OPTN

Briefing to the OPTN Board of Directors on

Improve Deceased Donor Evaluation of Endemic Diseases

OPTN Ad Hoc Disease Transmission Advisory Committee

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Improve Deceased Donor Evaluation of Endemic Diseases

Affected Policies:	*Policy 2.9: Required Deceased Donor Infectious Disease Testing*
Sponsoring Committee:	*Ad Hoc Disease Transmission*
Public Comment Period:	*January 19, 2023-March 18, 2023*

Executive Summary

OPTN *Policy 2.9: Required Deceased Donor Infectious Disease Testing* requires certain infectious disease testing be performed for deceased donors.[1] The purpose of these requirements is to minimize disease transmission through organ transplantation. The two most common donor derived parasitic infectious diseases reviewed by the OPTN Ad Hoc Disease Transmission Advisory Committee (DTAC) are Strongyloidiasis and Chagas disease. The parasite *Strongyloides stercoralis (Strongyloides)* causes Strongyloidiasis and the parasite *Trypanosoma cruzi (T. cruzi)* causes Chagas disease. Despite available strategies to mitigate risk, the DTAC continues to find transmissions of these pathogens.

The DTAC proposes modifying policy to require antibody screening for *Strongyloides* of deceased donors and *T. cruzi* antibody screening of deceased donors born in endemic areas for Chagas disease. The Organ Procurement and Transplantation Network (OPTN) will maintain a list of countries currently classified as endemic for Chagas disease by the Centers for Disease Control and Prevention (CDC). If an antibody screen is positive for *T. cruzi*, the Committee proposes a sample be submitted for confirmatory testing by the organ procurement organization (OPO) within 72 hours. Any information regarding potential disease transmission must be communicated to medical staff responsible for the recipient's clinical care at the transplant program as soon as possible, but no later than 24 hours after becoming aware of the potential disease transmission, which is in line with the requirement for all deceased donor test results.[2]

This revision of OPTN policy aims to maintain transplant recipient safety through infectious disease testing by minimizing disease transmission through organ transplantation. The Committee will evaluate the success of this proposal through monitoring deceased donor derived transmission events.

[1] OPTN Policy 2.9: Required Deceased Donor Infectious Disease Testing (Accessed March 16, 2023) https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf.
[2] OPTN Policy 15.1: Patient Safety Contact (Accessed March 16, 2023) https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf.

Purpose

The universal deceased donor screening requirement for *Strongyloides* and the targeted deceased donor screening approach for *T. cruzi* aims to decrease donor-derived transmission from organ transplantation. *Strongyloides* and *T. cruzi* are endemic diseases that have high potential for morbidity and potential mortality if transmitted to recipients. As organ offer patterns continue to change, increased awareness and communication for potential endemic diseases across regions is necessary.

Background

In 2022, the Endemic Diseases Subcommittee of the DTAC reviewed the potential gaps in education and policy regarding certain endemic diseases that presented significant patient safety risks, and for which identification and treatment strategies exist but are not in common use. Diseases are endemic to a region when they are consistently prevalent in that specific area. The Subcommittee included subject matter experts from the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA), along with Committee representatives from OPOs. The OPTN Membership and Professional Standards Committee wrote a memo to the DTAC on opportunities to improve patient safety, noting concerns regarding a lack of standardized testing and reporting practices of OPOs for endemic diseases.[3] *Strongyloides* and *T. cruzi* were identified in this process as two pathogens that should be evaluated. The Committee received support from the OPTN Organ Procurement Organizations, Transplant Coordinators, and Operations and Safety Committees on this proposal. The OPTN Data Advisory Committee endorsed the data collection in this proposal.

Strongyloides

Strongyloides is a soil transmitted roundworm that infects the human small intestine causing the chronic disease known as strongyloidiasis.[4] The parasite is endemic to tropical and subtropical regions, but its presence has arisen in more temperate locations as well, including the United States, Japan, Australia, and Italy.[5]. Strongyloides is common in these regions because the environment is ideal for the parasite to thrive. Strongyloides is mostly found in areas that are relatively warm and moist, in rural areas, and in areas associated with agricultural activity. However, it can occur anywhere as global prevalence increases.[6] While the global prevalence is generally estimated to be somewhere between 30 to 100 million infected persons, more recent estimates have shown a prevalence of at least 370 million.[7]

There are multiple causes of strongyloidiasis among solid organ transplant recipients: a recent acquisition or reinfection in an endemic area, a reactivation of chronic strongyloidiasis infection, or a

[3] Ad Hoc Disease Transmission Advisory Committee, OPTN, meeting summary for February 14, 2022, accessed April 13, 2023, https://optn.transplant.hrsa.gov/media/jn4p42r3/2022_02_14_dtac_open_summary.pdf.
[4] Nutman, Thomas B. "Human Infection with Strongyloides Stercoralis and Other Related Strongyloides Species." *Parasitology*, vol. 144, no. 3, 16 May 2016, pp. 263–273., https://doi.org/10.1017/s0031182016000834.
[5] Ibid.
[6] Centers for Disease Control and Prevention. "CDC - Strongyloides - General Information - Frequently Asked Questions." Centers for Disease Control and Prevention. Centers for Disease Control and Prevention, September 2, 2020. https://www.cdc.gov/parasites/strongyloides/gen_info/faqs.html.
[7] Bisoffi, Zeno, et al. "Strongyloides Stercoralis: A Plea for Action." *PLoS Neglected Tropical Diseases*, vol. 7, no. 5, 9 May 2013, https://doi.org/10.1371/journal.pntd.0002214.

donor-derived infection.[8] From 2012 to 2017, 44.8% of recipients who received organs from a donor with *Strongyloides* developed a donor-derived infection.[9] Of those recipients with donor-derived infection, 30.8% died of transmission related causes.[10] In another retrospective study of 2008-2017 cases, the proportion of disease transmission events from positive *Strongyloides* antibody screening tests increased and subsequently the proportion of proven and probable cases decreased. [11]Proven transmissions occur when a donor tests positive for a disease and transmits the disease to a recipient. A probable transmission occurs when one or more recipients have data suggestive of a transmission from a donor. A retrospective cohort study of potential donor derived Strongyloides transmission events adjudicated[12] by the Committee from 2008-2017 shows the increase in the number of donors screened and the decrease in actual transmissions is consistent with OPOs increasing the use of *Strongyloides* antibody screening tests as well as subsequent notification and prophylactic treatment in recipients when the donor has tested positive. 2009 showed 41.7% of *Strongyloides* cases reported to the committee were adjudicated as proven or probable, which decreased to zero in 2017.[13]

Since 2008, there have been 39 proven or probable recipient transmissions of *Strongyloides* adjudicated by the Committee. In addition, 603 recipient transplants were adjudicated as intervention without disease transmission (IWDT). This means that recipients of a donor with *Strongyloides* received treatment preventing the transmission. Universal screening will identify infected donors, allow targeted treatment of recipients of organs from positive donors, and decrease the risk of transmission of an infection that currently affects 370 million people worldwide.

