

NAFG-2009-v1

**Guidelines for the
Completion of the National
Application Form for Ethical
Approval of a Research
Project**

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Ethics Committee Requirements

Health and Disability Ethics Committees

Please ensure applications are correctly collated. Each set should contain all the papers and forms being submitted, except where only 2 copies are required (eg company protocols and investigator brochures), ready to be sent to each committee member. Applications received incorrectly collated eg separate sets of each document may be returned at the researcher's expense.

Committee details	Number of copies required	Copies of drug company protocols/ investigator brochures	Format of application presentation (see Note, page 3)
Northern X Regional Ethics Committee 3rd Floor, Unisys Building, 650 Great South Road, Penrose Private Bag 92-522, Wellesley Street Auckland northernx_ethicscommittee@moh.govt.nz	1 original plus (single sided, paper clipped) 12 double sided	2	Staple double sided copies at left-hand corner
Northern Y Regional Ethics Committee 3rd Floor, BNZ Building, 354 Victoria Street PO Box 1031, Hamilton notherny_ethicscommittee@moh.govt.nz	1 original plus 12 double sided	2	Staple double sided copies at left-hand corner
Central Ethics Committee 2nd Floor, 1-3 The Terrace PO Box 5013, Wellington central_ethicscommittee@moh.govt.nz	1 original plus 12 double sided	2	Do not staple – use bulldog clips or paper clips
Upper South A Ethics Committee 4th Floor, 250 Oxford Terrace PO Box 3877, Christchurch uppersouth_ethicscommittee@moh.govt.nz	1 original plus 12 double sided	2	Do not staple – use bulldog clips or paper clips
Upper South B Ethics Committee 4th Floor, 250 Oxford Terrace PO Box 3877, Christchurch uppersouth_ethicscommittee@moh.govt.nz	1 original plus 12 double sided	2	Do not staple – use bulldog clips or paper clips
Lower South Ethics Committee 229 Moray Place PO Box 5849, Dunedin lowersouth_ethicscommittee@moh.govt.nz	1 original plus 12 double sided	2	Do not staple – use bulldog clips or paper clips
Multi-region Ethics Committee 2nd Floor, 1-3 The Terrace PO Box 5013, Wellington multiregion_ethicscommittee@moh.govt.nz	1 original plus 12 double sided	2	Do not staple – use bulldog clips or paper clips

National Co-ordinator for Ethics Committees: NC_ethicscommittees@moh.govt.nz

Accredited institutional ethics committees

Auckland University of Technology Ethics Committee

Private Bag 92-006, Auckland
email madeline.banda@aut.ac.nz

Lincoln University Human Ethics Committee

PO Box 84, Canterbury
Davidsm2@lincoln.ac.nz

University of Otago Ethics Committee

PO Box 56, Dunedin
gary.witte@stonebow.otago.ac.nz

UNITEC Research Ethics Committee

Private Bag 92-025, Auckland
ethics@unitec.ac.nz

University of Auckland Human Subjects Ethics Committee

Private Bag 92-019, Auckland
l.lon@auckland.ac.nz

Victoria University of Wellington Human Ethics Committee

Katy.Miller@vuw.ac.nz

Massey University Regional Human Ethics Committees

Albany

Private Bag 102-904, Auckland
M.L.Turner@massey.ac.nz

Palmerston North

Private Bag 11-222, Palmerston North
P.L.Broad@massey.ac.nz

Wellington

Private Box 756, Wellington
P.L.Broad@massey.ac.nz

Guidelines for Word Processing

Moving around the form

The information in the application form is presented as a series of tables, and the input areas where applicants type are table cells. Use the tab or arrow keys on your keyboard or the mouse to navigate to the table cells to begin typing. The table will expand as you type into each cell. You are able to view the layout of the table by ensuring that the paragraph markers are on (**T**ools → **O**ptions → **N**on-Printing **C**haracters → **A**ll).

Applications should be word processed using the same format and numbering as the application form. Ensure the font used to answer the question is easy to read (that is, not italic).

Page formatting

Do *not* delete 'Page Break' and 'Section Break' breaks. Do not remove headers and footers, or other information to gain more room. Margins should not be altered and must be no less than: 1.5 cm top, 1 cm bottom, 1 cm right and 2.5 cm left. Removing these breaks or changing the margins will seriously affect the formatting of the form.

The form has been designed to give sufficient room for your answers. Where an answer needs six lines, six lines are formatted, but where an answer only needs one line, one line is formatted. Please note the number of lines allowed for each question before attempting to answer the question and *make sure that no extra lines are used*.

Page limits are fixed

Page limits should be strictly adhered to. However, if the page overruns and cannot be further condensed, attach the additional information as an appendix. The page numbers in the application form must not be amended. You may find it helpful to print out the application first to help you to keep to the set page limits. Each answer must appear on the same page as the appropriate question.

The print preview option (**F**ile → **P**rint **P**review) will allow you to view the overall layout of the document before printing. Every endeavour should be made to ensure that the completed application form is the same in size and format as the original form. The submission of incomplete or unformatted application forms to ethics committees will result in delays for the applicant.

General Information for Applicants

Researchers should complete the application form in conjunction with the Health Research Council (HRC) Guidelines on Ethics in Health Research (available on the HRC website – <http://www.hrc.govt.nz> or from the HRC).

If your research involves genetic technology, notes entitled *Ethical Considerations Relating to Research in Human Genetics* are available from the HRC or the Health and Disability Ethics Committees' website <http://www.newhealth.govt.nz/ethicscommittees>.

Investigators conducting a clinical trial in human participants should obtain the Interim Good Clinical Research Practice Guidelines (August 1998) from the Ministry of Health business unit New Zealand Medicines and Medical Services Safety Authority (Medsafe) website <http://www.medsafe.govt.nz>

1. Applications should be word processed using the same format and numbering as the application form. Ensure the font used to answer the question is easy to read (that is, not italic).
2. The original and 12 copies should be forwarded to the appropriate ethics committee (see page 1).
3. Questions must be either answered or marked not applicable. Where indicated, enclose copies of information sheets, consent forms, questionnaires and other relevant documentation at the back of the application form.
4. Checklist for applicants: If an incomplete application is received, the principal researcher will be advised and the application will not be placed on an agenda until the missing documentation is received. The only documentation that may be pending are:
 - locality assessment by organisation
 - response letter from the group providing Māori consultation – the process undertaken and the result must be clearly stated in the application form
 - SCOTT approval.
5. In the case of pharmaceutical trials, please enclose one or two copies of the manufacturer or distributor's protocol and investigator's brochure as per the ethics committee's requirements listed on page 1. The relevant sections of the application form must also be completed in full. It is **not** acceptable to refer to the company's protocol in lieu of answering the questions in full.
6. The application form can be downloaded from the Health and Disability Ethics committees website <http://www.newhealth.govt.nz/ethicscommittees/> or the HRC's website <http://www.hrc.govt.nz/>
7. If approved, ethical approval will be given for up to a maximum of five years, contingent on annual reports being received.
8. Please allow at least two months for the ethical review process to be completed.
9. After a research proposal has been reviewed and its comments sent out to the researcher the researcher will have three months from the date of that letter to respond to the committee's requests.
10. The responsibility for obtaining ethical approval lies with the principal investigator and not with anyone else (for example, a pharmaceutical company).
11. The ethics committee is to be advised of **any** changes to the protocol, including changes in investigators.

12. Accompanying these Guidelines are:

- Appendix 1 How to apply to the Standing Committee on Therapeutic Trials (SCOTT)
- Appendix 2 How to apply to the Gene Technology Advisory Committee (GTAC)
- Appendix 3 New Zealand Researched Medicines Industry Guidelines on Clinical Trials:
Compensation for injury resulting from participation in industry sponsored clinical trials
- Appendix 4 How to apply to the National Radiation Laboratory (NRL)
- Appendix 5 Complaints procedures.

Part 1: Basic Information

Q2 Short project title (lay title)

Use language that is readily understandable by laypersons. This title is also to be used on the consent form and information sheet.

Q3 Principal investigator's name and position

If this is supervised work then the supervisor should be listed as the principal investigator unless the student being supervised is a PhD candidate in which case the principal investigator may be either the student or the supervisor.

Q5 Principal investigator's qualifications and experience in the past five years

What qualifications and experience does the principal investigator have in this type of research? Please include a brief biographical statement outlining relevant experience. You do not need to include a curriculum vitae.

Q9 Locality organisations

Include the organisation hosting the research and any organisations in which recruitment will be carried out if these differ from the researcher's organisation. Advise on the locality assessment form if another organisation is providing some of the assessment, eg, the researcher's organisation may assess their suitability to do the research (Part 2, Q1) and the organisation through which participants will be recruited may assess the suitability of the local research environment (Part 2, Q2).

Q10 Closed meetings

All applications and related correspondence are subject to the Official Information Act 1982. If you wish an application to be heard in a closed meeting, please provide a reason in accordance with the Official Information Act. If an application is heard in a closed meeting, only the decision will be listed in the minutes; any requirements or comments will be listed in 'closed' minutes.

Please note, applications heard in a 'closed' meeting are still subject to the Official Information Act 1982. Before an application or any other papers are released, the researcher will be asked to advise why they should be withheld but the final decision rests with the committee. If applications are withheld, the requester may seek a review of this decision from the Ombudsman.

Q12 Decisions from overseas ethics committees

Decisions are requested from overseas ethics committees because in the past, studies have been declined overseas and this was not mentioned in the New Zealand application.

Reports from other committees may be requested.

Q13 Human tissue

- (1) Human tissue under the Human Tissue Act 2008 “means material that –
- (a) is, or is derived from, a body, or material collected from a living individual or from a body; and
 - (b) is or includes human cells; and
 - (c) is not excluded, for the purposes of some or all of the provisions of this Act, by subsections (2) or (3)”.

Subsection (2) refers to a human embryo or human gamete. These are covered under the HART Act 2004 and any research involving human embryos or human gametes are required to be submitted to the Ethics Committee on Assisted Reproductive Technology.

Subsection (3) refers to cell lines derived from human cells.

For further information on human tissue definitions, see the guidelines on Part 5, page 28.

Q17 Lay summary

Please write in language that will make the project comprehensible to laypersons, that is, using non-technical language.

Q20 Duration of project

A final report will be required within three months of completion of the study (including collection and analysis of follow-up data). The report may not necessarily be the formal published results.

Q22 Clinical trial registration

It is recommended that clinical trials be registered with the Australian and New Zealand Clinical Trial Registry (ANZCTR). The ANZCTR (available at <http://www.actr.org.au>) meets the requirements of the ICMJE register policy and is consistent with the proposed World Health Organization (WHO) portal, which will allow a one-stop search of worldwide registers to improve fragmentation of current registries and establish standards on the scope and content of trial registration. The ANZCTR is not limited to randomly controlled trials and includes a wide definition of clinical trial.

“Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes (WHO / ICMJE 2008 definition) should be registered, including early phase uncontrolled trials (phase I) in patients or healthy volunteers (WHO Recommendation / ICMJE policy). If in doubt, registration is recommended”
(ANZCTR website)

The HRC is the co-ordinating agency for New Zealand and will work closely with the National Health and Medical Research Council (NHMRC), who has funded the establishment of the register.

There is an ethical duty to participants to provide access to information about ongoing, completed and published clinical trials to allow informed decision-making.

Part 2: Ethical Principles

A. Validity of research

(Operational Standard Paragraphs 53–59)

Q A1 Aims of the project

Avoid using jargon to describe the project.

Include a list of all relevant references and copies of key publications useful in providing background information for the ethics committee.

Q A2 Scientific background of the research

If the project has been scientifically assessed, include a copy of the scientific review of the project. An ethics committee has a duty to review the scientific validity of the proposal in instances where the proposal has not been assessed by a peer-review mechanism. Review by a supervisor or colleague, or any one individual, is not scientific assessment.

