Guidelines on the Use of Human Tissue for Future Unspecified Research Purposes

Submissions summary

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1 Introduction

In June 2006, the Ministry of Health (the Ministry) released *Guidelines on the Use of Human Tissue for Future Unspecified Research Purposes: Discussion document* for public consultation. The discussion document:

- provided background on the use of human tissue for future unspecified purposes
- explored the kinds of developments in research that are creating the need for tissue collections without a specific research purpose
- reviewed the current regulatory framework in New Zealand with respect to informed consent for the donation and use of human tissue
- outlined some examples of current international thinking on the issue
- discussed the ethical issues associated with this type of tissue use.

The discussion document also contained proposed national guidelines, developed to clarify New Zealand's approach to the use of human tissue for future unspecified research purposes. The proposed guidelines aimed to protect individuals' autonomy and respect the importance of informed consent, while allowing participants to consent to use of their tissue in future unspecified research.

The feedback from the public consultation provided important and useful information that has been fed into the process of finalising the guidelines on the use of human tissue for future unspecified research purposes.

This document summarises the feedback the Ministry received on the *Guidelines on the Use of Human Tissue for Future Unspecified Research Purposes: Discussion* document. The feedback from the public consultation has provided important and useful information that fed into the process of finalising the guidelines on the use of human tissue for future unspecified research purposes.

Consultation process

Consultation centred on the *Guidelines on the Use of Human Tissue for Future Unspecified Research Purposes: Discussion document* (Ministry of Health 2006).

The discussion document was released on 29 June 2006 and was sent to about 200 individuals and organisations that had a known interest in regulating the use of human tissue for future unspecified research purposes. The organisations included:

- consumer organisations
- research groups
- advisory committees
- advocacy groups
- ethics committees
- universities
- District Health Boards.

A media statement was issued when the document was released, and information about the consultation was placed on the Ministry's website. Submissions on the proposed guidelines closed on 11 August 2006. The Ministry received and accepted several requests for extensions to this timeframe.

Purpose of consultation

The guidelines were developed by collecting evidence from literature, analysing international experiences and looking at New Zealand's regulatory framework. Information gained through consultation was also important in helping to develop the policy.

The consultation on the guidelines has provided important information about:

- cultural, ethical and spiritual views on the research use of human tissue for future unspecified research purposes
- possible omissions/conflicts in the proposed guidelines that need to be clarified before the guidelines are implemented
- New Zealanders' perspectives on informed consent and research uses of donated human tissue.

To gain this information, the discussion document included a submission booklet that posed questions focusing on key aspects of the guidelines.

Participants in consultation

The Ministry received 48 written submissions in response to its request for feedback. A breakdown of the participants in the consultation process is contained in the following table and more detail is provided in Appendix 1.

The Ministry is very grateful to all those who participated in the consultation process. The information provided was extremely valuable for finalising the guidelines on the use of human tissue for future unspecified research purposes.

Table 1: Breakdown of submissions on the *Guidelines on the Use of Human Tissue for Future Unspecified Research Purposes: Discussion document*

Written submissions	**Number of responses**
Individuals*	13
District Health Boards and service providers	8
Research groups	6
Government agencies and advisory committees	5
Ethics committees	5
Universities and specific departments	5
Advocacy groups	2
Religious groups	2
Women's groups	2
Total written submissions	48

* A submission signed by more than one person has been counted as one submission. Two similar submissions, submitted by the same person, have been counted as one submission.

2 Overarching Themes

From the feedback on the proposed guidelines, the Ministry has identified the following overarching themes. These themes indicate how submitters view the use of human tissue for future unspecified research purposes.

Support for the use of human tissue for future unspecified research

Many submitters commented on the importance of, and expressed support for, the use of human tissue in future unspecified research. Some submitters considered tissue samples to be a precious resource, and suggested that it is vital to have the ability to establish collections to provide tissue for future research projects.

It was noted that, particularly for rare disorders or specific types of cancer, it can take many years to build up a statistically significant collection. Therefore, consent for future research is needed so that when research using human tissue is proposed, a suitable number of tissues will have already been collected and research can be undertaken in a timely manner.

It was also suggested that research utilising human tissue collections would, in future, become the vehicle for new treatments for serious illnesses and hopefully even cures for diseases such as cancer. A number of submitters argued that the potential for harm is so slight in this type of research, and the potential for good is so great, that future unspecified research use of tissue should be encouraged.

Withdrawing consent

It was noted by submitters that one of the most important aspects of informed consent is the right of research participants to withdraw consent at any time. In light of this, some submitters expressed concern that the proposed guidelines allowed for a donor's personal information to be delinked from their stored tissue samples, thus excluding any possibility of the donor being able to withdraw their consent in the future.

However, other submitters argued that delinking tissue is the best way to safeguard donors' privacy. They commented that little harm (if any) could result for the donor from the research use of delinked tissue.

A number of submitters said that if the guidelines prohibited the delinking of donated tissues, New Zealand researchers would not be able to contribute tissue to some international studies that required all tissue to be delinked. These submitters were concerned that, as a result, New Zealand cancer patients could be excluded from some international clinical trials and other research projects.

International research collaborations

Some submitters expressed concern at the possibility of New Zealand tissue samples being sent overseas. These submitters were particularly concerned with the:

- lack of control donors/ethics committees would have over tissue samples sent offshore
- potential lack of ethics committee review of international research projects that would utilise the tissue samples
- potential for tissue samples to be used in overseas commercial collaborations
- inability to ensure Māori tissue samples are stored, used and discarded in a culturally appropriate way.

Other submitters, however, commented on the substantial benefits that can result from New Zealand's collaboration with international research groups. It was noted that New Zealand is a small country with insufficient numbers of potential research participants and resources to undertake many types of research alone. It was argued that international collaborations are vitally important if New Zealand is to have a role in advancing scientific knowledge. Some submitters questioned whether New Zealand would be able to continue to benefit from international research, if we refuse to contribute tissue samples to international tissue banks.

Proxy consent for future unspecified research involving children

In situations where children are requested to participate in research, the requirement for consent is more complex. This is because, in general, children do not consent themselves; instead the child's legal guardians give consent, and such consent is called 'proxy consent'.

Submitters were evenly divided over the question of parental proxy consent for future unspecified research use of delinked tissue samples. Some submitters commented that parents make decisions everyday that impact on their children's interests. It was pointed out that most of these decisions can never be revisited or changed by the children once they turn 16 or become competent.

A few submitters commented that no harm could ever come to a child if their tissue sample were delinked and advocated for delinking to occur in every situation.

Many submitters, however, argued that the guidelines should prohibit the possibility of parental proxy consent for future research where donated tissue samples would be delinked. The main reason given was that such parental proxy consent would foreclose any possibility of a child later withdrawing consent to the use of their tissue sample for future unspecified research. Some submitters considered that the right to withdraw consent was more important than participation in research. A few considered that children's future choices' should be preserved and that delinking their tissue samples should only occur with the consent of the child, not proxy consent from parents.

Ethical review

Many submitters emphasised the importance of ethical review of all New Zealand research using stored tissue samples.

Submitters were divided about how to ensure tissue samples sent overseas are used only in ethically sound research that respects the donors' wishes.

Some submitters felt that aspects of the proposed guidelines contradicted the *Code of Health and Disability Services Consumers' Rights* and the *Operational Standard for Ethics Committees* and asked how ethics committees would address this conflict.

Others expressed concern about the quality of ethics review in New Zealand and recommended that the guidelines be finalised in a way that would eliminate inconsistency in ethics committees' decision-making processes.

