Human Research Ethics Handbook

Commentary on the National Statement on Ethical Conduct in Research Involving Humans
Human Research Ethics Handbook

Commentary on the National Statement on Ethical Conduct in Research Involving Humans

Endorsed 25 October 2001
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- fostering and supporting a high quality and internationally recognised research base;
- providing evidence based advice;
- applying research evidence to health issues thus translating research into better health practice and outcomes; and
- promoting informed debate on health and medical research, health ethics and related issues.

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PREFACE

THE DEVELOPMENT OF THE HUMAN RESEARCH HANDBOOK

In February 1998, the Australian Health Ethics Committee (AHEC) decided to seek tenders for the preparation of a manual for what were then known as institutional ethics committees. AHEC was then developing the National Statement on Ethical Conduct in Research Involving Humans and it was thought that such a manual would be a valuable aid in the use of the National Statement.

The tender was let to a consortium referred to in this document as the Editorial Committee. The Committee commissioned the writing of the drafts of the manual from the many contributors referred to as consultant authors. The members of the Editorial Committee and the consultant authors are acknowledged and listed on the following page.

That draft was then reviewed by members of AHEC in the 1997–1999 triennium. A limited process of consultation was undertaken with experienced institutional ethics committee members. As a result of responses from these processes, the material in the draft was re-ordered into the present layered structure of commentary, research ethics and research law collection. AHEC appointed A/Professor Colin Thomson, Deputy Chair of AHEC, to undertake the process of re-organisation of the material and to coordinate the ongoing development of the Handbook.

A one-day roundtable examination of this re-structured draft by a wide range of people representing ethics committees, researchers and lay people resulted in some further refinement, including editing and indexing. The final stage has involved professional editing, indexing and conversion to an electronic format. Further comments were then sought from AHEC members and some ethics committee members.

A deep debt of gratitude is owed to the Editorial Committee, consultant authors and commentators, who provided the substantive material for AHEC and NHMRC. In particular, AHEC wishes to acknowledge and warmly thank A/Professor Colin Thomson for the time and energy he dedicated to the skilled editing of the Handbook and for guiding all involved to the successful conclusion of this important project. AHEC has good reason to believe that the present volume will provide lasting assistance and guidance to human research ethics committees. That said, AHEC recognises, as did the original editorial committee, that the work is not complete. Experience will expose further matters on which advice and clarification is needed. In issuing the Handbook, AHEC accepts the responsibility of maintaining an active role in its continued revision, updating and development, and invites comments and suggestions for improvements and additions.

DISCLAIMER

This Handbook has been designed to provide recommendations only, for the assistance and guidance of Human Research Ethics Committee members, researchers and research participants. The Australian Health Ethics Committee does not warrant that the information contained in them is in every respect accurate or complete, and it is not responsible for any errors or omissions or the results obtained from the use of such information. Readers are encouraged to consider critically the information and suggestions contained in these parts of the Handbook and to make up their own minds in relation to the relevant issues and facts.
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INTRODUCTION

The primary purpose of the Human Research Ethics Handbook is to help Australian Human Research Ethics Committees (HRECs) assess and facilitate the ethical conduct of research involving human participants and resolve the challenges encountered during this process. The Handbook’s starting point is a widespread commitment to both the integrity of the ethics committee process and its importance in relation to research practice, and to making this process more effective.

The Handbook contains guidance for HRECs in their interpretation and application of the National Statement on Ethical Conduct in Research Involving Humans, thereby helping them maintain and improve the quality of their work. It provides information for researchers on substantive and procedural issues, and is a resource for potential research participants. It is open to the addition of new material and the development of new perspectives and viewpoints.

It should be understood that the Handbook is intended to provide information, and explanation. The National Statement remains as the primary and definitive source of ethical principles governing the conduct and review of research involving humans.

The Commentary on the National Statement, is designed to explain why a paragraph in the National Statement has been included, identify the ethical premises on which a paragraph is based, suggest how it might be implemented by an HREC or researcher, clarify a questioned interpretation or relate it to another paragraph(s).

The Research Ethics Collection, presents the issues confronting ethics committees and researchers within the context of discussions about specific topics and areas of research practice.

The Research Law Collection, presents concise and accessible accounts of legal issues in human research.

The Australian Health Ethics Committee (AHEC) believes that this approach is the one most likely to provide a text that is accessible, sensitive to the various contexts within which ethical issues arise in research practice, and flexible enough to allow continuous updating and revision as new developments occur in particular areas. AHEC believes that the topic-based approach also permits the experiences of researchers and ethics committee members to be drawn upon and provides a framework for ongoing feedback from the users of the Handbook.

The Handbook is designed to be used by individuals with widely differing personal, philosophical and ethical perspectives. To achieve this, AHEC has adopted the view that the diversity of opinions and outlooks in the community should be acknowledged and reflected. Accordingly, it has attempted to identify contentious and unresolved issues as well as those about which there is a significant degree of consensus. Consequently, contributions from a wide range of people have been brought together, including ethics committee members, community representatives, clinical researchers, social scientists, lawyers, ethicists and those active in other areas where specific issues might arise. As a result, the volume as a whole provides some concise accounts of relevant ethical issues, as well as practical guidance where difficult decisions need to be made.

The Handbook seeks to promote uniformity in ethics committee practices throughout Australia, while still allowing for variation in relation to local contexts. Although AHEC has been careful to avoid endorsing any particular ethical theory, some generalisations have been made where the Committee believes that these will be helpful in a practical setting.
Although is it is intended for use on a day-to-day basis, the Handbook should also provide a stimulus for continuing discussion and debate about the ethics of research practice in Australia. It should be seen as part of an ongoing process of development and change in research practice in Australia. It performs a number of functions, including summarising current practices, reflecting critically on current standards and providing practical guidance. Above all, however, it should be useful to ethics committee members, researchers, research participants, regulatory bodies and policy makers.

**A note on structure and relationships between parts of the Handbook**

The Commentary on the National Statement is arranged by reference to the National Statement, using its paragraphs as headings (and page numbers in relation to the Preamble of the National Statement) preceded by the initials ‘NS’. No commentary has been added to those paragraphs whose origins, ethical premises, implementation and interpretation are, at present, clear.

The Research Ethics Collection contains extended discussion of topics in research ethics, arranged alphabetically. Material in the Research Ethics Collection that is relevant to passages in the Commentary is identified and cross-referenced.

The Research Law Collection contains accounts of legal issues and is arranged in alphabetical order of topics. Material in this collection that is relevant to passages in the Commentary is identified and cross-referenced.

### ABBREVIATIONS

<table>
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AHEC</td>
<td>Australian Health Ethics Committee</td>
</tr>
<tr>
<td>ANCAHRD</td>
<td>Australian National Council on AIDS, Hepatitis C and Related Diseases</td>
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<tr>
<td>ARC</td>
<td>Australian Research Council</td>
</tr>
<tr>
<td>AVCC</td>
<td>Australian Vice-Chancellors’ Committee</td>
</tr>
<tr>
<td>CTTAC</td>
<td>Clinical Trials and Treatments Advisory Committee (of ANCAHRD)</td>
</tr>
<tr>
<td>CTN</td>
<td>Clinical Trial Notification Scheme</td>
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<tr>
<td>CTX</td>
<td>Clinical Trial Exemption Scheme</td>
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<tr>
<td>GTRAP</td>
<td>Gene and Related Therapies Research Advisory Panel</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome</td>
</tr>
<tr>
<td>HREC</td>
<td>Human Research Ethics Committee</td>
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<tr>
<td>IPPs</td>
<td>Information Privacy Principles</td>
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<tr>
<td>NHMRC</td>
<td>National Health and Medical Research Council</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised Control Trial</td>
</tr>
<tr>
<td>TGA</td>
<td>Therapeutic Goods Administration</td>
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PREAMBLE TO THE NATIONAL STATEMENT

The full text of the Preamble is an important component of the National Statement. It describes the purpose of the Statement and the historical context, both international and national, in which the Statement has emerged.

In the section headed ‘Statutory considerations’ on page 3 of the Statement, there is an explanation of how the Statement is designed to fulfil the statutory responsibility of the National Health and Medical Research Council as well as meeting wider goals.

The section headed ‘The meaning of ethics and research’ on page 3 is essential reading. It first outlines the scope of research ethics then explains how the term ‘research’ is to be understood in the Statement, thus indicating the scope of the responsibility of Human Research Ethics Committees (HRECs).

