29 May 2009

RE: Draft Ethics and the exchange, sale of and profit from products derived from human tissue: An Issue Paper

Thank you for the opportunity to provide comments on the draft issues paper: Ethics and the exchange, sale of and profit from products derived from human tissue.

The Eye Bank Association of Australia and New Zealand Inc. (EBAANZ) was formed to promote cooperation, communication, consistency and reliability of service between Eye Banks for the benefit of donors, donor families, ophthalmic surgeons and tissue recipients. All Eye Banks in Australia and New Zealand are members of the Association. Among EBAANZ's stated purposes are 1) the support of eye tissue research, both basic science and clinical, to advance understanding of eye disorders and treatments and 2) the development and implementation of policies and Standards for best practice in eye donation and banking.

Given EBAANZ’s current role, expertise and experience in the field we feel it is it is appropriate to comment on those aspects of this issues paper that relate to the interface between human tissue donation and human tissue products. Therefore, we have limited our comments to a general affirmation of the approach the Committee has taken, and the key principles upon which this approach is based. In addition, we present some suggestions towards further clarification of human tissue as distinct from human tissue products. We also seek to correct some factual inaccuracies in the issues paper that have, no doubt, partially arisen from the confusion between human tissue for transplantation and human tissue products.

General comments

EBAANZ supports the Committee’s approach towards the issues along with its primary focus on ethical issues regarding commercialization of human tissue products. This distinction between human tissue and human tissue products appears to be a useful framework and, as stated in the paper, its focus is appropriate given recent public consultations and the broad public support for prohibition on commercialisation of trade in human tissue.

In particular we support the principles towards human tissue as espoused in the issues paper that

- Property or ownership should not be applied to human tissue.
- Maintain the ban on for-profit commercialism of human tissue for transplantation

We support the Committee’s current view and approach towards human tissue products and

- Encourage the development of legislation and guidelines relating to human tissue products
- Believe that the concept of “attenuation” being applied to describe the loss of significance between a donor and the product derived from human tissue is a useful one
- Support the use of a properly and fully informed consent process as an effective means of protecting donors and families, including that tissue donors are informed of downstream commercialisation possibilities and informing them that commercial uses are strictly limited by effective ethical regulation
Consent Issues

Currently the EBAANZ Medical and Quality Standards for Eye Donation and Eye Tissue Banking (available at [www.ebaanz.org](http://www.ebaanz.org)) include a section on necessary elements of an informed consent for eye donation. Included among a list of relevant items are – 1) the purpose(s) for which these tissues will potentially be utilised, 2) permission for research, clinical training or education obtained as a separate explicit consent and 3) information on possible use for cosmetic procedures or applications involving commercial gain (if this is applicable to the tissue being consented).

Currently we are unaware of any human tissue product derived from the donation of human eye tissue that has been put to a commercial or cosmetic application anywhere in the world. However, Eye Banks do provide human tissue for research purposes, either free of charge or on a cost recovery basis, and there is potential for human tissue products with a commercial value being developed from this research. Therefore:

- Consent for known commercial applications of derived human tissue products could be included in an informed consent process.
- Consent for research purposes is currently obtained (when applicable). However, what is not clear is:
  - the extent of information that should be supplied on the type of research that is to be conducted (separate items of tissue or genetic material could be distributed to a large number of research groups – is it necessary to specifically list every known research application that the material to which the material could potentially be distributed)?
  - whether or not consent in this instance allows for the use of stored tissue for future currently unknown research applications (that may or may not have commercial potential)?
  - what are the responsibilities, rights, entitlements and liabilities of the Eye Bank within this chain of custody?

In reality it may be difficult to predict with any confidence at the time of consent the extent and nature of a chain of custody (from collection, processing, conversion to tissue products, manufacture, exchange, sale and final use). This poses difficulties, both in the degree of specificity to which donors are entitled to know of potential uses (the issues paper Q11), and also difficulties informing the donor or donor’s family if a product with commercial potential has been developed from donated human tissue (issues paper Q12) especially if the product is highly attenuated or the development comes some time after the original tissue donation.

Question 12 also neglects to consider that many donations are after death – and therefore the donor themselves cannot be informed. This raises interesting ethical questions regarding the next-of-kin with or without supporting consent from the donor. Do the next-of-kin have the same ethical considerations as the donor?

- The Committee should deliberate if there are different ethical considerations, and thus requirements, between the donor versus the next-of-kin in regards to consent for commercial use and the outcome of commercial use.

