

Trade in human tissue products

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In Australia, trade in human tissue is prohibited by state law, and in ethical guidelines by the National Health and Medical Research Council (NHMRC) — the *National statement on ethical conduct in human research*¹ and *Organ and tissue donation by living donors: guidelines for ethical practice for health professionals*.² However, Australian statutes and ethical guidelines about uses of human tissue have been established without specific regard to commercial activities involving products derived from these tissues.

There have been several areas of increased or new commercial activity involving human tissue products, including the manufacture of products from human tissue, such as:

- bone screws and bone putty;
- collagen products;
- acellular dermis (which is derived from human tissue, but no longer contains human cells);
- preserved injectable fascia lata particles derived from screened cadavers;³
- a range of blood products;
- live culture products, including those derived from human stem cells (embryonic or adult-derived) for therapy or research, that might in themselves become a saleable commodity (eg, mesenchymal stem cell products such as replacement tracheas);⁴
- diagnostic products; and
- non-medical uses of human tissue or human tissue products, such as in the manufacture of human collagen for cosmetic use.

In addition, large-scale purpose-built human research biobanks have been developed. While primarily for academic medical research, these biobanks retain potentially identifiable genomic material from the original specimen donor, as well as intellectual property, and this raises specific ethical concerns. Profit could potentially be derived from discoveries made from the use of specimens in such biobanks.

Distinguishing tissue products from source tissue

Legal and ethical restrictions prohibit payments to donors of tissue and their families, but once the tissue has been subjected to some kind of manufacturing process, it is considered freely available for commercial applications as a human tissue product.

Between the donation of human tissues (which are not permitted to be bought or sold) and the manufacture of saleable products from those tissues, a practical legal and ethical distinction may have arisen that has not been articulated in any legislation or guideline. There appears to be an assumption that once human tissue becomes a tissue product (and this includes cell lines), it may be offered for sale, that a price may be paid, and that profits may accrue to those who manufacture and sell the products.

Risk to blood, bone marrow and eye banks and organ transplantation

Blood, bone marrow and eye banks, and the practice of organ transplantation depend on human tissue not being treated as property, but as being subject to custodianship and used for the purpose for which it was donated.

ABSTRACT

- Trade in human tissue in Australia is prohibited by state law, and in ethical guidelines by the National Health and Medical Research Council:
 - *National statement on ethical conduct in human research*;
 - *Organ and tissue donation by living donors: guidelines for ethical practice for health professionals*.
- However, trade in human tissue products is a common practice especially for:
 - reconstructive orthopaedic or plastic surgery;
 - novel human tissue products such as a replacement trachea created by using human mesenchymal stem cells;
 - biomedical research using cell lines, DNA and protein provided through biobanks.
- Cost pressures on these have forced consideration of commercial models to sustain their operations. Both the existing and novel activities require a robust framework to enable commercial uses of human tissue products while maintaining community acceptability of such practices, but to date no such framework exists.
- In this article, we propose a model ethical framework for ethical governance which identifies specific ethical issues such as:
 - privacy;
 - unique value of a person's tissue;
 - commodification of the body;
 - equity and benefit to the community;
 - perverse incentives; and
 - "attenuation" as a potentially useful concept to help deal with the broad range of subjective views relevant to whether it is acceptable to commercialise certain human tissue products.

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A major concern is that if a laissez faire situation persists in relation to human tissue products, then ownership may be the paradigm for tissue products and the ethical issues may only be resolved through case law when tested in court. Unfortunately, legal judgments accepting unfettered ownership could endanger the social capital that exists in the donation of human tissue for transplantation and research in Australia. Such a risk is of particular concern for organisations like blood, bone marrow and eye banks, and for solid organ transplantation programs, which depend on goodwill. This goodwill may be threatened if the commercial industry in human tissue products is seen to be operated in a way that is not consistent with the wishes or values of the donors. Donors of human tissue typically presume that the tissue will be used for the benefit of the community through transplantation and research, rather than for profit to individuals. Thus, decisions by courts to attribute ownership would be controversial, and could

significantly undermine donors' trust. There may be an unwillingness to donate tissue if profits are being drawn from products manufactured from donated human tissue.

