



Review Article

Bioethics of Xenotransplantation Following the First Clinical Pig-Organ Transplants

Isabel Hansen^{1*}, Nikos Georgiou² and Sylvie Zielinska³

¹Department of Bioethics, Nordic Institute of Public Health Ethics, Finland

²Department of Philosophy, Nordic Institute of Public Health Ethics, Finland

³Institute for Health Policy and Ethics, Baltic Institute of Medical Humanities, Sweden

ABSTRACT

The first clinical pig-to-human heart and kidney transplants, followed by FDA-cleared clinical trials of pig kidney xenotransplantation, have moved xenotransplantation ethics from thought experiment to active clinical practice.

This review examines four fault lines that recent clinical experience has sharpened: informed consent obtained from terminally ill patients under conditions of genuine scientific uncertainty and open-ended, lifelong monitoring obligations; the infection-risk obligations that xenotransplantation creates toward close contacts who never consented to anything; the welfare status of genetically engineered source pigs bred specifically as organ donors; and the justice concerns raised by who is offered an experimental organ first as the field moves toward structured trials.

We also review the regulatory response, including the shift from case-by-case compassionate-use authorization toward formal clinical trial pathways and the legislative gaps that reviewers argue existing organ-transplant and biologics frameworks leave unaddressed.

Across these domains, the recent literature converges less on solutions than on a sharper description of where existing ethical and regulatory frameworks fail to fit xenotransplantation's particular risk profile.

We conclude that defensible progress requires uncertainty-forward consent processes, enforceable and evolving welfare standards for source animals, extended surveillance obligations for close contacts, and allocation frameworks designed before, rather than after, demand for pig organs exceeds supply.

Keywords: xenotransplantation; informed consent; animal welfare; zoonotic risk; organ allocation

Citation: Hansen I, Georgiou N and Zielinska S (2025) Bioethics of Xenotransplantation Following the First Clinical Pig-Organ Transplants. *Bioethics*. 1(1):01-05.

Corresponding Author: Isabel Hansen

E-mail Address: i.hansen@niphe.fi

Article History: Received 23 December 2024 | Accepted 21 March 2025 | Published 14 June 2025

Copyright: © 2025 Isabel Hansen, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited (<https://creativecommons.org/licenses/by/4.0/>).

INTRODUCTION

For decades xenotransplantation occupied an unusual place in bioethics: a field with an enormous literature

on hypothetical risks and almost no lived clinical experience to test it against. That changed abruptly between 2022 and 2024, when genetically engineered pig hearts and kidneys were transplanted into human recipients under compassionate-use authorizations, followed by the first FDA-cleared clinical trials of pig kidney xenotransplantation [1]. The move from thought experiment to bedside has not resolved the field's ethical debates so much as sharpened them, because the questions that mattered in the abstract -- informed consent under radical uncertainty, lifelong infection surveillance, the welfare of the source animals, and who gets access first -- now have real patients, real surgical teams, and real regulatory case files attached to them [2]. Earlier surveys of pig-to-human xenotransplantation bioethics anticipated much of this agenda before any clinical case existed, cataloguing consent, safety, and animal-welfare concerns that the 2022-2024 cases have since made concrete [3].

The pattern across the early cases is broadly similar. Patients who received the first pig hearts and kidneys were not eligible for conventional allografts and faced near-certain death without an experimental option, which is precisely the population in which the ethics of first-in-human research becomes most fraught: consent obtained under desperation is still consent, but it is consent extracted under conditions that make refusal almost unthinkable [4]. Commentators writing immediately after the first pig-to-human heart transplant noted that the surgical and immunological questions, while formidable, were in some ways more tractable than the consent and oversight questions the case raised [5]. This review surveys where the ethical literature has landed on four fault lines that recent clinical experience has made concrete: informed consent and the therapeutic misconception, infection risk and the obligations it creates toward people who never agreed to anything, the welfare status of genetically modified source animals, and the justice concerns raised by who is offered these experimental organs first.

CONSENT UNDER RADICAL UNCERTAINTY

Standard research consent assumes that risks, even serious ones, can be enumerated with reasonable specificity. Xenotransplantation consent cannot fully meet that standard, because some of the risks -- particularly the possibility of a novel zoonotic infection crossing from pig to human -- are, by definition, risks whose nature cannot be described in advance [6]. Ethicists reviewing the first clinical cases have argued that consent documents therefore have to be explicit about the limits of what is known, rather than translating scientific uncertainty into falsely reassuring language, and that patients facing terminal illness are especially vulnerable to overestimating a novel intervention's likely benefit -- the therapeutic misconception in its starkest form [7].