The Preamble comments on the dynamic context of research in Australia on page 8 and introduces categories of security for personal information on page 9.

GUIDANCE OR PRESCRIPTION?

The section headed ‘Structure and interpretation’ on page 10 explains, how the first part of the National Statement (NS 1.1–1.21) relates to the parts that follow.

In this part of the Preamble, it is stated that all research involving humans ‘must conform’ to the principles and values in that first part of the Statement. Earlier in the Preamble, the National Statement is described as providing ‘guidance for rather than prescription of ethically sound research design and practice’.

What is intended is that paragraphs 1.1–1.21 of the National Statement contain essential matters that HRECs are to consider in determining whether any research proposal is or is not ethically acceptable. It is this sense that the expression ‘must conform’ is intended to convey. The conclusion reached by any HREC will be the result of giving such consideration to these principles as well as other parts of the National Statement and other relevant guidance. It is in this sense that the National Statement is described as providing guidance and not prescription.
1. PRINCIPLES OF ETHICAL CONDUCT

The primary purpose of this Statement of ethical principles and associated guidelines for research involving humans is the protection of the welfare and rights of participants in research. The ethical and legal responsibilities which researchers have towards participants in research reflect basic ethical values of integrity, respect for persons, beneficence and justice. The responsibilities set out below accord with accepted moral and scientific principles set out in declarations, conventions and guidelines listed in Appendix 1. The principles in NS 1. Principles of Ethical Conduct are intended to apply to the interpretation and the use of all subsequent parts of this Statement.

The ethical principles and values contained in NS 1.1–1.21 are applicable to all research involving humans. They are not replaced or superseded by any of the more specific paragraphs in the National Statement. Recourse to these generally applicable principles and values will often assist the resolution of dilemmas in the use of more specific paragraphs.

INTEGRITY, RESPECT FOR PERSONS, BENEFICENCE AND JUSTICE

NS 1.1

The guiding value for researchers is integrity, which is expressed in a commitment to the search for knowledge, to recognised principles of research conduct and in the honest and ethical conduct of research and dissemination and communication of results.

The Joint NHMRC/AVCC Statement and Guidelines on Research Practice http://www.health.gov.au/hfs/nhmrc/research/general/nhmrcavc.htm provides a concise summary of one of the essential elements of the basic ethical value of integrity, namely the standards for sound scientific research practice. In other respects, this paragraph refers to a value or a set of virtues of researchers with integrity. (See also the Research Ethics Collection, 'Ethical theory', page 41).

In relation to each proposal presented to it, a Human Research Ethics Committee (HREC) should be satisfied that the researcher(s) responsible will conduct the research with integrity.

NS 1.2

When conducting research involving humans, the guiding ethical principle for researchers is respect for persons which is expressed as regard for the welfare, rights, beliefs, perceptions, customs and cultural heritage, both individual and collective, of persons involved in research.
The purpose of this principle is to ensure that research participants are treated in ways that respect their dignity as persons. See also the Research Ethics Collection.

**Points to consider**

- Does the research respect the inherent dignity of all the participants?
- Are the welfare, rights, beliefs, perceptions, customs and cultural heritage of all participants respected in the research design?
- Where the research involves a collectivity or collectivities as participants, how are those components respected at the level of the collectivity?
- Does the research involve participants who are competent to decide for themselves?
- Does the research involve participants whose capacity for making informed choices is impaired or who otherwise have diminished autonomy?
- How is the research designed to respect participants capable of making informed choices and also those with diminished autonomy?

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**NS 1.3**

*In research involving humans, the ethical principle of beneficence is expressed in researchers’ responsibility to minimise risks of harm or discomfort to participants in research projects.*

As with respect for persons, beneficence embraces a range of related ideas. It includes avoiding harm to others as well as promoting their wellbeing. Within the context of research ethics, this is also often thought to include the idea of benefits to society as a whole flowing from the results of the research enterprise. However, the National Statement focuses on minimising the risks of harm and discomfort to research participants. Therefore, for Australian HRECs, beneficent concern is directed at the effects on individuals and communities of participation in, or exclusion from, research projects. This means that priority should be given to protecting research participants from harm. (See the Research Ethics Collection, ‘Beneficence’, page E3.)

**Points to consider**

- What risks of harm arise in the proposed research?
- What is the magnitude of each of these risks?
- What is the probability of each of these risks?
- Has the researcher minimised these risks, either in the design or conduct of the research, to a satisfactory extent?
- Have all reasonable efforts been made to minimise each aspect of the risks involved in the research project?

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**NS 1.4**

*Each research protocol must be designed to ensure that respect for the dignity and wellbeing of the participants takes precedence over the expected benefits to knowledge.*
This principle of respect for the dignity and welfare of research participants entails the rejection of research practices that sacrifice the welfare and lives of humans in the pursuit of knowledge. Research that involves deception is a clear example of research that infringes this principle, because generally it fails to respect the dignity of the participants involved.

The principle requires researchers and HRECs to give primary consideration to the effects of their participation on the dignity and welfare of participants. The expression ‘dignity and welfare’ has a wide meaning in order to include every aspect of participation.

The principle focuses on the dignity and welfare of people as participants. Respect for their dignity and welfare can be given precedence even in research that holds no promise of benefit to participants.

**Points to consider**

- Have the risks and benefits of the research proposal been identified and fully evaluated? Do the potential benefits justify any risks?
- Does the research project involve an unacceptably high degree of risk to participants in the light of the expected benefits of the research?
- Have participants been adequately advised of the risks and benefits involved in the project?
- Where the major potential benefit from the project will accrue to certain members of society in the future, rather than to the individuals actually taking part in the study, has this been made clear to potential research participants?
- Where a research project involves people capable of making an independent and considered decision about participation, to what extent may analysis of risks and benefits by an HREC be overly protective of participants?
- Where a research project involves vulnerable people as potential research participants, or those unable to make independent and considered decisions, have sufficient measures been included in the research proposal to protect these people from harm?
- Are there provisions in the research proposal for continuing review and monitoring of data regarding efficacy and safety of the ongoing research process?

**NS 1.5**

The ethical value of justice requires that, within a population, there is a fair distribution of the benefits and burdens of participation in research and, for any research participant, a balance of burdens and benefits. Accordingly, a researcher must:

(a) avoid imposing on particular groups, who are likely to be subject to over researching, an unfair burden of participation in research;

(b) design research so that the selection, recruitment, exclusion and inclusion of research participants is fair; and

(c) not discriminate in the selection and recruitment of actual and future participants by including or excluding them on the grounds of race, age, sex, disability or religious or spiritual beliefs except where the exclusion or inclusion of particular groups is essential to the purpose of the research.
Justice can be understood variously to include fair treatment, equitable distribution of benefits and burdens within a society, or equal recognition and equal access to participation in society. Within the context of research practice, justice is generally understood to involve an obligation to share the benefits or burdens of research fairly throughout society. Justice as fairness (in which equality or restoration from unlucky burden is the primary concern), comparative justice (in which need is the primary distinction), and distributive justice, (in which need and socially distinguishing factors can be combined) can all be applied in assessing research proposals.

HRECs should scrutinise the proposed means of recruiting research participants in order to ensure that all groups within society are treated fairly with regard to participation in research. This involves protecting certain groups from unfairly bearing the burdens of research, while at the same time protecting other groups from unfair exclusion from the research process and, therefore, from the potential future benefits of that research.

**Points to consider**

- What is the justification for selecting certain people for recruitment and excluding others?
- Are these justifications based on the design of the research?
- Are potentially vulnerable people to be approached for recruitment? Why? How are these potential participants to be protected against exploitation?
- Is the recruitment process conducted in such a way that the privacy of potential participants is respected, and their right to refuse to participate acknowledged?
- Do recruitment methods, such as advertising, ensure that potential participants are given a clear account of the purpose of the researcher’s approach?
- Are the participants representative of the population intended to benefit from the research?

**NS 1.6**

The proportion of burdens to benefits for any research participant will vary. In clinical research, where patient care is combined with an intent to contribute to knowledge, the risks of participation must be balanced by the possibility of intended benefits for the participants. In other research involving humans that is undertaken solely to contribute to knowledge, the absence of intended benefits to a participant should justly be balanced by the absence of all but minimal risk.

