OPTN Ethics Committee
Meeting Summary
October 1, 2025
Teleconference

Andy Flescher, PhD, Chair
Sanjay Kulkarni, MD, Vice Chair

Introduction

The Ethics Committee ("Committee") met via teleconference on 10/1/2025 to discuss the following agenda items:

1. Welcome and Announcements
2. Workgroup Updates
3. Review First Draft: Xeno White Paper
4. Collaborating Committee Question and Answer: Xeno White Paper

The following is a summary of the Committee's discussions.

1. Welcome and Announcements

No decisions made.

The Chair welcomed the Committee members and presented the agenda. The Chair remarked that the Committee has a few points to discuss regarding the xenotransplantation white paper, highlighting the need for alignment. The Chair emphasized the importance of discussion towards achieving consensus.

The Chair noted that the Committee will be meeting to vote on the Xenotransplantation White Paper on November 20th, 2025, and urged participation at that meeting.

OPTN Contractor staff also notified the Committee of upcoming Board of Directors meetings, and noted that OPTN Directive information is available on the OPTN site. OPTN contractor staff shared updates on the allocation out of sequence directive and the donation after circulatory death (DCD) policy development directive,

The Ethics Representative on the Allocation Out of Sequence Workgroup explained that this Workgroup has been divided into 3 subgroups focusing on expedited placement, policy compliance, and offer efficiency. The Ethics Representative explained that the policy compliance team is evaluating non-compliance and considering how to notify of non-compliance and encourage increased compliance.

The Chair provided an update on the DCD policy development directive, noting that the DCD Policy Development Workgroup is focusing on developing a sensible checklist to ensure appropriate protocols are followed during DCD donation processes. The Chair remarked that this Workgroup was subdivided into a pause point subgroup and deceased donor family communication.

The Chair remarked positively that the Ethics Committee is being tapped to support these OPTN directives.

Summary of discussion:

There were no further questions or comments.

2. Workgroup Updates

The Committee received an update on the Allocation Out of Sequence Workgroup, the DCD Policy Development Workgroup, and the Modify Living Donor Psychosocial Evaluation Policy Workgroup.

No decisions made.

Summary of Presentation and Discussion:

The Ethics Representative on the Allocation Out of Sequence Workgroup explained that this Workgroup has been divided into 3 subgroups focusing on expedited placement, policy compliance, and offer efficiency. The Ethics Representative explained that the policy compliance team is evaluating non-compliance and considering how to notify of non-compliance and encourage increased compliance.

The Chair provided an update on the DCD policy development directive, noting that the DCD Policy Development Workgroup is focusing on developing a sensible checklist to ensure appropriate protocols are followed during DCD donation processes. The Chair remarked that this Workgroup was subdivided into a pause point subgroup and deceased donor family communication.

The Chair remarked positively that the Ethics Committee is being tapped to support these OPTN directives. The Chair emphasized that the Ethics Committee is well regarded in the OPTN.

OPTN Contractor staff provided an update on the Modify Living Donor Psychosocial Evaluation Policy Workgroup, sharing that the MPSC is currently investigating prior living donor deaths, including suicides, that were reported between October 2024 and September 2025. The Ethics Committee representative on this Workgroup emphasized that this number of deaths is higher than usual, noting that 6 deaths were attributed to suicide. OPTN contractor staff explained that the overall concern is with the psychosocial evaluation and whether updates may be needed. This Workgroup has met twice, and has reviewed reported death cases, finalized a data request, drafted and finalized a memo to Living Donor programs, and initiated discussion of potential project work, including literature review, survey, policy change, and guidance options. The Living Donor Committee will then consider sending the project to the Policy Oversight Committee for project approval. An Ethics Committee representative on the Workgroup explained that there is also a focus on the quality of follow-up, and consideration for increased standardization. The other Ethics Committee representative added that demographic information is important to understanding these cases, particularly in consideration of the vulnerability taxonomy.[1]

One member asked if the Modify Living Donor Psychosocial Evaluation Policy is expecting to update policy within the next few months. OPTN contractor staff explained that the Living Donor Committee first needs to agree to send the project to the Policy Oversight Committee for approval, and the Policy Oversight Committee would need to approve the project as well before a policy change could go forward. The Workgroup will continue to meet once a month, for now. OPTN contractor staff noted that the Workgroup has considered utilizing special public comment, but that it is not expected to go out in January public comment. OPTN contractor staff explained that this project is moving forward as fast as possible.

[1] Ross LF, Thistlethwaite JR. Developing an ethics framework for living donor transplantation. J Med Ethics. 2018 Dec;44(12):843-850. doi: 10.1136/medethics-2018-104762. Epub 2018 Jul 4. PMID: 29973389.

3. Review Xenotransplantation White Paper Draft

The Committee discussed key points in the Xenotransplantation White Paper Draft as the paper continues to be drafted.

The Chair and Vice Chair will incorporate the major discussion points below into the next draft of the white paper. No decisions are final.

Presentation Summary:

In introduction of the drafting process, the Chair explained that this draft has been mindful of word count, emphasizing the importance of explaining these complicated issues in understandable and concise ways. As a result, some pieces have been cut, but are preserved in prior drafts. The Chair explained that the Committee will review the next draft at the next meeting, with continued editing to address major concerns post-meeting. The Committee will meet and vote to send the paper to the Policy Oversight Committee for January Public Comment in November.

Current Paper Outline:

1. Introduction and Background
2. Sections I, II, III, IV
3. Conclusions – not yet written
4. Appendix:
    a. Glossary
    b. Scenarios and positions chart – suggested

Discussion summary:

The member who suggested the positions chart explained that a chart listing all the possible situations for xenotransplantation and how the Committee's conclusion about management could be applied to that situation would be helpful. This chart could also refer to the reasoning and logic behind the Ethics Committee recommendation. Another member remarked that drafting this chart could reveal gaps in clarity in the paper, which could help the Committee improve upon the draft. The member recommended that the Committee be substantively involved in the drafting of the chart, and expressed support for its development and inclusion.

The Chair explained that the initially recommended chart only included 5 scenarios, but that it may be more difficult for the Ethics Committee to consider how the analysis translates to specific recommendations and considerations.