In our view, the interests of the community and of donors and their families are best protected by extending custodianship of human tissue to include human tissue products, regulated by ethical guidelines developed by the NHMRC. Providing relevant information and obtaining consent are fundamental to the exchange of this custody. Information and consent processes should therefore aim to ensure that tissue donors are informed of downstream uses and possibilities for commercialisation.

Lack of regulation

There is a gap between existing guidelines and legislation regarding consent processes for the exchange, trade and commercialisation of human tissue products. For instance, there appears to be no current requirement that donors be informed of commercial applications of products derived from their donated tissue. The NHMRC national statement¹ prohibits the sale of human tissue, requiring that donors of tissue must be given an explanation that they will not benefit financially from any future commercialisation of a cell line. However, it makes no requirement that they be informed about any commercial potential from tissue products. The development of ethical guidelines on commercial uses of human tissue products would help determine when commercial use may be ethically permissible, and what restrictions are needed to protect individuals and maintain community support for such activities.

Attenuation and human tissue products

The commercial use of human tissue products has been distinguished in practice from the commercial use of human tissue. However, it is a difficult distinction to make. What, for instance, is the difference between tissues removed from a person's body and cells that have been grown in culture from that tissue? If the cells retain genomic information, then the same privacy concerns and issues to do with obtaining relevant information about the donor or donor family's health would apply to both the tissue removed and the cells cultured from it. Nevertheless, a distinction does appear to be made in practice, and this is based on a subjective attitude toward the tissue and the cells cultured from it that does not necessarily have a scientific rationale.

A notion that may both help explain why there are different attitudes toward human tissue and any products derived from it, and that may inform ethical decisions about commercial applications is that of attenuation. A tissue product may be considered to be "attenuated", in a subjective sense, when it has lost significance to the donor and donor's family. This recognises that a person's attitude toward commercial uses of human tissue products may not be based on objective criteria, such as when it has lost significant properties like genetic material. For instance, someone may not object to their hair being sold by their hairdresser even though it may contain cells with their genetic material in it, but would object to someone selling acellular dermis derived from them after their death.

From an ethical point of view, privacy issues are different in situations where the genomic material has been lost compared with where it is intact (which may permit identification). It stands to reason that if the genomic significance has been lost, then the uses of the tissue would not be specific to donors or their families. There

would therefore seem to be a loss of significance of the tissue for that donor and their family, and thus it may objectively be perceived to be attenuated. However, we must recognise that such objective reasoning may not be acceptable to some members of the community.

The NHMRC national statement states that human tissue should always be regarded as potentially identifiable because it contains genomic information.¹ The sensitivity about genomic material seems to depend on whether the genomic information can be accessed. It may matter to some if attempts are made to identify the donor source or their family or grouping in such a way that attributable information is obtained. It may also matter if there is value in the product that is unique to the individual or family.

The requirement in the national statement for consent, or at least a waiver of the need for consent, granted by an ethics committee, for secondary uses of pathology specimens, even for non-genetic applications,¹ suggests that there are community concerns about the use of these human tissue products. Instances like the scandals that arose out of the retention of organs at Alder Hey Children's Hospital in Liverpool in the United Kingdom⁵ remind us that the public may have very different views from those of the medical community about the importance of disclosure of the uses of human tissue and tissue products.

Specific ethical considerations

To protect the existing tissue donation practices, their social capital and the values on which they depend, we propose that even if it is accepted that attenuation differentiates a human tissue product so that it may justifiably be made available for commercial purposes, the following questions should be considered in determining if not-for-profit trade or for-profit commercialisation exemptions should be allowed.

- Is community benefit likely to be derived that would offset the negatives of commercialisation, and will equity of access to those benefits be maintained?
- If the human tissue product has genomic significance to individual donors or their families, will the right to privacy be maintained and will information derived from the material that is relevant to the future health of the donor or their genetic relatives or another group be provided back to them?
- Might members of the community consider the commercial use of a particular product to be ethically unacceptable because it commodifies the human body and treats it as an object?
- If the value of the human tissue product derives from a property that is unique to the individual donor or donor family, might trade be seen as exploitive and likely to undermine willingness to donate?
- Might perverse incentives arise from the commercial use of the product — that is, might the manner in which the incentive for the donation, trade, exchange or commercialisation of human tissue lead to behaviour by or toward the parties involved, in ways they otherwise would not behave, or behaviour that may place them at risk of harm?