It is essential that a careful assessment is made of both burdens and benefits. Burdens of research include not only its risks but also the inconveniences or disruptions to participants’ lives that may be caused by their participation. In order to determine whether the burdens of participation are justified, it is ethically acceptable to balance these burdens by the benefits for participants. Where there are no intended benefits to participants, it is unethical to accept anything more than a minimal level of burden to participants.
Points to consider

- Have the risks of the research proposal been identified and fully evaluated? Do the potential benefits for participants justify any risks?

- Have participants been adequately advised of the risks and benefits involved in the project?

- Where a research project involves vulnerable people as potential research participants (that is, those unable to make independent and considered decisions), have sufficient measures been included in the research proposal to protect these people from harm?

- Are there provisions in the research proposal for continuing review and monitoring of data regarding efficacy and safety of the ongoing research process?

- In research involving significantly more than minimal risk, is the consent process comprehensive and clear?

CONSENT

NS 1.7

Before research is undertaken, whether involving individuals or collectivities, the consent of the participants must be obtained, except in specific circumstances defined elsewhere in this Statement (see paragraphs 1.11, 6.9, 14.4, 15.8, 16.13).

The ethical and legal requirements of consent have two aspects: the provision of information and the capacity to make a voluntary choice. So as to conform with ethical and legal requirements, obtaining consent should involve:

(a) provision to participants, at their level of comprehension, of information about the purpose, methods, demands, risks, inconveniences, discomforts, and possible outcomes of the research (including the likelihood and form of publication of research results); and

(b) the exercise of a voluntary choice to participate.

Where a participant lacks competence to consent, a person with lawful authority to decide for that participant must be provided with that information and exercise that choice.

The importance of informed decision-making

This paragraph identifies three essential components of an effective consent, namely, that it be based on information, that it be voluntary and that it be made by a person competent to make that choice.

Information

The paragraph identifies the type of information that needs to be provided to participants and then reminds researchers that the manner and form of provision of the information needs to be carefully considered.
Voluntariness

In general terms, it may be acceptable to use people as a ‘means’ to gaining knowledge for the future if these people are also treated as ‘ends in themselves’, in particular, they are able to make a free and informed decision to participate. If individuals are free to do so, and if they understand the aims of the research, the risks, burdens and potential future benefits, then inviting them to participate will generally not constitute exploitation by the researcher. (See the Research Ethics Collection, ‘Consent’, page E29; see also the Research Law Collection, page L7, for a discussion of the legal aspects of consent.)

Competence

People are competent to give consent if they are adults or ‘mature minors’ and are able to understand what the procedure involves and to consent to it. Clearly, competence may be difficult to assess in certain situations. (See Research Law Collection page L13, for further discussion of this issue.)

Complexity and legality

Informed consent is an unavoidably complex ethical issue. Questions may be raised about what constitutes sufficiently informed consent; whether research participants are sufficiently able to appreciate the significance of risks, ‘randomisation’, and other scientific concepts; whether decisions to participate in research are ever ‘free’; and whether fully informed consent is always necessary.

Points to consider

- Do the recruitment and decision-making processes included in the research proposal ensure adequate protection of the freedom of participants to decide whether or not to participate in the project?
- Do the recruitment processes included in the research proposal provide for a disclosure of the types of information listed in this paragraph?
- Do the recruitment processes included in the research proposal provide for a manner and form for disclosure of that information appropriate to the research participants?
- Are all participants likely to be competent to decide whether or not to participate? If not, how is this addressed in the research proposal?
- If the researcher plans not to seek consent from potential research participants, is this justified?

NS 1.8

A person may refuse to participate in a research project and need give no reasons nor justification for that decision.

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Informed agreement to participate is one possible result of the informed choice process, an informed decision not to do so is the other possible result. An individual's choice not to participate in research should be respected, whether the individual has reasons or not. HRECs need to be satisfied that the freedom to decide not to participate is clearly presented.

**NS 1.9**

*Where consent to participate is required, research must be so designed that each participant's consent is clearly established, whether by a signed form, return of a survey, recorded agreement for interview or other sufficient means.*

There are some contexts where written evidence of a person's consent to participate may not be necessary, or may pose a more significant threat to participants than the protection that written evidence of consent is meant to provide. For example, in research involving anonymous surveys into illegal or socially stigmatised activities, requiring written evidence of consent may identify participants and so put them at risk of social harm or legal prosecution. Although consent is still required in these situations, the completion of consent forms that identify participants is likely to be inappropriate. Such situations require the researcher and the HREC to identify clearly the process of consent that will be followed and how the fact of that consent will be evidenced.

**Points to consider**

- Is written evidence of consent to be sought from participants? If not, why not?
- Are there special features of the context that make written consent inappropriate?
- Is the process by which participants can consent to participate clearly described?
- How will the fact of consent be evidenced?

**NS 1.10**

*The consent of a person to participate in research must not be subject to any coercion, or to any inducement or influence which could impair its voluntary character.*

HRECs need to assess whether there are any inducements offered to potential participants that would limit the voluntariness of their choice to participate or to refuse to do so. Any payment to participants should not be so great as to constitute an inducement to take part in the project. Inducements may invalidate consent by making it more difficult for participants to assess the risks and benefits of research, encouraging them to expose themselves to risk of harm. See the Research Ethics Collection, 'Consent', page E29.

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Points to consider

- Have participants been subject to any type of coercion, whether actual or perceived?
- Is there potential for misuse of participants’ trust, for example in their physician if she or he is inviting them to participate in research?
- Does the recruitment or selection process incorporate payments or rewards of any sort? If so:
  - What is the type and level of payment or reward?
  - Are they necessary? If so, why?
- Is there a risk that inducements may cause potential participants, or researchers, to overlook possible harms involved in the research project?
- Does the recruitment process protect people from being coerced or unduly influenced to participate?

NS 1.11

It is ethically acceptable to conduct certain types of research without obtaining consent from participants in some circumstances, for example, the use of de-identified data in epidemiological research, observational research in public places, or the use of anonymous surveys. (See 14. ‘Epidemiological research’ and 17. ‘Research involving deception of participants, concealment or covert operation’.)

Some research may be justifiable even though consent, or written consent, is not sought from participants. However, the risks of participation should be minimal and the research process should not involve any intrusion into the participant’s daily activities.

This paragraph recognises such limited exceptions to the requirement for participant consent. It does not exempt that research from ethical review, which, in appropriate circumstances may be suitable for expedited review, for which see N.S. 2.27–2.29.

NS 1.12

A participant must be free at any time to withdraw consent to further involvement in the research. If any consequences may arise from such withdrawal, advice must be given to participants about these before consent to involvement in the research is obtained.

HRECs need to be satisfied that, at the time participants are asked to consent to participate, they are fully informed of the consequences of exercising their right to withdraw from the research, including withdrawal of information or material.

Points to consider

- Will research participants be able to have their samples or data withdrawn from the research project if they wish to do so?
• Has this been made clear in information documentation and consent forms?
• Does the research design place any restriction on retrieval of data or samples? If so, is this restriction made clear to potential participants? Is it in written form?
• If there are any restrictions on withdrawal of samples or data, does the HREC consider this to be justifiable?

RESEARCH MERIT AND SAFETY

NS 1.13

Every research proposal must demonstrate that the research is justifiable in terms of its potential contribution to knowledge and is based on a thorough study of current literature as well as prior observation, approved previous studies, and where relevant, laboratory and animal studies.

All research involving humans needs to have both value and validity. That is, the research must demonstrate that, because of prior research, it is justifiable to seek the information to which the research is directed. Second, the research needs to be so designed that it is likely to lead to the discovery of new knowledge. HRECs need to be satisfied that these conditions are met, and may need to draw on expertise outside their membership for advice. (See NS 2.19.)

Points to consider

• Is there a clear hypothesis?
• Is the research likely to yield new knowledge, enhance understanding or clarify existing uncertainty?
• Has this, or similar, research been carried out before in the same, or similar, contexts?
• Could a systematic review of the literature demonstrate the importance of the research question?
• Do the researchers have the necessary expertise to analyse and interpret the results of the research project?
• Has a statistician been involved in the preparation of the research proposal? If not, should a statistician be consulted?
• Has the research project been designed to account for, or avoid, biases in participant selection, data collection, data analysis and data interpretation?