A few submitters argued that ethics committees should respect the right of donors to consent to research of their choice.

3 Summary of Submissions

The following summary of submissions has been organised to match the order of the questions posed in the original discussion document.

1. Do you think it is reasonable to ask patients and research participants to give some form of consent to future unspecified use of their tissues in research?

Allowing consent to future unspecified use of a donor's tissue is a shift from current requirements for consent, where donors are well informed of the use of their tissue for a specific research study. Consenting to future unspecified research would mean donors would not be fully informed as to the use of their tissue in future research studies.

The vast majority of submitters agreed that it is reasonable to ask potential donors to give some form of consent for future unspecified use of their tissues in research.

Many submitters commented that individual donors have a right to participate in research of their choice and that it would be disempowering, patronising, paternalistic and unethical to deny donors the option of consenting to future unspecified research. One submitter noted that it is important that ethics committees do not, in a paternalistic fashion, remove the right of individuals to consent to research of their choice. It was noted that this right is written into statute, under *The HDC Code of Health and Disability Services Consumers' Rights Regulation 1996* (the *Code of Health and Disability Services Consumers' Rights*).

One submitter noted that a lot of people may not be concerned how their tissue is used and that there should be provision for this tissue to be used in an anonymised way, totally delinked, with basic consent.

A number of submitters commented that tissue collected for future unspecified use is an invaluable resource that enables important medical research to be undertaken.

One submitter commented that if the conditions imposed on future use of tissue are too cumbersome, the use of that tissue becomes impossible, too difficult or too expensive.

Another submitter recommended that tissue banking for future research not be made impossible by too many administrative barriers or unreasonably high consent requirements.

Some submitters argued that storing tissues for future unspecified research makes best use of donated tissue, as individuals can make a single tissue contribution to many research projects. This was considered particularly important for research into rare disorders because it takes so long to accumulate a statistically significant collection of tissue for such disorders.

Right to withdraw consent

Some submitters suggested that giving people the option of relinquishing all control over the storage and use of their tissue for future unspecified research breaches the *Code of Health and Disability Services Consumers' Rights*. It was argued that even though consent may be obtained from a donor for ongoing storage and use of their tissue for unspecified research purposes, under the *Code of Health and Disability Services Consumers' Rights*, the donor retains the right to ask for the return or disposal of their tissue.

One submitter argued that the right for any person to change their mind is inherent in the principles of informed consent and that the proposed guidelines do not adequately protect this right.

One submitter commented that the proposed *Guidelines on the Use of Human Tissue for Future Unspecified Research Purposes* should be consistent with the *Universal Declaration on Bioethics and Human Rights* (2005). The submitter said that the guidelines must make it clear that donors have the unequivocal opportunity to change their mind and to withdraw their consent at any time and for any reason without disadvantage or prejudice.

Another submitter cited the *Operational Standard for Ethics Committees*, which states, 'individuals have the right to discontinue treatment or to withdraw from participating in research at any time' (paragraph 26). This submitter was concerned that the *Operational Standard for Ethics Committees* conflicted with the proposed guidelines and suggested that this would leave ethics committees is a difficult situation.

However, other submitters argued that there might be cases where the public benefit would justify delinking tissue, even though the practical effect would be to preclude the revocation of consent. It was acknowledged that any public benefit should be both substantial and demonstrated before this happens.

Ethics committee approval

Many submitters asserted that it was reasonable to ask individuals to give consent to future unspecified research as long as the future research projects would be reviewed and approved by a New Zealand health and disability ethics committee.

However, one submitter argued that it is impractical and unnecessary for researchers to seek approval from a New Zealand ethics committee when tissue is held overseas as part of an international collaborative group research project. Instead, approval should be sought from an accredited ethics committee in the country hosting the tissue bank.

Tissue banks

One submitter commented that tissues collected for unspecified research should be collected, where at all possible, by a large repository, such as a tissue bank, whose governance and operation is transparent, to help maintain public trust and confidence in New Zealand health research.

Another submitter advocated for the creation of such a tissue bank in New Zealand, so that tissue donated by New Zealanders would remain in the country.

Overseas research

A few submitters commented on the relationship between New Zealand research and international research. One submitter commented that contributing tissue to overseas studies is an essential part of collaborative research. It was argued that being able to contribute to international research projects is vitally important.

Another submitter noted that some research projects require highly specialised units, techniques or equipment to achieve their end points. It was argued that these resources might not be available in New Zealand. It was noted that in the case of rarer diseases, New Zealand cannot collect sufficient sample numbers to obtain statistically significant results, and in such situations, it is essential to combine the samples with those collected internationally to undertake meaningful research.

One submitter suggested that if New Zealand research groups cannot provide samples to international studies, the applicability of the results to New Zealand's population might be compromised.

Opposition to future unspecified research

A small number of submitters were opposed to future unspecified research. The main reasons given were:

- a lack of trust in the integrity of researchers, especially of foreign-based research organisations
- reluctance to send New Zealand tissue samples to overseas tissue banks
- the possibility that tissue samples could be delinked, which denies donors the right to withdraw consent for the use of their tissue sample.

2. What information do you think should be provided to potential research participants?

The requirement to provide research participants with information regarding the use of their tissue is a fundamental ethical principle. Information requirements currently exist under the Operational Standard for Ethics Committees. The purpose of this question is to determine whether there are any additional information requirements needed for future unspecified research.

The majority of submitters thought that potential research participants should be provided with as much information as possible regarding the potential use of their tissue in order to make an informed decision.

A few submitters recommended that the decision to donate tissue for future unspecified research should be separated from all other decision-making, such as the decision to consent to specified research or the decision to send tissue overseas for diagnostic purposes.

One submitter commented that where no information can be given, donors should be told this, and why.

A couple of submitters considered that the information sheet and consent form should be made as simple as possible for potential donors. It was suggested that the *Operational Standard for Ethics Committees* could include a generic information sheet for future unspecified research.

Another submitter commented that researchers must appreciate that seeking consent for future unspecified research would be a more time consuming process than attaining informed consent for specified research as there are more topics to cover and many of these may require indepth explanations.

Some submitters agreed with the information to be provided to potential research participants on possible use of their tissue as set out in the proposed guidelines. However, the majority of submitters made suggestions regarding the information that should be provided to potential research participants. Suggestions included the following.

Collection

- A background and description of the rationale behind collection of tissues for unspecified research, explaining the potential benefits.
- An explanation of:
  - why the person is being approached for tissue
  - what tissue will be taken
  - how the tissue will be collected and what risks are involved
  - how the tissue will be processed.

Storage

- A description of how the tissue will be stored and managed.
- Details of the organisation under whose auspices tissue storage is taking place, the relationship of that organisation with the treating clinical team obtaining consent and the lines of accountability/responsibility.
- An explanation of:
  - how the tissue will be identified (for example, whether the samples will be coded, delinked or anonymised)
  - the fact that if the tissue samples are delinked, then the decision to do this is irreversible and may prevent data obtained from research being of direct benefit to the donor (It also removes the possibility of withdrawal of consent to future use.)
  - the type of demographic and clinical data about the donor that will be stored with the tissue specimens
  - who may have access to tissue samples, and under what conditions
  - any limitation on duration of storage, if known.

Disposal/withdrawal of consent

- A description of tissue disposal methods.
- Provisions for withdrawing consent (where it is possible to do so).
- An explanation of:
  - what will happen to the tissue if the donor dies or is not contactable
  - whether tissue can be returned and when.