Describe the scientific basis of the project

This description should contain sufficient background detail information to allow the ethics committee to understand the relevance, importance and originality of the proposal. Where similar research has already been done, include the justification for the current research, including references. Technical terms and jargon should be minimised.

Q A3 Study design

Describe the study design in adequate detail to make clear how many participants will be in various groups, what procedures will be performed and what samples will be taken. How will randomisation be carried out? Describe all tests on samples. Attach diagrams and charts to illustrate if necessary.

Q A4 Participants

4.2: If there are other over riding restrictions on numbers or there is truly no information to base a valid power calculation on and the type of study does mean a pilot study is necessary, then this should be explained.

Information on the values of all parameters used in power calculations need to be given.

Copies of any advertisements/recruitment notices should be included with the application (refer also to question D2).

Q A5 Statistical method

5.3: Ensure if a statistician's name is given as having been consulted that they have sighted the relevant sections of the application, prior to it being submitted and have agreed to their name being quoted.

5.4: Questionnaires – If questionnaires are still being developed, the study cannot be given final ethical approval until the final version of the questionnaire has been reviewed. Ensure each version of the questionnaire has a version number and date. Draft schedules should be included with the application.

However, where the application proposes to engage in some form of qualitative research, such as participatory action research, the requirements of ethics committees to see completed questionnaires may be waived as is consistent with the nature of the research. In these instances, the committee will require evidence of the processes by which the research will be advanced and the experience and qualifications of the researcher.

Q A7 **Publication of results**

If the results go to the sponsor before publication, seek assurance from the sponsor that there will be no undue delay and that adverse results will be published.

Q A8 **Funding**

Investigators and their host institutions are entitled to adequate and reasonable reimbursement for their own time on the project. All funds should be paid to a specified account.

Q A9 **Incentive payments**

In the context of research, the **ethical issue of payment (in money or kind) or reward** for carrying out the project – including any payment (in money or kind) or reward for *recruiting* participants – is generally reviewed under three main categories:

- i) payment (in money or kind) or reward received by research investigators, host departments or host institutions [this is considered under Question A9];
- ii) payment (in money or kind) or reward received by participants recruited into studies [this is considered under Question E10]; or
- iii) payment (in money or kind) or reward received by individuals/organisations who recruit participants into studies but who are not involved in the research as research investigators [this is considered under Question A9].

Note:

- that (i) raises *ethical concerns* that require *closer scrutiny* by an accredited ethics committee
- that (ii) raises issues requiring review by an accredited ethics committee into whether or not any payment (in money or kind) or reward, or benefit of any sort, offered to any participant constitutes *undue inducement*
- that (iii) raises concerns that are generally considered *unethical*.

The researcher should provide relevant information, and the accredited ethics committee reviewing the proposed project should be satisfied that any payment (in money or kind) or reward for carrying out the project – including for recruiting participants into the project:

- (a) **would not** likely influence the findings of the research;
- (b) **would not** likely constitute an undue inducement to individuals to participate in the project; and
- (c) **will be** disclosed to individuals when recruiting them as research participants for the project (in the circumstances where the researcher does not intend to make any disclosure, justification must be provided to the ethics committee).

For clarity, any 'payment (in money or kind) or reward' received for carrying out the project – including for the recruitment of participants to a project includes:

- (a) any gift or loan (for example, gift or loan of expensive equipment)
- (b) any sponsored international travel
- (c) any financial interest (for example, ownership or equity interest in a company involved with/directly related to the research)
- (d) any potential reward (for example, creation of a patentable product or system and income from such rights).

The researcher(s) should provide details about the following:

- (a) The total monetary value, or where appropriate, the specific monetary value, about the payment (in money or kind) or reward, for example:
 - payment per participant
 - access to technology/equipment/medication
 - sponsored international travel.

(Please note that an accredited ethics committee **may seek additional information**, for example, information about costs to the researcher, department or institution that will be incurred, including the cost of tests, resources and staff time consumed as part of project requirements.)

- (b) How such payment or reward (in money or kind) will be received (for example, paid as a lump sum or in instalments to the researcher personally, according to number of participants recruited or to an audited trust or research account).
- (c) Whether participants recruited into the project will be **informed of the fact** that such payment (in money or kind) or reward will be received, for example, in the **information sheet** (if not, please explain and justify why not).
- (d) Whether any other individual/organisation will receive any payment (in money or kind) or reward for recruiting participants to the project (for example, a finder's fee for recruiting participants paid to any individual/organisation who will not be involved in the research as an investigator).

Any payment (in money or kind) or reward received for conducting the project – including for recruiting participants into the project – should *reasonably* reflect the actual cost of work carried out for the research; personnel costs should reasonably reflect standard rates for the professional involved.

The issue of what is reasonable may be decided on a *case-by-case basis*, and accredited ethics committees may decide that the payment or reward at issue should not exceed a certain percentage above standard rates of payment or reward.

B. Minimisation of harm *(Operational Standard Paragraphs 60–68)*

Q B6 Justification of procedures where research is non-therapeutic or innovative should be given, together with levels of acceptable risk.

Q B7 Use of National Health Index

- If the researcher is to make use of the National Health Index (NHI), they should state whether the information so obtained is linked or unlinked. If the research will use unencrypted information, then ethics committee approval is required.
- The researcher should state what risks to privacy are inherent in the study and what measures will be taken to safeguard the information.
- Are there any privacy issues that impact particularly on ethnic groups? For example, there may be privacy issues for a group of people rather than for individuals.
- If a privacy impact assessment has been completed, the outcome of this assessment should be described.

Attach copies of any questionnaires and interview guidelines being used.

Q B12.1 The GP should be advised if the study may impact on the patient's health either now or in the future. If the study is a Phase I study, not informing the GP should be an exclusion criterion.

Q B13 If there is no data safety monitoring board (DSMB), clear criteria for terminating the study must be explained in question B16. These criteria need to show some independence from the researcher or sponsor.

Q B16 If any form of radiation is being used see Appendix 4. Where, for the purposes of the study, there is only one more exposure of the same x-ray or a low risk scan that is being given to the participant for therapeutic purposes, then an NRL assessment is not usually required by the ethics committee.

Q B17 Will any medicines be administered? If yes, complete a ***Form for Registered and Unregistered Medicines (NAF Part 4)*** except where the medicine will be given regardless of entry into the trial (eg, anaesthetic) and that medicine is not being studied in any way. If the drugs are not registered, then SCOTT approval is required (see appendix 1).

Q B18 Resource implications

Researchers should include the use of staff time, drugs and equipment in their assessment of resources.

C. Compensation for harm suffered by participants *(Operational Standard Paragraphs 87–95)*

Information regarding compensation provisions should be included in the information sheet.

All applications involving treatment by, or at the direction of, a registered health professional as part of the research must be accompanied by the appropriate statutory declaration for harm (Form A or Form B).

'Registered health professional' means a chiropractor, clinical dental technician, dentist, medical laboratory technologist, medical practitioner, medical radiation technologist, midwife, nurse, occupational therapist, optometrist, pharmacist, physiotherapist, or podiatrist. The registered health professional must hold an annual practicing certificate or an interim practice certificate and must be acting in accordance with any conditions on that certificate.

ACC recently consulted on a proposed change of this definition to “registered health professional means a registered health professional of a type defined in regulations made under this Act”.

A treatment injury is defined as (Injury Prevention, Rehabilitation and Compensation Act 2001, Section 32).

- (1) **Treatment injury** means personal injury that is –
 - (a) suffered by a person –
 - (i) seeking treatment from one or more registered health professionals; or
 - (ii) receiving treatment from, or at the direction of, one or more registered health professionals;
 - (b) caused by treatment; and
 - (c) not a necessary part, or ordinary consequence, of the treatment, taking into account all the circumstances of the treatment, including –
 - (i) the person’s underlying health condition at the time of the treatment; and
 - (ii) the clinical knowledge at the time of the treatment.
- (2) **Treatment injury** does not include the following kinds of personal injury:
 - (a) personal injury that is wholly or substantially caused by a person’s underlying health condition
 - (b) personal injury that is solely attributable to a resource allocation decision
 - (c) personal injury that is a result of a person unreasonably withholding or delaying their consent to undergo treatment.
- (3) The fact that the treatment did not achieve a desired result does not, of itself, constitute **treatment injury**.
- (4) **Treatment injury** includes personal injury suffered by a person as a result of treatment given as part of a clinical trial, in the circumstances described in subsection (5) or subsection (6).
- (5) One of the circumstances referred to in subsection (4) is where the claimant did not agree, in writing, to participate in the trial.
- (6) The other circumstance referred to in subsection (4) is where –
 - (a) an ethics committee –
 - (i) approved the trial; and
 - (ii) was satisfied that the trial was not to be conducted principally for the benefit of the manufacturer or distributor of the medicine or item being trialled; and
 - (b) the ethics committee was approved by the Health Research Council of New Zealand or the Director-General of Health at the time it gave its approval

Treatment (Injury Prevention, Rehabilitation and Compensation Act 2001 s33)

For the purposes of determining whether a treatment injury has occurred, or when that injury occurred, **treatment** includes –

- (a) the giving of treatment
- (b) a diagnosis of a person’s medical condition
- (c) a decision on the treatment to be provided (including a decision not to provide treatment)
- (d) a failure to provide treatment or to provide treatment in a timely manner
- (e) obtaining, or failing to obtain, a person’s consent to undergo treatment, including any information provided to the person (or other person legally entitled to consent on their behalf if the person

does not have legal capacity) to enable the person to make an informed decision on whether to accept treatment

- (f) the provision of prophylaxis
- (g) the failure of any equipment, device, or tool used as part of the treatment process, including the failure of any implant or prosthesis (except where the failure of the implant or prosthesis is caused by an intervening act or by fair wear and tear), whether at the time of giving treatment or subsequently
- (h) the application of any support systems, including policies, processes, practices and administrative systems that –
 - (i) are used by the organisation or person providing the treatment; and
 - (ii) directly support the treatment.

Form A or Form B?

Form A should be completed if the research **is not** principally for the benefit of the manufacturer or distributor of the medicine or item being trialled. Form B should be completed if the research **is** principally for the benefit of the manufacturer or distributor of the item being trialled. The following factors may be considered in determining whether or not a trial is principally for a manufacturer's or distributor's benefit:

- (a) Who is initiating the proposed research study? That is, is the proposed research study investigator-initiated or the result of an approach to the investigator from a pharmaceutical company or any other company involved in health research?
- (b) Who is designing and planning the hypothesis to be tested and/or research questions to be asked in the proposed research?
- (c) Will the director of the proposed research study or other investigators involved in the study be receiving any direct financial remuneration either as an employee or as a consultant of the pharmaceutical company or any other company involved in the proposed research?
- (d) Is the pharmaceutical company or any other company involved in health research putting any unreasonable restrictions or delay on the timely publication of the results of the study?
- (e) Is the pharmaceutical company or any other company involved providing any funding and/or materials for the proposed research?

Please note that provision of funding and/or materials for the research that is provided by a company or any other company involved in health research should not of itself be determinative of whether the trial is principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is conducted (*Compensation for Injuries Caused as a Result of Participation in a Clinical Trial and the Role of Ethics Committees Guidelines*, December 1993, Ministry of Health and ACC).

If the research is not principally for the benefit of the manufacturer or distributor (Form A), participants may be eligible for compensation for treatment injuries under section 32 of the Injury Prevention, Rehabilitation, and Compensation Act 2001. In addition, participants may be eligible for compensation for other personal injuries (such as sprains or fractures) under other provisions of the Injury Prevention, Rehabilitation, and Compensation Act 2001. Investigators/institutions should ensure that they have sufficient indemnity insurance to compensate participants for harm that does not qualify for compensation under the Injury Prevention, Rehabilitation, and Compensation Act 2001.