NS 1.14

All research proposals must be so designed as to ensure that any risks of discomfort or harm to participants are balanced by the likely benefit to be gained.

The ethical difficulty with analysing risks and benefits in relation to research practice is that the risks are not often borne by the people for whom the possible benefits will accrue. Given this, potential benefits are unlikely to outweigh the risks for individual research participants. However, researchers and HRECs need to be satisfied that such risks as participants are exposed to are justified by the benefits expected from the research. To reach this decision, HRECs must carefully assess and quantify the magnitude and probability of the risks to participants and the expected benefits to participants and to others.

Points to consider

- Have the risks to participants and the benefits to participants and others been clearly identified and quantified?
- Where the major potential benefit from the project will accrue to certain members of society in the future, rather than to the individuals actually taking part in the study, has this been made clear to potential research participants?
- Where a research project involves vulnerable people as potential research participants, or those unable to make independent and considered decisions, have sufficient measures been included in the research proposal to protect these people from harm?

NS 1.15

Research must be conducted or supervised only by persons or teams with experience, qualifications and competence appropriate to the research. Research must only be conducted using facilities appropriate for the research and where there are appropriate skills and resources for dealing with any contingencies that may affect participants.

Researchers and HRECs should assess the relevant experience, qualifications and competence of researchers to conduct the proposed research. This should involve identifying who, among teams of researchers, will conduct each phase of the research process, including recruitment of participants. Facilities need to be appropriate for the scientific needs of the research. The HREC will need to be satisfied that appropriate facilities are available in the institution(s) in which the research is to be conducted. These will need to include facilities to meet any physical, emotional or other needs of participants that result from their participation.

Points to consider

- Does the research protocol make clear who will conduct each phase of the research?
- Is there satisfactory evidence of the experience, qualifications and competence of each of the researchers?
• Are there appropriate facilities for the conduct of the research?
• Are there appropriate facilities for the needs of participants?

ETHICAL REVIEW AND CONDUCT OF RESEARCH

NS 1.16
Research projects involving humans must be reviewed by a Human Research Ethics Committee (HREC) and must not be undertaken or funded unless and until approval has been granted.

Ethical approval should be gained prior to research being funded or undertaken. Institutions need to ensure that their research approval processes make this clear to researchers and provide clear unequivocal evidence of approval. Where conditions are required to be met before commencement, procedures should provide clear evidence that they have been met.

NS 1.17
A researcher must suspend or modify any research in which the risks to participants are found to be disproportionate to the benefits and stop any involvement of any participant if continuation of the research may be harmful to that person.

HRECs should be satisfied that researchers are aware of an obligation to suspend or modify research and, by NS 2.37, will require notification of such situations. There are two situations in which research is to be modified or suspended: first, where risks to participants are disproportionate to benefits (of research) and, second, where a participant may suffer harm.

NS 1.18
The results of research (whether publicly or privately funded) and the methods used should normally be published in ways which permit scrutiny and contribute to public knowledge. Normally, research results should be made available to research participants.

There is limited social, ethical or scientific value in carrying out research if the results are not published or otherwise disseminated, since the research thereby fails to contribute to the advancement of knowledge, research practice or policy.6 Publication of research results may also serve to minimise misconduct by researchers, such as plagiarism and scientific fraud.7

HRECs should be satisfied that researchers have considered appropriate ways in which research findings can be disseminated.

In the past, publication in professional journals was considered adequate dissemination of research results. However, there is an increasing expectation from research bodies, research participants and consumer groups that participants be informed of the results of research they have participated in, or that may have implications for their ongoing wellbeing. Nevertheless, the communication of research results raises some difficult ethical issues. These are discussed in the Research Ethics Collection—see under ‘Research, communication of results’, page E141.

Points to consider

- Will participants be advised of research results? If not, why not?
- Have the researchers declared their intention to submit the results of their research for publication or other means of dissemination? If not, why not?
- Is the planned method of feedback of information to participants appropriate to the type of research being undertaken?
- Is the HREC satisfied that the researcher has considered the importance of peer review of research findings prior to public release?
- Is the HREC satisfied that the researcher has justified any limitations imposed by ‘commercial-in-confidence’ considerations?

NS 1.19

Where personal information about research participants or a collectivity is collected, stored, accessed, used, or disposed of, a researcher must strive to ensure that the privacy, confidentiality and cultural sensitivities of the participants and/or the collectivity are respected. Any specific agreements made with the participants or the collectivity are to be fulfilled.

HRECs need to assess carefully the processes of collection, storage, access to and use of personal information, and determine whether those processes will in fact achieve the degree of protection that is promised to participants.

Mere assurances in participant information sheets that information will be kept confidential should not be accepted as adequate unless the research design will achieve that result.

For further discussion of legal aspects of confidentiality and privacy, consult the Research Law Collection under ‘Confidentiality’ page L7 and ‘Privacy’ page L43.

NS 1.20

Where the records and results of research contain information of clinical significance it is the responsibility of both the researcher and the institution or organisation to maintain the security and storage of records and results so as to enable any necessary follow-up studies to be carried out.

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The obligations of researchers and institutions are directed to the minimisation of risks of harm to participants.

HRECs need to assess whether such information is likely to be generated from the research and be satisfied that arrangements are in place to secure that availability.

Separate consent for any follow-up studies should normally be obtained.

**NS 1.21**

Where research is conducted in an overseas country under the aegis of an Australian institution or organisation, the research must comply with the requirements of this Statement as well as the laws and guidelines of that country.

This paragraph is intended to establish, as a minimum standard for ethical conduct of research involving humans undertaken by an Australian institution, the requirements of the National Statement. Those standards and none lower are to apply to such research wherever conducted. Compliance with the laws and guidelines relevant to the conduct of research of the country in which the research is conducted is also required but in addition to those of the National Statement.

For a further discussion related to this paragraph, see the Research Ethics Collection under ‘International research’, page E105.
2. HUMAN RESEARCH ETHICS COMMITTEES

Research proposals involving human participants must be reviewed and approved by a Human Research Ethics Committee (HREC) which is established by and advises an institution or organisation regarding ethical approval for research projects. Requirements are set out for:

- institutions or organisations in establishing HRECs;
- researchers in submitting research proposals to HRECs; and
- HRECs in considering and reaching decisions regarding those proposals and in monitoring the conduct of approved research.

NS 2.1

Institutions and organisations in which research involving humans is undertaken must individually or jointly establish, adequately resource, and maintain an HREC composed and functioning in accordance with this Statement.

Institutions or organisations are required to set up Human Research Ethics Committees (HRECs). (For useful discussions of the Australian system of research ethics review, see the Research Law Collection under ‘Research, regulation of’, page L45).

Where two or more institutions agree, one HREC may be used to review research conducted in each institution. HRECs need sufficient resources in staffing and equipment to complete all the tasks involved in reviewing research proposals and monitoring the conduct of approved research. Institutions need to have processes for appointing members of HRECs and establishing that the HREC is functioning in accordance with the National Statement.

An institution or organisation whose review of research fails to comply with the National Statement may be deemed ineligible to retain or receive funds for research from the National Health and Medical Research Council or the Australian Research Council. This consequence would require a decision by one of these two bodies.

NS 2.2

The institution or organisation must, when establishing an HREC, set out its terms of reference including the scope of its responsibilities, relationship to non-affiliated researchers, accountability, mechanisms of reporting, and remuneration, if any, for members.

Terms of Reference

Terms of Reference should be clear, concise and accessible to committee members, researchers and non-members. They may include any of the following:
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- purpose of the HREC;
- responsibilities within the institution or organisation, including legal responsibilities;
- relationship to the organisation, as well as other parts of the organisation;
- sub-committees and other HRECs within the institution;
- scope of responsibility, including definition of research to be reviewed and relationships (if any) to non-affiliated researchers;
- reporting to the institution (management, board and council);
- composition of the committee;
- minimal categories of membership;
- appointment of members and terms of appointment;
- reimbursement and payment, if any, to members;
- induction and support of new members;
- education and training;
- procedures for:
  - meetings
  - recording decisions
  - rules of functioning
  - expedited review
  - researchers and HREC applications
  - monitoring ongoing research
  - complaints
  - investigations
  - appeals
  - hearings

See also NS 2.13

- suspension or discontinuation of research; and
- providing compliance reports to the Australian Health Ethics Committee.

Individual institutions may decide to include additional items.