Use of tissue in research

- An explanation of:
  - whether research participants will be entitled to specify any restrictions on future research use of their tissue
  - whether tissue samples may be used in commercial research collaborations
  - whether the tissue samples could be sent overseas and, if so, what regulatory/ licensing framework would apply
  - the fact that tissue sent overseas may not receive the kind of ethical review that occurs in New Zealand
  - the fact that potential donors will not have any control over their tissue if it is delinked and sent overseas
  - whether the tissue will be used in the development of therapies
  - whether the participant will be informed when new research is proposed on their tissue
  - whether information generated by research on tissue samples could have significant negative impact on a donor's ability to take out health insurance
  - whether any future research might involve genetic analysis
  - how benefit would accrue from use of the tissue.

Cultural issues

- A discussion of different cultural views of tissue research.
- An explanation of the fact that the donors may want to discuss the possibility of donating tissue with their family or whānau.
- A broader discussion on the cultural impact on storing and disposing of tissue.

Information

- An explanation of:
  - the fact that donors will not own any intellectual property that may arise from any future research
  - whether any information learnt from research using the tissue would be fed back to the donor, and how this would occur

- whether any future information about the donors would be requested or taken from their records
- whether future researchers would be able to collect further data on the donor (that is, outcomes) without the donor's knowledge.

Other issues

- An explanation of:
  - whether researchers might wish contact the donor in the future
  - whether provision has been made for genetic counselling to be available to donors if required
  - the fact that the donor would not receive payment if the research became financially lucrative
  - the fact that the research would be enhanced by the availability of tissue with broad consent and retained links.

3. Do you think the options for consent are reasonable and practicable? What other options could or should be provided to potential research participants?

Providing options to research participants is an essential part of the consent process. The range of options will determine how much scope researchers have to use donated tissue, and how much involvement a donor will have with any future research.

Some submitters considered that the options for consent outlined in the proposed guidelines were reasonable and practicable. The majority of submitters accepted that donors should be offered the following broad options:

1. The right to refuse the use of tissue samples in future unspecified research.
2. The right to permit the use of tissue samples for future research use without restriction.
3. The right to permit the use of tissue samples with restrictions.

Many submitters made suggestions about the type of restrictions donors should be able to place on the use of their tissue (option 3 above). Suggestions included the following restrictions:

- Permitting the use of tissue samples for research under specific conditions or for particular types of research.
- Permitting the use of anonymised/coded/delinked tissue samples.
- Permitting the use of tissue samples in principle but with the understanding that the donor be contacted for each proposed future research use.
- Permitting the use of tissue samples in New Zealand only.
- Permitting the use of tissue samples in 'low-risk' research only.
- Refusing third-party researchers access to tissue samples.

- Refusing researchers access to medical files.
- Refusing to allow tissue samples to be used in commercial research collaborations.
- Refusing to allow tissue samples to be used for research on certain topics.
- Refusing to allow the tissue samples to be immortalised.

Option 3 generated much discussion, and submitters were often polarised in their views over what type of restrictions donors should be able to place on the use of their tissue sample. Many submitters argued strongly that donors should be able to specify as many restrictions on the use of their tissue sample as they wished. This was considered essential because of the boundless nature of possible research and to give donors some measure of control. One submitter commented that if any option presented in the proposed guidelines were not to be made available to donors, this should be made clear to the donors.

A few submitters supported making the options given to donors discretionary. One submitter commented that although the options offered in the proposed guidelines covered a good range, it was important not to make the options mandatory for every research project. The submitter argued that if the options become mandatory, New Zealand would be excluded from participating in some international studies where it is not possible to give all these options. One submitter suggested that, for clarity, the guidelines could include the wording '*Where practicable*, options could include ...'. One submitter was concerned that there was no criterion for researchers on how to determine which of the options should be provided.

One submitter commented that there might be research proposals where participants would be given only one option, for example, having their tissue sample sent overseas for future unspecified use by unspecified groups. Some submitters had concerns about this possibility. However, others argued that as long as prospective donors were given clear information about what they are consenting to, this lack of options did not need to be a barrier to such research.

A few submitters requested that the options presented in the proposed guidelines be clarified. One submitter commented that the list of options was not comprehensible and would only serve to confuse some participants. It was recommended that the options available to donors be written in accessible language, with a list of definitions for technical terms and an explanation of difficult concepts. In particular, the submitter felt that the language of coded information, anonymity, disposal methods and collaborating researchers needed to be clarified. The submitter suggested that the various issues and possibilities could be illustrated by providing examples of what the different consent options mean and what can happen with a tissue sample.

Options that should not be offered

Some submitters considered that some options should not be offered to donors. For example, it was considered unreasonable and impractical for researchers to recontact donors to obtain consent to use their tissue samples for each future research project. One submitter commented that this would be particularly difficult for donors suffering diseases like cancer where mortality is high. Another submitter suggested that it may

be distressing for the family/next of kin to be asked to consent to further research, even if this was the donor's wish. Alternatively, it was noted that the tissue donor might be terminally ill and not in a reasonable state to consider such options.

Third-party and commercial use of tissue samples

Other submitters considered that some options should be mandatory. One submitter thought that it would be prudent to always obtain consent for the use of tissue samples in 'commercial' research, even if the main goal is to improve health care treatments or knowledge about basic human biology. The submitter commented that all future research has the potential to be commercial, and possibly international. Similarly, it was argued that third-party tissue use almost always occurs if future research occurs, so it is not appropriate to deny donors the option to refuse third-party use.

One submitter noted that it might not be possible to separate commercial from non-commercial use easily as privately/publicly funded collaborations become more common.

Another submitter noted that due to the sensitive nature of issues relating to human tissues and the associated DNA, it essential that the appropriate safeguards are put in place so that tissue donated for altruistic reasons could not be used by any researcher or organisation for personal financial gain.

Administrative challenges

A couple of submitters were concerned about the burdensome administrative challenges that could be associated with an extensive list of options. These submitters felt that it may be harder and more expensive for researchers to keep track of what samples can be used for each research project. One submitter noted that compliance costs of such systems could become onerous to small research organisations or programmes funded by charities. However, other submitters disagreed, arguing that with computer data management it is relatively easy to sort tissue samples with respect to what the donor has approved.

Unidentified or delinked tissue

Some submitters expressed a preference for all tissue samples to be delinked. It was argued that unless the research has direct clinical relevance for participants, all samples should be delinked because this is the best way to safeguard participants' privacy and confidentiality. One submitter commented that while this means that participants lose their right to withdraw their samples from that particular research project, it offers maximum protection of participants' privacy.

However, an equal number of submitters disagreed with this position, arguing that the correlation of laboratory findings with clinical information may be pivotal to future research and advancement of disease treatment; hence the use of delinked tissue samples may negate the benefit of tissue donation. It was also noted that reidentifiability preserves the possibility of some important processes for donors, for example, the ability to withdraw consent and for children to reconsent in the future.

One submitter noted that the eventual non-identification of tissue also has implications for preferred cultural processes and outcomes. If either of these factors were to cause a reduction in the willingness of Māori to give consent, then we would be contradicting the dictums of the Treaty of Waitangi.
One submitter noted that in some proposed studies involving the use of delinked tissue samples, particularly those that might be regarded as sensitive or controversial, it may be useful to seek community feedback on the proposed research in addition to formal ethics committee approval.

4. Do you think there should be any requirements on the use of information derived from tissues that are donated for future unspecified research use that are additional to or distinct from those already required in relation to other research with human tissue?

Where research is planned at the time of consent, it is more likely that researchers will be able to provide donors with clear details on how the information derived from the research will be used. When tissue is donated for future unspecified research, such clarity may not be possible. This question explores whether there should be any additional or distinct requirements for the use of information derived from tissues that are donated for future unspecified research.