Presentation Summary:

First draft discussion: Reconcile key points in White Paper

- How do the rights of research participants weigh on the scenarios presented in the paper?
- What is the viability of considering a xenotransplant trial candidate "active" on the waiting list?
- Further discussion:
    - Option of a moratorium, wherein a xenograft trial participant would be granted a period of time on the waiting list in an inactive status following the xenograft
    - Discussion of inactive accrual of wait time vs. moratorium

Rights of Research Participants

The Chair asked if it's more appropriate to consider a research participant as a volunteer who is owed a great debt of gratitude, or as a person who is fortunate to have been chosen as a clinical participant and recipient of an organ. The Chair remarked that the paper is not about selection criteria, but it is important to consider the rights of the participants to opt out, and if they opt out, what rights they then have. The Chair remarked that, obviously, any clinical trial participant always has the right to opt out at any time. The Chair offered a scenario where a patient who received a

The Chair explained that the Committee's comments held a notion that insinuated at points that the clinical trial participant understood that to date, xenotransplants have not succeeded for longer periods of time, and therefore has a right to anticipate the xenotransplant's failure and thus is conferred additional prerogatives in terms of wait listing. The Chair continued that this viewpoint may double down on respect for persons at the expense of social justice and utility. The Chair expressed discomfort at how the Paper will be perceived by the larger transplant community with the emphasis that came in clinical participants' rights.

Active vs. Inactive Waiting List Time

The Chair offered a scenario where a patient has a currently functioning xenograft and is actively listed on the waiting list, and thus is considered eligible for a human graft. The Chair explained that this is an inappropriate way of describing what would and should happen. The Chair agreed that it is helpful to understand active listing as an option, but explained that it is not a viable ethical option. The Chair continued that Committee leadership wants to ensure the paper strongly conveys that. The Chair added that other members of the Committee disagree, and noted that there are some work arounds about the options available to clinical participants.

The Chair noted that it is important for the Committee to talk these issues through together before continuing to draft the White Paper, in order to ensure consensus and alignment.

Discussion summary:

One member emphasized the friction between the ethical and the practical, noting that a patient could be active on the waitlist, but practically and realistically, a program wouldn't retransplant them while they had a functioning xenotransplant. The member explained that because xenotransplant is so rare, there could be undue influence that a patient may feel they should take part in the xenotransplant trial because they believe they will be owed and more likely to receive a human graft later if the xenotransplant fails.

The Chair remarked that, to say that someone wouldn't get a functioning allograft during the time in which the received xenograft is functioning, is not to say that, should that xenograft fail, the patient wouldn't immediately go from inactive to active. The Chair continued that it's the anticipatory piece is logistically and ethically problematic.

A member shared that they had read accounts from xenotransplant recipients, and shared that from one participant's perspective, they had a choice to continue on dialysis and wait 7-10 years to receive a kidney transplant or to pursue xenotransplant. The member explained that the patient saw xenotransplant as a bridge to an allograft. The member shared that this candidate is still on the waiting list, but that they are not sure if the patient is active or inactive. The member continued that if the patient was listed as active, he could still receive allograft kidney offers. The member explained that if he is listed as inactive, the patient would not receive an allograft offer, even if it was an appropriate match. The member expressed interest in discussing a similar situation, explaining that it is in the interest of science for the patient to stay in the trial. The member remarked that they feel it could be an

ethically viable option for the patient to be active on the allograft list so that the patient doesn't miss a chance at allograft transplant.

Another member remarked that the principle will always be that the system should not give a kidney to a patient with functioning kidneys, be it xenotransplant graft or deceased donor graft or living donor graft. The member explained that this principle will guide most transplant programs to determine whether and how to list a patient. The member noted that, in the scenario offered, if a patient with a functioning xenograft has an eGFR of 30-40 over 20 years post-transplant, the program may decide to remove that patient from the waiting list, because the kidney is functioning. The member explained that it is not an automatic decision, but one that programs will consider holistically.

One member explained that they are more interested in the idea of obligatory beneficence and respect for persons towards the recipients. The member remarked that this is a novel situation, and that one of the current trials is not a clinical trial, and so has no weight on equipoise. The member added that it's not yet standard of care. The member remarked that the term "rights" needs to be removed, and that the Ethics Committee needs to focus on what the ethical obligations to the xenotransplantation participants are. The member noted that the original principles for use in bioethics[2] were written for research participants, and it's from them the idea of obligatory beneficence comes.

The Chair noted that one of the things about the Beauchamp and Childress text is that it balances these principles. The Chair noted that these things can be true weighed against the other principles, namely the utilization – or stewardship of scarce resources – and social justice. The Chair explained that transplantation is a zero sum game and there is a social justice issue in consideration of the other candidates on the waiting list. The Chair agreed that this is unique, and it is important to get right the actual situation of xenotransplantation. The Chair continued that a participant in a xenotransplantation trial is much more likely to be fortunate recipient of a life saving graft as opposed to a risk taking participant who is owed a debt of gratitude. The Chair continued that it's not just logistical, but ethical. The Chair added that furthermore, in considering perception, the Ethics Committee is not pursuit.

The Chair asked how the member would respond to those considerations. The member responded that there are obligations to participants in research and that must be considered in balancing the principles. The member explained that the participants are not being told that this is for their benefit, and that would be the therapeutic misconception to be avoided. The member remarked that the characterization of these clinical trial participants as fortunate to receive a graft implies this misconception, and that this characterization shouldn't be used in considering these research participants. The member concluded that these participants are not in it for their own benefit. The Chair responded that this is a claim about which there is a diversity of opinion, and disagreed. The Chair invited other responses.

A member noted that previously, the Vice Chair had made a point that the system does not transplant people with a functioning kidney. The member continued that this cuts through a lot of the objections, noting that if the kidney is functioning, the patient could be accruing a lot of time inactively on the list, but at that moment, that patient is not a candidate to receive an allograft. The member expressed support for this principle. The member posed a hypothetical that xenotransplant recipient is taking medications that make them sick or weak and the xenograft is allowed to go non-functional or be removed. At the point at which the patient had a non-functioning kidney, the patient could be made active with accrued waiting time. The member continued that the hypothetical being discussed currently

[2] Beauchamp T, Childress J. *Principles of Biomedical Ethics*: Marking Its Fortieth Anniversary. Am J Bioeth. 2019 Nov;19(11):9-12. doi: 10.1080/15265161.2019.1665402. PMID: 31647760.

is a patient who has a xenotransplant graft that is then essentially swapped out for a human allograft. The member continued that this doesn't make sense.