**Institutions and organisations may appoint more than one HREC**

In some situations an institution or organisation may form more than one HREC. This may be appropriate in large organisations, such as some universities and hospitals, where the volume of research proposals reviewed is extremely high and proposals originate from many different disciplines. In this arrangement, each HREC formed must be composed according to NS 2.6. Institutions need to clarify responsibilities of each such committee.

For a discussion of legal aspects of the formation and operation of HRECs, see the Research Law Collection under 'Human Research Ethics Committees' on page L33.
HREC's with small workloads

The Report of the Review of the Role and Functioning of Institutional Ethics Committees (March 1996) suggests that where committees meet infrequently or review few proposals, concerns arise about the 'time spent serving on committees', as well as about maintaining the 'breadth and depth of experience needed by committee members to maintain an adequate level of review.' The report therefore invites committees with small workloads, such as those reviewing fewer than 50 research proposals a year, to 'consider the possibility of amalgamation' with another committee.9

However, the report also acknowledges that there may be good reason for maintaining a committee even though the number of research projects reviewed is small. This would be appropriate if the research reviewed was of such a specialised nature that the necessary expertise would be difficult to replicate on a committee dealing with a wider range of proposals.

NS 2.3

The institution or organisation (individually or jointly) must accept legal responsibility for decisions and advice received from the HREC and indemnify its members.

Whether an HREC operates in an advisory capacity only or has other authority, the institution or organisation is responsible for its advice or decisions.

Individual members of HREC's have legal as well as ethical responsibilities in relation to the protection of the interests of research participants. Therefore, they could be sued by, for example, an injured participant or an aggrieved researcher.10 Thus, institutions must indemnify each member of its HREC for liability for acts done in accordance with its terms of appointment.11

NS 2.4

Researchers without affiliation to an institution or organisation with an HREC must ensure that the project is approved by an established HREC. There should be an agreement between the institution or organisation and researchers that defines the approval, conduct and monitoring of research, and who carries legal responsibility for it.

All research involving humans conducted in Australia should be reviewed by a properly constituted HREC. When an institution or organisation decides to permit their HREC to consider and approve research with which it has no connection, there must be an appropriate formal agreement between the parties.

NS 2.5

The primary role of an HREC is to protect the welfare and the rights of participants in research and the primary responsibility of each member is to decide, independently, whether, in his or her opinion, the conduct of each research proposal submitted to the HREC will so protect participants.

Members of HRECs are not appointed to represent any interest in the research process—that is, that of a researcher, other research interests or participants. Each member of the HREC has the same responsibility, in reaching a decision whether or not to approve a research proposal, to protect the welfare and rights of the research participants. The decision-making process can involve the assessment of competing considerations of the value of research and the risks to participants, but should not be seen as adversarial.12

Each committee member is expected to reach a decision independently, that is, according to their judgment of all the material available, including the opinions of other HREC members and expert advice. A decision is independent in the sense that it is the committee member’s decision and not that of any other person or entity.

Further discussion in this area can be found in the Research Ethics Collection under ‘Human Research Ethics Committees: Approval of Research’, page E84.

COMPOSITION

NS 2.6

The minimum membership of an HREC is seven members, being men and women, comprising:

(a) a chairperson;

(b) at least two members who are lay people, one man and one woman, who have no affiliation with the institution or organisation, are not currently involved in medical, scientific, or legal work, and who are preferably from the community in which the institution or organisation is located;

(c) at least one member with knowledge of, and current experience in, the areas of research that are regularly considered by the HREC (eg. health, medical, social, psychological, epidemiological, as appropriate);

(d) at least one member with knowledge of, and current experience in, the professional care, counselling or treatment of people (eg. medical practitioner, clinical psychologist, social worker, nurse, as appropriate);

(e) at least one member who is a minister of religion, or a person who performs a similar role in a community such as an Aboriginal elder; and

(f) at least one member who is a lawyer.

Chairperson
The chairperson should be chosen for her or his ability to draw on the experience of all members, including lay members and those with specialist expertise, and to demonstrate respect for each member’s view. The chairperson also has responsibility for managing the agenda and making sure that all relevant items are covered and adequately recorded.

Further guidance to the chairperson’s role in relation to committee meetings can be found in other paragraphs of the National Statement. That role is likely to include:

- considering whether the committee is sufficiently informed on all aspects of research protocols (2.8);
- overseeing arrangements for meetings (2.15);
- being satisfied that all views of absent minimum members have been received and considered (2.16);
- presiding over decision-making (2.17);
- inviting researchers to attend meetings (2.18);
- seeking advice from experts (2.19);
- monitoring conflicts of interest (2.19, 2.20);
- overseeing recording of decisions (2.14, 2.30); and
- establishing a complaints process (2.40)

The chairperson is likely to be called upon to perform duties beyond those related to HREC meetings. These could include overseeing procedures, monitoring approved research and receiving reports, and being involved in expedited review.

The Chairperson is likely to be called on to communicate with other HRECs in multi-centre research approval arrangements (3.4, 3.5), and to be required to represent the HREC within the institution and in discussions with researchers and other HRECs.

Lay members
The qualifications for lay members are their independence from the institution and their non-involvement in medical, scientific or legal work. Those recruited from the community in which the institution is located are more likely to understand that community and how its members would view involvement in research. And those who have no experience in professions associated with research on human beings are more likely to bring a truly lay perspective.

Person with knowledge of, and current experience in, areas of research regularly considered by the committee
There may need to be more than one member in this category. For instance, where a university HREC regularly considers educational, psychological, medical and sociological research, the HREC will need the opinions of members with relevant knowledge and experience in each field.¹³

Person with knowledge of, and current experience in, the professional care of people

This category of member is included because such a person has contact with potential or typical participants in research and has insights into the possible impact of research on such people.

Minister of religion

The rationale for including a minister of religion is that this person ‘holds the importance of humanity and human life above all else’.14 Through the experience of pastoral care and mixing widely throughout the community, a minister of religion is usually in a position to understand the views of many people.15

A person who is a lawyer

This member should have professional qualifications but need not be currently in legal practice. The role of the lawyer on an ethics committee is to ‘advise the committee on legal implications of research considered or decisions taken and whether formal legal advice is necessary’; the attributes required are ‘good judgment and experience in dealing with people’, as well as competence in ‘critical thinking and experience in the clarification of issues’.16

Further discussion of the membership categories can be found in the Research Ethics Collection under ‘Human Research Ethics Committees: Membership: Minimum requirements’, page E71, and ‘Appointment’ page E73.

**NS 2.7**

The institution or organisation must ensure that the membership will equip the HREC to address all relevant considerations arising from the categories of research likely to be submitted to the HREC. For example, an experienced medical practitioner should be included if the HREC considers research protocols which involve any physically invasive procedures or medical interventions, (eg. surgical, pharmacological, physiological, technological, or nutritional intervention).

This paragraph adds detail to the basic institutional responsibility set out in NS 2.1. Where additional members are needed, NS 2.9 is relevant.

**NS 2.8**

An HREC must ensure that it is sufficiently informed on all aspects of a research protocol, including its scientific and statistical validity, that are relevant to deciding whether the protocol is both acceptable on ethical grounds and conforms with this Statement. This may necessitate appointment of additional members with specific expertise.

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14 ibid.
HRECs need to be satisfied that the research design can produce valid results and can protect the welfare and rights of research participants. To be satisfied, an HREC may seek or receive advice from an individual, a scientific committee in its institution, an external expert, or it may include an additional person who has specific expertise in the particular type of research. For more information on research design, see the Research Ethics Collection, ‘Research, design and purpose’ page E143.

It is not possible to provide a comprehensive list of relevant considerations for every research approval. However, the following matters will usually require consideration:

The project

- Is there a clear hypothesis?
- Is the research question useful? Is the research worthwhile?
- Is the research likely to yield new information, enhance understanding or clarify existing uncertainty?
- Has this, or similar, research been carried out before in the same, or similar, contexts?
- Can the research proposal be supported by a systematic review of the literature that would demonstrate the importance of the research question and that it builds upon the results of previous research?
- If indicated, have perspectives of potential participant groups, the wider community, or other disciplines been incorporated into the research proposal?
- Are the aims of the proposal clear?
- Does the value of the project appear to be adequate to justify its conduct with humans?