Form B studies

If the research is principally for the benefit of the manufacturer or distributor (Form B), participants will not be eligible for compensation for treatment injuries in relation to treatment given as part of the trial. Investigators/institutions should ensure that they have sufficient indemnity insurance to compensate participants in accordance with the New Zealand Research Medicines Industry (RMI) Guidelines of Clinical Trials (RMI Guidelines).

Participants should be advised to check whether participation in the research project would affect their status with regard to existing or contemplated indemnity cover, such as medical insurance, life insurance and superannuation.

If the research is for the benefit of the manufacturer or distributor, then, unless there are particular circumstances that would make this unnecessary, an ethics committee would expect the company to provide, **as a minimum**, at least the level of compensation that is provided by ACC (see <http://www.acc.co.nz>). Payment of medical expenses only is not considered to be within the spirit of the RMI Guidelines. If a company agrees to abide by the RMI Guidelines, because compensation will only be paid for a serious and enduring injury and not for an injury of a temporary nature, then it can be inferred that payment of medical expenses alone would not necessarily be sufficient compensation for someone whose injury prohibits them from working/driving/doing housework, etc, and the amount of compensation payable should take into account the type of compensation that would be needed by someone with an ongoing disability, for example, home help, childcare, mobility allowance and transport, as well as medical expenses.

Indemnity insurance

The current Research Medicines Industry Guidelines (August 2008) allow for compensation from the drug company to be abated (potentially by 100%) to the extent that injury has arisen through a significant departure from the agreed protocol (3.4.1) or the wrongful act or default of a third party (3.4.2). This means that the participant may not receive any cover under the sponsor's indemnity insurance and may have to commence legal action against the researcher and/or the researcher's institution in order to receive compensation.

Sponsor indemnity

Q C5.3 A current insurance certificate covering the specific study is required from the sponsor. This indemnity should specify per participant cover. An updated certificate should be provided each year with the annual report.

Researcher and institution indemnity

If the sponsor excludes cover for a significant deviation from the protocol or negligence by the investigator, research staff, the hospital or institution, evidence of indemnity cover for the institution(s), the researcher and all staff providing treatment (as defined by the Injury Prevention, Rehabilitation and Compensation Act 2001 s33) must be provided to the reviewing committee. Once it has been provided, it will be kept on file and is not required with subsequent applications until renewed. One document may be provided if it covers the institution and all research staff.

D. Privacy and confidentiality *(Operational Standard Paragraphs 48–56)*

Copies of the consent form and the information sheet that are issued to participants must be included with the application form. The two forms should be adapted to provide local contact information.

Specific consent to inform a GP of an individual's results or participation in the project should be included on the consent form. If it is regarded as essential to inform the GP of the individual's results or participation, then a participant's refusal to provide such consent should constitute an exclusion criterion.

Principal investigators should make themselves familiar with the requirements of the Privacy Act (1993) and the Health Information Privacy Code (1994).

Guidance notes entitled *Health Research and Privacy: Guidance Notes for Health Researchers and Ethics Committees* are included as part of the HRC Guidelines for Researchers. These notes, which include guidance on the storage of data and access to registers, are available from accredited ethics committees or the HRC.

E. Informed consent *(Operational Standard Paragraphs 28–43)*

Principal investigators should make themselves familiar with the provisions of the Code of Health and Disability Services Consumers' Rights, obtainable from the office of the Health and Disability Commissioner.

Consent should be obtained in writing, unless there are good reasons to the contrary. If consent is not to be obtained in writing, the justification for not doing so should be given and the circumstances under which consent is obtained should be recorded. A protocol should be attached, indicating the form of words to be used on the consent form.

F. Cultural and social responsibility *(Operational Standard Paragraphs 73–82)*

F1–F4

Section F enshrines four fundamental positions. They are:

- i. The need for culturally safe research practice. Here, research involving participants from specific ethnic or socially identified groups (even when small numbers from each group are involved) must involve those participant groups in the research process as full participants having equal analytical importance as those categories having larger numbers.

Where a particular ethnic or socially identified group is the principal subject of the research, there must be engagement with appropriate parties, and the way this will be achieved must be outlined in the application. Engagement may reflect a range of relationships, including consultation, collaboration, and/or research partnership.

- ii. The need to focus on reducing health inequalities, Here the researcher will demonstrate how the research will contribute to achieving equity of outcomes for those population groups most in need within the public good health system.
- iii. The need to recognise that all health research carried out in Aotearoa is of relevance to Māori. How relevant is a decision to be made by Māori. Importantly, describing the context and the relevance of the proposed research to Māori will serve as a prerequisite to determining the scope and kind of consultation required.
- iv. The need to strengthen and develop the number and quality of Māori health researchers. Whenever appropriate the research team will contain suitably qualified Māori researchers.

In this vein, it will be important for researchers to outline in the application how the study's approach to sampling allows for robust analysis and evaluations to be made of Māori populations.

Guidelines for Researchers on Health Research Involving Māori are available from the HRC at <http://www.hrc.govt.nz> for guidance on generic consultation with Māori. Such consultation is only exempted when the sole focus of the research is on a specific non-Māori ethnic group.

The guidelines assert that Māori consultation is a vital step in developing a research project that:

- a) involves Māori as participants, or
- b) is on a topic of particular relevance to Māori health.

Therefore in summary, completing the questions in Section F will require that the applicant articulates the context and the relevance of the proposed research to Māori and the possible consequences for Māori health outcomes. The greater the degree of relevance to Māori then the greater the expectation of participation of Māori and hence consultation expectations in addition to the minimum requirements of evidence of engagement from institutionally based Māori expertise or local iwi/hapū.

In giving effect to the Treaty of Waitangi applicants therefore must engage and formally consult with Māori. The Treaty principle of relevance here is rangatiratanga, that is, Māori determining for themselves the relevance of the proposed research to Māori. This implies that as best research practice in these situations Māori should also be active participants in the research as ongoing partners.

Researchers should also take into account the Operational Standard for Ethics Committees, 2006, paragraph 378 bullet point 4, which states:

“Other issues which should also be considered include:

- the strengthening and development of Māori health researchers”.

F5 and F6

Complete these sections if the research is specific to any of these groups or is likely to involve a large number of participants from any of these groups. Separate answers are required for each ethnic group because what is appropriate may be quite different.

As for Māori populations, if research does focus on participants from other ethnic groups then the applicant(s) should discuss how their approach to sampling reflects this quality.

F7

Ensure information about whether the study drug/s are available at the end of the study and whether there is any cost is clearly stated in the information sheet.

Part 4: Declarations

Where there is more than one locality, a Part 4 signature page is to be submitted by the principal investigator for each locality. Co-investigators who are managers should have another senior manager sign Part 4 declaration 2.

Form A: Declaration of eligibility of a clinical trial for consideration of coverage under accident compensation legislation

This form is to be completed and the statutory declaration signed by the registered health practitioner who is providing treatment as part of the research. It should be forwarded to the appropriate ethics committee together with the documents seeking ethical approval for the proposed study.

The information provided must be sufficiently detailed to enable the ethics committee to be satisfied that the proposed research is not conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the research is carried out.

The provision of this information will enable the ethics committee to be satisfied that participants in the clinical trial will be considered for cover under accident compensation legislation for injury caused as a result of their participation in the research.

Note: Applicants conducting a research study that is conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is carried out should complete Form B.

Form B: Declaration of provision of compensation for injury for participants in a research study for a pharmaceutical company or any other company involved in health research

This form is to be completed and the statutory declaration signed by the applicant. It should be forwarded to the appropriate ethics committee together with the documents seeking ethical approval for the proposed study and appropriate assurance from the pharmaceutical company or any other company involved in health research.

The information provided must be sufficiently detailed to enable the ethics committee to be satisfied that:

- the proposed research is conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the research is carried out
- participants in the proposed research project will receive an acceptable level of compensation from a pharmaceutical company or any other company involved in health research in the event of injury to participants resulting from their involvement in the proposed research study.
- researchers and institutions have indemnity cover to provide an acceptable level of compensation in the event of injury to participants resulting from any researcher or research staff deviating substantially from the trial protocol.

Note: Applicants applying for approval for a research study that is not conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the research is carried out should complete Form A.

Locality assessment

What is locality assessment?

In addition to ensuring that their proposed studies would meet established ethical standards, if conducted in an appropriate locality, investigators are also responsible for ensuring that any location they propose for study conduct is appropriate and that they have made the relevant local arrangements. Each locality organisation in or through which there is to be substantial recruitment or in which the study will be conducted is then responsible for checking that the investigator has met this second responsibility. If the study is not to be conducted in or through any locality organisation, this check is instead an ethics committee responsibility.

A study conducted wholly within a single ethics committee region might be conducted in several different locality organisations within that region. Conversely, a national study might be conducted in just one locality organisation – for example, one that houses a national database of health information.

What is a locality organisation's responsibility?

It is the locality organisation's responsibility to check that:

- the investigator's local role in the study is appropriate (for example, any conflict the investigator might have between her or his local roles in research and in patient care has been adequately resolved)
- the resources (other than funding, which often depends on ethics committee approval) and/or facilities that the study requires locally have been identified, are appropriate and are available (for example, the proposed study use would not conflict with any other health or disability support service use that should have priority, and any potentially affected parties have been notified; or any relevant local equipment, and processes to ensure confidentiality, are adequate)
- the investigator has identified and satisfactorily addressed any cultural or other issues *specific* to the locality or to participants for whom study recruitment or participation is primarily at the locality
- the investigator will include the key local contact details in the information sheet for participants (for example, the investigator's local or 0800 number and contact details for advocacy services and for any other important local services).

The ethics committee, or in the case of a clinical trial of a non-registered drug the Standing Committee on Therapeutic Trials (SCOTT), will check the general capability of the investigator(s) to conduct the study. In the case of the Multi-region Ethics Committee, this might sometimes involve liaising with the relevant regional ethics committee. Such liaison might also be needed to check that particular groups are not being invited to participate in too much research at once. Locality assessment should then simply check that any local role played by these 'generally capable' investigators is also appropriate.

For the purposes of this locality assessment, the investigator need submit only the locality assessment form to the locality organisation (and not, for example, the information sheet, consent form or full ethics committee application form). Each locality organisation may make its own decision as to whether this locality assessment check and sign-off for ethics committee review also doubles as its overall approval for study conduct at its locality. Some locality organisations may wish to ask further questions or to take the matter through further processes. Any such further issues or processes are not part of ethics committee review, and ethics committee approval does not depend on them.

What is a locality organisation?

For the purposes of locality assessment, a 'locality organisation' is an organisation through which substantial study recruitment or conduct is to take place. A key purpose of defining the locality organisation in this way is to ensure that, where a proposed study has significant potential to impact on health or disability services, the investigator satisfactorily addresses this issue. Note the consequence that the locality organisation is *not* necessarily the same as the investigator's employer organisation or the study's funder or sponsor organisation. For example, if the proposed study involves access to health records held by the National Screening Unit, then that is the locality organisation. This means that even if the investigator were funded by the HRC or the Ministry of Health or were employed by a university none of these three organisations would be a locality organisation. As another example, if the study involved a community-based intervention that took place in premises and facilities of Ngāti Porou Hauora, then that would be the locality organisation no matter who funded the study or employed the investigator.

Locality organisations have responsibilities for the good conduct of the activities within their organisations, whether or not locality assessment processes are in place. Statutory sources for accountability of locality organisations to the local community of health services consumers include: the Health and Disability Commissioner Act 1994; the New Zealand Public Health and Disability Act 2000; the Injury Prevention, Rehabilitation, and Compensation Act 2001 and the Health Practitioners Competence Assurance Act 2003.