One member agreed, and clarified that they were not talking about the hypothetical where a xenograft recipient receives an allograft transplantation while the xenograft is still functioning. The member clarified that the question relates to how clinical trial participants are classified. The member expressed that in principle, it is important to uphold the value of protecting and acknowledging the vulnerability of people who become research participants. The member added that utility should not run over the respect for human persons. The Chair agreed, noting that this could be a footnote that characterizes the xenotransplant clinical trial participant, capturing all of the nuance.

The Chair reminded the Committee that the characterization of a clinical trial participant is not the main goal of the paper, though it is relevant. The Chair explained that the Ethics Committee begins with receiving a xenotransplant recipient and works from there. The Chair remarked that the Committee made headway on the active and inactive waiting list discussion.

A member agreed with commitments to research participants, and noted that generally, the obligations of researchers to participants is relatively straight forward, especially with consideration of obligations for remedy and care after a decision to withdraw from the trial. The member continued that the difference here is that while the xenotransplant trial participants do have rights, the enterprise that has the capacity and potential to provide those remedies isn't just the research group, but is the entire transplant system. The member continued that the question then becomes what the transplant system owes the xenotransplant trial participant. The member asked if participation in xenotransplantation trial sets apart participants as a class from other patients waiting for an allograft, and whether things like graft performance and medical need should be considered. The member continued, asking if the system should be treating participants as a class and grant them certain interests that the system has to honor, or if the participants should be treated similarly to other patients. The member expressed that they are not convinced that there is something about xenotransplant graft function as opposed to another bridge therapy. The member continued that their position would be that eligibility to be listed as active and then to accept an offer should be based primarily on clinical status.

The Chair posed a hypothetical that xenotransplant patients should be treated the same as other patients waiting for an organ. The Chair explained that clinical trial participants could experience, as a result of participation, psychological distress or physical hardship, and that those participants should never be deprived the option of withdrawing. The Chair continued that potentially, these participants could develop into worse condition as a result of participation. The Chair remarked that there is a distinction to be drawn between how the system categorically treats people as a default and what is subsequently done as the system learns what happens in real time. The Chair remarked that one of the drafting groups considered this thoroughly. The Chair offered that this distinction could be a way out of this further conundrum.

The Chair noted that at the outset, all patients who are awaiting a kidney are treated the same, with no special precedence given to the recipient. The Chair continued that as things occur because of participation in xenotransplant, that could warrant additional priority. The Chair continued that one wouldn't assume that xenotransplant participation gives a patient a boost or qualifies them for active listing as a classification. A member remarked that there seems to be consensus that one's status as a xenotransplant participant does not change the criteria used to determine a patient's eligibility to be actively listed on the waiting list. The member continued that eligibility does not change by virtue of being a xenotransplant participant.

The member remarked on the hypothetical situation where a xenotransplant recipient is considered as having a functioning kidney, and thus would not be eligible to receive a human allograft. The member made a distinction that this patient has a function pig kidney, not a functioning human kidney. The member asked that the medical criteria for when that patient should be considered active could change. The member asked whether following xenotransplant, if the organ is removed, dialysis is the same as prior to transplant, or if a second transplant impacts access. The member continued that it may not be fair to assume that a functioning pig kidney is the same as a functioning human kidney. The Chair continued that "function" depends on the same eGFR qualification and considerations.

The Chair remarked that this paper will have to make certain assumptions, particularly as the information required to answer certain questions is simply unavailable.

One member asked whether the performance of the xenograft matters regarding the obligations the transplant system has to the participant. Another member responded that the graft performance does not, because individual benefit is not being promised. However, if graft performance is being linked to active status on the list, that depends. The member continued that as a rule, patients are neither rewarded nor punished for being in a clinical trial in terms of their eligibility for the next standard of care treatment. The originally asking member noted that benefit cannot be promised, but the Committee is agreeing that performance is a relevant consideration when considering active status. The member continued that active status is the only remedy or best standard of care. The other member remarked that it's a case by case. The member continued that if a patient chooses to participate in a clinical trial, they should be able to opt out of participation; whether or not they should be eligible for an allograft depends. The originally asking member responded that, recognizing a participant's absolute right to withdraw from a xenotransplant trial at any time, the question then becomes what obligations the transplant system has to resolve the consequences of the decision to withdraw. The member continued that is it that the system has an obligation to prioritize them as a class, even if they withdraw while having a functioning graft. The member asked if it would be ethically defensible for a patient to refuse a functioning xenograft on the background of an absolute right to withdraw and therefore to fix it with allograft access. The Chair remarked that any one can withdraw from any clinical trial, period. The Chair continued that this doesn't have to be answered definitively, but that this group can develop guide posts. The Chair explained that once a patient withdraws from a clinical trial, what priority the patient receives at that moment in time will depend on other things that will have been learned through their experience.

One member emphasized that the question being considered as whether, as a class, the research participants get to keep active status while having an operational xenograft, or if that status is suspended and those patients only given a particular status on the waitlist after failure or the decision to withdraw, maybe including explant. The member continued that it does matter whether or not they maintain active status while having a functioning xenograft as opposed to only getting active status after a decision to withdraw and being explanted.

The Chair continued that another consideration is what should be communicated to the patient about the consequences of withdrawing, and would that communication constitute any form of coercion.

A member remarked that the Committee is talking in cycles, and that this issue has already been resolved in the transplant community even outside of xenotransplantation. The member added that the rule of thumb is simply that if the kidneys are functioning well enough, even if listed, the patient will not be active. The member explained that, for example, a program may have a few polycystic kidney disease patients listed with GFR that dips to 18 or 15; those patients may have improved kidney function, but they remain inactive until their function falls again. The member continued that a candidate's participation in a xenotransplant will never be missed. If a patient has received a xenotransplant but

opts out, that patient will need to follow withdrawal protocol. The member continued that if a patient withdraws from a xenotransplant trial, then it must be decided whether they're a candidate for deceased donor transplant. The member continued that at this point, it's not subject to a simple yes or no because there are numerous variables and factors that determine whether a patient is a candidate for transplant. The member continued that, if the patient has an eGFR of 70 at the point of withdrawal, the program is not going to transplant that patient.