The majority of submitters considered there should not be any requirements on the use of information derived from tissue samples that are donated for future unspecified research use in addition to or distinct from what is already required in relation to information about other research with human tissue samples.

Many submitters argued against a requirement to inform donors of individual research results. Some submitters commented that to offer all donors individual research results would not necessarily be meaningful, could create confusion and uncertainty, as well as being an additional burden on research resources.

It was noted that the likelihood research will yield information useful to the treatment of a donor's particular condition is very small. One submitter commented that it takes many years for research to produce useful information, and many research endeavours, for various reasons, do not generate the kind of data that would have clinical significance for patients.

One submitter commented that it is difficult to give specific results on a donor's own tissue sample because research data are experimental, and need to be confirmed by further testing before being used in clinical care.

One submitter argued that there is no need for a specific requirement that information collected in the course of research be directly fed back to the donor, because the benefit to individual donors will accrue indirectly through the ongoing outcomes of research.

Recontacting donors

Much of the discussion in the submissions focused on the practicality of having to recontact donors with results of research, many years on from when the tissue was initially donated. Some submitters thought having to recontact donors would be an additional burden for researchers and would be impractical for the following reasons:

- The tissue may have been delinked.
- The participant may be deceased.
- The research may be taking place overseas.
- Donors may not be able to be located.

However, one submitter commented that the fact that some donors may not be able to be given the results of future research because their contact details are out of date does not mean that even donors whose contact details are still available should not be given their future results.

A few submitters recommended that contact to offer results be individualised. It was suggested that tissue donors should be given the choice of whether or not they be contacted in future with research results. It was recommended that research participants bear some responsibility for maintaining up-to-date contact details if they require information.

One submitter noted that there is a range of options available for feeding general research results back to tissue donors, some of which do not require researchers to contact the donors personally, for example:

- setting up websites that contain research results
- generating a mailing list to be used to send out general findings
- sharing information through scientific publications, meetings and public seminars/ talks as well as with the media
- providing donors with a contact phone or fax number that they could use to obtain research results/proposals
- sending reports to support groups, giving presentations to support group meetings and providing articles for support group newsletters
- developing an extension to the organ donor register that would be updated regularly with research information for tissue donors.

Other submitters argued that researchers must contact the donor or their blood relatives if any information of possible importance to their health is discovered during the course of the research, with consultation from an appropriate ethics committee when required. One submitter commented that information derived from tissues may be relevant to the clinical treatment of a patient and could lead to the discovery of better health treatments for that patient. It was argued that in such cases, there might be an ethical requirement to inform the patient and their clinician. However, it was also noted that if a donor has opted for their tissue sample to be completely anonymised, then such improvements to their clinical care would not be possible. A couple of submitters recommended that all

samples be deidentified but not totally anonymised so that important information could be relayed back to the donor.

One submitter commented that care must be taken to ensure that any information given to participants is both accurate and can be understood by a layperson. It was noted that while it will often not be possible for medical representatives to discuss study results with donors in person, this option should be made available to the donor when practicable, particularly in cases where the information is sensitive or may easily be misinterpreted.

5. Do you agree that there is no need for ethics committees to require any additional safeguards of participants' interests with respect to New Zealand researchers accessing samples donated for future unspecified research? If you do not agree, what safeguards would you propose?

All New Zealand research involving human tissue samples is subject to ethical review. This question explores whether there is a need for additional safeguards in order to protect participants, in situations where samples are accessed by other researchers.

The majority of submitters agreed that there is no need for ethics committees to require any additional safeguards of participants' interests with respect to New Zealand researchers accessing samples donated for future unspecified research.

Several submitters reiterated the need for each research project to be reviewed by an ethics committee but commented that this should be the only requirement for future unspecified research projects. It was noted that the current safeguards by which researchers must abide (for example, the *Operational Standard for Ethics Committees*) are comprehensive. It was suggested that a review of the adequacy of these safeguards in two or three years' time would be helpful in determining whether further measures are needed.

One submitter commented that where tissue banks comply with ethical guidelines and have clear governance structures, there is no need for New Zealand ethics committees to require additional safeguards with respect to accessing tissue samples.

A couple of submitters suggested that anybody collecting tissues for research should have procedures, policies and audit processes approved by the appropriate ethics committee.

One submitter recommended that tissue donation to a centralised repository should be encouraged where possible. It was suggested that ethics committees only allow groups with a good track record, funding and high quality research design to access banked tissue. It was noted that any tissue, but in particular rare tissues, should not be consumed in low quality research projects.

Overseas banks

One submitter commented that there might be a need for additional measures for the use of tissue samples gathered for overseas banks. However, another submitter

suggested that the only safeguard required for overseas use is that researchers' access to tissue samples be conditional on approval of an accredited ethics committee in the country hosting the tissue bank.
One submitter suggested that there should be additional safeguards to protect the consent conditions of donated tissue when tissue banks are bought or sold, or policies governing collections are changed.

Another submitter suggested that additional safeguards are necessary to ensure that the New Zealand researchers collecting the initial sample maintain some responsibilities for future research conducted on the samples collected.

Oversight committee

A couple of submitters suggested that an oversight committee be established as an additional level of safeguard for tissue research. It was suggested that an oversight committee would ensure that samples would be shared in a responsible and ethical manner.

Extent of committees' power

One submitter commented that the ethics review system gives too much power to ethics committees to waive people's rights under law in certain circumstances and expressed concern that there is no real supervision or policing of the committees' decisions.

One submitter recommended that ethics committees consider research applications in a consistent fashion and avoid arbitrary differences between committees. The submitter considered that the guidelines should be specific so that individual ethics committees would not be able to determine additional safeguards on a case-by-case basis.

6. What would constitute a reasonable level of assurance to ethics committees that samples sent overseas will be subject to appropriate governance and ethical review? Is any additional assurance required over and above that currently sought when consent is given for tissues to be sent overseas for specified research?

It is possible that future unspecified research might be conducted overseas. When this occurs, the procedures for governance and ethical review of samples used in such future research are more difficult to enforce. Therefore ethics committees and research teams must be confident that the procedures for governance and ethical review are adequate to ensure that participants' wishes are respected.

Some submitters commented that no additional assurance is needed over and above that currently sought for tissues to be sent overseas for specified research. It was suggested that the issues are the same for any research being carried out in another country where there is a New Zealand connection or interest. One submitter commented that, for either specified or unspecified research, an ethics committee must have sufficient information to be able to assure itself that the ethical procedures governing use of the tissue overseas are up to the same standards as the procedures governing use in New Zealand.

A few submitters considered that the requirement proposed in the guidelines (that future overseas research must be subject to review by a committee or review board that conforms to the International Ethical Guidelines for Biomedical Research Involving Human Subjects) is a very adequate safeguard.

One submitter disagreed, commenting that this requirement was insufficient in itself to assure participants that rigorous ethical review would be carried out. The submitter suggested that ongoing audit and monitoring of what happens to the samples once they have gone overseas is needed.

Many submitters made suggestions about the information New Zealand ethics committees would need to receive to be reasonably assured that samples sent overseas would be subject to appropriate governance and ethical review. Suggestions for information needed included:

- the reputation, accreditation and international standing of the tissue bank/research group
- the procedures for storage, handling and disposing of the tissue by the bank/ research group
- a clear outline of what would be done with the tissue overseas, what linked information would be sent and what would be done with any remaining tissue
- a list of individuals and organisations having access to the tissue samples
- clarification on whether the overseas group would be working in collaboration with a New Zealand research group
- details on where the collection would be located and what legal oversight would in place to govern the collection
- the audit and monitoring procedures of the tissue bank/research group
- the authority and constitution of the overseas ethics committee that would approve applications
- the nature and standard of ethical review in the country where the tissue would be held
- the regulatory or licensing requirements of the country where the tissue would be held.