Trypanosoma cruzi

T. cruzi is a protozoan parasite which typically infects a patient through the bite and subsequent fecal or urine contamination from a triatomine bug and causes Chagas disease.[14] Other paths of transmission include in utero mother-to-baby, contaminated blood products, or via an organ transplanted from an infected donor.[15] *T. cruzi* is currently endemic to many parts of Latin America including Mexico, Central America, and South America, but not the Caribbean Islands, and an estimated eight million people globally are infected.[16] The list of countries classified as endemic for *T. cruzi* by the CDC include:

- Mexico
- Belize
- Costa Rica
- El Salvador

[8] La Hoz RM, Morris MI. "Intestinal parasites including Cryptosporidium, Cyclospora, Giardia, and Microsporidia, Entamoeba histolytica, Strongyloides, Schistosomiasis, and Echinococcus: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice." Clin Transplant. 2019 Sep;33(9):e13618.
[9] Kaul, Daniel R., et al. "Ten Years of Donor-Derived Disease: A Report of the Disease Transmission Advisory Committee." *American Journal of Transplantation*, vol. 21, no. 2, 5 July 2020, pp. 689–702., https://doi.org/10.1111/ajt.16178.
[10] Ibid.
[11] La Hoz RM, Vece G, Danziger-Isakov L, Florescu D, Malinis M, Lilly K, Strasfeld L, Wood RP, Tlusty S, Wolfe CR, Michaels MG. Donor Derived Strongyloidiasis, a Preventable Event . Am J Transplant. 2019; 19.
[12] The Committee uses a categorization system to classify potential donor derived transmission events reported to the OPTN.
[13] Ibid.
[14] WHO Expert Committee on the Control of Chagas Disease. "Chapter 2. Basic Information on Chagas Disease." *Control of Chagas Disease: Second Report of a WHO Expert Committee*, World Health Organization, Geneva, 2002, pp. 2–35. https://apps.who.int/iris/bitstream/handle/10665/42443/WHO_TRS_905.pdf?sequence=1&isAllowed=y.
[15] CDC. "Chagas Disease - Epidemiology & Risk Factors." *Cdc.gov*, Centers for Disease Control and Prevention, 11 Apr. 2022, https://www.cdc.gov/parasites/chagas/epi.html.
[16] Ibid.

- Honduras
- Guatemala
- Nicaragua
- Panama
- Argentina
- Bolivia
- Brazil
- Chile
- Colombia
- Ecuador
- Guyana
- Suriname
- French Guiana
- Paraguay
- Peru
- Uruguay
- Venezuela[17]

The Committee confirmed with CDC representatives that this list has remained consistent for decades.

Recipients of a solid organ transplant from a *T. cruzi* infected donor are at risk of donor-derived infection, with recipients of a heart transplant carrying the highest risk due to the parasite's affinity for the heart muscle and the associated cardiac complications.[18] Acute *T. cruzi* infection causes substantial morbidity and mortality in the post-transplant setting if not recognized and treated early.[19] Morbidity is the state of being symptomatic or unhealthy for a disease or condition. It is usually represented or estimated using prevalence or incidence. Mortality is related to the number of deaths caused by the health event under investigation.[20] Severe complications from active infection also include meningoencephalitis and death.[21] In a study of organ donors that were seropositive for *T. cruzi* from 2001-2011, 13 of 14 donors were either born in Latin America or their mothers were.[22] Out of 32 recipients transplanted from a *T. cruzi*-seropositive donor from 2001-2011, 75% of heart recipients, 20% of liver recipients, and 13% of kidney recipients developed a donor-derived infection. Four of the five

[17] Centers for Disease Control and Prevention. "Chagas Disease: What U.S. Clinicians Need to Know." August 2012, https://www.cdc.gov/parasites/cme/chagas/lesson_1/5.html#:~:text=Endemic%20Countries&text=cruzi%20transmission%20occurs%2C%20or%20occurred,%2C%20Peru%2C%20Uruguay%20and%20Venezuela.

[18] La Hoz RM, Morris MI. Tissue and blood protozoa including toxoplasmosis, Chagas disease, leishmaniasis, Babesia, Acanthamoeba, Balamuthia, and Naegleria in solid organ transplant recipients- Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019 Sep;33(9):e13546.

[19] Chin-Hong PV, Schwartz BS, Bern C, Montgomery SP, Kontak S, Kubak B, Morris MI, Nowicki M, Wright C, Ison MG. Screening and treatment of chagas disease in organ transplant recipients in the United States: recommendations from the chagas in transplant working group. Am J Transplant. 2011 Apr;11(4):672-80. doi: 10.1111/j.1600-6143.2011.03444.x. Epub 2011 Mar 14. PMID: 21401868.

[20] Hernandez JBR, Kim PY. Epidemiology Morbidity And Mortality. [Updated 2022 Oct 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK547668/

[21] Colin J Forsyth et. Al. "US Chagas Diagnostic Working Group, Recommendations for Screening and Diagnosis of Chagas Disease in the United States" The Journal of Infectious Diseases, Volume 225, Issue 9, 1 May 2022, Pages 1601–1610, https://doi.org/10.1093/infdis/jiab513.