The Chair discussed several action items:

1. Two members will write up what does justice to the experienced perspective of the clinical trial participant in such a way that does not foreclose options for that individual, as a footnote
2. Two members will write address the basic understanding of how both human allografts and xenoallografts are assessed as functioning, and can it be assumed if the answer to that question is the same for both. As a footnote, the write up needs to highlight what it looks like to have a xenograft that is functioning and what it looks like to have a xenograft that is no longer functioning
3. The paper will need to raise the questions that arise if a participant decides to withdraw; the Ethics Committee is not in a position to answer these questions.

The Chair continued that the third item should also include feedback from the Patient Affairs Committee, particularly because answers to these questions will need to be communicated to the patients.

A member noted that functioning and non-functioning is defined by whether or not the patient needs dialysis. Another member commented that GFR could also define functioning. One member volunteered to define a functioning allograft as an eGFR of 20 or more; non-functioning or primary failure as an eGFR less than 20 or the patient needs dialysis. The member added that there is a still a question of whether this deceased donor definition is generalizable for xenotransplant. The Chair continued that this definition could be inserted. One member remarked that the simplest approach would be to use the same definition of organ failure as is used to qualify patients for the waitlist. The member continued that a xenograft recipient with an eGFR of 50 is not likely going to be put on dialysis. The member explained that there isn't a need to develop a different definition of functioning or non-functioning kidneys. The member continued that liver recipients would still be serviced by the MELD, regardless of whether they received a xenograft. The member remarked that kidney waiting time accrues while a patient is inactive.

One member remarked that when talking about the effect of graft performance and medical need, there is a difference between considering these as the basis for access to the waiting list, as opposed to graft performance on the freedom to withdraw from a trial. The member continued that on the one hand, graft status should not have any effect on the freedom of a trial participant to withdraw from a trial. At the same time, graft performance carries weight on access to active status. The member emphasized that it doesn't affect a participant's right to withdraw, nor does it affect the obligation to remedy the consequences of withdrawing, but it does carry weight as to whether or not the patient has access to active status on the waiting list. Another member offered that the Committee could create another category between active and inactive of "xenotransplant trial status," such that a participant with an eGFR greater than 20 but an infection due to the nature of the graft could have a discrete category. The member asked if such a discrete category would make sense. Another member emphasized that this then creates a new class of candidates who are xenotransplant recipients, and that it becomes important to justify the standing of that class relative to others in the transplant system. The member continued that, if it's giving them a different kind of pathways, what is the impact to other patients who

are also looking to receive organs from the same supply. The member continued that it is important to ask whether that becomes a pathway that grants special or accelerated access relative to others.

A member responded that this assumes that research participants are gaining from the research, and noted that the fairness issue can be taken off the table. The Chair remarked that others disagree, adding that intentions of the participant aside, there is objectively a benefit for the participant that must be considered. The member continued that if it's in an FDA approved clinical trial, then equipoise is assumed, such that the benefits likely outweigh the harms, but there is no guarantee. The member continued that this lack of guarantee makes it not a fairness issue to others on the waiting list. The member continued that a xenotransplant recipient who has an eGFR greater than 20 and no other symptoms that then withdraws and has that xenotransplant remove could not automatically demand to be on the waitlist in the same way that they would have been had they not received a xenotransplant. The Chair raised that the emphasis in the case of xenotransplantation should be on benefit.

One member asked how success is being measured in the trials, asking if that science holds the same for a xenograft kidney as for an allograft kidney. The Chair remarked that this is the assumption he had been making, and asked if there was any reason to think this wasn't true. The Chair noted that further nephrologist input can be requested, and that the Committee will follow up.

The Chair asked for confirmation that the Committee seems to be reaching consensus that failure cannot be anticipated given past performance, but that the Committee is receptive to immediately actively listing once failure occurs and further calibrating priority recommendations based on the things that happen as a result of clinical trial participation. The Chair noted that this addresses the distinction between anticipation and immediately after organ failure. The Committee agreed.

A member remarked that it is good to represent all of the positions in the paper.

The Chair explained that there is a distinction between inactive listing where the candidate is accruing time but not eligible to receive offers while the graft is function and the moratorium concept wherein a xenograft trial participant would be granted a period of time on the waiting list in an inactive status following the xenograft. The Chair shared that Committee leadership's sense is that inactive listing is the most appropriate option.

One member explained that a patient is accruing time while inactive, so it's either continuous inactive or moratorium inactive. With continuous inactive, the patient still accrues time but is not eligible for the offer. In the alternative, with the moratorium concept, that the patient accrues time for a period up to the end of the moratorium duration. The member explained that the question is whether the Committee recommends indefinite accrual of time in the inactive status or whether the Committee feels that a ceiling should be put on the amount of time accrued in the inactive. The Chair shared that the concept of a moratorium was discussed by the OPTN Board of Directors (the Board), and that the Committee is doing its diligence in considering the moratorium.

One member expressed concern that xenograft recipients accruing time would have an impact and potentially disadvantage those patients who are active on the waiting list. Another member responded that if the patient is listed as inactive, they won't appear on the match run. The member continued that if the xenograft participants are left active on the list and have more time or priority based on points, then those patients may appear ranked in front of other patients who have less waiting time. The concerned member asked if there should be a moratorium on accruing waiting time.

A member remarked that the challenge with the indefinite waiting time is that the patient then gets benefit both from a functioning graft and the accrual of the wait time. The member remarked that the alternative is that there could be a period of time where the accrual of wait time stops. The member

continued that theoretically, in either case, there isn't a disadvantage to candidates who are active because the xenograft recipient is inactive.

The Chair expressed feeling strongly on behalf of respect for persons, expressing support for inactive listing with continuous accrual of waiting time. The Chair asked if the Committee feels that is an inappropriate recommendation. The Chair added that if at some date when xenotransplant as bridge therapy may become standard of care, this question could be reassessed. The Chair remarked that this is an opportunity for the Ethics Committee to make a concrete recommendation.