Certainly the Eye Banks seek more guidance in this area through the development of national guidelines and (as the issues paper discusses) the development of legislation to cover the issues surrounding the exchange of human tissue towards the development of human tissue products.

Legislation

Page 22 and 23 of the issues paper discusses legislation issues. It is interesting that the example given of ministerial exemption to the provisions of the Human Tissue Act relates to bone screws and bone putty – both human tissue products rather than human tissue (as defined in this issues paper). It is reasonable to assume that the human tissue was originally donated on the assumption that it would be used for not-for-profit purposes (which is covered by the Act). However what is not covered is the aspects of the exchange (from tissue to tissue product) and nor is a legal framework provided for the appropriate uses, regulation and commercialism of products (as distinct from tissue).

The issues paper could perhaps express these differences more clearly – the law needs to provide

1. a clearer distinction between human tissue and human tissue products (along the lines of the definition provided in this issues paper),
2. provide a legal framework relating to the exchange (this would relate to the transfer of custody implications – the points between tissue banking, bio banking and transformation into human tissue products) and
3. provide a legal framework for the appropriate uses, regulation and commercialism of products

Definitions
The issues paper has correctly identified a difference in the use of human tissue product (as it relates to this issues paper) and the TGA’s use of the word product (the TGA uses the term to also include the original donated tissue).

We believe that there is a need to highlight this difference even further. The use of the term “product” by the TGA is in keeping with the manufacturing terminology used by regulators in this area, although this is by no means universal in universal use by regulators (the FDA for example uses the terms Human Cell, Tissues and Cellular and Tissue-Based Products (HCT/P) and Canada continue to use the term human tissue to apply to the originally donated tissue). The universal use of use of the term “product” by the TGA has lead to confusion in this area, not only in their approach to human tissue for transplant regulation (applying a quality systems approach similar to that of the manufacture of pharmaceuticals and manufactured medical devices) but also in the confusion and commoditisation of human tissue items as seen in some aspects of the Doyle Report into Prostheses Listing Arrangements.

• We suggest that there is a need to further highlight the differences in the use of the term “product” in regard to TGA manufacturing principle use, and the use intended in regard to the exchange, sale and profit from products derived from human tissues.

In addition, the phraseology and terminology used throughout the Issues Paper can contribute to the confusion between human tissue for transplantation purposes and human tissue products. For example human tissue products are sometimes referred to as being transplanted, while at other times human tissue is referred to being used for therapeutic purposes (the two being freely interchanged). In some instances there is confusion between the functions and operations of a Tissue Bank and that of a Bio Bank (“Tissue Bank” here being used in its generic sense to cover Organ Procurement Organisations, Eye Banks and Tissue Banks).

Page 20 of the Issue Paper states “……increased commercial opportunity has emerged for those engaged in human tissue collection”. In this context the term “human tissue collection” should imply collection for or by a Bio Bank for Bio Banking purposes. However it could be confused with the donation of organ eyes or tissues primarily for transplant purposes. In addition, the word “collection” can be used as either a noun or a verb; further contributing to confusion over Bio Banking or donation for transplantation purposes.

Therefore we suggest that to better define terms, avoid confusion and resist commoditisation of human tissue provided for transplantation –

• The use of the word ‘transplant’ could be restricted to that of human tissue (i.e. unprocessed such as hearts, kidneys, corneas, fresh bone) - not human tissue products. “Therapeutic use” for human tissue products could be used instead.
• The term “human tissue collection” should not be used as it can be interpreted in the sense of an action or in the sense of an object– the term Bio Banking (and Bio Bank) could be used instead.
• The use of the term Eye Bank or Tissue Bank (Eye Banking and Tissue Banking) should be restricted to the donation and transplantation of human eyes or tissues. The term Bio Bank (Bio Banking) could used for as all other processes which may involve the
  o Modification of human cells for storage (where the transfer incurs a fee that covers more costs than those associated with storage and handling of the donated tissue) for purposes of research or transformation into human tissue products and
  o Manipulation of human cells that allows them to be exchanged for use in research (where the transfer incurs a fee)
This doesn’t preclude a Tissue Bank undertaking Bio Banking functions. However it may have implications for the governance of different functions within a single entity (see later).
Some members also feel that the difference between human tissue and human tissue products is not well-defined in the Issues Paper. We appreciate that absolute definitions may be difficult considering that a key concept in this determination, “attenuation”, is indeed a subjective concept in itself and perhaps has to be determined on an individual basis (perhaps by an ethics committee). For example, much is made of cellular or acellular nature in determining degree of attenuation. Yet many human tissues used for transplantation, such as heart valves, may be considered acellular in nature because the intent in storage is to preserve the mechanical properties of the tissue rather than the cellular properties. Indeed, only solid organs, corneas and isolated pancreas islets could be considered to be preserving the true cellular nature of the tissue. Not forsaking our concerns regarding the TGA’s controversial manufacturing terminology, a useful tool in combination with the concept of attenuation may be the TGA’s use of “degree of manipulation” in its classifications of human tissue and tissue products.