One submitter commented that New Zealand ethics committees are unlikely to always have the information necessary for evaluating overseas ethics committees that may subsequently be approving research for particular tissue banks. Some submitters suggested that a degree of trust has to lie with the regulatory regime of the country to which the samples are sent. It was argued that the risks have to be balanced against the benefits of participating in international research projects.

It was noted that internationally, standards of ethical review vary widely. A couple of submitters commented that it needs to be clearly explained to prospective tissue donors that New Zealand ethics committees cannot control the use, storage and disposal of samples sent overseas. One submitter suggested that because there are fewer restrictions on use of human tissue for unspecified research, the potential for actual abuse is greater than in cases where tissue use has been limited to a specific project. The submitter considered that the only way to overcome this situation would be to implement an internationally agreed and recognised system of accreditation and auditing for research institutions.

One submitter suggested that there are two options available for ensuring that samples sent overseas are subject to appropriate governance and ethical review:

1. Ethics committees could require that samples be sent only to countries with similar guidelines to New Zealand, with ethical oversight, or to countries that comply with the World Health Organization's International Ethical Guidelines for Biomedical Research Involving Human Subjects.
2. Ethics committees could require that research donors understand that their samples may be sent overseas to collaborators (or others) whose research is not subject to ethical review. Donors could then decide whether to donate under these conditions.

A few submitters commented that it would be preferable for any research using tissue samples from New Zealanders sent to overseas tissue banks to be subject to review by a New Zealand health and disability ethics committee. However, it was noted that this might not always be practical.

One submitter commented that if any future research use of New Zealand sourced tissue was required to be referred back to a New Zealand ethics committee for approval, New Zealand's participation in international research and potentially, New Zealand's ability to access those same overseas banks, would be limited. It was argued that it is reasonable to allow New Zealand material to be released from an overseas tissue bank for an approved research project without further ethical review in New Zealand provided that New Zealand ethics committees can be satisfied that the future process will be safe and also that the donor clearly understood the nature of the consent to use at the time they gave that consent.

One submitter argued that tissue from New Zealand should not be allowed to be sent overseas for anything other than nominated, specific research. Concern was expressed that New Zealand standards of ethical review will not be applied in overseas settings. It was argued that this is a particular problem for Māori, as it is unlikely that overseas facilities or ethics committees will be familiar with Māori protocols for handling and disposing of tissue.

7. Do you think it is reasonable to permit tissue samples from children to be delinked or anonymised on the basis of parental proxy consent, even though this will foreclose any possibility of children later withdrawing consent to the use of their tissue for future unspecified research?

The current Operational Standard for Ethics Committees *affirms the right to withdraw consent (paragraph 26), and the* Code of Health and Disability Services Consumers' Rights *provides for people to give consent when they are able; this is usually by the time they are 16 years of age. This question explores the conflict between the rights of children to later withdrawal consent and the rights of parents to give proxy consent for their children's tissue to be delinked and used in future unspecified research.*

Overall, there was a wide divergence of opinion on this issue. Many submitters agreed that it is reasonable to permit tissue samples from children to be delinked on the basis of parental proxy consent, even though this will foreclose any possibility of children later withdrawing consent to the use of their tissue for future unspecified research. Others disagreed, expressing concerns based on children's rights to consent.

Parental autonomy

It was noted that parents and guardians routinely make decisions affecting their children's interests. A couple of submitters commented that it is not possible for all decisions made by parents to be revisited by children when they reach the age of consent. One submitter suggested that if parents were denied the ability to contribute their child's tissue to research, the child might miss the opportunity to benefit from new therapies or preventative strategies. One submitter said that at the time of providing consent, parents are acting in what they consider to be the best interests of both the child and the wider community. The submitter considered that, given parental altruistic motives, it is unreasonable to require children to consent at the age of 16 to the use of their tissue for future unspecified research. Therefore, it was recommended that parental proxy consent be accepted whether or not tissue is anonymised.

Delinking children's tissue

Some submitters considered that delinking samples would safeguard child participants. One submitter commented that if a child's right to withdraw from research once they reach 16 years of age were upheld, children would be exposed to risks associated with the protection of their privacy and confidentiality. The submitter commented that in the absence of any argument relating to clinical relevance, these risks outweigh the benefits of retaining the option of withdrawing consent.

One submitter suggested that if tissue samples were delinked, no harm could occur and commented that it is hard to imagine a scenario in which a child might wish to withdraw consent. Another submitter argued that donation of delinked tissue is very unlikely to be *contrary* to the child's interests. It was suggested that a blanket insistence that researchers retain children's tissue in an identifiable form would also pose an additional and unwarranted burden on researchers in cases where there is otherwise no need for such a link to be maintained. Another submitter noted that New Zealand's privacy law does not require a secondary consenting process for collection, use and disposal of information when a child becomes competent or turns 16.

A few submitters thought the proposal was reasonable, with qualifiers. For example, some submitters thought it was reasonable to permit tissue samples from children to be delinked or anonymised on the basis of parental proxy consent only if:

- the child is incapable of giving any assent at the time of donation
- there are sound research reasons for doing so
- the research has the potential for public benefit
- it is made clear that future withdrawal of the sample is not possible.

Gillick competence test

Many submitters said that the competence of a child to make a decision must be considered in terms of Gillick competence, whereby children under the age of 16 years can give legally effective consent if they understand the nature and consequences of the decision they have been asked to make. Submitters argued that if children younger than 16 years are competent, they have the legal right to make an informed choice about the future use of their tissue samples, and the guidelines should reflect that legal position. It was also argued that the right of retrieval (and withdrawal of consent to usage) should be extended to Gillick-competent children and not just those who have attained the age of 16 years. It was recommended that Gillick-competent children have all of the same rights in respect of their tissue as adults.

Concerns regarding delinking children's tissue

A number of submitters argued that it is not reasonable to permit tissue samples from children to be delinked or anonymised on the basis of parental proxy consent. The main reason given was that it would foreclose any possibility of children later withdrawing consent to the use of their tissue for future unspecified research.

One submitter commented that a decision to anonymise tissue samples should only be done in special circumstances and should be an active decision by the donor. Therefore, it was argued that while adults are entitled to make this decision for themselves, they should not make this decision for their children. The submitter suggested that, when they reach an age of competence, children might make this decision for themselves if they wish to do so.

One submitter commented that children should have their future choices preserved as much as possible. It was argued that children, once competent, should be able to withdraw their tissue sample from a tissue bank or direct the destruction of any of their identifiable tissue taken with parental consent before their age of competence.

Another submitter said that a parent's or guardian's consent can only properly be given in the child's best interests, so it may be questionable whether consent to retention and use of deidentified tissue for research purposes is legitimate. One submitter commented that the fact that a child's tissue might have less to contribute because it needs to remain identifiable to safeguard the autonomy of the person from whose body it came (until he or she is of an age to exercise his or her autonomy) is a small concession.

A few submitters recommended that the guidelines require a child's tissue sample to be linked always, to facilitate the preservation of the child's autonomy and rights regarding reconsenting or withdrawing consent in respect of their tissue. It was argued that the potential benefits of retaining the tissue sample in a linked and identifiable form were not elucidated in the discussion document.