One member asked if the waiting time accrual is being framed as compensation or remedy or incentive for participation in the trial. The Chair noted that is a subsequent question, but that consists of the points mentioned previously about equipoise and the contribution of clinical trial participants. The Chair remarked that it doesn't necessarily need to be framed. The member expressed support for inactive listing with continuous waiting time accrual, adding that it is important to be thoughtful about how to respond to criticism that the clinical trial participant is receiving excess benefit of having both a functioning graft and accruing waiting time.

The Chair asked if any Committee members were not okay with recommending that xenotransplant recipients are listed inactively with continuously accruing waiting time. A member agreed, but noted that how this is framed is important. The member explained that given that currently, these are not considered equivalent therapies, the Committee feels it's fair for those xenotransplant recipients to remain inactively listed and accruing waiting time, at least for those organs allocated by time. The member continued that in the future, when these therapies are considered either a bridge to an allograft transplant or equivalent therapies, this may need to be readdressed. Another member agreed.

The Chair asked if any members support the moratorium idea over inactive listing with continuous waiting time accrual, noting the latter is more favorable to the clinical trial participants.

One member remarked that the term "equivalent therapy" is better than standard of care because it reinforces that the xenotransplant recipient is not receiving undue benefit. The Chair explained that standard of care is a term often used, and added that the Committee can utilize a foot note that notes equivalent therapies may be a better term, but the language is not yet finalized.

The Chair remarked that it seems the Committee has reached consensus about recommending inactive listing with continuous waiting time accrual for xenotransplant clinical trial participants, and not something less favorable.

The Chair added that it may not make sense for the Committee to weigh in on the completely independent of what a xenotransplant clinical trial participant is insofar as it bears on the rest of the Paper, and recommended thoughts on that be woven into other parts of the Paper. A member agreed.

4. Collaborating Committee Question and Answer: Xenotransplantation White Paper

The Chair provided an overview of the Ethical Analysis of Possible Impacts of Xenotransplantation on Human Allograft Organ Allocation White Paper, and members of collaborating OPTN Committees provided comment.

The Committee will incorporate a section in the White Paper to discuss how ethics may differ when considering xenotransplantation as a specific bridge therapy.

Presentation summary:

This paper will focus on how xenotransplantation will interface with the human allograft allocation system. The paper will also evaluate the ethical issues related to appropriate access to allograft allocation for xenotransplantation candidates and recipients.

In April of 2024, a memo on this topic was submitted by the Ethics Committee to the OPTN Executive Committee. Support from the Executive Committee and HRSA was confirmed. The paper is anticipated to go out for public comment in January 2026, and go to the Board in June of 2026.

This paper includes questions of how xenotransplantation interfaces with the human organ allocation system and thorough analysis of allograft waitlist status, timing, and priority of xenotransplant graft recipients. Initial listing, accrual of waitlist time, active or inactive status on waitlist, whether harms or benefits are incurred as a result of participation in xenotransplantation, how those should be reflected in status, and finally, whether there is some notion of reciprocity for those who participate in xenotransplantation trials in terms of priority status.

The paper does not include changes to policy, bylaws, or data collection; xenozoonosis, privacy rights, and the tension that exists between third party public health concerns and autonomy/privacy rights; animal rights; human subjects ethics questions; other issues that are out of scope.

The major questions discussed in the white paper include:

- How does the eligibility to participate in a xenotransplant clinical trial impact the eligibility for and timing of a patient's initial waitlisting for a deceased donor allograft?
- How, if at all, should receiving a xenotransplant in a clinical trial impact a patient's continuing active status on the allograft waiting list?
- How should prior receipt of a xenotransplant affect eligibility to be listed for a subsequent deceased donor allograft?
    - Compensating for harms and accounting for benefits question
- Should former clinical trial participants with a failed xenograft receive special consideration for subsequent receipt of a deceased donor allograft
    - Priority points question

The Committee had extensive discussion on what it means to be a xenotransplant trial participant and if this should bear on any sorts of initial priority for that person by virtue of their clinical trial participation in determining waitlist status and timing. The Committee also discussed whether waiting time should accrue under active or inactive status, or whether there should be a moratorium on waiting time.

Discussion questions:

- Are there any major questions or concerns about the paper?
- Are there ethical considerations not addressed?
- Does the paper overview, as provided, address relevant ethical principles of organ transplant – nonmaleficence, respect for persons, and utility?

<u>Discussion summary:</u>

The Chair of the Heart Committee asked how the Paper handles the issue of xenotransplant being used as an alternative to allograft transplantation instead of as a bridge to allotransplantation. The Chair of the Heart Committee continued that, in the pediatric transplant community, there is a perspective of xenograft hearts as an alternative to ventricular device implants because they can be size matched and received on demand; this is particularly in the early stages of xenotransplant where outcomes are less predictable. The Chair of the Heart Committee explained that, in such a case, it would be preferable to maintain a xenotransplant recipient on the waiting list actively at status.

The Chair responded that the analysis begins at the point in time that someone defacto is a clinical trial participant. The scope of the paper does not weigh in on whether a patient should have one therapy or another; the paper begins at the point of selection. The Chair explained that why and how a patient is selected for xenotransplant is relevant to future analysis. The Chair noted that the paper is self aware that the technology is advancing and that empirical assumptions made at one point in time will be superseded by a different set of empirical assumptions at a subsequent point in time. The Chair continued that as xenotransplantation is revealed to be a more sustainable kind of therapy, there becomes a subsequent concern for accruing two different benefits from two different pathways at once; at this point in time it's not as pressing of a concern. The Chair explained that the Paper denotes the present state and the future state may diverge.

The Chair of the Heart Committee asked if the White Paper takes a position on whether someone can maintain a high status of urgency despite having a xenotransplant.

The Chair explained that currently, the White Paper takes the position that the viability of a xenotransplant is assessed by the same criteria by which a human allograft is judged; such that a graft is functioning if the candidate's eGFR is above 20. The Chair continued that that person is not eligible to be actively listed, but that eligibility changes when the graft is no longer functioning. However, that person is eligible to be inactively listed and accruing waiting time.