The researchers

- Do the researchers have necessary qualifications, competence and experience?
- Are there adequate arrangements to ensure that members of the research team are aware of relevant ethical and legal obligations?

The funding

- What is the relationship between the source of funding and the aims of the project?
- Does that relationship have any implications for the ethical conduct of the project, especially the recruitment of participants, the character of information sought or the freedom to publish the results?

Other HREC approval

- Where applicable, are the reasons given by another HREC, either for approval or the imposition of conditions, consistent with the HREC's own opinion?

Research methodology

- Are all aspects of the research methodology clearly described?
- Is the HREC satisfied that the methodology is appropriate to the achievement of the aims of the project?

Recruitment of participants

- Is it clear how participants will be recruited?
- Do the recruitment methods respect participants’ rights to the confidentiality of their affairs?
- Are the proposed participants appropriate in number and kind?
Burdens of research

- Are the burdens and risks of research to participants clearly identified and have appropriate measures been taken to minimise these?
- Is the balance between the burdens and risks to participants and the aims and benefits of the project such as to warrant approval?

Incentives for participation

- Are financial or other rewards proposed to be given to participants?
- Are these of such a size or value that they may unduly influence the freedom of participants to withdraw or otherwise protect themselves from risks?

Consent

- Are the ways in which participants will be approached clearly described?
- Is the information to be provided to potential participants adequate in content and appropriate in form?
- Do the proposed methods of securing consent to participate provide a) sufficient time to consider the decision; b) evidence that participants understood their choices, and c) sufficient opportunities to ask questions and re-consider?

Discontinuing participation

- Are the ways in which participants are advised of their freedom to withdraw sufficient in content and frequency?

Information protection

- Is it clear who will (and who will not) have access to information collected during the project?
- Are the proposed storage and security measures adequate?
- Are participants clearly informed that information they provide will be used only for the project?
- What measures are proposed to protect the confidentiality of information in the course of the project and are these adequate to give the degree of protection promised to participants?
- Are the manner and form in which results will be published clearly described, and do they adequately protect the confidentiality of information and privacy of participants?

Legal issues

- Does the project involve subject matter or conduct which may give rise to legal vulnerability of participants or researchers? Are adequate precautions to be taken?

In addition to these recurrent issues, some research requires particular additional attention, either because of the vulnerability of the intended participants or the type of research. Research with vulnerable participants that needs additional consideration includes:

- research involving children (see NS 4.1–4.4);
- research involving participants with intellectual or mental impairment, including temporary impairment, for example as a result of alcohol or drug-induced intoxication (see NS 5.1–5.4);
- research involving persons in highly dependent medical care situations (see NS 6.1–6.10);
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- research involving persons in dependent or unequal relationships (see NS 7.1–7.3);
- research involving collectivities (see NS 8.1–8.2);
- research involving Aboriginal or Torres Strait Islander communities (see NS 9, which refers to NHMRC Guidelines on Ethical Matters in Aboriginal and Torres Strait Islander Health Research [1991]).

Types of research requiring additional attention include:
- research involving ionising radiation (NS 10)
- research involving assisted reproductive technology (NS 11)
- clinical trials (NS 12.1–12.13)
- epidemiological research (NS 14.1–14.13)
- research using human tissue samples (NS 15.1–15.9)
- human genetic research (NS 16.1–16.16)
- research involving deception (NS 17.1–17.2)

**NS 2.9**

If an institution or organisation appoints additional members it should ensure that the membership continues to reflect both the diversity of the categories of members listed in paragraph 2.6, including gender, and the relative proportion of institutional to non-institutional members.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**APPOINTMENT OF MEMBERS**

**NS 2.10**

The institution or organisation may recruit members for an HREC in such a manner and shall appoint them for such a period and on such terms and conditions as it determines.

Institutions and organisations may develop explicit policies to ensure that appropriate people are recruited to HRECs. In developing such policies, the points made in NS 2.6 about attributes, desired qualities of members and minimum categories of membership should be considered. See also the Research Ethics Collection under ‘Human Research Ethics Committees: Membership: Minimum requirements’, page E71.

The term of appointment of members is a decision for the institution. It may be advisable to include the time period in the written Terms of Reference. The benefit of maintaining some continuity of membership by overlapping terms of office could be considered.

Traditionally, members of HRECs have provided their services on a voluntary basis; some institutions offer ‘sitting’ fees, and others are required to pay fees by the legislation under which they operate. The appropriateness of payments to members of HRECs is an issue.
to be determined by individual institutions. The National Health and Medical Research Council supports the payment of reasonable expenses such as travel, parking and additional child care.

**NS 2.11**

Members are to be appointed for their expertise and not in a representative capacity.

HREC members must reach their decisions independently, and not on behalf of or in accordance with any identifiable interest. See also NS 2.5.

**NS 2.12**

Members must receive a formal notice of appointment and assurances that the institution or organisation will provide legal protection in respect of liabilities that may arise in the course of bona fide conduct of their duties as committee members.

Members need a full and clear statement of their responsibilities and any other information or documentation that will enable them to fulfil their roles. This should include copies of the National Statement, the Terms of Reference of the HREC and any previous reports on the committee’s activities. It should also include any other relevant material about the committee’s processes, procedures and protocols, and an up-to-date list of members’ names and contact information, including the administrative support person and other relevant personnel.

**PROCEDURES**

**NS 2.13**

Institutions and organisations and their HRECs must establish working procedures concerning:

- frequency of meetings;
- preparation of agendas and minutes;
- distribution of papers prior to meetings;
- presentation of research protocols;
- timely consideration and review of research protocols;
- methods of decision making;

The IEC Report cautions that ‘Where a sitting fee is paid care should be taken to ensure that this does not result in an apparent or actual conflict of interest for the member(s) concerned.’ It would not be appropriate, for example, for payment to members to be related in any way to funds received from any person or organisation with a financial interest in the approval of research projects reviewed by that committee. pp.47–48.
prompt notification of decisions;
reporting of adverse occurrences;
appropriate monitoring;
receiving complaints;
advising institution(s) or organisation(s) to discontinue a research project;
fees, if any, to be charged; and
confidentiality of the content of protocols and of committee proceedings.

For a discussion of meeting frequency, agendas and minutes, applications forms and methods of decision-making, see the Research Ethics Collection, ‘Human Research Ethics Committees’, page E67-88.

Some commentary on the other items for working procedures appears in relation to the following paragraphs:
– Distribution of papers before meetings—NS 2.15
– Methods of decision-making—NS 2.17
– Reporting of adverse occurrences—NS 2.37, 2.38
– Monitoring—NS 2.33–2.38
– Complaints—NS 2.39–2.43
– Suspension of research—NS 2.44–2.45

**NS 2.14**

An HREC may approve, require amendment of, or reject a research proposal on ethical grounds. The HREC must record decisions in writing and should include reasons for rejection.

HRECs should inform researchers in writing of decisions and, in the event of rejections or recommended amendments, the reasons for those decisions.

**NS 2.15**

Meetings of an HREC must be so arranged as to allow, wherever possible, all members to be fully informed by receipt of all relevant papers and the opportunity to attend.

The agenda, including copies of research proposals, should be distributed to all members prior to the meeting, allowing sufficient time for reading. Some committees also distribute a copy of relevant grant applications to members who are selected to lead the committee review process, while others distribute comments from members and responses from the researchers.
Committees benefit by regular attendance of members at all meetings. Members are then in a position to consider ethical issues within the context of a range of points of view. This promotes informed discussion and consensual resolution of conflicting views.

**NS 2.16**

Where there is less than full attendance at a meeting, the Chairperson must be satisfied, before a decision is reached, that the minimum membership listed in paragraph 2.6 have received all papers and have had an opportunity to contribute their views and that these have been recorded and considered.

This paragraph is designed to ensure that all HREC decisions are the result of consideration of the views of each of the categories of members listed in NS 2.6.

HRECs need to establish procedures to enable members who are unable to attend a particular meeting to contribute, prior to that meeting, views on each protocol to be considered. Written comments may be communicated by any convenient method, including email or facsimile. The chairperson is responsible for ensuring that these views are recorded and considered at the meeting.

Some committees establish a quorum that needs to be met before the committee can proceed with a meeting. A quorum serves the important purpose of ensuring a degree of discussion, but needs to be realistic, taking into account the mechanism required by this paragraph.

