

Trade in Human Tissue Products¹

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Trade in human organs and tissues is prohibited in many jurisdiction but permitted in some others. Most ethical guidelines for human research also consider trade in organs to be unethical.

In 2008, Pope Benedict told scientists and bioethicists meeting at the Pontifical Academy for Life that the worldwide illegal organ trade often made victims of innocent people, including children.

The Pope noted that buying and selling of human organs is a lucrative business for suppliers and countries that allow foreign "transplant tourists" to have operations they cannot get at home. Organs are often bought from poor peasants and sometimes harvested from condemned prisoners. He condemned abuses in transplantation and organ trafficking, which often hit innocent people such as children as abominations.²

However, despite the general rejection of trade in human organs, trade in human tissue *products* is a common practice especially for the purposes of reconstructive orthopaedic or plastic surgery. Rapid advances in biotechnology has resulted in novel human tissue products such as the creation of a replacement trachea using human mesenchymal stem cells. In addition, biomedical research is now extensively underpinned by the use of human tissue products such as cell lines, DNA and protein provided through biobanks. Cost pressures on these have forced consideration of commercial models to sustain their operations.

There are however complex issues involved such as, privacy, the unique value of a person's tissue, commodification of the body, benefit to the community and perverse incentives that arise from the type of commercial use. There are questions about whether there is adequate regulation to implement an ethical framework to regulate commercial activities involving human tissue products.

Commercial activities involving human tissue products

The law in some jurisdictions and the existing ethical guidelines were usually established without specific regard to commercial activities that involve human tissue products. Specifically there have been several areas of increased or new activity involving human tissue products such as:

- The establishment of large-scale purpose-built human research biobanks that may be used for genomic sequencing and profiling that may retain identifiable

¹ The author, Prof Nicholas Tonti-Filippini chaired an Australian Government enquiry into the Commercialisation of Human Organs and Human Tissue and acknowledges the contributions of the members of the committee, especially the deputy chair, Dr Nik Zeps, the staff of the NHMRC secretariat and the many people who made public submissions to the enquiry.

² <http://www.reuters.com/article/idUSTRE4A658820081107>

genomic material from the original tissue donor, and also may be used to derive intellectual property and therefore potential profit from discoveries made from human biological specimens;

- The manufacture of therapeutic products from human tissue, such as bone screws and bone putty, collagen products or acellular dermis (which though derived from human tissue no longer contain human cells), preserved injectable fascia lata particles derived from screened cadavers,³ and a range of blood products;
- The development of 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;
- The possibility of non-medical uses of human tissue or human tissue products, such as in the manufacture of cosmetic products.

The effect of the legal restrictions would seem to have prohibited any form of payment to donors of tissue and their family, but once the tissue has been subjected to some kind of manufacturing process, it is often considered freely available for commercial applications as a human tissue *product*.

Somewhere between the process of obtaining the human tissues, which may not be bought or sold, and the manufacture of saleable products from those tissues, a legal and ethical distinction would seem to have been made in practice but, as far as we are aware, not articulated in any legislation or guideline. That is, whilst human tissue products that originate from human tissues may not involve payment to the donors or their families, once the tissue becomes a tissue product there would appear to be an assumption that the product may be offered for sale, a price paid and profits accrue to those who manufacture and sell the products. The distinction between what is a human tissue and what is a human tissue product has also not been articulated and the some products, such as stem cell lines, may retain the original genomic sequences of the source donor.

An Ethical Framework for the Commercial use of Human Tissue Products

If the interests of the community and of donors and their families are to be protected, the existing ethical ban on for-profit commercialisation of human tissue for transplantation could be retained, but there may be some circumstances in which products derived from human tissue may be used commercially, within a context of ethical guidelines that are monitored by government agencies.