One submitter suggested that tissue samples without clinical data or health history are of very limited value in research and that research information needs correlation with clinical outcome.

A few submitters suggested that tissue samples be stored in a bank in a coded fashion that allows retrieval in the event that a parent or a young person reaching the appropriate specified age no longer wishes the material to be stored for future unspecified research.

A couple of submitters commented that there are risks and potential harms involved in denying adolescents the right to withdraw consent to future unspecified research uses of their tissue that extend beyond merely physical risks. Such risks include:

- losing privacy
- losing autonomy
- finding the use of one's own genetic information in the pursuit of research to be morally, spiritually or culturally abhorrent
- having one's genetic information used in a study that may unwittingly contribute to the construction of new groups (based on arbitrary and non-obvious patterns and statistical calculations) that puts oneself and others at risk of stigmatisation and discrimination.

Right of children to withdraw their consent

A couple of submitters argued that the proposed guidelines contradict the *Operational Standard for Ethics Committees* because they do not require children to consent at the age of 16 to their ongoing participation in a research project. It was suggested that the *Operational Standard for Ethics Committees* and the *Code of Health and Disability Services Consumers' Rights* provide an expectation that donors have the right to withdraw consent when they are of an age to make their own choice. One submitter requested that the conflict be clarified to prevent confusion for ethics committees.

Some options for preserving children's ability to reconsent at the age of 16 (or when they are Gillick competent) were suggested:

- Researchers could make their best endeavours to keep track of families who had given consent for their children's tissues to be used for future unspecified research purposes and seek reconsent.
- Researchers could work on a presumption of consent to future unspecified research purposes if the child or family establishes no contact within a specified timeframe of the child's 16th birthday.

- Research on a child's tissue sample with the proxy consent of the child's parents only could be subject to a time restriction that forbids the future use of such tissue in any research (not of direct benefit to the child) where no reconsent has been received from the child by their 16th birthday.
- Someone (family or institution) could take on the responsibility of remembering that proxy consent has been given, either so that the child knows that they need to approach the institution to give or withdraw consent or so that the institution can (at a suitable age) approach the child for reconsent. If the institution carries the responsibility for recontacting the child, the institution will need to retain up-to-date contact details for that child.

It was also suggested that implementing a default disposal period of 10 years would largely resolve any concerns in relation to children.

8. Would participants be adequately protected and timely review of low-risk research enhanced, if provision were made for delegated authority to the chairperson of an ethics committee to include:

- **use of anonymised tissue; and**
- **use of tissue where the participant has given consent for future unspecified research use of their tissue?**

In situations where tissue is anonymised or where donors have already given consent for future unspecified research, using their tissue samples may require fewer protections to safeguard the donor. This could decrease the involvement of ethics committees and result in a quicker and more efficient approval process for researchers.

Several submitters considered that participants would be adequately protected and timely review of low-risk research enhanced, if provision was made for authority to be delegated to the chairperson of an ethics committee, in the situations specified. It was noted that ethics committee chairpersons are already able to approve low-risk research under delegated authority.

Limits on a chairperson's delegated authority

One submitter commented that delegated authority for a chairperson should not be extended to include approval for the use of tissue that is not anonymised. The submitter argued that non-anonymised samples pose a greater risk to donors' privacy, which requires a greater degree of scrutiny.

However, another submitter commented that the issue is not whether the tissue is anonymised or donated for unspecified use but whether the nature of the proposed research is ethically acceptable. That submitter said that some proposals will be uncontroversial and straightforward and could be approved under delegated authority.

A few submitters were concerned that 'low-risk' research was not defined. One submitter commented that expedited ethical review might be appropriate in some situations but that such review should be used as sparingly as possible to avoid any lowering of standards/safeguards. Another submitter recommended that guidelines be developed around when delegated approval can occur. One submitter considered that two or three people could carry out a review more quickly than just the chairperson.

Opposition to delegated authority

Several submitters considered that delegated authority was not appropriate under any circumstances. Some submitters thought that review by an accredited ethics committee is essential to maintain public confidence and trust in health research. One submitter commented that it is premature to delegate approval of use of anonymised tissue for research to the chairperson and that all proposals to use human tissue for research should be considered in full committee. Another submitter commented that ethics committees provide essential oversight to ensure respect of all values donors might hold and that samples are utilised in the most efficient, rewarding and responsible projects.

One submitter commented that unspecified research, by its very nature, requires careful consideration in every case and this should require a full-committee decision. Another submitter said that an ethics committee chairperson might not be comfortable being solely responsible for an ethics review. One submitter said that the chairperson of an ethics committee could not be expected to take on delegated authority in cases where researchers might wish to fast-track research approval. The submitter commented that there is the danger of allowing 'carte blanche access' and use of tissue that has already been consented for future unspecified use. It was argued that it is crucial that such situations not occur and all research be reviewed by ethics committees in the same rigorous manner.

One submitter commented that such a provision would not adequately protect donors because researchers' ideas about low risk are not necessarily correct nor in agreement with the tissue donor's ideas about risk.

9. Are there any additional issues related to consent for future unspecified research use of human tissue that need to be considered in any guidelines for research? If so, what are they, and what considerations would you want to emphasise?

Several submitters raised additional issues. These have been grouped as follows.

Governance of tissue collections

A couple of submitters considered that governance of tissue collections was an important consideration for future unspecified research use of tissue. One submitter said that all tissue banks, whether based in New Zealand or overseas, should be required to have a well-documented governance structure and clear guidelines for ownership of, access to and means of return or disposal of tissue.

It was noted that not all situations where consent is approved would involve large reference tissue banks; in some cases the guidelines may be applied to individual researchers with small laboratories and small numbers of samples. A couple of submitters noted that it could be difficult for small collections to offer a similar level of well-defined collection, storage, tissue access policies and defined governance that a larger tissue bank would provide. One submitter said that the governance requirements for such situations and associated financial implications need to be considered to ensure that small research facilities are not disproportionately disadvantaged.

Timeframe

It was suggested that consideration be given to whether permission to store tissue or to use tissue for research would be for a specific timeframe and whether the researcher would have to reapply for ethics committee approval. One submitter commented that ethics parameters and community beliefs and standards change over a period of time and it seems unwise to approve research for an indefinite period of time.

Cultural concerns

One submitter commented that it is important to support cultural diversity and opinion throughout the consent process. It was also considered important that people of a particular cultural background and belief not be prevented from participating in research because another group does not agree with the process.

Another submitter noted that it is unclear from the discussion document how some of the cultural, ethical and spiritual questions would be addressed under the guidelines.

Deceased persons

One submitter recommended that those in possession of deceased persons should be able to give consent for the future unspecified use of tissues from the deceased, as per current practice for specified use of tissues. However, in cases where the deceased has indicated full or partial prohibition of the use of their tissues, the submitter believed that the deceased's request should be upheld.

Public register

Another submitter recommended that the guidelines require the establishment of a publicly available register of information to allow the public to know what sort of tissue banks exist and what sort of approved research projects are using stored tissue.

10. Do you have any other comments on the proposed guidelines?

This section lists comments that have not been included elsewhere in this document.

The Human Tissue Bill

- It would have been the best use of resources to wait to develop the guidelines until after the Human Tissue Act 1964 had been reviewed and revised legislation enacted. In reviewing the Act, many of the issues relating to the use of human tissue would be assessed, and it is very likely that any guidelines for the unspecified use of human tissue prepared now will need to be rewritten to ensure consistency with the new Act.
- One of the structures being proposed under the Private Member's Human Tissue (Organ Donation) Amendment Bill 2006 is an Organ Donor Register (the Register). Currently the Register is limited to organ donors, but it is logical to add donor tissue to the Register. This is an appropriate extension of the current Human Tissue Act and would strengthen the guidance for ethical approval.