[22] Huprikar S, Bosserman E, Patel G, et al. Donor-derived Trypanosoma cruzi infection in solid organ recipients in the United States, 2001-2011. Am J Transplant. 2013 Sep;13(9):2418-25.

recipients had symptomatic disease. Death was related to Chagas disease in one recipient, but all four recipients died.[23]

Since 2008, there have been 17 *T. cruzi* cases reported to the DTAC. Seven of these cases were adjudicated as proven or probable transmissions of *T. cruzi* by the Committee with two recipient deaths.

Proposal for Board Consideration

The DTAC proposes universal antibody testing of deceased donors for *Strongyloides* and targeted antibody screening of *T. cruzi* for deceased donors born in countries currently classified as endemic for Chagas disease by the CDC. If an antibody test screen is positive for *T. cruzi*, the Committee proposes requiring confirmatory testing. The Committee proposes two new separate data fields for Chagas confirmatory testing and a new question on whether the donor was born in a country currently classified as endemic for Chagas disease under the 'infectious diseases' tab in the OPTN Donor Data and Matching system.

Strongyloides Antibody Screening

The Committee proposes the requirement of universal *Strongyloides* antibody screening to increase patient safety and reduce donor derived transmissions. Universal screening is being proposed versus targeted screening due to the movement of an estimated 30 to 100 million infected individuals and the lack of clear endemicity.[24] The Committee believes that testing is readily available and accurate for OPOs. In 2022, 27 of 57 (47.4%) OPOs reported at least one *Strongyloides* test result.[25] While there has been an increase in donor screening for *Strongyloides*, a 2021 survey revealed that only 24% of OPOs are screening for this prevalent disease.[26]

There is a high rate of prevention of disease transmission if treatment is provided and the therapy used is benign.[27] The Committee proposes that results do not need to be required pre-recovery since organs can still be utilized with a positive screening test due to the availability and effectiveness of treatment. This Committee proposes that FDA licensed, approved, cleared, or Class 1, 510(k)-exempt tests and laboratory developed tests (LDTs) be used for *Strongyloides* screening to ensure testing is available to the community. The addition of Class 1, 510(k)-exempt tests and LDTs is a change from public comment and was added in collaboration with FDA representatives to mitigate the community's concerns over limited availability of testing for *Strongyloides.*

[23] Ibid.

[24] Puthiyakunnon S, Boddu S, Li Y, Zhou X, Wang C, Li J, Chen X. Strongyloidiasis--an insight into its global prevalence and management. PLoS Negl Trop Dis. 2014 Aug 14;8(8):e3018. doi: 10.1371/journal.pntd.0003018. PMID: 25121962; PMCID: PMC4133206.

[25] OPTN, Data request prepared for the Ad Hoc Disease Transmission Advisory Committee, April 21, 2023, pp. 1.

[26] Theodoropoulos NM, Greenwald MA, Chin-Hong P, Ison MG. Testing deceased organ donors for infections: An organ procurement organization survey. Am J Transplant. 2021 May;21(5):1924-1930. doi: 10.1111/ajt.16552. Epub 2021 Mar 11. PMID: 33621430.

[27] Requena-Méndez A, Buonfrate D, Gomez-Junyent J, Zammarchi L, Bisoffi Z, Muñoz J. Evidence-Based Guidelines for Screening and Management of Strongyloidiasis in Non-Endemic Countries. Am J Trop Med Hyg. 2017 Sep;97(3):645-652. doi: 10.4269/ajtmh.16-0923. Epub 2017 Jul 27. PMID: 28749768; PMCID: PMC5590585.

T. cruzi Antibody Screening and Confirmatory Testing

The Committee proposes the requirement of Chagas screening if a donor was born in a country currently classified as endemic for Chagas disease by the CDC. These endemic countries are located in Latin America. The OPTN will maintain a list of these countries. Chagas disease is often a fatal disease with a high mortality rate in transplant recipients. In 2022, 38 of 57 (66.7%) OPOs reported at least one test result for *T. cruzi.*[28] Only 37% of 47 OPOs responding to a 2021 survey reported testing for *T. cruzi*.[29] The Committee modified the proposal post public comment to remove the requirement that *T. cruzi* screening results be available pre-transplant. This was in response to feedback from the community that it would not be possible for many OPOs to be compliant with this requirement. The screening testing for Chagas does not have adequate sensitivity and specificity, so a confirmatory test is proposed to ensure accuracy.[30] The CDC uses an algorithm to confirm a positive screening test, but as proposed, OPOs would also have the option to ensure that confirmatory testing is completed using two different FDA cleared, approved, or licensed antibody diagnostic tests. Four assays have been U.S. Food and Drug Administration (FDA) cleared for diagnostic use.[31]

If a donor's birthplace is unknown, the Committee proposes that the donor is not required to have a *T. cruzi* screening test conducted. This is in response to balancing risk and minimizing delays for organ allocation time.