Ownership or Custody of human tissue products

There is much debate about whether ownership is an appropriate concept to apply to human tissue. and the products derived from its tissue. If a *laissez faire* situation persists, then the ownership of human tissue products may only be resolved through case law when it is tested in court. Unfortunately, such cases tend to be controversial and if brought to court could raise questions that might endanger the social capital that exists in the donation of human tissue for transplantation and research in many

³ Burres, S 2001 'Preserved Particulate Fascia Lata for Injection: A New Alternative', *Dermatologic Surgery* vol. 25, (10) December, pp. 790-794

countries. Such a risk is particularly of concern to the Blood Banks, the Eye Banks and the Bone Marrow Banks that in many places exist on the basis of good will altruistic donations and the latter may be threatened if the development of a commercial industry in human tissue products is not regulated in such a way as to protect the interests of the community and of donors and their families. 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, and controversial court cases may significantly undermine their trust.

The interests of the community and of donors and their families could be protected by the continued use of the notion of custody in relation to human tissue and human tissue products, and that custody be regulated by the development of enforceable ethical guidelines, including allowing commercialization of some human tissue products subject to approval by an appropriate Government regulatory agency.

The change of custody of human tissues and human tissue products may happen in several ways:

- Gift – where custody is transferred without a fee or benefit in return;
- Not for Profit Exchange or Trade - includes payment for transfer of custody or for access (to tissue or a product derived from human tissue) but no more than for the purposes of cost recovery⁴; or
- Commercialisation – trade where a fee is charged for the purpose of making a profit.

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 commercialisation possibilities. There is a gap between the existing guidelines and legislation regarding consent processes for the exchange, trade and commercialisation of human tissue products. For instance, there would appear to be no current requirement that donors be informed of commercial applications of products derived from their donated tissue. Most ethical guidelines for human research prohibit the sale of human tissue and contain the simple statements to the effect that donors of tissue must be given an explanation that the research participants will not benefit financially from any future commercialization of cell lines, but make no requirement that they be informed about any commercial potential from tissue products. The development of ethical guidelines regarding commercial uses of human tissue products would assist with determining when commercial use may be ethically permissible and the restrictions that are needed to protect individuals and maintain community support for such activities.

Attenuation and Human Tissue Products

⁴ Note that there is some ambiguity about not-for-profit agencies seeking to charge fees that are greater than actual cost for that service, in order that the fee charged for that particular service offset the costs of other services. Strictly such a charge greater than cost is a profit and is a commercial activity rather than not-for-profit-exchange. However such a 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 other activities of the not for profit agency. Such subsidies should be transparent, approved by the relevant authority and the donors informed.

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 a cell removed from a person's body and cells that have been grown in culture from that cell, especially if the genomic information remains intact? The same privacy issues and issues to do with obtaining relevant information about the donor or donor family's health would seem to apply to both the cell removed and the cells cultured from that cell.

A notion that would seem to assist in making ethical decisions about commercial applications of tissue products is that of attenuation. That is, a tissue product may be considered to be 'attenuated' in a subjective sense when it has lost significance to the donor and donor family.

Objectively a product may be considered to be attenuated when it has lost significant properties such as cellular or genomic properties or the reason for inclusion does not use these significant properties. For instance, there would seem to be little significance attached to human collagen because it does not contain genomic information and it appears that no-one objects to it being sold for profit.

Where the genomic material has been lost, the privacy issues are different compared to intact genomic material which may permit identification. It stands to reason that if the genomic significance has been lost, then the uses of the tissue would seem not to be specific to the donor source or their family. There would therefore seem to be a loss of significance of the tissue for that donor and their family, and thus it may be perceived to be attenuated.

For example, pathology samples that were once considered to be abandoned by the general public can now be analysed for valuable genomic material. These samples could once have been considered to have become attenuated. Today, however, with the advent of genomic uses, the original samples and derived products may take on great significance. The donor, the family or the community may be greatly concerned with what happens to the tissue or the final use of the human tissue product.

It needs to be emphasised that the presence of genomic material does not necessarily indicate that there will be sensitivities about any derived products. It rather depends on whether the genomic information may be accessed, whether attempts may be made to identify the donor source or their family or grouping in such a way that attributable information is obtained and whether there is value in the product that is unique to the individual or family, such as a sequence for an antibody to a cancer. Some national ethical guidelines⁵ state that human tissue should always be regarded as potentially identifiable because of genomic information but others such as the Canadian ethical guidelines⁶ have taken a view that such samples can be regarded as 'traceable' but that this may require access to further information that is controlled and therefore renders them functionally anonymised. The situation varies in different jurisdictions as to the comprehensiveness of genetic data banks and the control of them.