Importation of tissue

- A couple of submitters asked whether guidelines would be developed to regulate the importation of tissue for research into New Zealand. The view was expressed that before tissue from overseas was imported into New Zealand, ethics committees should satisfy themselves that appropriate ethics approval has been obtained in the jurisdiction where the tissue was collected. It was recommended that where there is no process for ethical review in the country of origin, New Zealand ethics committees should be able to satisfy themselves that the standards applied to the collection and prior use of the tissue outside New Zealand respected the spirit of ethical practice held within New Zealand.

Framework

- The proposed guidelines provide guidance for the initial approval of the collection of tissue but offer no ongoing support or accountability for the future unspecified research uses once they emerge.
- There is no overarching framework that sets out general principles and guidelines for all tissue handling and use. The result is a fragmented and sometimes contradictory set of systems and protocols. This lack of cohesion means that the same tissue may be treated differently depending on circumstance or the situation within the health system.
- Little attention is given in the consultation document to the actual one-off consent process. The one-off consent process appears too casual and represents an unwarranted trust in the researcher downplaying potential harm.
- There needs to be some way of ensuring that researchers are accountable for following the protocols agreed to by ethics committees.

Māori concerns

- In regard to confidentiality and storage issues, consideration could be given to the concept of Māori guardianship (kaitiaki).
- The proposed guidelines provide little consideration and recognition of potential issues for Māori. Issues concerning the body are of particular significance to Māori culture. The body is considered tapu (sacred) and therefore requires specific consideration and respect.
- The guidelines are not clear on how Māori issues or Māori rights under the Treaty of Waitangi are to be considered.
- Researchers should be required to work with Māori to ensure that Māori donors are aware of the cultural ramifications of an agreement to donate tissue for unspecified future use.
- The level of consideration and recognition given to the Māori within this document is excellent.

Privacy

- The potential for researchers to access sensitive information is miniscule compared to that accepted within our public health system in which thousands of employees have potential access to a much greater amount of information.

Other issues

- Incompetent living people (apart from children) and the deceased are excluded from the guidelines. There seems to be a reason in principle to extend the proposed guidelines to cover these groups to make unspecified future use permissible.
- The proposed guidelines will not have the force of law, and ethics committees will implement them. As such, a more prescriptive process is needed for the ethics committees who will implement and apply the guidelines to the potential research situations.
- The guidelines should not apply retrospectively.
- How long will the protocol that is currently under development last after it has been codified?
- The guidelines should clarify whether two separate consents need to be sought for the collection and the future use of a tissue.

Appendix 1: Participants in Consultation

Individuals

Ian Campbell
Peter Ganly
Michael Gough
Deborah Lawson
Stephen Macdonald Luke
Kelvin Lynn
Ian M Morison
Lorraine Neave
Nicola Peart and Mark Henaghan
Bridget Robinson
C Sorby
Robert Welch
Phil White

District Health Boards and service providers

Auckland District Health Board
Canterbury District Health Board
Capital & Coast District Health Board
Counties Manukau District Health Board
MidCentral District Health Board
Family Planning Association (FPA) New Zealand
Starship Children's Health
Wairarapa District Health Board

Research groups

Cancer Society Tissue Bank
Christchurch Clinical Studies Trust, Standing Committee on Therapeutic Trials (SCOTT) and Medicines Assessment Advisory Committee (one submission)
Medical Research Institute of New Zealand
Paediatric Oncology Steering Group
The Royal Society of New Zealand
Wellington Blood & Cancer Centre

Government agencies and advisory committees

Health and Disability Commissioner
Human Rights Commission
National Ethics Advisory Committee
Office of the Privacy Commissioner
Toi te Taiao: The Bioethics Council

Ethics committees

Health Research Council (HRC) Ethics Committee
University of Auckland Human Participants Ethics Committee
Massey University Human Ethics Committee: Southern A
Multi-region Ethics Committee
Health and Disability Ethics Committees Chairs' Group

Universities and specific departments

University of Auckland
Research Advisory Group, University of Otago
Department of Pathology, University of Otago
Department of Anatomy and Structural Biology, University of Otago
Massey University

Advocacy groups

New Zealand Organisation for Rare Disorders
Right To Life New Zealand

Religious groups

The Nathaniel Centre (The New Zealand Catholic Bioethics Centre)
InterChurch Bioethics Council

Women's groups

Women's Health Action Trust
National Council of Women of New Zealand

Appendix 2: Review of Proposed Guidelines

The following analysis outlines how the proposed guidelines were revised to account for the key issues raised in the submissions.

In general there was support for the use of human tissue for future unspecified research purposes, and support for the proposed guidelines. Accordingly, the finalised guidelines allow consent for future unspecified research, with a number of requirements around the information that must be provided to inform such consent.

The guidelines are intended to sit alongside the *Operational Standard for Ethics Committees*. However, because the guidelines specifically deal with issues related to future use of tissue, they will take precedence over the *Operational Standard for Ethics Committees* on any points of conflict.

Key areas of concern raised by submitters

Information to be provided to donors

The majority of submitters thought that potential research participants should be provided with as much information as possible, to ensure that any consent is truly informed. Information relating to the collection, storage, disposal and use of tissue, withdrawal of consent, and cultural issues, was discussed.

The Ministry accepts that tissue donors should be provided with as much information as is possible. However, it is noted that the extent of information regarding the future use of tissue is going to be limited because the use in the future is unspecified. Therefore the Ministry believes that researchers should attempt to provide as much information as is practical.

A number of comments made by submitters have been added to Part II of the finalised guidelines (information to be provided). Under the finalised guidelines, researchers must provide information such as: whether tissue will be delinked, whether tissue will be sent overseas and whether a donor will be contacted in the future.

Options to be provided to donors

The majority of submitters commented on whether donors should have the option to "permit the use of tissue with restrictions". Many submitters argued strongly that donors should be able to specify as many restrictions on the use of their tissue sample as they wished. This was considered essential because of the boundless nature of possible research and to give donors some measure of control.

Conversely, a couple of submitters were concerned about the burdensome administrative challenges that could be associated with an extensive list of options. These submitters felt that it may be harder and more expensive for researchers to keep track of what samples can be used for each research project. One submitter noted that compliance costs of such systems could become onerous to small research organisations or programmes funded by charities.

It is acknowledged that an option to donate tissue with restrictions would pose challenges for researchers. The intention, however, of having such an option is to provide a balance between protecting the interests of tissue donors and allowing researchers to obtain tissue samples. Such an option may appear burdensome for researchers. However, researchers ultimately have the choice whether to use a tissue sample with restrictions or not. It should be noted that the options are not mandatory. Rather, sufficient options should be provided to donors. In situations where such an option would not appear to be overly burdensome, it is likely that such an option will be expected to be offered by researchers.

Unidentified or delinked tissue samples

Unidentified or delinked tissue samples created the most contention amongst submitters. Some argued that delinking a donor's tissue sample from the donor's background information provides the utmost privacy for the donor. However, others were concerned with the effects on research if a donor's clinical information could not be related to their sample. Delinking tissue raised a number of other concerns relating to the donor's right to withdraw their consent and children's right to revisit consent given by their parents.

Despite the concerns raised regarding delinked samples, the finalised guidelines make it clear that donors can donate delinked tissue samples. Under Part III of the finalised guidelines (options for consent), donors must be offered a number of options, and the option of donating a delinked sample is one of these options.