Overall Sentiment from Public Comment

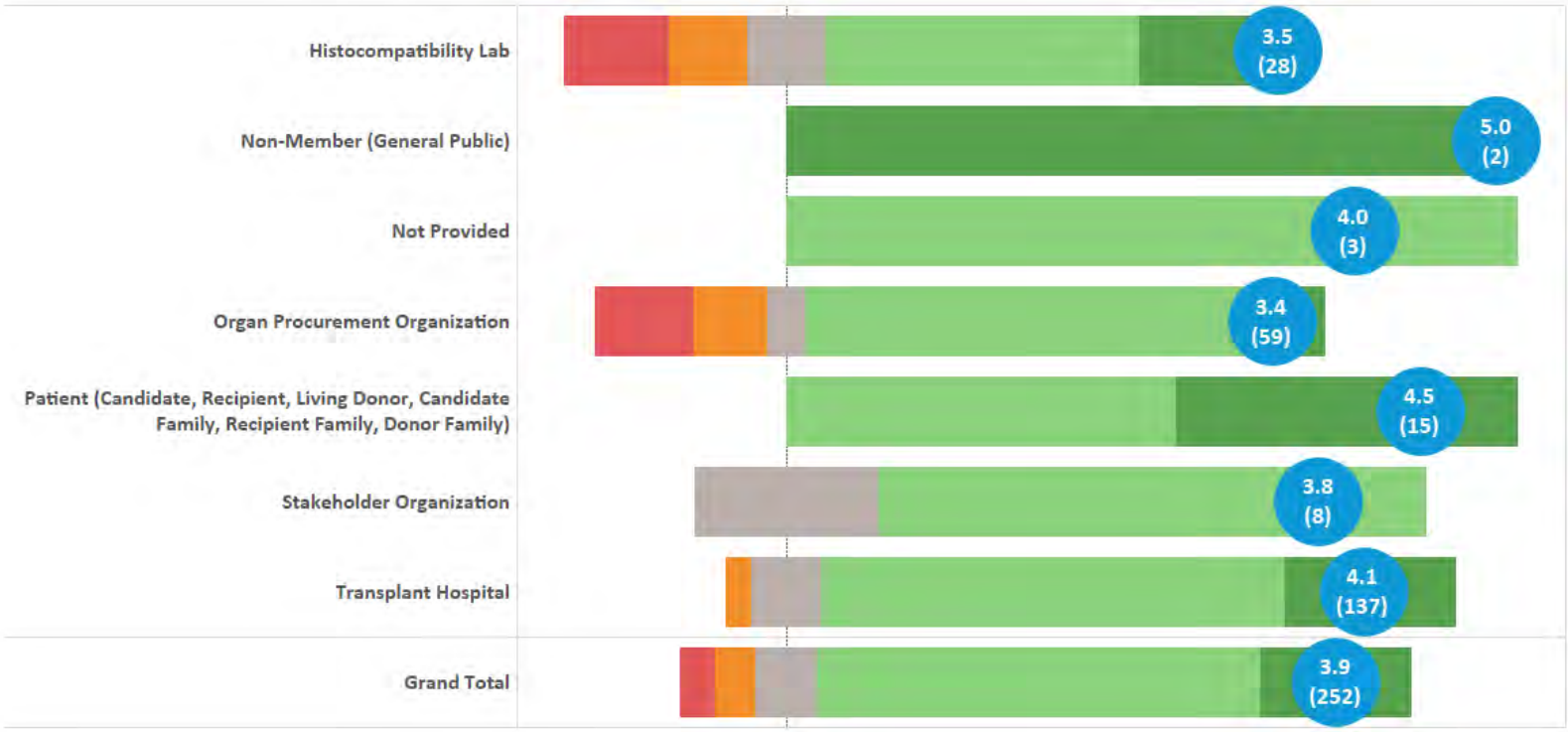
This proposal was out for public comment from January 19, 2023 to March 18, 2023. It was generally supported by most respondents with an overall sentiment score of 3.9. Most member types supported or strongly supported the proposal. However, there was opposition in several categories, with some strong opposition among histocompatibility labs and OPOs. This could be attributed to concern over additional cost of testing, concern over availability of assays, and concern over allocation delays.

Sentiment is collected on public comment proposals and measured on a 5-point Likert scale from strongly oppose to strongly support (1-5). These reports are helpful to spot high-level trends but are not meant as public opinion polls or to replace the substantive analysis below. Below are graphics that illustrate the sentiment received through public comment.

[28] OPTN, Data request prepared for the Ad Hoc Disease Transmission Advisory Committee, April 21, 2023, pp. 1.
[29] Theodoropoulos NM, Greenwald MA, Chin-Hong P, Ison MG. Testing deceased organ donors for infections: An organ procurement organization survey. Am J Transplant. 2021 May;21(5):1924-1930. doi: 10.1111/ajt.16552. Epub 2021 Mar 11. PMID: 33621430.
[30] Kelly EA, Bulman CA, Gunderson EL, Irish AM, Townsend RL, Sakanari JA, Stramer SL, Bern C, Whitman JD. Comparative Performance of Latest-Generation and FDA-Cleared Serology Tests for the Diagnosis of Chagas Disease. J Clin Microbiol. 2021 May 19;59(6):e00158-21. doi: 10.1128/JCM.00158-21. PMID: 33762363; PMCID: PMC8316041.
[31] Colin J Forsyth, Jennifer Manne-Goehler, Caryn Bern, Jeffrey Whitman, Natasha S Hochberg, Morven Edwards, Rachel Marcus, Norman L Beatty, Yagahira E Castro-Sesquen, Christina Coyle, Paula Stigler Granados, Davidson Hamer, James H Maguire, Robert H Gilman, Sheba Meymandi, US Chagas Diagnostic Working Group, Recommendations for Screening and Diagnosis of Chagas Disease in the United States, ***The Journal of Infectious Diseases***, Volume 225, Issue 9, 1 May 2022, Pages 1601–1610, https://doi.org/10.1093/infdis/jiab513.

The following graphic shows sentiment received from all respondents (regional meeting, online, and email) by their stated member type. Again, there was overall support for the concept, demonstrated by a sentiment score of 3.9. OPOs and histocompatibility labs, however, showed a slight opposition to the proposal, demonstrated by a 3.4 and 3.5 sentiment score.