A further complication is that the terms of consent do not end at the surgical bar. Recipients of the first pig organs agreed, as a condition of participation, to lifelong virological monitoring, restrictions on activities that could transmit an infection to others, and in some cases post-mortem examination -- obligations that extend well past the point where a typical research subject's involvement would be considered concluded [8]. Whether a patient facing organ failure can meaningfully weigh commitments that persist for the rest of their life, at the moment they are also weighing near-certain death against a novel procedure, has become one of the more closely argued questions in the recent literature, and reviewers of the regulatory pathway note that the FDA's expanded-access and compassionate-use routes were not originally designed with this kind of open-ended, lifelong obligation in mind [9].

INFECTION RISK AND OBLIGATIONS TO THIRD PARTIES

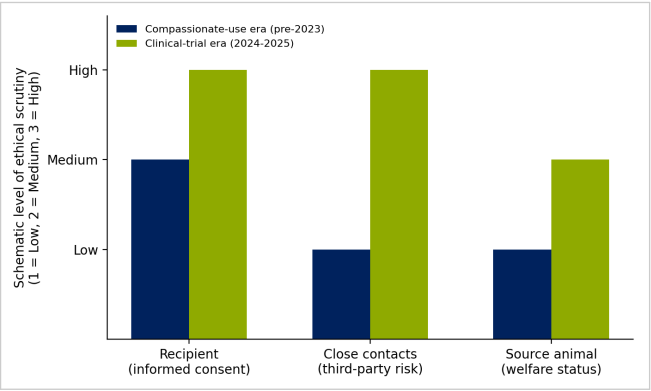
Xenotransplantation is unusual among experimental therapies in that its principal safety concern is not confined to the patient who consents to it. Cross-species infection, whether from a known porcine endogenous retrovirus or an unanticipated pathogen, could in principle spread beyond the recipient to family members, healthcare workers, or the wider public, which means the consent of the recipient alone cannot settle the ethics of proceeding [10]. This has prompted a distinct ethical literature on the standing of "close contacts": people who did not choose to participate in the trial but who may be asked to accept surveillance, testing, or behavioral restrictions of their own because of a risk they had no say in creating.

Recent reviews of the biological evidence describe the risk of a transmissible zoonosis from current-generation genetically modified pigs as low but not zero, and argue that "low but not zero" is exactly the category of risk that public health ethics has the most trouble handling cleanly, since it does not justify halting research but also does not permit treating the risk as negligible [11]. The first clinical renal xenotransplantation trial built its protocol around exactly this tension, incorporating extensive pre- and post-operative virological screening explicitly to generate the kind of surveillance data that earlier, more improvised compassionate-use cases could not provide [12]. Table 1 summarizes how the ethical weight assigned to different categories of xenotransplantation risk has shifted as clinical experience has accumulated, and Figure 1 presents the same shift schematically across the recipient, close-contact, and source-animal domains discussed in this review.

Table 1. Shift in the ethical weight assigned to major xenotransplantation risk categories between the compassionate-use era and the current clinical-trial era.

Risk domain	Compassionate-use era (pre-2023)	Clinical-trial era (2024-2025)	Primary driver of change
Recipient informed consent	Case-by-case, improvised documentation	Structured trial consent with explicit uncertainty disclosure	FDA-cleared trial protocols
Close-contact / third-party risk	Rarely addressed explicitly	Formal surveillance and disclosure obligations proposed	Zoonosis literature and case reports
Source-animal welfare	Ad hoc, facility-specific practice	Proposed formal welfare principles for GM pigs	Published welfare frameworks (2025)
Allocation / justice	Single-patient compassionate use	Trial eligibility criteria; allocation debate for future scale-up	Movement toward structured trials

Figure 1. Schematic comparison of the level of ethical scrutiny applied to recipients, close contacts, and source animals in the compassionate-use era versus the current clinical-trial era. Illustrative representation of the shift described in the literature, not derived from a quantitative study.



ANIMAL WELFARE AND THE STATUS OF GENETICALLY ENGINEERED SOURCE PIGS

The organs now being transplanted come from pigs subjected to extensive genetic modification -- typically a combination of gene knockouts to remove immunogenic markers and human transgene insertions to improve compatibility -- raised in biosecure facilities and euthanized at a time dictated by a human recipient's surgical schedule rather than any welfare consideration of the animal's own life course [13]. Whether this arrangement is ethically different from other forms of animal use in biomedical research, or represents something categorically new because the animal is engineered specifically to be treated as a compatible parts source for a different species, remains genuinely contested. Some

bioethicists argue that the degree of genetic modification and the animal's functional role as a living organ repository make the moral distance from ordinary laboratory animal use larger than proponents acknowledge [14], while others maintain that if the research is otherwise justified, welfare concerns are better addressed through concrete standards for housing, handling, and euthanasia than through opposition to the practice itself [15].