A locality organisation's check that the investigator has satisfactorily addressed the locality issues can be seen as part of the locality organisation meeting its responsibility for the quality and appropriateness of the services delivered or studies conducted within it. One consequence of this is that any organisation that is competent to host a study must also be competent to conduct locality assessment for that study.

Locality organisations have the power to withdraw a favourable locality assessment, if significant concerns arise in relation to locality issues after sign-off. Any such move would, in effect, also withdraw ethics committee approval for study conduct at that locality. Thus, it is important that the locality organisation first communicate with the investigator about any intention to withdraw its favourable locality assessment. If favourable locality assessment is withdrawn, the locality organisation must notify this to the ethics committee as well as to the investigator.

If a locality organisation has any comments that might bear on a revision to the application form, information sheet or consent form, it should make these to the investigator as currently, it is the investigator's responsibility to submit to the ethics committee any changes they wish to make to the ethics committee application form, generic information sheet or generic consent form. If the investigator wishes to make any changes that affect the locality assessment, such as changes to local contact details, these should be sent to the locality organisation.

When to use the form locality assessment – by ethics committee

1. Use this form when there is no study locality organisation, for example, when neither study recruitment nor study conduct takes place through or in any locality organisation. For example, the study might recruit participants through public advertisement alone, or from the electoral roll, and the recruitment might only be conducted in public places or in university or other employer premises where there is no significant potential for impact on health or disability services. Where there is no study locality organisation, it is an ethics committee responsibility to check that the investigator has satisfactorily addressed any locality issues.
2. Use this form when the investigator and the locality organisation are, or are in effect, one and the same. For example, the investigator might also be the lead person in the organisation through which recruitment takes place or in which the study is to be conducted; or the locality organisation might be the primary funder of the study. In such cases, that organisation's locality assessment would in effect be a self-assessment or would at least be subject to significant influence by the party to be assessed.

3. To enable the committee to complete an assessment, ensure the questions are fully answered. The examples are given as a guide to the type of questions that may need to be addressed.

Is locality assessment required prior to submitting an application to the ethics committee?

The processes of ethics committee review and locality organisation checking of locality assessment may proceed in tandem. The investigator may: (1) submit completed locality assessment to the ethics committee with the ethics committee application form or (2) submit the ethics committee application form without having completed locality assessment. In case (1), the ethics committee administrator would check this completed locality assessment and inform the ethics committee that this assessment has been done. In case (2), the ethics committee would inform the investigator that its approval is conditional on subsequent completion of that locality assessment. A copy of the letter of conditional ethical approval would be sent to the locality organisation.

Is favourable locality assessment required for all sites prior to ethical approval being confirmed?

For some studies (for example, HRC-funded studies), favourable locality assessment from *all* proposed locality organisations may be required for the study to be viable or worthwhile. In such cases, ethics committee approval for study conduct at *any* locality will be conditional on administrator receipt of favourable locality assessment from *all* locality organisations. In some other studies, however, this is not required. In many multi-national studies, for example, study viability or worth is not significantly affected by how many New Zealand localities participate. In such cases, ethics committee approval for study conduct at *each* locality should simply be conditional on administrator receipt of favourable locality assessment from *that* locality.

If a study amendment raises considerable locality issues, then a new locality assessment may be required.

What is the role for Māori in locality assessment?

Locality assessment is distinct from consultation with Māori (a key guidance document for which is: *Guidelines for Researchers on Health Research Involving Māori*, available from the HRC at: <http://www.hrc.govt.nz/maoquide.htm>). In relevant cases, it is the researcher's responsibility to consult with Māori and an ethics committee responsibility to check that this consultation has been conducted satisfactorily. Consultation with Māori will assist the researcher to identify and address issues for Māori regarding study conduct at the particular locality in question but may also address ethical issues that go beyond 'locality' matters. In addition, not all locality issues are particular to Māori.

Researchers and locality organisations (and, in the relevant cases, ethics committees) should address locality issues, or check that they have been addressed, in a manner that is consistent with the principles of the Treaty of Waitangi, as set out in He Korowai Oranga: Māori Health Strategy. In some large organisations, there are processes that involve approval from a MRRC (for example, Auckland DHB) or from a Māori Health Advisor (for example, Hutt Valley DHB).

Information required for trials involving administration of medicines.

(Refer to the *Interim Good Clinical Practice Research Guideline* (August 1998), Ministry of Health, <http://www.medsafe.govt.nz>.)

This form is to be completed for trials that involve administration of medicines including non registered medicines except where the medicine will be given regardless of entry into the trial (eg, anaesthetic) and that medicine is not being studied in any way. A separate form must be submitted for each medicine. For registered medicines, attach a copy of the data sheet published by the manufacturer and approved by the Ministry of Health.

Substances such as nutritional compounds become medicines under the Medicines Act 1981 (the Act) if they are being administered for a therapeutic purpose. Therefore such trials require SCOTT consideration and approval by the Director-General of Health under section 30 of the Act.

For medicines that are not currently registered in New Zealand, an ethics approval may be given on the understanding that the study cannot lawfully proceed in New Zealand unless the trial has been considered by the Standing Committee on Therapeutic Trials (SCOTT) and approved by the Director-General of Health. If the trial has already been approved by the Director-General of Health, and you are now seeking an ethics approval, please attach a copy of the notification of approval.

Pro forma for consent form

Please follow the structure of the pro forma below in your consent form, which should be printed on the letterhead of the institution of the principal investigator.

Note: The Code of Health and Disability Services Consumers' Rights requires written consent for all experimental health care procedures. Consent forms for all participants should be identical, except for contact/advocate details where appropriate.

Request for interpreter (to be included on all consent forms)

English	I wish to have an interpreter	Yes	No
Deaf	I wish to have a NZ sign language interpreter	Yes	No
Māori	E hiahia ana ahau ki tetahi kaiwhaka Māori/kaiwhaka pakeha korero	Ae	Kao
Cook Island Māori	Ka inangaro au i tetahi tangata uri reo	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu	E	Nakai
Sāmoan	Ou te mana'o ia i ai se fa'amatala upu	loe	Leai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	loe	Leai
Tongan	Oku ou fiema'u ha fakatonulea	Io	Ikai
	<i>Other languages to be added following consultation with relevant communities.</i>		

It is important that consent forms being used by researchers include the following information/phrases:

1. The form should be clearly labelled with the heading Consent Form.
2. The form should include the name of study in language that will be easily understood by the participants.
3. The points covered by the following phrases should be included in language that will be easily understood by the participants.
 - 3.1 I have read and I understand the information sheet dated _____ for volunteers taking part in the study designed to _____. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given.
 - 3.2 I have had the opportunity to use whānau support or a friend to help me ask questions and understand the study.
 - 3.3 I understand that taking part in this study is voluntary (my choice), and that I may withdraw from the study at any time, and this will in no way affect my *future health care/continuing health care/academic progress/employment*. (Insert only the phrases that are most appropriate.)

- 3.4 (Insert if relevant, where the research involves a vulnerable participant.) I have had this project explained to me by .
- 3.5 I understand that my participation in this study is confidential and that no material that could identify me will be used in any reports on this study.
- 3.6 *(Insert only when appropriate.)* I understand that the treatment, or investigation, will be stopped if it should appear harmful to me.
- 3.7 *(Insert for Form A and B trials.)* I understand the compensation provisions for this study.
- 3.8 I have had time to consider whether to take part in the study.
- 3.9 I know who to contact if I have any side effects from the study.
- 3.10 I know who to contact if I have any questions about the medication used in this study or about the study in general.
4. The following clauses, if applicable to the research project, should be included in the body of the consent form.
- 4.1 I agree to an approved auditor appointed by either the sponsoring pharmaceutical company, ethics committee or the regulatory authority or their approved representative and approved by the ethics committee reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study. Yes No
- 4.2 I consent to the researchers storing a specimen of my blood (or other tissue) for its later use as a part of this study or other research **or** Yes No
- 4.3 I consent to blood samples being destroyed at the end of the study. Yes No
- 4.4 I consent to blood samples being sent to . Yes No
- 4.5 I am aware that the proposed study will involve analysis of my genetic make-up. I consent to such an analysis being performed. Yes No
- 4.6 I understand that if I consent to such analysis, no rights will be created for the researcher/sponsor to my genetic information. Yes No
- 4.7 I am aware that the proposed study may involve storage of my genetic make-up, and I give my consent to such storage. Yes No
- 4.8 I consent to my DNA/tissue sample being stored for future research into *(specific research, for example, diabetes, heart)* subject to ethical approval being given by a New Zealand-accredited ethics committee. Yes No
- 4.9 I consent to my interview being audiotaped/videotaped. Yes No
- 4.10 I wish to receive a copy of the results. *Participants should be advised that a significant delay may occur between data collection and publication of the results. Alternatively 'I would like the researcher to discuss the outcomes of the study with me'.* Yes No
- 4.11 I agree to my GP or other current provider being informed of my participation in this study/the results of my participation in this study. Yes No

5. I _____ (*full name*) hereby consent to take part in this study. (Refer to Guidelines where participants are vulnerable.)

Date:

Signature:

Full names of researchers:

Contact phone number for researchers:

Project explained by:

Project role:

Signature:

Date:

Notes:

1. A copy of the consent form is to be retained by each participant and (in the case of patients) a copy is to be placed in the medical file.
2. In a Phase I study, a participant's decision not to inform their GP or primary health provider of their participation in a trial should be an exclusion criterion. Otherwise, consent to contact the GP should be the participant's choice. If there is a safety concern, it is up to the investigator to make a decision as to the person's eligibility for inclusion in the study.

Footer: version number and date.

Guidelines for the preparation of information sheets

Note: Information sheets should be prepared on the appropriate letterhead of the principal investigator's institution. Information sheets for all participants should be identical except for the principal investigator's contact/advocate details as appropriate. A footer containing the project title, version and page number must be included on each page. Information sheets and consent forms may be numbered separately or as one document.

1. General

The information sheet for participants in a study is very important. Not only does it set out the aims and methods of the study, but it also establishes the credibility and the responsibility of the investigator. It can be difficult to strike the balance between providing what the patient or participant should know and providing too much information.

The information sheet and consent form in a multi-region study should be identical except for local information, for example, name and contact details of the researchers and health and disability advocate.

Information should be written in a way that is helpful and clear. Not all people have the same command of the English language. Some for whom English is a second language may have special difficulties. The aim should be to produce documents that can be easily read by all participants.

The information sheet should be headed with the study title, using language that is appropriate for a layperson.

Obviously, all the details covered will not be appropriate for all studies. Sections 5 to 8 below may raise questions that participants may wish to have answered. The information sheet does not have to be in question and answer form. If you have any questions about these forms, please do not hesitate to contact the administrator of the appropriate ethics committee for advice.

2. The text

Some methods for improving the comprehensibility of the text.

- 2.1 Use positive phrasing. Negative sentences should be used only when emphasising actions to be avoided.
- 2.2 Avoid reassuring language in describing side effects.
- 2.3 Whenever possible, use active rather than passive sentences.
- 2.4 Use short sentences with only one or two ideas. Avoid sentences with complex and multiple clauses.
- 2.5 Avoid jargon. If possible, use common words.
- 2.6 Place 'inviting' questions as headings before relevant parts of the text, for example, 'What are the side effects of the medicine?'.
- 2.7 Group related items under subheadings.
- 2.8 Include the little words in the text. Omitting words such as 'in', 'this', 'the', 'you' sometimes leads to misunderstanding.
- 2.9 Avoid abbreviations or use of initials for terms.