The Chair of the Heart Committee noted that this answers the question for kidney, but that for heart, the question isn't just end organ function. The Chair of the Heart Committee provided an example, noting there are patients in ventricular assist devices that are bridges to transplant, and the more ventricular assistance that is needed, the higher urgency the patient is. The member continued that, in the case of a xenotransplant, especially for a pediatric patient, the question is not whether the graft provides adequate output, but rather how long the graft will do that and what the complications will be of providing the xenotransplant as an alternative to or a bridge to human transplant. The Chair of the Ethics Committee remarked that this hasn't yet been thoroughly thought through, and noted that language on how to think it through is welcomed.

A member noted that organs other than kidney are allocated by need. The member explained that the Ethics Committee had not yet felt that xenografts are to be a bridge to allograft transplant. The member continued that the Ethics Committee is looking at current state, where the vast majority of xenotransplants are considered investigational devices. The member added that it may come down to the individual organ committees to say what qualifies the status, as it wouldn't be appropriate necessarily for the Ethics Committee to say what makes sense for each organ individually. The Chair agreed.

An OPTN Liver Transplantation Committee representative noted that ultimately, guiding principles of non-maleficence and respect for autonomy are going to be very similar among different organ types, but utility and urgency are going to be very different organ to organ. The member asked how the Ethics Committee is going to consider that the ethical issues for different organs may be different, given that the way these grafts fail and the urgency when they fail is going to differ based on the organ type.

The Chair explained that there is a working definition about what constitutes success or failure with regard to a kidney graft, and the Committee defers to other Committees about the answer with regard to other organs. Regardless of those definitions, the Chair explained, the conceptual position that the Committee is going to take is that while those organs are considered functioning, those patients will not be actively listed and waiting time will continue to accrue. The Chair continued that the patients will be active status at the point in time that those organs are no longer functioning.

The Chair of the Heart Committee expressed disagreement. The Chair of the Heart Committee presented a hypothetical scenario where a patient is 6 months old with single ventricle heart disease and pulmonary vascular resistance. The Chair of the Heart Committee explained that a single ventricular assist device (VAD) can't be put in. The Chair of the Heart Committee continued that the options for this patient would be either a biventricular assist device In with a bridge to transplant mortality of 50 percent, or a xenotransplant. The Chair of the Heart Committee continued that it's not clear how the xenotransplant is going to do, and the best data is that the xenotransplant may give 3 months-1 year of life, which is on par with the average waiting time for a status 1A patient. The Chair of the Heart Committee added that the xenotransplant is now a viable alternative to providing the same type of support that a ventricular assist device would provide for a patient with dilated cardiomyopathy who can safely be bridged with a VAD. The Chair of the Heart Committee explained that if the hypothetical 6-month old patient were to receive a xenotransplant and be inactive until the graft fails, that patient is going to die on the waiting list. The Chair of the Heart Committee continued that this would put up barriers to the idea of pediatric xenotransplantation even if it becomes completely viable. The Chair of the Heart Committee advocated that the each Organ Committee needs to have autonomy over what constitutes reactivation and the urgency of transplant for someone that has a xenotransplant. The Chair of the Heart Committee offered that xenotransplant could be the first "liver-assist device," and for a patient who would otherwise die as a 1A liver candidate, a xenotransplant may provide an alternative that provides a bridge on active listing of 3-6 months instead of days. The Chair of the Heart Committee continued that in the case of liver, that Committee may want to leave those patients as actively listed unless there are clinical trials indicating xenotransplant as a viable alternative to an allograft.

The Chair of the Ethics Committee asked if the case is being made that it doesn't make sense to write this paper across all organs, that there should be separate papers with regard to each separate organ, and that Kidney should be set aside from the other organs.

The Heart Committee Chair responded uncertainty about answering that question, but shared that there are opinions on how things should be handled for Heart candidates.

A Liver Committee representative offered that this could be addressed by looking at the ethical principles of different scenarios – such as xenotransplant as a replacement for a functioning human allograft, or xenotransplant as a bridge and urgency occurs when xenotransplant fails. The Liver Committee representative explained that Liver and Heart would fall into the question of how long is the allograft going to keep going, and when it fails it will likely fail quickly and urgency will be high. The Liver Committee representative continued, noting tha t a third question is what the ethical considerations are for human allograft if a patient experienced harm because of accepting a xenotransplant.

The Heart Committee Chair commented that there may be a dichotomy that needs to be drawn on the use of xenotransplant. The Heart Committee Chair continued that, in the future, it could be foreseen that in adult heart transplant, xenotransplant could be a destination therapy or an alternative, especially for patients who may not be a candidate for an allograft. The Heart Committee Chair continued that for pediatrics, there may need to be a different approach, and there may need to be different approaches for when an organ is being used as an alternative to transplant versus when it's being used as a bridge to a transplant.

The Chair explained that the White Paper thinks through questions of fairness, and that the Committee didn't have the sufficient ability to predict likelihoods in an emerging technology about what will happen with different organs. A member remarked that the Committee felt it would be necessary to rely on the individual organ Committees for specific criteria and ideas about bridge therapies. The member continued that one group did discuss about how the process could work for VAD as a bridge, but that it may not have been in scope to be organ specific. The member shared that several scenarios were

considered, starting with accepting a xenotransplant at a point when it's still considered part of a clinical trial and very unproven. The member added that for those patients, it's uncertain about whether or not a xenotransplant is likely to be beneficial; these patients should be considered differently than a scenario where xenotransplant is a standard of care or proven to be an equivalent treatment to a human allograft.

The Chair of the Heart Committee explained that in the early days, it's difficult to predict that different populations are going to have different applications for xenotransplant. The Chair of the Heart Committee continued that for adult heart transplant, the patients who can't get an allograft are going to the beneficiaries of xenotransplant. In this case, xenotransplant could be an alternative to a heart transplant. The Heart Committee Chair continued that for a younger patient, it is going to be a patient who is higher risk or has access issues because of size. The Heart Committee Chair continued that the Paper should not disturb equipoise over who is going to benefit from a xenotransplant, and noted that taking a position about periods of inactivity on the waiting list would disturb equipoise and change behavior for experimental design.

The Chair of the Ethics Committee commented that other Committee members made that point, and that the recommendation was initially developed in trying balance principles of organ transplantation as a zero sum game and the perspective of patients who did not receive a xenotransplant. The Ethics Committee Chair continued that the logic may not apply equally to kidney as it does to other organs.