A recent set of proposed welfare principles for genetically modified pigs used in xenotransplantation attempts to operationalize this second position, specifying minimum standards across breeding, housing, and clinical use that source-animal facilities would be expected to meet regardless of the animal's ultimate role as an organ donor [16]. Whether such standards can be enforced consistently across the small number of specialized biotech firms currently supplying research-grade source animals is a separate and largely unanswered question; the literature on animal engineering for xenotransplantation notes that welfare oversight has generally lagged the pace of genetic innovation rather than kept pace with it [17]. A parallel debate has emerged around thoracic-organ xenotransplantation specifically, with clinicians calling for an explicit, value-based framework for deciding when the balance of risk to the recipient and burden on the source animal justifies proceeding, rather than leaving that judgment implicit in individual surgical teams' case-by-case decisions [18].

JUSTICE, ACCESS, AND WHO GETS THE EXPERIMENTAL ORGAN FIRST

Every one of the first clinical pig-organ recipients was selected because they had exhausted, or were ineligible for, the conventional allograft waiting list -- a selection criterion that is defensible on compassionate-use grounds but raises a harder question once xenotransplantation moves toward routine clinical trials and, eventually, an approved therapy: who should be offered a pig organ, and on what basis, once demand plausibly exceeds a still-limited supply of biosecure source animals [19]. Some proponents present xenotransplantation as a partial solution to organ scarcity precisely because it could, in principle, decouple transplant access from the number of human donors -- a framing that recent critics argue understates how much biosecure, genetically engineered organ production will cost and how unevenly that cost is likely to fall across health systems [20].

The justice concern is not confined to who receives an organ; it extends to who bears the risk of participating in an unproven therapy before its safety profile is established. Reviewers of the field's regulatory trajectory have noted that early xenotransplantation recipients function, in effect, as safety data generators for a therapy that wealthier patients and health

systems may benefit from only once the technology has matured past its riskiest phase [21]. Whether this amounts to exploitation, or is simply what first-in-human research always requires of its earliest participants, is a question the recent cardiac and renal xenotransplantation literature has raised without fully settling [22].

REGULATORY AND LEGISLATIVE RESPONSES

Regulators have moved cautiously but concretely since the first clinical cases. The FDA's clearance of formal clinical trials for genetically modified pig kidney transplantation marked a shift away from case-by-case compassionate-use authorization toward a more structured evidentiary pathway, one that requires the kind of systematic safety and efficacy data that individual compassionate-use cases, however informative, could not generate on their own [23]. Legislative and regulatory reviews published since 2023 broadly converge on the view that existing biologics and organ-transplant frameworks were not built with xenotransplantation's particular combination of infection risk, lifelong monitoring obligations, and third-party exposure in mind, and that dedicated regulatory guidance -- rather than adaptation of existing categories -- is likely needed as trials scale up [8]. Reviews of the broader ethical and regulatory landscape have made similar points about the mismatch between existing frameworks and the novel risk profile xenotransplantation presents, particularly regarding long-term recipient monitoring obligations that most transplant regulatory frameworks do not currently mandate [24]. Solid-organ xenotransplantation has drawn most of the recent regulatory attention, but the same gaps apply to liver xenotransplantation, where reviewers note that societal and regulatory preparation has lagged well behind the pace of surgical and immunological progress [25], and to adjacent neurotechnology fields such as brain-computer interfaces, where commentators have drawn direct parallels to xenotransplantation's combination of novel biological risk and inadequate existing oversight categories [26].

CONCLUSION

The clinical arrival of pig-to-human organ transplantation has not resolved the ethical questions that xenotransplantation has posed for decades; it has made them concrete enough to argue about with specifics rather than hypotheticals. Consent obtained from patients facing terminal illness, under conditions of genuine scientific uncertainty and lifelong post-transplant obligations, strains standard research-ethics frameworks in ways that are now visible in actual case reports rather than thought experiments. Infection risk creates obligations that extend to people who never consented to anything, source animals occupy a welfare category that existing biomedical research norms were not built to address,

and the justice question of who bears early risk versus who eventually benefits remains open as the field moves from compassionate use toward structured trials. None of these problems has a single clean solution, but the literature reviewed here suggests a workable orientation: honest, uncertainty-forward consent processes; enforceable welfare standards for source animals that keep pace with genetic innovation rather than trailing it; surveillance obligations extended, with appropriate limits, to close contacts; and allocation frameworks for future trials designed before demand for pig organs actually exceeds supply, rather than improvised once it does.