**NS 2.17**

An HREC should endeavour to reach decisions by general agreement. This need not involve unanimity, but failure to agree may require an extension of time to reconsider the research protocol and its possible amendment, especially when any member is not satisfied that the welfare and rights of participants are protected.

Committees are encouraged to respect the expression of a diversity of views and to allow the time necessary to review all concerns. Full consideration of all relevant perspectives fosters greater confidence in the committee’s decisions and the advice it offers.

**NS 2.18**

An HREC may invite the researcher(s) to be present for discussions of the research and may request amendments to the research protocol.

HRECs need to be sufficiently informed about each research protocol (NS 2.8). Interviewing researchers is one means to this end.

Some HRECs require all researchers presenting proposals to attend an interview, while others restrict such interviews to proposals involving contentious ethical issues, invasive or potentially risky procedures, or the need for clarification. Interviews provide opportunities for detailed assessment of the proposed research, for provision of information about its conduct, for clarifying the capacity of the researchers to fulfil their responsibilities and for negotiating possible amendments to research proposals. Interviews can contribute to a cooperative working relationship.

Communication between individual HREC members and researchers should be in accordance with procedures established by the HREC.

**Confidentiality of protocols and proceedings**

Documents are submitted to an HREC for the sole purpose of consideration and, if thought fit, approval. Generally speaking, HRECs should regard this as confidential material. They should take care to prevent it being disclosed outside of the HREC except for the purpose for which it was provided, for example obtaining an opinion from an expert. Where a committee thinks consultation within the research or wider communities is desirable, or where it wishes to share its experiences with other committees, it should seek the consent of the parties involved or omit potentially identifying information.

These strategies could also be applied when inviting interested researchers and others to attend committee meetings.

**NS 2.19**

An HREC may seek advice and assistance from experts to assist with consideration of a research protocol, but must be satisfied that such experts have no conflicts of interest in relation to the research project under consideration arising from any personal involvement or participation in the research, any financial interest in the outcome or any involvement in competing research.

See also comments on NS 2.20 and the Research Ethics Collection, ‘Conflicts of interest’, page E25.

**NS 2.20**

An HREC shall ensure that no member of the committee adjudicates on research in which that member has any conflict of interest including any personal involvement or participation in the research, any financial interest in the outcome or any involvement in competing research.

When an HREC member has, or could be seen to have, a conflict of interest, that member should withdraw from the meeting when that project is being assessed. The absence of the member concerned should be recorded in the minutes. In addition, a committee member in this situation should not discuss the project with other members or attempt to influence the committee in any way. Where a member is an investigator, the HREC may choose to invite that member to answer questions about the project before the member withdraws from the meeting.
HRECs relying on the advice of sub-committees or advisory bodies should also seek assurance that members of these groups will declare any conflict of interest and comply with the process described above.

Institutions need to develop clear policies and definitions of conflicts of interest.

See also comments on paragraph 2.19 and the Research Ethics Collection, ‘Conflicts of interest’, pp E25-27.

**NS 2.21**

A researcher must disclose to the HREC the amount and sources or potential sources of funding for the research and must declare any affiliation or financial interest when proposing and when reporting the research. The HREC must consider the extent to which it should disclose that information about funding sources.

Researchers must disclose funding sources, affiliations or financial interests so that HRECs may consider whether there is any actual or perceived conflict between the researcher’s personal and professional involvement in the proposed research. Disclosure of such conflict is a recognised means of protecting a person from later criticism. For this reason, the HREC must consider whether the affiliation or financial interest, or any payments to be received by the researcher, ought to be disclosed to the research participants. An explanation of the HREC’s reasons for so deciding should be provided to the researcher.

Further discussion can be found in the Research Ethics Collection, Conflicts of interest, page E25-27.

**Points to consider**

- What parties have interests in the specific research setting and exactly what are their interests?
- Is a primary purpose of the research project commercial?
- Does a researcher face a conflict of interest with regard to the obligations of, or pressures involved in, having more than one professional role in relation to a specific research project?
- Is sponsorship from industry likely to limit scientific communication in order to protect proprietary information?
- Have researchers fully disclosed any financial interests relating to the research project? Is any payment to researchers fair and not excessive?

**NS 2.22**

A researcher must include, in the research proposal, a statement of the ethical considerations involved in the proposed research and an HREC must be satisfied that the research protocol gives adequate consideration to participants’ welfare, rights, beliefs, perceptions, customs and cultural heritage both individual and collective.
The ways in which HRECs can be satisfied that a researcher has given adequate consideration to the characteristics of participants are often illustrated in research with vulnerable populations. Further information can be found in the Research Ethics Collection, ‘Children and young people, research involving’ page E5, ‘Gay men and lesbians, research involving’, E43, ‘HIV/AIDS, research involving’ page E57, or ‘Terminally ill people, research involving’, page E161.

**NS 2.23**

An HREC should not communicate directly with a research sponsor on matters relating to the protocol or ethics of a project, but the institution or organisation and the sponsor may have direct communication on matters relating to administration, indemnity and insurance.

Any undue influence, or appearance thereof, in HREC review of research is to be avoided. Normally, an HREC will communicate with the researcher or the institution who in turn will communicate with the sponsor, where necessary.

In some types of research, notably clinical trials, it will be important for the HREC to be aware of the regulatory requirements imposed on the research.

**NS 2.24**

All documents and other material used to inform potential research participants should be approved by the HREC including plain language information sheets, consent forms, questionnaires, advertisements and letters of invitation.

It is important that potential participants in research are properly informed before they decide whether to participate. The process of recruiting participants begins with the first information they receive about the research, and HRECs need to recognise that this paragraph refers to ALL documentation used in those processes, These will include newspaper, radio, television or other public advertisements, and not only information sheets and consent forms.

**ADVOCATES AND INTERPRETERS**

**Advocates**

**NS 2.25**

An HREC must consider whether an advocate for any participant or group of participants should be invited to the HREC meeting to ensure informed decision making and understanding by these participants.
Advocates may help an HREC decide on the best ways of providing information to potential participants and the most appropriate process by which potential participants can exercise their choice whether or not to participate.

**Interpreters**

**NS 2.26**

Where research involves the participation of persons unfamiliar with the English language (or the language in which the research is to be conducted), an HREC must ensure that:

(a) the participant information statement has been translated into the participant’s language; and

(b) an interpreter is present during discussions with the participants about the project. Normally the interpreter should be independent, but when the research proposed is of minimal risk, an English-speaking relative or friend may be acceptable.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**EXPEDITED REVIEW FOR MINIMAL RISK RESEARCH**

**NS 2.27**

An HREC may establish procedures for expedited review of research involving minimal risks to participants and in so doing may depart from the requirements of paragraphs 2.15, 2.16 and 2.17 and if so, must determine:

(a) the class or classes of research to which an expedited review procedure is to apply;

(b) the scope of the Chairperson’s authority;

(c) the delegation of tasks to sub-committees;

(d) the relationship between the Chairperson of the full Committee, and the Chairpersons of such sub-committees; and

(e) the method of reporting and ratification of decisions by the full Committee.

This involves a departure from the usual requirements that all materials are considered by all committee members who participate in decision-making. The justification for this type of review is that the research involves minimal risk to participants, not that speedy approval is needed. In this situation, the HREC delegates assessment of a proposal to a small number of reviewers. These reviewers are usually given the authority to approve a proposal subject to ratification by the full committee.

In some circumstances, often created by research funding time constraints, a faster review than is normally available is sought. Where the research involves more than minimal risk, there is not a clear justification for departing from the normal review process of an HREC meeting.

For further discussion of expedited review, see the Research Ethics Collection, 'Human Research Ethics Committees, Expedited review', page E86.
NS 2.28

Research with potential for physical or psychological harm should generally not be considered for expedited review. This includes drug trials, research involving invasive physical procedures and research exploring sensitive personal or cultural issues.

Other situations where review would not normally be expedited include where vulnerable populations are involved or where conflicts of interest may arise, such as those between the roles of clinician and researcher, or teacher and student. Expedited review is never justifiable solely on the grounds of a researcher’s claim to the need for urgent review of their project.