3. Layout and typography

- 3.1 The print size should be large enough to be read by all age groups.
- 3.2 The text should be spaced appropriately.
- 3.3 Use bold lower case in titles (except for the initial letter of the first word) as this is more distinct, and easier to read, than full capitals.
- 3.4 Indent the first line of a paragraph.
- 3.5 Use Arabic numerals (for example, 4, 5, 6) not Roman numerals (iv, v, vi).
- 3.6 Numbers are easier to read as numbers rather than words.
- 3.7 Exclusion clauses should be in bold or underlined for emphasis.

4. The content

Each page of the information sheet should be numbered.

Principal investigator: Include the full name, position, address and local contact telephone number of the principal investigator and/or the contact person. (Include details of the supervisor, if this is a student protocol.)

Title: The study title should be in language appropriate for a layperson.

Introduction: The information sheet should begin with an invitation to take part ('You are invited to take part in ...'), a comment on the time available to the proposed participant for considering whether to take part and a statement on the proposed participant's right not to take part.

5. Participation

Include statements such as:

1. 'Your participation is entirely voluntary (your choice). You do not have to take part in this study, and if you choose not to take part you will receive the standard treatment/care available.'
 For non-treatment based studies, (or where appropriate) replace 'You will receive the standard treatment/care available' with 'This will not affect any future care or treatment'.
 Where there is a student/supervisor or student/student relationship, the following statement should be used: 'This will not affect your academic progress'. If appropriate, use 'This will not affect your employment'.
2. 'If you do agree to take part in the study, you are free to withdraw from the study at any time, without having to give a reason, and this will in no way affect your future health care/continuing health care/academic progress.' (Insert only the phrase(s) that is/are most appropriate.)
 'Participation in this study will be stopped should any harmful effects appear or if the doctor feels it is not in your best interests to continue.'
3. If the study involves children, include in the information sheet for parents:
 "Your child has the right to consent to participate in research when they are capable of understanding what the study involves and the risks. If your child is unable to fully understand, their assent must be obtained unless your child is unable to communicate."
 "Your child's refusal to participate must be respected unless your child will receive therapy for which there is no medically acceptable alternative, where the risk is justified by the anticipated benefit or where the anticipated benefit to the risk is likely to be at least as favourable as any available alternative."

6. About the study

Include:

1. An explanation of the aims of the study.
2. How participants were selected for this study, and who selected them.
3. How many participants will be involved.
4. Where the study will be held.
5. What the time span for the study will be.
6. What will happen during the study (that is, clearly explain what procedures will take place, including the number and length of visits, number and type of samples taken, total time involved, other investigations (for example, any interview – how long it will take, how it will be recorded, what will happen to transcripts/tapes after the study) and why the tests or procedures are necessary).
7. What will happen to samples after the study is concluded (if blood samples are going overseas indicate that these will be destroyed (if relevant)).
8. If participants are being randomised, an explanation of what this means, for example, 'selected by chance by a computer'.

7. Benefits, risks and safety

Explain all the following in layperson terms:

1. The benefits of the study.
2. The risks and/or inconveniences of the study (list all possible side effects of any medication or procedures that are part of the study and their likely incidence).
3. Whether medication will continue to be available at the completion of the study and at whose cost.
4. Outline the inclusion and exclusion criteria.
5. If pregnancy testing is compulsory, include the statement: 'We realise that pregnancy will not occur for all women for a variety of reasons, but because of safety issues, one of our requirements for taking part in the study is a negative pregnancy test'.
6. Whether the study is therapeutic or non-therapeutic. Where children will be participants, include whether they will receive therapy for which there is no medically acceptable alternative, where the risk is justified by the anticipated benefit or where the anticipated benefit to the risk is likely to be at least as favourable as any available alternative.
7. Whether taking part in the study will cost anything, and whether participants will receive any payment or reimbursement of expenses.
8. Whether any other treatments are available, and if so, what the advantages/disadvantages of these are.
9. If a placebo is to be used include an explanation, for example, 'A placebo is a "dummy" medicine. If you are given a placebo while taking part in this study you will not get any expected effects from the medicine that is being studied'.
10. While it is important to state that participants may receive no benefit from participating in a trial, it can be stated that participants may benefit from the extra monitoring they will receive.
11. What happens if there are any ill effects from the trial? What compensation will be available?
12. If appropriate, include 'If you have private medical insurance, please check with your insurance company before agreeing to take part in the trial. You should do this to ensure that your participation will not affect your medical insurance'.
13. Include a full explanation of the company's compensation cover for participants, including exclusions, and a description of the circumstances in which participants would have to sue to obtain compensation.

8. General

Include the following:

1. 'Will my GP be told I am in the study?' (if applicable).
2. 'What will happen at the end of the study?' (include a comment on onward referral/future care if applicable).
3. 'Where can I get more information about the study?'
4. 'If I need an interpreter, can one be provided?'
5. 'You may have a friend, family or whānau support to help you understand the risks and/or benefits of this study and any other explanation you may require.'
6. For studies using interviews or questionnaires, state 'You do not have to answer all the questions, and you may stop the interview at any time'.
7. In clinical trials, include the statement 'You will be issued a card to confirm your participation in a clinical trial. This card should be presented at the time of any treatment received during your participation in the trial'.

8. For studies where participants are health professionals, include the statement 'If you have any queries or concerns regarding your rights as a participant in this study, you may wish to contact your professional organisation'.
9. 'If you have any queries or concerns regarding your rights as a participant in this study, you may wish to contact an independent health and disability advocate:
Free phone: 0800 555 050
Free fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz'
10. Details of any travel or accommodation allowance payable should be included.

9. Confidentiality

Include the following statement: 'No material that could personally identify you will be used in any reports on this study'.

Explain what identifiers will be used to identify specimens. These should be minimal to protect participants' privacy. You should obtain the consent of participants to use identifiers.

Information should also be included that explains how records will be stored to ensure details are kept confidential throughout the duration of the study and what will happen to records after completion of the study.

If the notes/results need to be checked by anyone else, for example, the study sponsors (these should be listed), this should also be included on the information sheet and consent form.

10. Results

How can participants get the results of this research, and where will the results be published? Explain that there may be a delay between data collection and publication of results. Alternatively, offer to discuss the outcomes with the participant on an individual basis by appointment.

11. Genetic technology studies only

In some research, it will be necessary to explain genetic technology. The following wording is not mandatory and should be simplified where necessary for participants' understanding:

'Each person has a DNA make-up (their genes) that is different from that of everybody else (except in the case of identical twins). This genetic make-up is a mixture of the genes of our parents. The precise way genes are mixed varies from child to child within the same family, so having the same parents does not mean that two children will have exactly the same genes. We already know that some health conditions and disorders are definitely inherited through the genes (hereditary conditions), but we do not know how many conditions are explained by genetic inheritance. Inherited genes may explain why some people are more resistant and some people more prone to disorders that have not yet been identified as hereditary. The research in which you are invited to participate will investigate genetic make-up to look for any link between an occurrence of a disorder and inherited genes.

'Because the research investigates genetic make-up, this identifies you as a participant as well as your particular genetic characteristics. This information is confidential and will not be disclosed, stored or used in any way without your informed consent.

'In particular the researcher/sponsor of the research will not claim any right, ownership or property in your individual genetic information or that of your kinship group, hapū or iwi, without having first sought and obtained your informed consent to the transfer of any such right, ownership or property. Your consenting to participate in DNA sampling for the proposed study will not be construed as creating any right or claim on the part of the researcher/sponsor to your genetic information.'

12. Statement of approval

Include:

- (1) 'This study has received ethical approval from the (insert name of committee) Ethics Committee, ethics reference number (insert ethics reference number).' or
- (2) 'This study has received ethical approval from the Multi-region Ethics Committee, which reviews national and multi regional studies, ethics reference number (insert ethics reference number).'

For those studies involving groups of employees, include a statement such as 'The Manager/ Supervisor/Director (as appropriate) has given permission for this study to be carried out'.

Conclude the information sheet with the following statement:

'Please feel free to contact the researcher if you have any questions about this study.'

Note: Include either Declaration A Trials (Compensation) or Declaration B Trials (Compensation) as appropriate on the information sheet (see description below).

Footer: version number and date.

Declaration A trials: to be included on information sheet under the heading "Compensation"

'In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation, and Compensation Act 2001. ACC cover is not automatic, and your case will need to be assessed by ACC according to the provisions of the Injury Prevention, Rehabilitation, and Compensation Act 2001. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors, such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses, and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

'If you have any questions about ACC, contact your nearest ACC office or the investigator.

'You are also advised to check whether participation in this study would affect any indemnity cover you have or are considering, such as medical insurance, life insurance and superannuation.'

Declaration B trials: to be included on information sheet under the heading "Compensation"

'The (insert name of committee) Ethics Committee has certified that this clinical trial is being conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which this trial is being carried out. This means that **if you suffer injury as a result of your participation in this trial, you will not be eligible for cover under accident compensation legislation.** Compensation, however, will be provided by (insert name of company) in accordance with the *New Zealand Researched Medicines Industry Guidelines on Clinical Trials: Compensation for injury resulting from participation in industry sponsored clinical trials.*

'These Researched Medicines Industry (RMI) Guidelines are only guidelines, and until your claim is assessed by the insurers of (insert name of company) it cannot be said with any certainty exactly what type or amount of compensation you will receive if you suffer injury as a result of your participation or what sort of injury will be covered. The guidelines require that compensation be provided by (insert name of company) where the injury you suffer is serious and not just temporary and is one caused by the trial medicine or item or where you would not have suffered injury but for your inclusion in this trial.

'The guidelines require that the compensation you receive be appropriate to the nature, severity and persistence of your injury. This means that you will be unlikely to receive compensation from (insert name of company) unless your injury is serious and not just temporary.'

You will also not receive compensation from (insert name of company) in this trial if (include other exclusions, for example, if mental injury is excluded this must be stated).

You might not receive compensation from (insert name of company) if your injury was caused by the investigators, if there is a deviation from the proposed plan of research, or if your injury was caused solely by you. If you are injured as a result of the trial, but your injury was caused by the investigators (or the institution/hospital where the trial took place) or as a result of a deviation from the proposed plan of research, you will **not be covered by** ACC and may have to pursue a civil action against the investigators (or institution). Ethics committees require that researchers and their institution have indemnity cover for such risk.

'You are also advised to check whether participation in this study would affect any indemnity cover you have or are considering, such as medical insurance, life insurance and superannuation.'

Note: If the trial includes placebo/standard treatment, the investigators will need to check with the company whether there is compensation for participants being using placebo treatment. If there is no compensation for this, it should be stated in the last sentence of paragraph four of the declaration above. The declaration should also make it clear why participants on placebo are not covered, for example, because there are not the same risks involved.

Part 5: Use of Human Tissue

Review and approval by an accredited ethics committee is required for any research project that involves any collection, use or storage of human tissue.

The Human Tissue Act 2008 came into force on 1 November 2008. The Act provides a framework for regulating the collection, storage and use of human tissue, primarily from deceased donors. It also regulates trading in tissue, export and import of tissue, the use of tissue for non-therapeutic purposes (eg, audit, anatomical examination, research and post mortem).

Definition of 'human tissue'

(From the Standard for collection or use of human tissue currently under development.)

Human tissue means material that is, or is derived from a body, or material collected from a living individual or a body, which includes human cells.

Examples of human tissue includes but is not limited to the following:

- (a) all or any part of a body (for example, brain, arm, leg)
- (b) human bone marrow
- (c) whole human organs (for example, heart, lungs, kidney, liver) or parts of them, (for example, heart valves)
- (d) human hair, nails, skin and other tissue (for example, eyes, corneas, tendons)
- (e) human blood and blood products
- (f) human mucus, sputum or urine
- (g) human stem cells or other human cells (for example, stem cells derived from human embryos)
- (h) human lung washouts
- (i) cell lines derived from human tissue.