The Vice Chair of the Heart Committee reiterated that for Heart, this would be similar to how mechanical devices are considered today, with xenotransplant seen as a destination therapy or a bridge to transplant. The Vice Chair of the Heart Committee explained that destination therapy may eventually fail and require mechanical support, at which case the patient with a failing xenograft would qualify for listing for a heart transplant and meet criteria for certain medical urgency status. The Vice Chair of the Heart Committee added that xenotransplants could be used as a bridge for transplant, especially for patients that don't tolerate VADs, and noted that those patients could be stable outpatients eventually awaiting an allograft, similar to those with durable devices. The Vice Chair of the Heart Committee explained that bridge to transplants on devices are seen as a ticking time to complication, and that would probably be seen similarly with xenotransplant, with a limited time of support before needing additional support.

The Ethics Committee Chair summarized consensus from clinicians that no one should be precluded from continuing to accrue time at active status because as a bridge therapy, things are precarious. The Chair continued that there is also a distinction between anticipating a time where the graft will fail and the time that it fails.

The Vice Chair of the Heart Committee explained that a clinician wouldn't be waiting for a graft to fail to do an allograft transplant. If it's a bridge to transplant, hopefully the patient would be stable until they have an opportunity to be transplanted, but they'd have to be active on the waiting list. Where that patient would fall in terms of medical urgency would be up to Heart Committee to decide. The Vice Chair of the Heart Committee noted that intuitively, it would fit with outpatient durable left ventricular assist device (LVAD) status 4, unless the patient required other support. The Vice Chair of the Heart Committee continued that infants would qualify like any other device as a status 1A, either inpatient or outpatient on a device.

One member clarified that the patient would be eligible for an offer even if they had a functioning graft. The Vice Chair and Chair of the Heart Committee agreed. The Vice Chair of the Heart Committee noted that their level of medical urgency would vary depending on how sick they are, which would be determined by the level of support required. The member then clarified that the relative priority after

already having maintained active status would be based on the Organ-specific Committee's recommendation. The Vice Chair of the Heart Committee agreed, noting that the candidate would be active and would not need to wait for the graft to fail before being eligible for an allograft.

The member asked if there would be an reason to distinguish between someone on a VAD versus someone on with a xenograft heart. The Vice Chair of the Heart Committee remarked that would be up to the OPTN Heart Committee to determine, but if it is being considered like a bridge to transplant, it could be compared to a VAD in a more straightforward way. The Vice Chair of the Heart Committee continued that if the patient is outpatient and stable, they would be active for transplant at status 4, and wouldn't be waiting for a complication from the xenograft.

An OPTN Liver Transplantation Committee representative noted that the future state can differ greatly from the current state. The Liver Committee representative offered that this could be considered across different outcomes. One scenario is that xenotransplant outcomes are equivalent to human allograft outcomes; another outcome is where the xenograft provides some benefit to the patient, but has inferior outcomes to human allograft and thus is used for bridge therapies. The Liver Committee representative continued that, in the second scenario, those patients should be listed actively and urgency based on likelihood of mortality, compared to other patients on the waiting list. . The Liver Committee representative continued that the third scenario addresses patients who may have been harmed by xenotransplant. The Liver Committee representative explained that in this case, that person's mortality has increased significantly and that patient should receive additional priority due to their urgency. The Chair of the Heart Committee commented that this is an interesting set of scenarios.

The Chair of the Ethics Committee expressed that it may be necessary to delineate different papers based on organ type.

The Liver Committee representative noted that, even for Kidney, there could still be a scenario where the patient is hurt by the xenotransplant, such as through sensitization. The Liver Committee representative continued that patient should receive the appropriate priority for their sensitization level.

One member remarked that the Paper as outlined is very similar to the Liver Committee representative's recommendation . The member explained that the Committee addresses a scenario where xenotransplantation is standard of care, and thus considered an equivalent therapy based on outcomes. The member explained that the Committee considered the scenario where a xenograft functions but less well than a human allograft as the clinical trial stage.

The Chair wondered if the Committee can coherently retain with qualification their earlier work to incorporate these issues.

The Vice Chair noted that being inactive does not preclude the medical urgency issue; if a patient has a medical need for transplant that is urgent, that patient can simply be made active. The Vice Chair continued that patients active on the list should be immediately ready to be transplanted.

The Vice Chair of the Heart Committee explained that when a VAD is used as a bridge to transplant, the patient is immediately active for transplant. The Vice Chair of the Heart Committee continued that a xenotransplant recipient may have a higher risk, and so would not necessarily be considered stable and appropriate to leave as inactive. The Vice Chair of the Heart Committee continued that it would not be appropriate to wait for a complication from the graft. The Vice Chair of the Ethics Committee responded that this depends on how the clinical trial is designed; if the primary endpoint of the trial is deceased donor transplant, then the patient should remain active, but if the clinical trial end points are different, then it does not make sense to maintain active status if there isn't intent to immediately transplant. The

Chair of the Heart Committee remarked that there could be an evolution in the length of time that a xenotransplant is viable, though this evolution can't be predicted. The Chair of the Heart Committee continued that behavior on how xenotransplant is used will likely shift; one way this could shift is use of xenotransplant as a bridge to transplant for pediatric patients. The Chair of the Heart Committee continued that suggesting that patients who have received a xenotransplant should not be active on the waiting list or be at a lower priority could preclude this use of xenotransplant as a bridge therapy. The Chair of the Heart Committee recommended that the White Paper distinguish between intents of therapy, and that it should be up to the organ-specific Committees to determine priority of candidates.

The Chair of the Ethics Committee noted that the last qualification is important, and noting that while a recommendation of inactive listing and continuous waiting time accrual may not be appropriate for heart and liver candidates, it may be acceptable for kidney candidates. The Heart Committee Chair agreed, and noted that in order to write a paper that addresses an overview of transplant ethics and the state of xenotransplantation may need more of a "zoomed out," non-organ specific view. The Heart Committee Chair noted that there could be risk in writing a position paper on the ethics of xenotransplantation for kidney but not the other organs, even for a short period. The Chair of the Ethics Committee agreed.

The Chair asked if it would be acceptable to rework the beginning of the paper to be self-aware in the manner specified and add a section discussing how ethics may differ when considering xenotransplantation as a specific bridge therapy. The Chair of the Heart Committee noted that this could be a reasonable way to approach this.