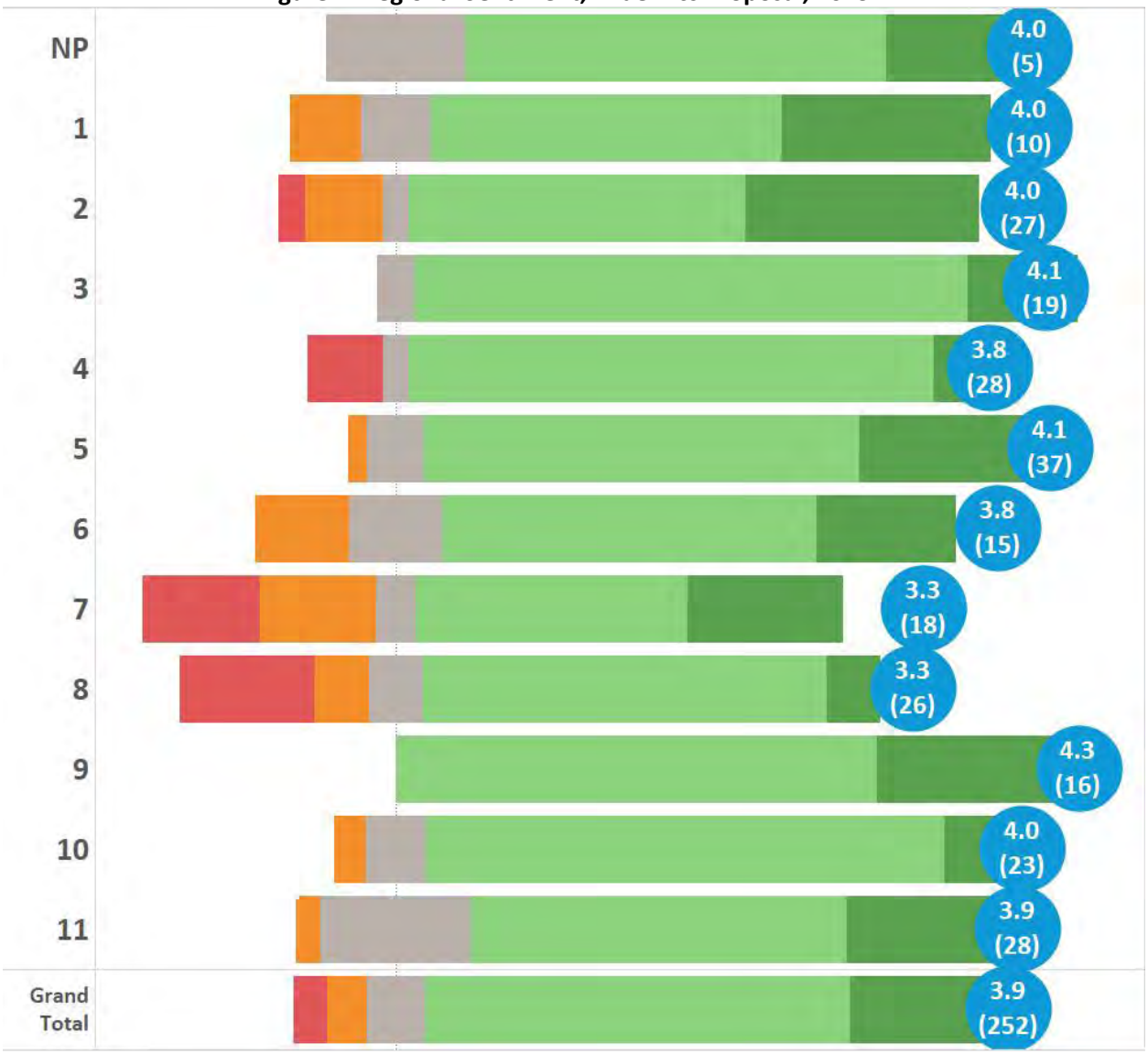
Figure 1: Sentiment by Member Type, Endemics Proposal, 2023[32]



[32] 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). The circles after each bar indicate the average sentiment score and the number of participants in is in the parentheses.

The following graphic shows sentiment received at regional meetings. Again, overall sentiment was supportive, as indicated by a total sentiment score of 3.9. Opposition was raised in all regions, mostly under the theme of stringent test result requirements that could delay allocation.

Figure 2: Regional Sentiment, Endemics Proposal, 2023[33]



Public comment feedback included suggestions for changes, primarily on removing the requirement for *T.cruzi* screening results to be available pre-transplant and concerns with cost and availability of testing.

Concern Over Cost and Availability of Assays

The proposal asked the community for input on what barriers are in place for OPOs to access *T. cruzi* and *Strongyloides* antibody and *T. cruzi* confirmatory testing. This proposal received feedback on the increased cost and limited availability of testing for *Strongyloides* and *T. cruzi*. This sentiment was shared

[33] Ibid.

in regions 1, 3, 4, 6, 8, 10, and 11. This theme was highlighted by six individual OPOs, the Association of Organ Procurement Organizations (AOPO), the OPTN Operations and Safety Committee, and the American Society of Transplantation (AST). Members noted that few labs in the United States meet the criteria for *Strongyloides and T. cruzi* testing as proposed. They emphasized this would increase cost and time burden for OPOs with deceased donor evaluations. The Committee worked with partners from the CDC and FDA to ensure that testing requirements can be met. Members also expressed concern over the bandwidth of the CDC to handle confirmatory testing for Chagas. CDC representatives assured the Committee that they can handle testing submitted through the CDC, and that OPOs have the option to use other laboratories to ensure that two different types of antibody diagnostic tests can be performed for confirmatory testing without going through the CDC.

OPOs commented that there is no current FDA approved, cleared, or licensed donor screening or diagnostic test for *Strongyloides.* The Committee's post public comment changes include permitting use of laboratory developed tests (LDTs) and FDA 510(k)-exempt tests for Strongyloides antibody to make this testing more available and affordable for OPOs and histocompatibility labs that perform infectious disease testing. An LDT is described by the FDA as, "…a type of in vitro diagnostic test that is designed, manufactured and used within a single laboratory."[34] These changes are supported by the Committee due to concern over testing availability from the community. The Committee consists of ex-officio representatives from the FDA who had no concerns over this change.

Concern Over *T. cruzi* Screening Results Pre-Transplant Requirement

This proposal received feedback that took issue with the pre-transplant requirement of *T. cruzi* screening results due to concerns with turnaround time from commercial laboratories. OPOs noted that *T. cruzi* screening tests can take longer than 24 hours to be available, and requiring results to be available pre-transplant could delay allocation and result in organs not being utilized. AOPO, AST, the OPTN Operations and Safety, Transplant Coordinators, and OPO Committees all shared this sentiment and voiced concern that this requirement may delay allocation. Because of this, the Committee decided to remove the requirement that *T. cruzi* screening results must be available pre-transplant from the policy proposal. The Committee made this post public comment change to appropriately balance preventing delay in allocation and patient safety. The Committee recognizes that Chagas disease is treatable if transmitted to a recipient if it is identified and treated early.