'Human tissue' also includes the human foetus and placenta. Any research that creates or uses a human gamete, a human embryo or a hybrid embryo must be referred to the Ethics Committee on Assisted Reproductive Technology (ECART) under the Human Assisted Reproductive Technology (HART) Act 2004.

Depending on the context of the proposed research, 'human tissue' may extend to include:

- molecular information about sub-cellular structures of that human tissue
- any other information derived there from (for example, information about heritable characteristics of individuals obtained by analysis of DNA sequences or by other means).

In some unique circumstances, research involving 'human tissue' may also include micro-organisms cultured from human tissue.

Human embryonic stem cell lines

For research on human embryonic stem cell lines refer to the Guidelines for Using Cells from Established Human Embryonic Stem Cell Lines for Research, Ministry of Health 2006 available at <http://www.ethicscommittees.health.govt.nz/moh.nsf/indexcm/ethics-resources-consultation-guidelines-stem-cell-use>. Contact the National Co-ordinator for additional questions relating to this research. (An additional Part 9 is under development.)

Māori or cultural issues that may be ethically relevant

Researchers and ethics committees should consider and reflect on whether there are any Māori or cultural issues that may be ethically relevant that could arise in the context where human tissue is involved in any research project.

The ethical issues and appropriate safeguards should be discussed and developed in consultation with the relevant iwi or cultural groups – details about the Māori or cultural issues that are ethically relevant and the safeguards that will be in place should be provided under section F (Cultural and Social Responsibility).

Seeking consent for a research project involving human tissue

The consent of the person from whom the human tissue was/will be obtained, or if deceased the appropriate consent from the family and confirmation that the deceased had not objected to becoming a donor, must be sought in relation to any collection, use or storage of the tissue for research. **In some rare and exceptional circumstances**, it may be ethically permissible to conduct research involving human tissue without consent, but such research must be prospectively reviewed and approved by a health and disability ethics committee or the Health Research Council Ethics Committee. The expectation is that consent for future use for research purposes will be obtained prospectively (see Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes).

Later use of stored human material in a future study

If human tissue is stored for *later use in a future study* and *specific consent* for that use has not been obtained previously or does not come within the scope of consent that was given, a new application will have to be submitted to an accredited ethics committee for review when any researcher proposes to carry out such a study. A copy of the original information sheet and consent form must be submitted with the application.

Transfer of human tissue sample overseas (for question 4)

Researchers and ethics committees should discuss and consider the appropriate ethical safeguards that should be in place to protect any human tissue sample that will be sent out of New Zealand.

Use of human tissue for future unspecified research purposes

Refer to the Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, Ministry of Health, 2007 available at <http://www.moh.govt.nz/moh.nsf/indexmh/guidelines-use-human-tissue>.

These guidelines also apply to any information that is derived from human tissue.

Consent to the future unspecified use of a person's tissue samples must be distinct from consent to collect the sample and distinct from consent to use the sample in specified research. Consent may be given for the unidentified or de-linked use of the donor's tissue sample. However, in such situations, the donor must be informed that they will not be able to withdraw their consent in the future.

Consent or assent must be obtained from a child to the level of their understanding. Where a child lacks the competency to give legally effective consent, the child's legal guardians can give proxy consent for the use of their child's tissue sample for future unspecified research, including for the tissue sample to be de-linked.

Unidentified/de-linked tissue means that the identity and personal information of an individual who has donated human tissue is no longer identifiable or linked to that individual's tissue sample.

Relevant documents that may be helpful

- Human Tissue Act 2008
- *Human Tissue and Biological Samples for Use in Research*. Operational and Ethical Guidelines, Medical Research Council (UK) (2001). http://www.mrc.ac.uk/pdf-tissue_guide_fin.pdf
- *National Statement on Ethical Conduct in Human Research*, National Health and Medical Research Council (Australia) (2007). See especially paragraphs page 21 and pages 39–40. <http://www.nhmrc.gov.au/publications/synopses/e35syn.htm>
- *Human Research Ethics Handbook. Commentary on the National Statement on Ethical Conduct in Research Involving Humans*. National Health and Medical Research Council (Australia) (2002). See especially pages E89–E98. <http://www.nhmrc.gov.au/publications/synopses/e42syn.htm>
- *Tri-Council Policy Statement: Ethical conduct for research involving humans*. Medical Research Council of Canada et al. (1998). See especially section 10. <http://www.nserc.ca/programs/ethics/english/policy.htm>

Part 8:

When a Participant is Unable to Make an Informed Choice

Refer to the following appendices in the Operational Standard for Ethics Committees 2006.

- Appendix 1: Guidelines for Health Research with Children
- Appendix 2: Research Involving People with Intellectual Disabilities: Issues of informed consent and participation
- Appendix 3: Research Involving Unconscious Participants.

Research with children

The ethics committee shall ensure that:

- there is minimal risk to the participants
- it has taken advice from independent child health experts, including kuia and koroua
- prior knowledge has been obtained through research with adults and animals
- no valid alternative to the use of children in the research is available
- a valid proxy consent (where children consent to participate in the research) has been obtained for each research participant. (Note: Proxy consent cannot authorise research that carries significantly greater risk to the research participant than normal clinical treatment would pose.)

The consent of a child of or over the age of 16 must be obtained and has the same effect as if the child were of full age. If the child is below the age of 16 but has the competence to understand the nature, risks and consequences of the research, the consent of the child must be obtained and that consent will have the same effect as if the child were of full age.

The views of children and others who are legally incompetent must be taken into account to the degree that they are capable of understanding. If there is someone able to consent on behalf of the participant eg, parents/caregivers of children, a standard parent/caregiver consent form should be used, not the statement by relative/friend/whānau. The child's assent must also be obtained unless the child is unable to communicate. The refusal of a child to participate in research must be respected unless the research procedures or interventions are intended to provide direct therapeutic benefit to the child and the risk is justified by the anticipated benefit or any anticipated benefit to the risk is likely to be at least as favourable to the child as any available alternative.

An information sheet and consent or assent form must be provided appropriate to the child's level of understanding.

Research with participants who are unable to consent themselves

The ethics committee shall also ensure that:

- there is minimal risk to the participants
- the researcher has signed a statement to the effect that they believe that the research is not adverse to the welfare of the particular patient
- a best possible substituted judgment has been reached, regarding the likely wishes of the participant
- the participant will be told of their participation as soon as practicable.

If participants are unable to consent themselves and there is no one legally able to consent for them (parents/guardians may consent for children) the investigator must comply with Right 7(4) of the Code of Health and Disability Services Consumers' Rights. The views of the consumer or other suitable persons who are interested in the welfare of the consumer and are able to advise the researcher should be taken into account using the Statement by Relative/Friend/Whānau. Such views are relevant to the decision about whether the research should be conducted on the incompetent participant, but whether the research is in the potential participant's best interests is also relevant. Therefore, in all cases where there is no person entitled to make an informed choice, sections 1.1 and 1.2 must be completed.

Appendix 1: How to Apply to the Standing Committee on Therapeutic Trials (SCOTT)

New medicines – clinical trials

Approval must be obtained before any clinical trial can be undertaken where any medicine to be used in the trial, including comparator and investigational medicines, is a new chemical entity and/or new or different dose forms, delivery systems or formulations of established medicines are to be used and the medicine does not have consent to be marketed in New Zealand. Approval is dependent upon a favourable recommendation from the Health Research Council's Standing Committee on Therapeutic Trials (SCOTT), and an accredited ethics committee for the study protocol.

Labelling

While the legislation requires that clinical trial medicines must be labelled 'to be used by qualified investigators only', the Ministry of Health (the Ministry) policy is to accept this wording or wording with a similar meaning, for example, 'for clinical trial use only'.

The application form can be obtained from: The Manager, Therapeutics Section, Ministry of Health, PO Box 5013, Wellington, or from the MedSafe website at: <http://www.medsafe.govt.nz>

The document is located under 'Regulatory Information' and is contained in volume three of the *New Zealand Regulatory Guidelines for Medicines*.

One copy of the completed application, accompanied by the supporting data and appropriate fee, should be sent to the Ministry at the address given above.

Four copies of the full application dossier are required by the SCOTT and should be sent at the same time as making the application to the chair of the committee:

Postal address:

Dr R Robson
Clinical Studies Trust
PO Box 2856, Christchurch
Attention: Celia Foley

Courier address:

Dr R Robson
Clinical Studies Trust
The Pegasus Centre, 31 Tuam Street, Christchurch
Attention: Celia Foley

Any correspondence arising from the application will be conducted through the Ministry.

The Director-General of Health will advise the applicant of the final outcome of the application within 45 days of its receipt. If the decision is made to decline the application, the reasons for declining will be provided.

All medicines distributed under these provisions must be labelled 'To be used by qualified investigators only'. It is the responsibility of the importer or manufacturer to ensure that the medicine is supplied only to an authorised investigator.

The importer or manufacturer must keep complete and accurate records of all quantities of the medicine so supplied and of the progress and results of the investigations. Six-monthly progress reports on the trial must be provided to the Director-General of Health. The Director-General of Health must also receive a copy of the results obtained at the completion of the trial.

Serious adverse effects

The sponsor must report all serious adverse events, which result in breaking the study code, to the Director-General of Health within three working days of being informed of the adverse event. These reports should be followed as soon as is practicable with an assessment of causality of the adverse event and a discussion of the possible impact of the adverse event on the future use of the product under investigation.

All other serious adverse events that do not result in breaking the study code and that are not specified as study end points should be recorded and presented to the ethics committee and/or the Director-General of Health as part of the regular reporting requirements of these bodies.

Note:

- A study designed solely to compare bioequivalence of a new medicine with one that is currently legally marketed, using healthy volunteers, does not require an application for approval.
- The requirement for SCOTT approval is linked to the formulation of the medicine being used in the clinical study. Where a clinical study of a new indication is using the formulation of a medicine that is normally distributed in New Zealand, (that is, the formulation has consent to market), approval by the SCOTT for the study is **not** required, but the approval of an accredited ethics committee is required. However, should the study formulation differ in any way from the formulation of a medicine that has consent to be marketed, then SCOTT approval is necessary.

Further information on the requirements for reporting, etc can be found in *Interim New Zealand Guideline for Good Clinical Research Practice* (August 1998) Ministry of Health.

Appendix 2: How to Apply to the Gene Technology Advisory Committee (GTAC)

GTAC reviews the following proposals for the purposes of seeking an exemption under Section 30 of the Medicines Act (1981) or as required by an accredited ethics committee or the Health Research Council or any of its committees:

1. Proposals for clinical trials that include the introduction of nucleic acids (genetically manipulated or synthesised in the laboratory) or genetically manipulated micro-organisms, viruses or cells into human subjects for the purpose of gene therapy or cell marking.
2. Proposals for clinical trials in which the introduction of nucleic acids (genetically manipulated or synthesised in the laboratory) or genetically manipulated micro-organisms, viruses or cells is designed to stimulate an immune response against the subject's own cells, as in the treatment of certain cancers.
3. Proposals for clinical trials in which nucleic acids either from or within cells from animal species are transferred into humans for the purpose of disease treatment, that is, xenotransplantation.
4. Proposals for clinical trials in which human nucleic acids have been introduced into the genome of an animal species, including genetically manipulated micro-organisms, for the purpose of developing products to be used for either disease prevention or treatment in human subjects.
5. Proposals for clinical trials involving vaccines in which nucleic acids (genetically manipulated or synthesised in the laboratory) or genetically manipulated micro-organisms, viruses or cells have been introduced to stimulate an immune response to antigenic determinants of an infectious agent.

