed May 15, 2023) https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf.

²¹ Durand et al, 2018, "Organs from deceased donors with false-positive HIV screening tests: An unexpected benefit of the HOPE act", <https://onlinelibrary.wiley.com/doi/full/10.1111/ajt.14993>.

²² OPTN Policy 14.4.A: *Living Donor Medical Evaluation Requirements* (Accessed May 15, 2023) https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf.

The Advisory Committee on Blood and Tissue Safety and Availability (ACBTSA) recently recommended to the United States Department of Health and Human Services (HHS) Secretary the removal of the statutory research and Institutional Review Board (IRB) requirements for kidney and liver HOPE Act transplants.²³ If the HHS Secretary removes these requirements for kidneys and livers, this would allow for wider adoption of HIV positive to HIV positive organ transplantation and make more organs available for all candidates. In this event, the number of donors with a positive HIV test result may increase, and correspondingly the rate of donors with a positive HIV test result but who do not have HIV infection may increase, therefore further emphasizing the need for this algorithm.

After further discussion with the Centers for Disease Control and Prevention (CDC) and the Health Resources and Services Administration (HRSA), the Committee has decided to put out a concept paper to determine the scope of the issue. This will help the Committee determine the need for an algorithm.

Project Plan

The Committee aims to gather relevant data to consider the creation of an algorithm that may be utilized by OPOs or living donor recovery hospitals to evaluate deceased or living donors, respectively, who have a positive HIV test result yet after additional testing or evaluation is conducted it is believed the donor is not infected with HIV. Living donor recovery hospitals often have more time to determine whether a donor who has a positive HIV test is HIV infected, so an algorithm may incorporate different testing options to help transplant teams make this determination.

The goal of this concept paper is to request feedback from the community to inform a future policy proposal. The timing of a future policy proposal may depend on the timing of the Committee's ability to determine the types of tests that will inform an algorithm. The Committee will not move forward unless the need from the community is clear, the data gathered through this concept paper justifies the use of an algorithm in allocation, and the Committee receives support from important stakeholders.

Progress So Far

The Committee formed a Workgroup that consisted of members from the Committee, MPSC, CDC, and the OPTN Heart Transplantation Committees. The Workgroup examined existing algorithms and considered the level of risk of transmission to recipients posed by each factor and the ability to mitigate risks through different or additional confirmatory testing criteria. The Workgroup considered risk criteria, HIV incidence, the timing of HIV tests, chimeric antigen receptor-T Cell therapy/Lentiviral gene therapy, and the use of HIV pre-exposure prophylaxis (PrEP). Ultimately, the Workgroup decided that the lack of data on false positive donors does not allow for a proposed algorithm that addresses these situations. This concept paper is an attempt to gather the data the Workgroup needs to rationalize the use of an algorithm for donors with HIV positive tests.

The Committee has presented the concept paper to the OPTN OPO and Operations and Safety Committees. They are in full support of an algorithm that may assess situations where a donor may not be infected although there is a positive HIV test result.

²³ Office of Infectious Disease and HIV/AIDS Policy (OIDP). "Fifty-Sixth ACBTSA Meeting November 17, 2022 - Meeting Summary." HHS.gov, January 10, 2023. <https://www.hhs.gov/oidp/advisory-committee/blood-tissue-safety-availability/meeting-summary/2022-11-17/index.html>.

NOTA and Final Rule Analysis

The Committee submits this proposal under the authority of the NOTA, which states, "In adopting and using standards of quality under paragraph (2)(E), the Organ Procurement and Transplantation Network may adopt and use such standards with respect to organs infected with human immunodeficiency virus (in this paragraph referred to as "HIV"), provided that any such standards ensure that organs infected with HIV may be transplanted only into individuals who- (A) are infected with HIV before receiving such organ..."²⁴ and under the authority of the OPTN Final Rule, which states, "Organs from individuals infected with human immunodeficiency virus (HIV) may be transplanted only into individuals who— Are infected with HIV before receiving such organs..."²⁵ If an algorithm is created due to the feedback gathered through this concept paper, OPOs could allocate organs from donors with a HIV positive test result through the standard match run if the algorithm concludes the donor to be HIV uninfected.

Conclusion

The Committee aims to gather relevant data to consider the creation of an algorithm that addresses:

1. What (if any) testing results could be used to classify a deceased donor as not infected with HIV although the donor has at least one positive HIV test result?
2. What (if any) test results could be used to classify a living donor as not infected with HIV although the donor has at least one positive HIV test result?
3. What (if any) clinical judgment or individual protocols would be appropriate and consistent with requirements to assess situations where the donor is not thought to be infected although there is a positive HIV result?

The Committee will use this concept paper to determine if the need from the community warrants the development of an algorithm and determine the level in which this algorithm could be used by OPOs and living donor recovery hospitals.

Considerations for the Community

- How often do OPOs or laboratories encounter donors who have at least one test that is positive for HIV but are not thought to be infected? Please be as specific as possible.
- Do OPOs need a testing algorithm to address donors who have at least one test that is positive for HIV but are not thought to be infected?
- Due to risk of transmission, does it make sense to create this algorithm only for pediatric donors?
- What percent of organs from donors with a positive HIV test are not utilized? Please be as specific as possible.
- How often are living donor recovery hospitals encountering living donors who have at least one test that is positive for HIV but are found not to be infected through confirmatory testing? Please be as specific as possible.

²⁴ 42 USC §274(b)(3)(a)

²⁵ 42 CFR §121.6(b)(1)(i)

- How often are OPOs and living donor recovery hospitals receiving positive fourth generation HIV test results for a SARS-CoV-2 positive donor? Please be as specific as possible.