The finalised guidelines state that donors must be provided with information including whether the donor's identity will remain linked with their tissue sample. The purpose of this is to ensure donors are well informed about whether their identity will remain with their tissue sample.

Right to withdraw consent

Despite widespread support for the use of human tissue in future unspecified research, a number of submitters were concerned that donors who had donated delinked samples would not be able to withdraw their consent to future research.

It is acknowledged that the right to withdraw consent is a well-established ethical principle, set out in the *Operational Standard for Ethics Committees* and the *Code of Health and Disability Services Consumers' Rights*. The right to withdraw consent is a significant right. However, the act of tissue donation does not create a right under the Code to withdraw tissue in the future. The right to withdraw consent relates to those actively participating in research.

In the finalised guidelines (under information that must be provided to potential donors), there is a requirement that those wanting to obtain tissue must fully inform donors that the donor will not be able to withdraw their consent in the future if they choose to donate tissue that will be delinked. Thus, under the finalised guidelines, it is clear that if a

donor consents to their sample being delinked, then they choose to relinquish the right to withdraw their consent in the future.

It is also acknowledged that it would be impractical for researchers to re-link tissue once it had been delinked, in order for donors to withdraw their consent.

Parental proxy consent

Submitters were divided on this issue. A number of submitters supported parental proxy consent because, in their view, parents routinely make decisions affecting their children's welfare, and they considered tissue donation to be no different. However, other submitters were concerned that in situations where parents consent to their children's tissue being delinked, in the future, children would not be able to withdraw consent for their tissue to be used.

The finalised guidelines require that a child gives consent to their tissue to be used where the child is competent to do so. This places greater emphasis on the views of the child who is donating tissue for future unspecified research. Where it is deemed that a child is not competent based on well-established competency tests, the child's legal guardians may give proxy consent for the child.

The finalised guidelines thus recognise that parental proxy consent is appropriate where a child is not competent to give consent. In such cases, if the child's legal guardians consent to the child's donated tissue being delinked, then the child will not be able to withdrawal their donated tissue or consent to its use in the future.

Recontacting donors

A number of submitters expressed concern with the requirement to recontact tissue donors. Those submitters argued that requiring researchers to recontact tissue donors would be an additional administrative burden on researchers, and in some cases donors might be difficult or impossible to recontact.

Other submitters argued that there are other less direct methods that could be used to feed information back to tissue donors, such as through websites or general mailing lists, sending reports to support groups, and providing donors with contact numbers that they could use to obtain research proposals and results.

On the other hand, a number of submitters supported recontacting donors, noting that information from the research might be of relevance to the donor.

It is acknowledged that options requiring researchers to recontact tissue donors may be burdensome on researchers. However, the option to be recontacted is not mandatory and in situations where an ethics committee is of the mind that such an option would be too burdensome, it is likely that such an option will not be required.

Tissue samples sent overseas

Many submitters had concerns about tissue samples being sent overseas for future unspecified research, because there would be a loss of control over their use (eg use would not be subject to approval of New Zealand ethics committees). Others, however, noted that contributing to overseas research is advantageous because of the collaborative effects of using a wide variety of samples and the potential for developing new treatments.

The finalised guidelines seek to balance the potential risks of sending tissue samples overseas with the potential benefits of international collaborative research. Under the finalised guidelines, researchers must provide donors with information stating whether their tissue sample is to be sent overseas. Researchers must also inform donors that if tissue samples are sent overseas, any future ethical review conducted overseas is likely to progress without New Zealand representation.

In any case, researchers will only gain ethics committee approval if the committee is satisfied that any future use of the tissue will have ethical and scientific review by a committee that conforms with the *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (Council for International Organizations of Medical Sciences and World Health Organization 2002).

The finalised guidelines thus set in place safeguards to ensure that donors are well informed and ethics committees are satisfied there will be appropriate ethics review in the country receiving the donor's tissue sample. The concept of an oversight committee was not considered necessary.

Delegated authority

Submitters had a diverse range of comments on this issue. Several submitters considered that participants would be adequately protected and timely review of low-risk research enhanced, if provision was made for authority to be delegated to the chairperson of an ethics committee.

However, several other submitters considered that delegated authority was not appropriate under any circumstances.

A few submitters noted that 'low-risk' research was not defined. One submitter commented that expedited ethical review might be appropriate in some situations but that such review should be used as sparingly as possible to avoid any lowering of standards/safeguards.

The finalised guidelines have been amended to exclude 'low-risk' research. It is recognised that the term 'low risk' research could be interpreted too widely and create inconsistent decisions amongst ethics committees.

However, under the finalised guidelines, ethics committee chairs can approve the use of delinked tissue samples. The rationale for this is that these samples do not directly affect individuals because these samples are no longer linked with the donor's identity.

Cultural issues

In light of submissions relating to cultural issues, the finalised guidelines have expanded the information requirements to include a requirement that information must be provided to potential donors, noting that they may wish to discuss the issue of tissue donation with those close to them: for example, family, whānau, hapū and iwi. This recognises the fact that, for some donors, donating tissue is an issue that requires wider discussion with those people close to them.

Under the finalised guidelines the use of the word 'individual' has been removed. The reason for this is to recognise that for some cultures, issues such as tissue donation and participation in research are a collective decision. However, as set out in the *Operational Standard for Ethics Committees*, paragraph 40, an individual is still ultimately free to give or withhold consent.

The Ministry considers that the guidelines and the existing ethics approval structure address the interests of Māori. Ethics committees have Māori representation and the finalised guidelines and *Operational Standard* explicitly refer to issues relating to Māori. The concept of Māori guardianship (Kaitiaki) has not been incorporated into the guidelines, however, this is an option which researchers and tissue banks may wish to incorporate into their operations.

Other issues

Governance of tissue collections

A couple of submitters considered that governance of tissue collections was an important consideration for future unspecified research use of tissue. One submitter said that all tissue banks, whether based in New Zealand or overseas, should be required to have a well-documented governance structure and clear guidelines for ownership of, access to and means of return or disposal of tissue.

Another submitter recommended that the guidelines require the establishment of a publicly available register of information to allow the public to know what sort of tissue banks exist and what sort of approved research projects are using stored tissue.

The Ministry accepts that the governance of tissue collections is an important aspect of tissue storage. Under paragraph 29, of the guidelines ethics committee's must be satisfied that organisations storing tissue samples, whether in New Zealand or overseas, have adequate governance structures, procedures and process in place to ensure donors' choices are respected.

In regard to a register of information, the Ministry is satisfied that the interests of the community and individual donors are adequately protected by the requirement that all research involving human tissue be approved by a Health and Disability Ethics

committee. These committees include community and consumer representatives, their minutes are available on the ethics committees' website and information is also published through annual reporting.

Timeframe

It was suggested that consideration be given to whether permission to store tissue or to use tissue for research would be for a specific timeframe and whether the researcher would have to reapply for ethics committee approval at some later date.

The guidelines do not specify any timeframe which consent applies to. In situations where consent has been approved for future unspecified use, there will be no need to reapply for ethics committee approval so long as the future use is not contrary to anything which was initially approved.

Importation of tissue

A couple of submitters asked whether guidelines would be developed to regulate the importation of tissue for research into New Zealand. The view was expressed that before tissue from overseas was imported into New Zealand, ethics committees should satisfy themselves that appropriate ethics approval has been obtained in the jurisdiction where the tissue was collected.

The issue of tissue importation is currently being considered under the review of the Human Tissue Bill. The current ethics approval framework within New Zealand requires that all research involving human tissue gain ethics committee approval.