Application process

Applications to the Ministry of Health for GTAC approval are to be made by letter, using *Guidelines for Preparation of Applications for GTAC Review*, available from the Health Research Council or from the Ministry of Health. The format used by GTAC is based on that used by the NH&MRC (Australia) and the Points to Consider, used by the FDA (USA). The fee or a letter seeking an exemption from the fee should accompany the application.

The application will be reviewed by GTAC within 30 days. The investigator may be required to attend a meeting with the committee to discuss the application.

GTAC will provide the Director-General of Health with their recommendation on whether the trial should be approved.

If a proposal involves materials that originate from the USA, the investigator will be required to meet the regulatory requirements of the FDA to obtain an export certificate. The Director-General of Health will not give approval for a Section 30 exemption until the appropriate documentation has been received and has been approved by the Ministry of Health.

Approval from an accredited ethics committee cannot be sought until the Director-General of Health has received a recommendation from GTAC that the trial under review should be approved.

When the Director-General of Health has received recommendations for approval from GTAC and an accredited ethics committee, written approval for an exemption under Section 30 of the Medicines Act (1981) will be given. Only then can the investigator proceed with the trial.

Investigators should ensure that they meet **all** the requirements of their host institutions with respect to making applications to gain approval from GTAC, relevant ethics committees, biosafety committees and the Environmental Risk Management Authority (ERMA).

Criteria for GTAC approval

GTAC will review applications to establish whether:

- (i) there is adequate scientific evidence from laboratory and experimental studies in animals to allow a trial in humans to proceed
- (ii) the proposed trial will provide a clinical benefit and scientifically useful information particularly in relation to safety and efficacy
- (iii) there is adequate information on the safety and toxicity of the materials to allow them to be used in a trial in humans
- (iv) the investigators have the qualifications, experience and track record to conduct the proposed trial
- (v) the investigators have conducted appropriate risk assessment of their proposed procedures.

A copy of the *Guidelines for Preparation of Applicants for GTAC Review* can be obtained from the Health Research Council, PO Box 5541, Wellesley Street, Auckland. Phone: (09) 379 8227; Email: info@hrc.govt.nz.

Appendix 3: New Zealand Researched Medicines Industry Guidelines on Clinical Trials: Compensation for Injury Resulting from Participation in Industry Sponsored Clinical Trials

(RMI Guidelines December 2008 – <http://www.rmianz.co.nz>)

Note: These guidelines are based on but differ from the Association of British Pharmaceutical Industry Guidelines.

Preamble

The Researched Medicines Industry Association of New Zealand Inc. favours a simple and expeditious procedure in relation to the provision of compensation for injury caused by participation in clinical trials. The association recommends, therefore, that a member company sponsoring a clinical trial should, without legal commitment, provide to the investigator – and through him/her to the relevant research ethics committee – a written assurance that the following guidelines will be adhered to in the event of injury caused to a patient that is attributable to participation in the trial in question. These guidelines are an adaptation of those used by the Association of British Pharmaceutical Industry.

1. Basic principles

- 1.1 Notwithstanding the absence of legal commitment, and having cognisance of the “no fault” nature of the New Zealand Accident Rehabilitation and Compensation Insurance Act, the sponsor company should pay compensation to patient-volunteers suffering bodily injury (including death) in accordance with these guidelines.
- 1.2 Where there is a difference of opinion as to if, on the balance of probabilities, the injury was attributable to the inclusion of the patient in the trial then the opinion of an independent mediator will be available at the cost of the sponsor company. The decision of the mediator will not be binding.
- 1.3 Compensation should be paid to a child injured in utero through the participation in a clinical trial of the subject’s mother as if the child were a patient-volunteer with the full benefit of these guidelines.
- 1.4 Compensation should only be paid for more serious injury of an enduring and disabling character (including exacerbation of an existing condition) and not for temporary pain or discomfort or less serious or curable complaints.
- 1.5 Where there is an adverse reaction to a medicinal product under trial and injury is caused by a procedure adopted to deal with that adverse reaction, compensation should be paid for such injury as if it were caused directly by the medicinal product under trial.
- 1.6 Neither the fact that the adverse reaction causing the injury was foreseeable or predictable, nor the fact that the patient has freely consented (whether in writing or otherwise) to participate in the trial should exclude a patient from consideration for compensation under these guidelines, although compensation may be abated or excluded in the light of the factors described in paragraph 4.2 below.

- 1.7 For the avoidance of doubt, compensation should be paid regardless of whether the patient is able to prove that the company has been negligent in relation to research or development of the medicinal product under trial or that the product is defective and therefore, as producer, the company is subject to strict liability in respect of injuries caused by the product.

2. Type of clinical research covered

- 2.1 These guidelines apply to injury caused to patients involved in clinical trials, that is to say, patients under treatment and surveillance and suffering from the ailment which the product under trial is intended to treat but for which a product licence does not exist or does not authorise supply for administration under the conditions of the trial (including Phase I, II and III clinical trials).
- 2.2 These guidelines also apply to injuries arising from Phase I studies in either patient or non-patient volunteers, whether or not they are hospitalised.
- 2.3 These guidelines do not apply to injury arising from clinical trials on marketed products (Phase IV) where a product licence exists authorising supply for administration under the conditions of the trial, except to the extent that the injury is caused to a patient as a direct result of procedures undertaken in accordance with the protocol (but not any product administered) to which the patient would not have been exposed had treatment been other than in the course of the trial.
- 2.4 These guidelines do not apply to clinical trials that have not been initiated or sponsored directly by the company providing the product for research.
- 2.5 Where trials of products are initiated independently by medical practitioners under the appropriate Medicines Act 1981 exemptions, responsibility for the health and welfare of patients rests with the medical practitioner alone.

3. Limitations

- 3.1 No compensation should be paid for the failure of a medicinal product to have its intended effect or to provide any other benefit to the patient.
- 3.2 No compensation should be paid for injury caused by other licensed medicinal products administered to the patient for the purpose of comparison with the product under trial.
- 3.3 No compensation should be paid to patients receiving placebo in consideration of its failure to provide a therapeutic benefit.
- 3.4 No compensation should be paid (or it should be reduced as the case may be) to the extent that injury has arisen through:
 - 3.4.1 a significant departure from the agreed protocol
 - 3.4.2 the wrongful act or default of a third party, including a medical practitioner's failure adequately to deal with adverse reaction
 - 3.4.3 contributory negligence by the subject.

4. Assessment of compensation

- 4.1 The amount of compensation paid should be appropriate to the nature, severity and persistence of the injury and should be no less than would be awarded for similar injuries by New Zealand's accident compensation scheme.
- 4.2 Compensation may be abated, or in certain circumstances excluded, in the light of the following factors (on which will depend the level of risk the patient can reasonably be expected to accept):
 - 4.2.1 the seriousness of the disease being treated, the degree of probability that adverse reactions will occur and any warnings given
 - 4.2.2 the risks and benefits of established treatments relative to those of the trial medicine known or suspected.

This reflects the fact that flexibility is required given the particular patient's circumstances. As an extreme example, there may be a patient suffering from a serious or life-threatening disease who is warned of a certain defined risk or adverse reaction. Participation in the trial is then based on an expectation that the benefit/risk ratio associated with participation may be better than that associated with alternative treatment. It is reasonable, therefore, that the patient accepts the high risk and should not expect compensation for the occurrence of the adverse reaction about which he or she was told.

- 4.3 In any case, where the company concedes that a payment should be made to a patient but there exists between company and patient a difference of opinion as to the appropriate level of compensation, it is recommended that the company agree to seek, at its own cost (and make available to the patient), the opinion of a mutually acceptable independent arbiter, and that this arbiter's decision on the appropriate payment to be made is binding.

5. Miscellaneous

- 5.1 Claims pursuant to the guidelines should be made by the patient to the company, preferably via the investigator, setting out details of the nature and background of the claim. Subject to the patient providing, on request, an authority for the company to review any medical records relevant to the claim, the company shall consider the claim expeditiously.
- 5.2 The undertaking given by the company extends to injury arising (at whatever time) from all administrations, clinical interventions or procedures occurring during the course of the trial but not to treatment extended, at the instigation of the investigator, beyond the end of the trial. The use of unlicensed products beyond the trial period is wholly the responsibility of the treating medical practitioner.
- 5.3 The fact that a company has agreed to abide by these guidelines in respect of a trial does not affect the right of a patient to pursue a legal remedy in respect of injury alleged to have been suffered as a result of participation. Nevertheless, patients will normally be asked to accept that any payment made under the guidelines will be in full settlement of their claims.
- 5.4 A company sponsoring a trial should encourage the investigator to make clear to participating patients that the trial is being conducted subject to the Researched Medicines Industry Association of New Zealand Incorporated Guidelines on Clinical Trials Compensation for Injury Resulting from Participation in an Industry-Sponsored Clinical Trial, and have available copies of the guidelines should they be requested.

Appendix 4: How to Apply to the National Radiation Laboratory (NRL)

National Radiation Laboratory (NRL) verification of research proposals involving the use of ionising radiation

What research proposals must be submitted to NRL for verification?

Any research project involving the intentional exposure of a person, as part of the project, to ionising radiation for diagnostic, therapeutic or other purposes where that exposure is not required for the clinical management of the person being exposed, ie, the individual being exposed is unlikely to receive any personal benefit.

What is NRL's role?

NRL is a specialist unit of the Ministry of Health and is the regulatory authority administering the *Radiation Protection Act 1965* (the Act) and *Radiation Protection Regulations 1982* (the Regulations). Two NRL specified codes of safe practice, *NRL C3* (NRL, 1994) and *NRL C5* (NRL, 1994), have requirements relating to the use of unsealed radioactive material and diagnostic x-ray equipment in medical research. The Act and the Regulations and codes of safe practice can be accessed through NRL's web site <www.nrl.moh.govt.nz>.

NRL's role is not to approve research proposals. Rather, it is to assist an ethics committee in evaluating a proposal by verifying as far as practicable that:

- responsibilities under the Act related to the use of radioactive materials and/or irradiating apparatus are being fulfilled, ie, an appropriate licence holder is responsible for the use of the radioactive materials and/or irradiating apparatus
- the calculated radiation doses to the volunteers are accurate
- the radiation risks are clearly explained to the volunteers.

Information required

Relevant sections of research proposals should be submitted to NRL at least 10 working days before the research proposal will be considered by an ethics committee. Relevant sections include:

- project title and contact details, including an email address and a contact fax number
- the name of a licensee (under the Act) who will take responsibility for the clinical direction of patient exposures to ionising radiation
- your dose/risk assessment for the radiation which is not needed for normal patient management. We require in your assessment an estimate of the 'effective dose' that an average patient would receive from this additional radiation. It must be specific to the facility and equipment being used and must include sufficient detail of its derivation for us to verify it
- a copy of the Patient Information Sheet that will be given to the volunteers. In particular, the section where you inform them of how much additional radiation they will be receiving and the associated explanation of the risk
- in the case that there will be multiple facilities around the country involved in delivering this additional radiation, then the facility specific information (questions 3 to 5) will need to be supplied for each of them.

There is no fee levied by NRL for ratification. Information should be sent to either:

Tony Cotterill, Team Leader, Regulatory
(Tony_Cotterill@nrl.moh.govt.nz); or

Glenn Stirling, Scientific Advisor
(Glenn_Stirling@nrl.moh.govt.nz)

Guidance on compiling a research proposal involving the exposure of volunteers to ionising radiation

The guidance given here conforms to the *International Commission on Radiological Protection's (ICRP) Publication 62* (ICRP 1993). This is the principal reference on the ethical and procedural aspects of participation of volunteers in biomedical research.