Support for Universal Screening for *T. cruzi* and Targeted Screening for *Strongyloides*

The proposal received a variety of feedback on when donors should be tested and under what circumstances. There were suggestions for the screening of all donors for *T. cruzi* and support for a targeted screening approach for *Strongyloides,* similar to what is being proposed for *T. cruzi* testing. Regional meetings provided feedback that travel history should be factored into testing requirements for *T. cruzi*. The OPTN OPO Committee and the OPTN Transplant Coordinators Committee expressed support for universal screening for *T. cruzi*. This was also suggested in regional meetings. AST stated that targeted screening for *Strongyloides* is more appropriate citing concerns about the prevalence of the

[34] Center for Devices and Radiological Health. "Laboratory Developed Tests." U.S. Food and Drug Administration. FDA, September 27, 2018. https://www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests.

disease. This sentiment was also shared at regional meetings. The Committee considered all the feedback and ultimately decided due to the data showing increased and wide prevalence for *Strongyloides* and more clearly defined areas of prevalence for Chagas disease, along with the variety of sentiment, the proposal for universal screening for *Strongyloides* and targeted screening for *T. cruzi* is well supported and adequate. This also aligns with the increased number of transmissions reviewed by the Committee of *Strongyloides* as opposed to *T. cruzi.*

False Positivity Rates of Assays

T. cruzi

Members voiced concern over false positivity rates of testing for *Strongyloides* and *T. cruzi*. Individual OPOs, the American Society for Histocompatibility and Immunogenetics (ASHI), AOPO, and regional meeting sentiment shared this concern.

The FDA has approved the use of Abbott Prism Chagas, Abbott ESA Chagas, and the ORTHO T. cruzi ELISA Test System for donor screening. There are two enzyme immunoassay (EIA) kits approved by the U.S. Food and Drug Administration (FDA) for blood and organ donor screening in the United States, the Ortho T. cruzi EIA test system (Ortho Clinical Diagnostics, Raritan, NJ, USA; approved December 2006) and Abbott Prism Chagas (Abbott Laboratories, Abbott Park, IL, USA; approved May 2010). The Ortho EIA is reported to have 100% sensitivity and 99% specificity in clinical trial data. However, the predictive value of a positive test will vary depending on the *T. cruzi* prevalence in the tested population.[35]

The Committee has also proposed confirmatory testing to mitigate false positive *T. cruzi* screening results. Two EIA test kits are FDA-cleared and are currently in use at commercial diagnostic laboratories. These are the Hemagen Chagas Kit (Hemagen Diagnostics, Inc., Columbia, MD, USA) and Chagatest EIA Recombinante v. 3.0 (Laboratorios Weiner, Rosario, Argentina). For the purpose of clinical diagnosis, no single assay has sufficient sensitivity and specificity to be solely relied on, therefore two serological tests based on different antigens (e.g. whole parasite lysate and recombinant antigens) and/or techniques (e.g. EIA and IFA, or EIA and RIPA) are used in parallel to increase the accuracy of the diagnosis.[36] Because of this, the Committee proposes to keep the original proposal requirement of submission of confirmatory testing through the CDC or performance of two different antibody diagnostic tests.

Strongyloides

The concerns over false positivity of *Strongyloides* screening tests are mitigated through affordable and unharmful treatment. The Committee emphasizes that organs can be utilized with positive assays and the correct treatment.

[35] Chin-Hong PV, Schwartz BS, Bern C, Montgomery SP, Kontak S, Kubak B, Morris MI, Nowicki M, Wright C, Ison MG. Screening and treatment of chagas disease in organ transplant recipients in the United States: recommendations from the chagas in transplant working group. Am J Transplant. 2011 Apr;11(4):672-80. doi: 10.1111/j.1600-6143.2011.03444.x. Epub 2011 Mar 14. PMID: 21401868.

[36] Ibid.

Insufficient Data to Support this Proposal

Some members stated this proposal is not justified by the data provided by the Committee. This limited feedback came from the International Society for Heart and Lung Transplantation (ISHLT), regional meetings, and individuals. The Committee recognizes and appreciates the burden of additional testing, which is why the testing requirements are tailored and balanced against the patient safety risk of transmission and severity of morbidity/mortality if transmitted. These are the two most common parasitic infections reviewed by the Committee. *Strongyloides* transmissions would be more prevalent if testing was not already completed by several OPOs, and treatment was not utilized. The Committee refers to the 603 recipient transmissions adjudicated as intervention without disease transmission since 2008.

Guidance and Education

There were requests from the community for guidance and education when implementing this proposal. Members asked for assistance in identifying assays that meet this policy requirement. Ex-officio CDC representatives were strongly supportive of this proposal and instrumental in its development. The Committee will work with CDC and FDA to ensure members are aware of available compliant testing.

Compliance Analysis

NOTA and OPTN Final Rule

The Committee submits this proposal under the authority of the National Organ Transplantation Act (NOTA), which states that the OPTN shall "adopt and use standards of quality for the acquisition and transportation of donated organs"[37] and under the authority of the OPTN Final Rule, which states, "[a]n OPTN member procuring an organ shall assure that laboratory tests and clinical examinations of potential organ donors are performed to determine any contraindications for donor acceptance, in accordance with policies established by the OPTN."[38] This proposal would assure that *Strongyloides* and *T. cruzi* testing of deceased donors is performed to determine if any additional measures should be taken to prevent transmission of parasitic infectious diseases for those who accept these donor organs.

OPTN Strategic Plan

This proposal aligns with the strategic plan goal to promote living donor and recipient safety by reducing transmission of parasitic infections through organ transplantation.

Implementation Considerations

Member and OPTN Operations

Operations affecting Transplant Hospitals

Modifications to deceased donor testing may require modifications to medical record systems, particularly for transplant specific modules.

[37] 42 USC §274(b)(2)(E).
[38] 42 CFR §121.6(a).

Transplant hospitals must also educate staff on changed criteria and risk discussion. Transplant hospitals will need to be prepared to receive and review additional infectious disease test results and have experts available to treat patients as medically appropriate.

Operations affecting Organ Procurement Organizations

OPOs will need to set up agreements or modify testing protocols to obtain lab testing for *Strongyloides* and *T. cruzi.* OPOs will need to modify their donor screening questions and documentation for identifying donors that were born in endemic countries for Chagas disease. Confirmatory tests will be needed for donors if a positive *T. cruzi* screening test is obtained.