⁵ Such as the Australian National Health and Medical Research Council "National Statement on Ethical Conduct in Human Research" 2007

⁶ Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans: <http://www.pre.ethics.gc.ca/english/policystatement/policystatement.cfm>

Specific Ethical considerations

Even if one accepts that attenuation differentiates a human tissue product such that it may justifiably be made available for commercial purposes, a Committee that I chaired suggested⁷ that the following considerations should also be used in determining if not-for-profit trade or for-profit commercialisation exemptions should be allowed, specifically,:

1. If a community benefit is likely to be derived from commercialisation that would offset the negatives of commercialization for the community and whether equity of access to those benefits is maintained;
2. If the use of the human tissue product has genomic significance to the individual donor or their family, whether the right to privacy and obligations to provide information derived from the material and relevant to future health of the donor or their genetic relatives or other grouping will be met;
3. If members of the community would consider the commercial use of a particular product to be ethically unacceptable because it commodifies the human body and treats it as an object;
4. If the value of the human tissue product derives from a property that is unique to the individual donor or donor family so that trade may therefore be seen as an exploitative and likely to undermine willingness to donate; and
5. If perverse incentives may arise from the commercial use of the product - that is, the manner in which the incentive for the donation, trade, exchange or commercialisation of human tissue leads to behaviour by or toward the parties involved, in ways they otherwise would not, or which may place them at risk of harm.

An example that may be useful to consider is 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 a research or manufacturing group either for free, or with 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 organ donor systems are maintained.

However, two concerns can be raised in this process. Cost recovery may be sufficient to cover the costs of a whole business not just the tissue handling (this may extend to research undertaken by the bank). Additionally, transferring custody of the sample to a for-profit organisation may undermine the altruistic nature of donation. The profit

⁷ The Committee's Issues Paper is soon to be published by the NHMRC and an article on the recommendations is forthcoming in the Medical Journal of Australia.

motive may diminish respect for the human body through commodification, and access to the benefits of research and therapy may be priced out of reach.

In the above example, the community may respond differently depending upon the use to which the sample is put. For instance, a different sentiment may be expressed by the community if the original tissue sample is rendered acellular and transformed into collagen for cosmetic purposes versus if the sample is rendered acellular and used for treatment for dermal ulcers or burns.

The use to which the sample is finally, or potentially, put is also important when considering whether commercialisation is ethically permissible. For instance, when assessing community benefit in the above example, community benefit would generally be regarded as more significant if the sample were used for therapy or research rather than manufacturing a cosmetic product. In other applications, if the donor cells remain intact, community members may be concerned about how their family member's DNA and related information may be used, especially because it may be identifiable or in principle re-identifiable.

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 the uniqueness of the donor rather than a novel approach or process. Commercialising and generating a profit from a tissue product which derives its value from a physical property unique to the donor, such as a particular genetic mutation, may also raise community concerns if people feel that the donor should share the profits. This would constitute material incentive and may erode community benefit and the altruistic nature of organ, bone marrow, eye and blood donation systems if people start to withhold donations unless profits were made available to them. For this reason ethical guidelines should prohibit commercial use of human tissue products if the value of a product is derived from a characteristic that is unique to the donor. In that way products may be exchanged and fees paid to recover costs but no profit should be obtained from such exchanges.

Commercialisation may also be ethically impermissible if it generates perverse incentives. That 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 the tissue donor for a tissue product developed from their tissue. Nevertheless care must also be taken to ensure those involved in retrieval, handling, storage and distribution of the human tissue and derived products do not then develop profit from properties that are unique to the donor, make profits in such a way that restricts the community benefit or prevents equity of access to the benefits, lose the chain of responsibility to the donors and their connections in relation to information gained from commercial or non-commercial applications where the information is relevant to the health of the donor and their connections, or otherwise themselves succumb to incentives to act perversely if there are commercial benefits for them to do so.