General principles

- The exposure of humans to ionising radiation at any level is considered to carry with it a risk of cancer induction and heritable effects (ICRP, 2007). For effects of a defined nature and severity such as skin erythema and cataracts there is a threshold-type dose-relationship. For these effects, below a certain level of dose to the vulnerable tissue, the probability of occurrence is essentially zero.
- The decision to expose volunteers to ionising radiation for research purposes must be clearly justified, ie, achieving greater good than harm. Considerations in the justification must include:
 - whether it would be possible to obtain similar information by using potentially less harmful means, eg, ultrasound or MRI
 - confirmation that individual volunteers are not being needlessly subject to multiple or repeat exposures
 - the weighing, where there is no obvious health benefit to a volunteer, of the potential benefit to society (by increase of knowledge) against the potential harm to the exposed individual.
- In therapy studies the selection of the radiation dose will be a compromise between delivering a dose sufficiently high to destroy a tumour while avoiding non-repairable damage to normal tissues. In all other investigations, the principle of keeping radiation doses as low as reasonably achievable must be applied, ie, ensuring the required information is obtained for the lowest 'effective dose'.¹
- Pregnant women must not be involved as volunteers in research projects involving irradiation of the fetus unless the pregnancy itself is central to the research. A volunteer of reproductive capacity should be offered a pregnancy test if there is any doubt that she might be pregnant.

Licensing under the Act

- The use of radioactive materials and/or irradiating apparatus in research projects involving radiotherapy, nuclear medicine and diagnostic radiology will require the involvement of an appropriately licensed radiation oncologist, nuclear medicine physician or a radiologist. Other projects will need the involvement of a person appropriately licensed to use radioactive materials and/or irradiating apparatus. Applications for licences should be made directly to NRL.
- Under the Act persons can use radioactive material and/or irradiating apparatus under the supervision or instructions of an appropriately licensed person.

¹ Effective dose is the radiation dose quantity most readily relatable to the overall risk of cancer induction or hereditary effects. The unit of effective dose is the Sievert (Sv).

Radiation risk assessments

- ‘Effective doses’ (except for therapeutic studies) and where necessary ‘equivalent doses’² should be calculated based on local equipment settings for all individual radiation exposures, eg, radiography views. Indicative effective doses from the literature or other sources can be used when there is confidence that the effective dose will be less than approximately 0.1 mSv, ie, representing a trivial level of risk (see Table 1). If necessary, reference should be made to a medical physics expert for advice.
- Table 1 taken from *ICRP Publication 62* should be used to band the level of risk to an individual or to a group of volunteers (using a representative person from the group) based on the summed effective doses from individual radiation exposures.

Table 1: Categories of risks and corresponding levels of benefit (ICRP, 1993)

Level of risk	Risk category (total risk)	Corresponding effective dose range (adults) (mSv)	Level of societal benefit
Trivial	Category I (~ 10 ⁻⁶ or less)	<0.1	Minor
Minor to intermediate	Category II IIa (~ 10 ⁻⁵) IIb (~ 10 ⁻⁴)	0.1–1 1–10	Intermediate to moderate
Moderate	Category III (~10 ⁻³ or more)	>10 ^a	Substantial

a To be kept below deterministic threshold except for therapeutic experiments.

Quantification of radiation risk

- The subject information sheet for volunteers must present a balanced and easily understandable description of the benefits and risks involved in the project. Relative radiation risk is best explained by comparing calculated ‘effective doses’ to the 2 mSv effective dose every person on average receives from natural background radiation every year.
- Care should be taken when deriving specific radiation risk values from calculated effective doses due to the substantial uncertainties involved. The recommendation given in *ICRP Publication 103* is that the nominal, overall fatal risk coefficient (age and sex averaged) of 5% per Sv (5.0 10⁻² Sv⁻¹) is appropriate for the purposes of radiological protection. The calculation of specific risk values for Category I exposures is inappropriate. For Category II and Category III exposures, any calculated risk should be represented as being indicative only.
- At younger ages (0-19 years) the probability of induction of cancer following exposure to ionising radiation is few times higher than the nominal value. Conversely, exposure at ages above 50 years the risk decreases reaching values of 0.2 to 0.1 of the nominal value at ages of 70–80 years.

² Equivalent dose is the most appropriate dose quantity when assessing the effects of radiation on an individual tissue. The unit of equivalent dose is the Sievert (Sv).

References

1. ICRP. 1993. Radiological Protection in Biomedical Research. ICRP Publication 62.
2. NRL. 1994. Use of unsealed radioactive materials in medical diagnosis, therapy, and research. NRL Code of Safe Practice C3.
3. NRL. 1994. Use of x-rays in medical diagnosis. NRL Code of Safe Practice C5.
4. ICRP. 2007. The 2007 recommendations of the International Commission on Radiological Protection. ICRP Publication 103.

Contact details

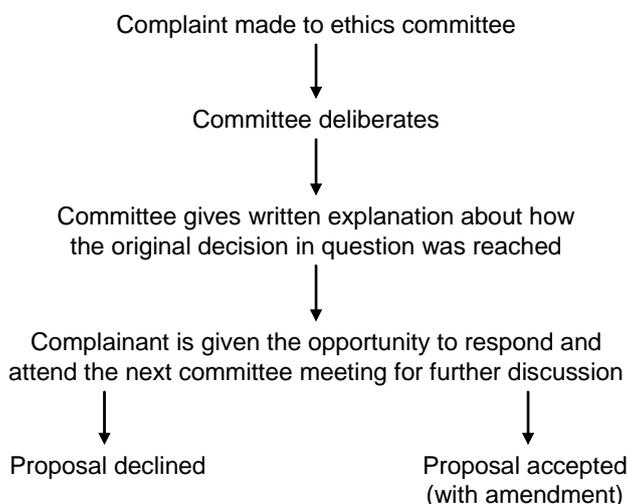
National Radiation Laboratory
108 Victoria Street
PO Box 25 099
Phone (03) 366 5059
Fax (03) 366 1156

Appendix 5: Complaints Procedure

Ethics committees should ensure that they have a written complaints process in place and that copies of the complaints procedure are available on request. Complainants should be kept informed about the progress of their complaints and should be informed in writing about the resolution of the complaint. All complaints should be recorded and included in the annual report of the ethics committee, which is sent each year to the Health Research Council Ethics Committee, the accrediting body and any other appropriate bodies. A copy of complaints received should be sent to the National Co-ordinator, Ethics Committees, Sector Policy Directorate, Ministry of Health, PO Box 5013, Wellington.

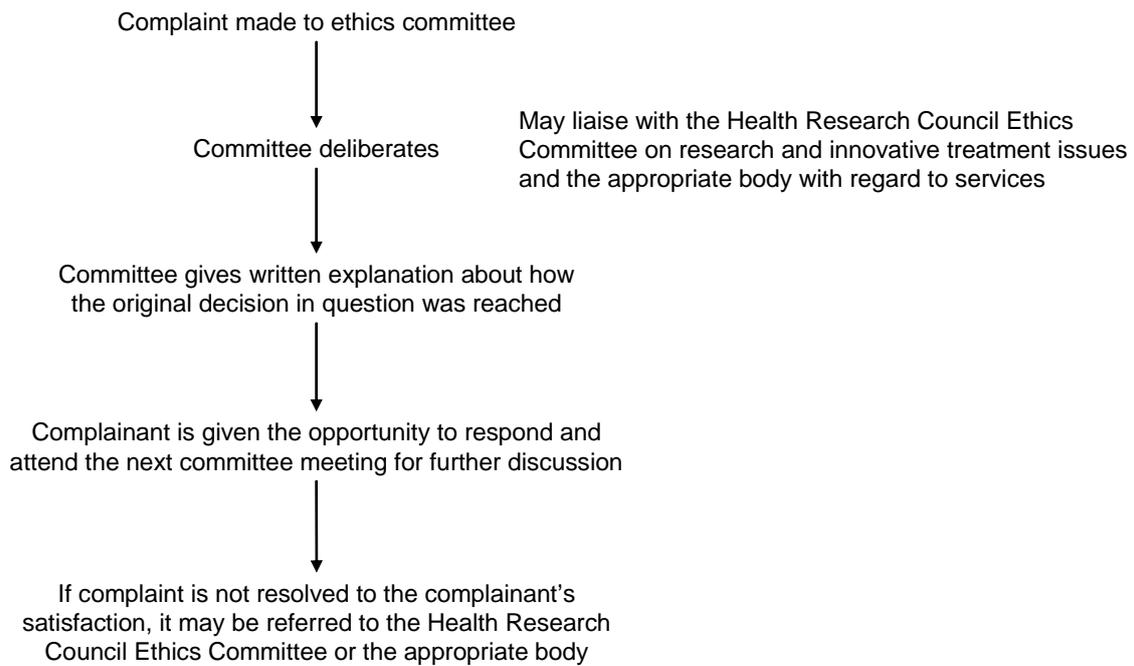
The complaints procedure should cover a range of situations. The following list should be regarded as the minimum required.

1. Complaint received from an applicant when a research proposal is declined



If the decision is still to decline the research proposal, researchers may seek a second opinion on research and innovative treatment proposals from the Health Research Council Ethics Committee and the appropriate body with regard to services.

2. Complaints received from individuals or providers other than the applicant about the decision-making process used by the committee in reaching a particular decision

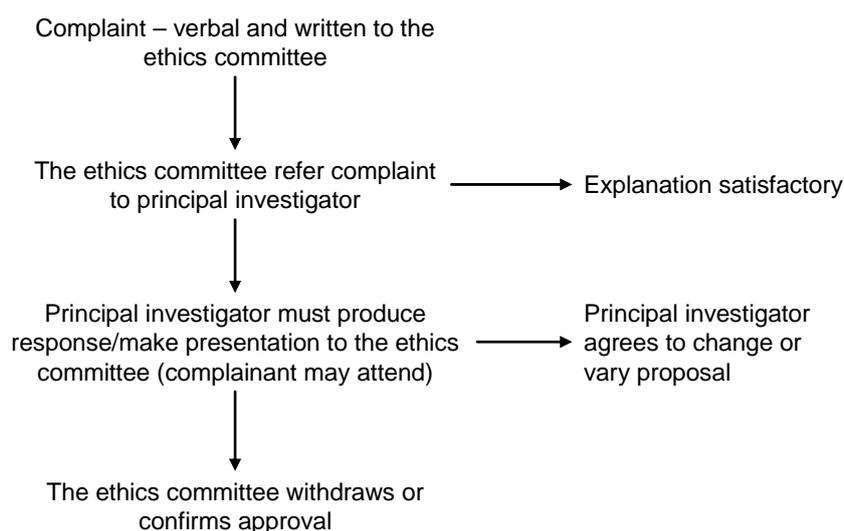


3. Complaint received from participants that research is not progressing according to terms agreed by the Ethics Committee

The ethics committee will send the complaint to the researcher and provide time for comment. The complaint must be in writing (an advocate working under the Health and Disability Commissioner Act 1994 may be contacted to assist in writing the complaint). It is possible for an ethics committee to warn the researcher and the provider that they no longer have protection from the legal redress that an ethics committee gives if a protocol has been altered without approval. The complainant will be kept informed.

Complainants have the option of either having the complaint dealt with by the ethics committee that gave the approval for the research, the Health Research Council Ethics Committee or the complaints procedure under Right 10 of the Code of the Health and Disability Services Consumers' Rights.

If the complaint is being dealt with by the ethics committee, that ethics committee can withdraw approval for research at any stage of the investigation. The process is as follows:



4. Complaints about the performance of Ethics Committee members

Such complaints may be received by the ethics committee itself or by the National Co-ordinator, Ethics Committees. In all instances, the Chair and members of the ethics committee will be informed of the issue and the matter will be resolved by the committee concerned, under the guidance of the Chair. The Chair is required to report to the National Co-ordinator, Ethics Committees on any complaints received about the process or behaviour, but the responsibility is entirely upon the ethics committee to follow up on the complaint to the point of resolution.