A Liver Committee representative recommended that the ethical principles should be defined, and active status determination made by the physician, not the allocation organization. The Liver Committee representative continued that the patient may not qualify for a kidney according to current standards, but the xenograft recipient may lose function more quickly than a standard kidney, and thus it should be up to the physician to determine when the patient should be made active. The Liver Committee representative added that the Committee could determine when it would be necessary for active status qualification to be determined in order to establish fairness.

The Chair of the Ethics Committee thanked the participants for their time and input. The Chair continued that the Paper may need to consider more specifically where xenotransplantation serves as a short term bridge therapy. The Chair continued that it is critical to thoroughly describe this scenario before the ethics are applied. The Heart Committee Chair noted that whether the xenograft functions for days, months, or a year, if it's considered a bridge to transplant, it's a bridge to transplant.

One member asked how to distinguish between a therapy as a destination or as a bridge. The member explained that it seems the implication is that the extent to which it's intended as a bridge means the patient should categorically stay in active status, but if it's a destination, then the patient would be accruing the benefit of destination therapy and therefore shouldn't simultaneously be getting the benefit of destination therapy and access to an allograft, in which case there are questions of fairness. The Chair of the Heart Committee explained that this is precisely the duality that can be drawn out, and offered to provide a few paragraphs to contribute to defining this dichotomy. The member remarked that the fairness issue from the standpoint of ethics is whether or not some patients have access to two destination therapies before another patient has access to one. The member continued that the Ethics Committee has concern about creating incentives that allow for certain patients to have two destination chances. The Heart Committee representative noted that human allograft transplantation is a destination therapy, and if a transplant fails, there are not any rules against listing a patient with a previous transplant for a second transplant. The member agreed, but noted that the question becomes

whether or not a patient remains active during the functioning period of the first destination therapy. The Heart Committee Chair agreed.

The Chair of the Ethics Committee remarked that, for the number of cases being considered at this point, the more realistic scenario is that xenotransplant just buys extra time. A member remarked that if de facto, the present scenario is that xenotransplant is only being used as a bridge, then the Committee should be responsive to that in the present. The Chair agreed. The member noted that if the technology advances to the point at which the xenotransplant is intended as a destination therapy, how that will be accommodated should be considered. The Chair agreed, but noted that the Committee discussed that question and determined that failure should not be anticipated, but a patient should be made active immediately in the case of organ failure. The Chair continued that the clinicians have been making the point that it moves faster than that.

A Liver Committee representative remarked that if a standard kidney graft functions for ten years and xenograft functions for 2 years, it's difficult to determine if the xenograft is a destination or a bridge. A member agreed. The Chair remarked that in that case, there is enough time to de facto list the patient immediately as active.

The Liver Committee representative responded, asking how it should be handled if the xenograft is going to fail differently than a standard kidney may fail, graft or otherwise. The Liver Committee representative asked if it is the urgency alone that dictates what should happen next. The Chair of the Ethics Committee remarked that this is the harms-benefits question, which the Ethics Committee does address.

The Vice Chair of the Heart Committee commented that if the intention of the xenotransplant is as a destination therapy, then the patient is not listed for an allograft until the xenograft fails. One member asked what the primary considerations are in the judgement between destination or bridge. The Vice Chair of the Heart Committee explained that xenograft transplantation could be thought of in the same context as LVADs, which are described as either a destination or a bridge. Destination therapy would be for those patients who are not a candidate for human allograft, which has been the case with the clinical heart xenotransplants that have occurred on a compassionate use basis. The Vice Chair of the Heart Committee explained that destination LVAD may be appropriate for a patient who doesn't prefer transplant. The Vice Chair of the Heart Committee continued that there is risk over time for LVAD patients of stroke or bleeding, and LVAD is used as a bridge to transplant in most patients using LVAD support. The Vice Chair of the Heart Committee added that this group of patients would be listed for transplant immediately due to risk over time of being on the LVAD.

The member asked if there was a clinical or evidence based distinction, noting that the exclusions that result in a patient getting the VAD as a destination are either by choice or by exclusion, and that patient would never have been otherwise eligible for the allograft primarily. The Vice Chair of the Heart Committee explained that would be by choice, and noted that qualify of life and risk and outcomes are poor with LVAD compared to transplant. The Vice Chair of the Heart Committee continued that if it were true that outcomes were poor with xenotransplant compared to allograft transplant, then xenotransplant would also be perceived as a bridge to eventual allograft transplant, as is done for LVAD currently.

The Liver Committee representative noted that the scope of this paper is not that patients are going to get xenotransplant as destination therapy the way it has been defined in discussion, adding that those patients are otherwise excluded from human allografts anyway.

The Chair of the Ethics Committee remarked that one problem of defining the intention of the therapy if that it's difficult to know the intention in every case and that this intention can evolve as technology advances. Others agreed.

The Chair thanked the representatives of other Committees for joining and for their input.

Next steps:

The Committee will continue to think through and discuss the suggestions made, with deference to the consideration of xenotransplant as a bridge therapy.

Upcoming Meeting(s)

- October 30, 2025, teleconference

Attendance

- **Committee Members**
  - Andrew Flescher
  - Sanjay Kulkarni
  - Annette L. Needham
  - Laura Jokimaki
  - Laura Madigan-McCown
  - Lois Shepherd
  - Sheila Bullock
  - Matthew Wilkinson
  - Sena Wilson-Sheehan
  - Gloria Chen
  - Bob Truog
  - Joel Wu
  - Felicia Wells-Williams
  - Oluwafisayo Adebiyi
  - Grace Lee-Riddle
  - Lisa Paolillo
- **HRSA Representatives**
  - None
- **SRTR Staff**
  - None
- **UNOS Staff**
  - Emily Ward
  - Lindsay Larkin
  - Cole Fox
  - Meghan McDermott
- **Other Attendees**
  - Megan Urbanski
  - Aaron Ahearn
  - J.D. Menteer
  - Richard Daly
  - Catherine Vascik
  - Steve Weitzen
  - Dennis Lyu
  - Neha Bansal
  - Prince Anand
  - Joseph Dinorcia
  - Shimul Shah
  - Marc Melcher