Cost recovery

Biobanks may depend on the ability to recover their costs. This raises a question about the circumstances when consent is altruistically provided by a donor's family for a not-for-profit tissue bank to retrieve, handle, store and distribute a sample of the donor's skin. The tissue bank may, in time, transfer custody of the sample

to researchers or a third party engaged in creating tissue products either for free, or for a small fee to cover the costs of handling the sample. At this stage, it may be argued that the ethical values so highly prized in the Australian donor system are maintained.

However, two concerns can be raised about this process. Cost recovery may be constructed in such a way as to cover the costs of a whole business, including any research undertaken by the biobank, and not just the tissue handling. There is some ambiguity about not-for-profit agencies seeking to charge fees that are greater than the actual cost for that service, in order to offset the costs of other services. Strictly, a charge greater than cost is a profit and is a commercial activity rather than not-for-profit exchange. However, such commercial use is likely to be viewed differently, given that no profit is paid to anyone.

For our purposes, "commercial use" means a for-profit activity not including a not-for-profit agency charging a fee greater than cost to subsidise its other activities. However, we propose that such subsidies should be transparent, approved by the relevant authority and that the donors be informed.

Community benefit

There is a significant concern that transferring custody of the sample to a for-profit organisation may undermine the altruistic nature of tissue donation. Some may be less willing to donate as a result, and some may believe that the profit motive diminishes respect for the human body through commodification. There may also be concern over the sorts of uses made, with therapeutic uses being more acceptable than cosmetic uses. Also, community access to the benefits of research and therapy (which may be assumed by donors) may be priced out of reach of those in need, and could alter community acceptance of such activity.

Unique value

In circumstances in which the tissue product has a value that is unique to the donor or the donor family, commercial use of the product could be seen as exploiting this uniqueness. Generating a profit from a tissue product that derives its value from a unique physical property, such as a particular genetic mutation, may also raise community concerns that the donor should share in the profits. This would constitute material incentive, and both community benefit and the altruistic nature of Australia's donor system may be eroded if people started to withhold donations unless profits were made available to them. For this reason, we propose that ethical guidelines should prohibit the commercial use of human tissue products if the value of a product is derived from a unique characteristic of the donor. The situation would be that products may be exchanged and fees may be paid to recover costs, but no profit should be obtained from such exchanges.

Perverse incentives

Commercialisation may also be unethical if it generates perverse incentives. Stipulating no fee is payable to the donor of tissue should ensure that there are no perverse incentives for donors to act in ways they otherwise would not, or in ways which may be to their detriment. We consider that the existing prohibition of material incentives for donating human tissue should be retained, including prohibition of any payment to tissue donors for tissue products developed from their tissue. This is important, as it

reduces the likelihood of fraud and of donors taking risks or placing recipients at risk by hiding relevant information.

Conclusion

We have argued that, although trade in human tissue should remain prohibited, it would be in the interests of the community to allow the continued development of trade in human tissue products, but only within ethical guidelines that protect the interests of donors and their families and the community.

There is a need to address the governance issues in implementing guidelines. For products related to research, the guidelines might be implemented by human research ethics committees. That would not seem to be a significant extension to their work, as research involving human tissue must be reviewed by them in any case. However, we envisage a need for the Australian Government to appoint an independent agency to implement ethical guidelines for non-research applications.

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Competing interests

Nicholas Tonti-Filippini has received reimbursement for travel costs and sitting fees to attend NHMRC Working Committee on Commercialisation of Human Tissue meetings. Nikolajs Zeps has received reimbursement of travel costs and sitting fees as a member of the NHMRC Working Committee on Commercialisation of Human Tissue, is employed to operate a biobank and undertake cancer research, and has been the recipient of an NHMRC grant to facilitate biobanking of cancer specimens.

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