- The committee should attempt to better clarify the differences between human tissue and human tissue products.

Corrections

**Figure 1, Page 16**

Figure 1 requires some correction. Corneas should not be used as an example of a human tissue product. It is clearly human tissue for transplantation (in this context in the same category as hearts, livers, and kidneys) and certainly one that clearly belongs to the far left of the figure in terms of attenuation.

The use of the word “transplant” in reference to bone putty (clearly a human tissue product and appropriately placed in the figure) seems inappropriate and confusing. Instead the use of the term “therapy” would assist in the clear distinction between the use of human tissue for transplants and the use of human tissue derived products for patient therapy (which may or may not involve a commercial aspect).

**Section 2.4 Cost Recovery and Profit Generation, Page 21, paragraph one**

This section discusses human tissue products and implies that Eye Banks recover cost associated with human tissue products. This is not the case – Eye Banks currently only provide human tissue. In contrast some Tissue Banks do provide what would be called human tissue products (such as bone putty). The correction and the distinction should be made. In addition, instead of using the term “research tissue bank” we suggest the use of a defined term “Bio Bank”.

**Section 2.6.3 Therapy, Page 31**

“Many of these therapeutic products are provided by those undertaking work that is closely related to transplantation such as eye banks and bone banks....”

As far as EBAANZ is aware therapeutic human derived products are not supplied by any Eye Banks. Currently Eye Banks only provide human tissue for transplantation and research – they are not involved in providing human tissue products.

In addition only one Eye Bank is a member of the ATBF. All Australian and New Zealand Eye Banks belong to the Eye Bank Association of Australia and New Zealand. The majority of bone banks, skin banks, heart valve banks and multi-tissue banks belong to the ATBF. The ATBF cannot be considered to be representative of the Eye Banking sector.

**Section 2.6.3 Therapy, Page 31 & 32**

The text indicates that “…all of these materials are presently taken from cadavers or cardiac dead donors” However-

1. Blood derived are given as an example – when clearly they are from living donors
2. Person is dead whether they are brain-dead or cardiac dead, and thus all are cadavers. Why the distinction between “cadavers” and “cardiac-dead donors” in the text?

**Section 2.6.3 Therapy, Page 32, last paragraph**

We can find no reference to the effect that the Australian Organ Donor Register lists human tissue products as within the scope of the Register. Therefore it seems incorrect to state that the Australian Government explicitly encourages donation of this material. Perhaps it implicitly encourages donation
of this material through the encouragement of tissue donation. However the Register does not cover consent for research purposes and therefore it is doubtful that it covers consent for anything other than donation of tissue (organs, eyes and tissues) for transplantation purposes.

**Other Issues**
Throughout the issue paper uses phrases such as “plastic surgeons deriving profit from human tissue products”, “Bio Banks deriving profit” and “the NH&MRC noted that undue focuses upon revenue rather than altruism has led to possible unethical behaviour…”. It would be of benefit if the issues paper provided (anonymous?) concrete examples of these activities so as to –

1. more clearly define what the Committee considers the derivation of profit and/or unethical behaviour
2. demonstrate whether this type of activity is widespread throughout the profession or if it is restricted to a certain sector, person, institution or business.

**Governance and conflicts of interest**
The Working Committee suggests that “payment of a fee that includes provision for a profit to an organisation that provides human tissue products should be limited to those agencies that produce and develop the product…..” p. 64.

In order to ensure and protect equity of access to human tissue, and to protect against perverse incentives in relation to donation of human tissue, we suggest that the Committee extend its recommendations to include -

- the governance of an organisation involved in the donation of human tissue should be separate and independent of the governance of an organisation that derives a profit from human tissue products.

Thank you in advance for the consideration of our comments.

Dr Graeme Pollock
*For and on behalf of the Eye Bank Association of Australia and New Zealand.*