This may involve technical modifications to their medical record systems and changes to data collection and reporting. Additional testing may require additional communication with transplant programs. OPOs will need to educate staff on the revised screening questions. Operational and documentation changes will be needed as well. OPOs will need to report results to the OPTN through the OPTN Improving Patient Safety Portal.

Operations affecting Histocompatibility Laboratories

This proposal is anticipated to minimally affect the operations of histocompatibility laboratories. Since there are no changes in histocompatibility testing, any changes would affect labs that perform infectious disease testing and/or archive donor blood specimens for OPOs.

Operations affecting the OPTN

This proposal would require implementation in the OPTN Computer System; specifically, the OPTN Donor Data and Matching System and the Data System for the OPTN.

This proposal requires the submission of official OPTN data that are not presently collected by the OPTN. The OPTN Contractor has agreed that data collected pursuant to the OPTN's regulatory requirements in §121.11 of the OPTN Final Rule will be collected through OMB approved data collection forms. Therefore, after OPTN Board approval, the forms will be submitted for OMB approval under the Paperwork Reduction Act of 1995. This will require a revision of the OMB-approved data collection instruments, which may impact the implementation timeline.

Resource Estimates

The OPTN Contractor estimates 780 hours for implementation. Implementation will involve updates to the OPTN Donor Data and Matching System to add new data fields for deceased donor infectious disease testing, education and training on the changes, and communication efforts about the changes. The OPTN contractor estimates 100 hours for ongoing support. Ongoing support will involve answering member questions and monitoring at 1-year and 2-years post-implementation.

Post-implementation Monitoring

Member Compliance

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

- Results of required *Strongyloides* testing
- Results of *T. cruzi* testing, if required
    - Evidence of the candidate being born in a country endemic to Chagas disease
    - Confirmatory *T. cruzi* testing, if there is a positive screening result for *T. cruzi*

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:

1. Volume of proven/probable *Strongyloides* or Chagas donor derived disease transmission events (PDDTE) cases reviewed by the OPTN DTAC that were submitted through the OPTN Improving Patient Safety Portal
2. Number/percent of deceased donors with a positive *Strongyloides* or *T. cruzi* screening test result reported on the DDR, and the associated overall distribution of *Strongyloides* or *T. cruzi* infectious disease test results for deceased donors

Conclusion

The policy change to require universal deceased donor antibody screening for *Strongyloides* and targeted *T. cruzi* screening for deceased donors born in countries currently classified as endemic for Chagas disease by the CDC is in response to donor derived patient safety events reviewed by the Committee. This proposal seeks to limit infectious disease transmission through organ transplantation while addressing patient safety concerns after determining *Strongyloides* and *T. cruzi* are the two most common causes of donor derived parasitic infections reviewed by the DTAC. This proposal aims to reduce preventable recipient morbidity and mortality from these infections.

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.

2.9 Required Deceased Donor Infectious Disease Testing

The host OPO is responsible for ensuring that *all* of the following infectious disease testing is completed in Clinical Laboratory Improvement Amendments (CLIA) certified laboratories, or in laboratories meeting equivalent requirements as determined by the Centers for Medicare and Medicaid Services (CMS):

1. Blood and urine cultures
2. Infectious disease testing for all potential deceased organ donors using FDA licensed, approved or cleared tests, as listed below:
    a. HIV antibody (anti-HIV) donor screening test or HIV antigen/antibody (Ag/Ab) combination test
    b. HIV ribonucleic acid (RNA) by donor screening or diagnostic nucleic acid test (NAT)
    c. Hepatitis B surface antigen (HBsAg) donor screening test
    d. Hepatitis B core antibody (total anti-HBc) donor screening test
    e. Hepatitis B deoxyribonucleic acid (DNA) by donor screening or diagnostic nucleic acid test (NAT)
    f. Hepatitis C antibody donor screening test (anti-HCV)
    g. Hepatitis C ribonucleic acid (RNA) by donor screening or diagnostic nucleic acid test (NAT)
    h. Cytomegalovirus (CMV) antibody (anti-CMV) donor screening or diagnostic test
    i. Epstein-Barr Virus (EBV) antibody (anti-EBV) donor screening or diagnostic test
    j. Syphilis donor screening or diagnostic test
    k. Toxoplasma Immunoglobulin G (IgG) antibody test

    Donor samples for all required HIV, HBV, and HCV testing must be obtained within 96 hours prior to organ procurement.

3. Infectious disease testing for all potential deceased lung donors using an FDA licensed, approved, cleared, or emergency use authorized, lower respiratory specimen test for SARS-CoV-2 (COVID-19) by nucleic acid test (NAT)

    Lower respiratory specimen test results for SARS-CoV-2 by nucleic acid test (NAT) must be available pre-transplant of lungs.

4. Infectious disease testing for all potential deceased donors for *Strongyloides* antibody, using either
    - an FDA licensed, approved, cleared, or Class 1, 510(k)-exempt test or
    - a Laboratory Developed Test (LDT), as described by the FDA.

5. Infectious disease testing for all potential deceased donors whose donor history reflects the donor's birthplace was in a country classified as endemic for Chagas disease by the CDC at the time of testing. The OPTN maintains a list of countries currently classified as endemic for Chagas disease by the CDC.

This testing must be performed using an FDA licensed, approved, or cleared donor screening test for *T. cruzi* antibody.

Within 72 hours of receipt of a positive *T. cruzi* antibody donor screening test, the host OPO must submit a sample for confirmatory testing. Confirmatory testing requires either

- submission through the CDC or
- performance of at least two different FDA licensed, approved, or cleared antibody diagnostic tests.