DECLARATIONS

Acknowledgements

The authors are grateful to colleagues in their respective bioethics and philosophy departments for helpful discussion during the preparation of this review.

Funding

This review received no external funding.

Conflict of Interest

The authors declare no conflicts of interest relevant to this work.

Author Contributions

Isabel Hansen conceived the review, coordinated the literature synthesis, and drafted the initial manuscript. Nikos Georgiou contributed the sections on animal welfare and regulatory responses and critically revised the manuscript for intellectual content. Sylvie Zielinska contributed the sections on informed consent and justice in allocation and provided final approval of the submitted version. All authors read and approved the final manuscript.

Ethics Statement

As a literature review synthesizing previously published, publicly available research and policy analysis, this article did not involve new data collection from human or animal subjects and did not require institutional ethics committee approval.

Data Availability

No new data were generated or analyzed for this review. All sources discussed are cited in the reference list and are publicly available through their respective publishers.

REFERENCES

1. FDA greenlights first clinical trials for genetically modified pig kidney transplants in humans (2024) American Kidney Fund.
2. Hurst DJ, et al. (2024) Pressing ethical issues relating to clinical pig organ transplantation studies. Xenotransplantation,

DOI:[10.1111/xen.12848](https://doi.org/10.1111/xen.12848).

3. Bioethics of xenotransplantation from pig to human (2023) Clinics.
4. Ethical Issues in Xenotransplantation: The First Pig-to-Human Heart Transplant (2022) The Annals of Thoracic Surgery.
5. Ethical Considerations for First-In-Human Pig Kidney Xenotransplant Clinical Trials (2023) The Hastings Center for Bioethics.
6. Xenotransplantation: Three Areas of Concern (2023) The Hastings Center for Bioethics.
7. Existing Ethical Tensions in Xenotransplantation (2023) Cambridge Quarterly of Healthcare Ethics.
8. Ethical and legislative advances in xenotransplantation for clinical translation: focusing on cardiac, kidney and islet cell xenotransplantation (2024) Frontiers in Immunology, DOI:[10.3389/fimmu.2024.1355609](https://doi.org/10.3389/fimmu.2024.1355609).
9. Should Xenotransplantation Surgeries Be Authorized Under the Food and Drug Administration's Expanded Access Pathway? (2025) AMA Journal of Ethics.
10. Hurst DJ, et al. (2024) Close contacts of xenograft recipients: Ethical considerations due to risk of xenozoonosis. Xenotransplantation, DOI:[10.1111/xen.12847](https://doi.org/10.1111/xen.12847).
11. Denner J (2026) Is There an Ethical Dilemma in Xenotransplantation? Xenotransplantation, PMID:42054234.
12. The First Clinical Renal Xenotransplantation Study (EXPAND): Evaluating Safety, Function, and Zoonotic Risks (2025) PMC.
13. Involuntary Donation: Animal Welfare and Xenotransplantation (2023) The Hastings Center for Bioethics.
14. In defense of xenotransplantation research: Because of, not in spite of, animal welfare concerns (2022) PMID:36573621.
15. George AJT (2024) Ethics, virtues and xenotransplantation. Clinical Ethics, DOI:[10.1177/02676591221140767](https://doi.org/10.1177/02676591221140767).
16. Ethical six principles for the welfare assurance of genetically modified pigs in xenotransplantation (2025) Organ Transplantation.
17. Animal engineering for xenotransplantation (2024) European Journal of Transplantation.
18. Ethical considerations in xenotransplantation of thoracic organs -- a call for a debate on value based decisions (2024) The Journal of Heart and Lung Transplantation.
19. Practical ethical concerns in allocation of pig kidneys to humans (2022) Clinical Kidney Journal.
20. Gunkel A, et al. (2025) Xenotransplantation: Injustice, Harm, and Alternatives for Addressing the Organ Crisis. Hastings Center Report, DOI:[10.1002/hast.5021](https://doi.org/10.1002/hast.5021).
21. Xenotransplantation Literature Update: January-June 2025 (2025) PMC.
22. Cardiac Xenotransplantation: Current State and Future Directions (2024) Circulation, DOI:[10.1161/CIRCULATIONAHA.124.070875](https://doi.org/10.1161/CIRCULATIONAHA.124.070875).
23. Successful Pig-to-Human Xenotransplant Paves the Way for Clinical Studies (2025) Kidney News.
24. Ethical and Regulatory Challenges of Xenotransplantation (2023) Biomedical Journal of Scientific & Technical Research.
25. Liver Xenotransplantation: Ethical and Societal Implications (2025) PMC.
26. Ethical Challenges in Xenotransplantation and BCIs (2025) European Society of Medicine.