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Proposed Data Collection

1 OPTN Donor Data and Matching System

2 Data Removals

Infectious Disease Data Field	Values	Recommended Changes and Comments
Chagas NAT	Current Selection Options: Positive Negative Not Done Indeterminate Pending	Remove from the OPTN Donor Data and Matching System

3 Data Revisions

Infectious Disease Data Field	Values	Recommended Changes and Comments
Strongyloides	Current Selection Options: Positive Negative Not Done Indeterminate Pending	Change field name to "Strongyloides Ab" under the 'Infectious Diseases' section in Donor Summary
Chagas	Current Selection Options: Positive Negative Not Done Indeterminate Pending	Change field name to "T. cruzi Ab Screen" under the 'Infectious Diseases' section in Donor Summary

4 Data Additions

Data Field	Values	Recommended Changes and Comments
Was the donor born in a country currently classified as endemic for Chagas disease by the CDC?	Yes, No, Unknown	Add to Donor Information under Donor Summary

Serial Data Collection in OPTN Donor Data and Matching System

Data Field	Values	Recommended Changes and Comments
Was T. cruzi (Chagas) Ab diagnostic testing performed on the donor?	Yes, No, Unknown	Add to Donor Summary under 'Other Infectious Diseases'
Specimen date	Date	Add to Donor Summary under 'Other Infectious Diseases'
Time	Time	Add to Donor Summary under 'Other Infectious Diseases'
Specimen Type	Serum Whole Blood Plasma	Add to Donor Summary under 'Other Infectious Diseases'
Hemodiluted Specimen	Yes, No, Unknown	Add to Donor Summary under 'Other Infectious Diseases'
Test Method	Antibody (IgG/IgM/IgA) Other, specify	Add to Donor Summary under 'Other Infectious Diseases'
Result	Positive Negative Indeterminate Pending	Add to Donor Summary under 'Other Infectious Diseases'
Comments	Free text	Add to Donor Summary under 'Other Infectious Diseases'

Data System for Organ Procurement and Transplantation Network

Data Removals

Infectious Disease Data Field	Values	Recommended Changes and Comments
Chagas NAT	Current Selection Options: Positive Negative Not Done Indeterminate Pending	Remove from the OPTN Donor Data and Matching System

8 Data Revisions

Infectious Disease Data Field	Values	Recommended Changes and Comments
Strongyloides	Current Selection Options: Positive Negative Not Done Indeterminate Pending	Change field name to "Strongyloides Ab" under the Infectious Diseases section in Donor Summary
Chagas	Current Selection Options: Positive Negative Not Done Indeterminate Pending	Change field name to "T. cruzi Ab Screen" under the Infectious Diseases section in Donor Summary

9 Data Additions

Data Field	Values	Recommended Changes and Comments
Was the donor born in a country currently classified as endemic for Chagas disease by the CDC?	Yes, No, Unknown	Add to Donor Information under Donor Summary

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Appendix A: Proposed Data Definitions

OPTN Donor Data and Matching System

T. cruzi (Chagas) Ab screen: Indicate whether the specimen that was used for the test was hemodiluted. Select Yes, No or Unknown from the drop-down list of options. Select the result of the test. If a test has been run but results have not been received, select Pending. If it is not known if a test has been run, select Not Done. If the results from an infectious disease test were inconclusive or equivocal, select Indeterminate. If the donor's birth place is unknown, testing is not required by policy.

Strongyloides Ab: Indicate whether the specimen that was used for the test was hemodiluted. Select Yes, No or Unknown from the drop-down list of options. Select the result of the test. If a test has been run but results have not been received, select Pending. If it is not known if a test has been run, select Not Done. If the results from an infectious disease test were inconclusive or equivocal, select Indeterminate.

Was T. cruzi (Chagas) Ab diagnostic testing performed on the donor?: Indicate whether T.cruzi Ab diagnostic testing was performed on the donor. Select Yes, No or Unknown from the choices. If "Yes" is chosen, additional data collection fields display. If the donor's birth place is unknown, testing is not required by policy.

Specimen Date: Enter the date the test was performed. The date must be in the following format: MM/DD/YYYY. A calendar link is available.
Time: Enter the time the test was performed.
Specimen Type: Select the type of the type of specimen from the drop-down list of options. Note: For specimens only, an indication of whether the specimen was hemodiluted.

- Blood

Examples include:
Plasma
Serum
Whole blood

- Other, specify

Hemodiluted Specimen: If the Specimen Type is "blood", then indicate whether the specimen that was used for the test was hemodiluted. Select Yes, No or Unknown from the drop-down list of options. If the specimen type is not Blood, then leave blank.

Test Method: Select the test method from the drop-down list of options.

- Antibody (e.g. IgG)

Result: Select the result of the test from the drop-down list of options. If a test has been run but results have not been received, select Pending. If the results from an infectious disease test were inconclusive or equivocal, select Indeterminate. Note: OPO users: Please be sure to include in your process steps to update with the final result. The result must be updated in DonorNet because the T. cruzi antibody diagnostic test data collection is not available on the TIEDI® DDR. Similar to culture reporting, the new T. cruzi antibody diagnostic test section will remain editable after Donor Organ Disposition (feedback) is complete.

- Positive
- Negative
- Indeterminate
- Pending

Comments: Enter documentation of other pertinent information regarding the test, such as when pending results are expected back. This field is optional.

Data System for Organ Procurement and Transplantation Network

Was the donor born in a country currently classified as endemic for T. cruzi (Chagas) disease by the CDC?: If the donor's birthplace is known, please use the linked OPTN resource to answer this question. If the donor's birthplace is unknown, please select 'unknown.'

Serology: For each of the infectious diseases listed, select the result of the test (**Positive, Negative, Not Done, Indeterminate).** These fields are **required**. (List of Serology Results codes)

HIV Serology Results
HIV Ag/Ab Combo Results
HTLV Serology Results
Syphilis Serology Results
Anti-CMV Serology Results
HBsAg Serology Results
HBcAb Serology Results
HCV Serology Results
HBsAb Serology Results
EBV (VCA) (IgG) Serology Results
EBV (VCA) (IgM) Serology Results
EBNA Serology Results
T. cruzi (Chagas) Ab Screen Results
West Nile Serology Results
Toxoplasma (IgG) Results
Strongyloides Ab Results

Was the donor born in a country currently classified as endemic for T. cruzi (Chagas) disease by the CDC?: If the donor's birthplace is known, please use the linked OPTN resource to answer this question. If the donor's birthplace is unknown, please select 'unknown.' If the donor's birthplace is unknown, T. cruzi (Chagas) testing is not required by policy.