NS 2.29

Where the Chairperson of an HREC considers that research may involve a departure from any of the ethical principles in this Statement, the protocol must be considered by the full Committee and cannot be dealt with by expedited review.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

RECORDING OF DECISIONS

NS 2.30

An HREC shall maintain a record of all research protocols received and reviewed, including:

- name of responsible institution or organisation;
- project identification number(s);
- principal researcher(s);
- title of project;
- ethical approval or non-approval with date;
- approval or non-approval of any changes to the protocol;
- the terms and conditions, if any, of approval of any protocol;
- whether approval was by expedited review;
- whether the opinion of another HREC was considered;
- action taken by the HREC to monitor the conduct of the research; and
- the relevance, if any, of the Guidelines for the Protection of Privacy in the Conduct of Medical Research.
This record is important for HRECs’ responsibilities for monitoring the conduct of approved research, the need for renewals of approval or amendments and statistical reporting to institutions and to the NHMRC (see NS 2.46–2.48).

NS 2.31

For multi-centre research proposals the HREC shall also record, from information provided from the researcher (see paragraph 3.7):

- details of other centres involved;
- the approval status of the study at each centre; and
- details of any amendments required at other centres.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

NS 2.32

An HREC shall retain on file a copy of each research protocol and application for HREC approval, including any information sheets, consent forms or relevant correspondence, in the form in which they are approved.

The National Statement does not specify a period for which these records need to be kept. For research data, the Joint AVCC/NHMRC Statement and Guidelines on Research Practice http://www.health.gov.au/hfs/nhmrc/research/general/nhmrcavc.htm recommends retention for a minimum period of five years, and 15 years for specific types of research such as clinical research. The time for which HREC records need to be retained may be determined by State or Territory legislation. Where there is no legislation, retention of HREC records for the same period as the data from the research project is advised.

MONITORING

NS 2.33

An institution or organisation and its HREC have the responsibility to ensure that the conduct of all research approved by the HREC is monitored by procedures and/or by utilising existing mechanisms within the institution or organisation which will ensure the achievement of the goals for monitoring as determined by the institution or organisation and the HREC.

Monitoring is defined in the National Statement on page 64. Monitoring should be designed to establish that a research project is being or has been conducted in the

manner proposed to, and approved by, the HREC. The conclusion could then be drawn
don that protection of the welfare and rights of participants—the primary purpose of the
National Statement and of HRECs—had been achieved.

In determining mechanisms for monitoring research, an HREC needs to take into account
how they can be implemented within the institution. There may be existing institutional
procedures that can be adapted or relied upon to achieve monitoring goals.

Further information can be found in the Research Ethics Collection under ‘Monitoring
research’, page E109.

**NS 2.34**

The frequency and type of monitoring determined by an HREC
should reflect the degree of risk to participants in the research
project.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**NS 2.35**

As a minimum an HREC must require at regular periods, at least
annually, reports from principal researchers on matters including:
(a) progress to date or outcome in the case of completed research;
(b) maintenance and security of records;
(c) compliance with the approved protocol; and
(d) compliance with any conditions of approval.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**NS 2.36**

An HREC may recommend and/or adopt any additional appropriate
mechanism for monitoring including random inspections of
research sites, data and signed consent forms, and/or interview,
with their prior consent, of research participants.

HRECs may apply monitoring measures additional to, or in place of, the regular reports
provided for under NS 2.35. Such additional measures should be designed to establish
that the research is being or has been conducted as approved. They may focus on a
specific element of the research, for example where a condition was attached on
approval, or on a report publishing the results of the research.

Existing mechanisms within an HREC's institution or organisation may help. For example,
quality control mechanisms could be modified to confirm that a research project is
progressing as approved. Or it may be appropriate to set up specific on-site monitoring
of the research process for a particular study. When an HREC decides that active
monitoring of a research project is necessary, committee members will need to consider who is the most appropriate person to carry this out.

**NS 2.37**

An HREC shall, as a condition of approval of each protocol, require that researchers immediately report anything which might warrant review of ethical approval of the protocol, including:

(a) serious or unexpected adverse effects on participants;
(b) proposed changes in the protocol; and
(c) unforeseen events that might affect continued ethical acceptability of the project.

Serious adverse effect is defined in Appendix 3 to the Statement as any untoward medical occurrence that at any dose:

- results in death
- is life threatening
- requires in-patient hospitalisation or prolongation of existing hospitalisation;
- results in persistent or significant disability/incapacity; or
- is a congenital anomaly/birth defect.

This definition is taken from the context of clinical trials.

An unexpected adverse effect is an adverse reaction, the nature or severity of which is not consistent with the applicable product information. HRECs need to be aware of the mechanisms for reporting such events that are part of multi-centre clinical trials and decide how they will assess the significance of reports they receive, particularly those from other research sites. HRECs should receive from researchers advice about the significance of the adverse events, their relation to the research and whether any amendments to the conduct of the research are required. Notes on and references to NS 12.2 about clinical trials contain further discussion.

**NS 2.38**

An HREC shall, as a condition of approval of the research proposal, require researchers to inform the HREC, giving reasons, if the research project is discontinued before the expected date of completion.

If an HREC is advised of the early discontinuation of a research project, it can assess whether any research participant has been or will be disadvantaged as a result. It can also be made aware that the research will not fulfil its goals.
COMPLAINTS

NS 2.39

An institution or organisation with an HREC shall establish mechanisms for receiving and promptly handling complaints or concerns about the conduct of an approved research project.

Further information can be found in the Research Ethics Collection, ‘Complaints’, page E17. See also NS 2.40, 2.41 and 2.42 following.

NS 2.40

An HREC must nominate a person to whom complaints from research participants, researchers, or other interested persons may be made in the first instance. This person or the HREC shall attempt to resolve these complaints.

At least one person should be designated to receive complaints, although two people may be necessary to carry out any investigation. Such a person may be the secretary or a member of the HREC, but is not required to be a member. ‘Complaints officers’ should be easily contactable, be seen to be easily approachable and have the authority to act promptly and appropriately. They should also be capable of dealing sympathetically with any concern that arises and be prepared to take action on the basis of verbal or written reports, whether these reports are from people who identify themselves or not. Adequate resources should be provided to allow complaints officers to carry out their functions.

NS 2.41

2.41 Where a complaint made under paragraph 2.40 cannot be resolved, the HREC must refer the matter to a person nominated by the institution or organisation to handle and resolve such complaints.

If the person nominated under NS 2.40 is connected with, or a member of, the HREC, then the appointment of a person under NS 2.41 not associated with the HREC would reflect a desirable standard of transparency.

NS 2.42

When information on the research is first provided to participants, the name or position and contact details of the person nominated by the HREC to receive complaints must be included together with the procedures for raising concerns or obtaining additional information on the research.
All details about how to make complaints should be given to all research participants as a routine part of the information they receive when they are deciding whether to participate or not. Collaborating researchers and research assistants also need to be informed. These details could be advertised throughout an institution and forwarded to any associated research bodies.

**NS 2.43**

An institution or organisation shall also establish procedures for receiving and promptly handling concerns or complaints from researchers about the consideration of their research protocol by an HREC.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**SUSPENSION OR DISCONTINUATION OF RESEARCH**

**NS 2.44**

Where an HREC is satisfied that circumstances have arisen such that a research project is not being or cannot be conducted in accordance with the approved protocol and that, as a result, the welfare and rights of participants are not or will not be protected, the HREC may withdraw approval, inform the researcher(s) and the institution(s) or organisation(s) of such withdrawal, and recommend to the institution(s) or organisation(s) that the research project be discontinued, suspended, or that other necessary steps be taken.

The HREC’s authority is normally limited to the withdrawal of ethical approval, notification of this decision to the researcher and the institution, and a recommendation to the institution that it take action to discontinue the research.

Institutions need to establish procedures to receive and act on such advice and recommendations.

**NS 2.45**

A researcher must not continue the research if ethical approval has been withdrawn and must comply with any special conditions required by the HREC.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.
COMPLIANCE REPORTS TO THE NHMRC

NS 2.46
The National Health and Medical Research Council (NHMRC), through the Australian Health Ethics Committee (AHEC), will audit the activities of HRECs to ensure compliance with this Statement.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

NS 2.47
An institution or organisation and its HREC shall provide information from its records to the NHMRC on request.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

NS 2.48
An institution or organisation and its HREC shall report annually to the NHMRC information relevant to its procedures including:
• membership/membership changes;
• number of meetings;
• confirmation of participation by required categories of members;
• the number of protocols presented, the number approved, and the number rejected;
• monitoring procedures in place and any problems encountered; and
• complaints procedures and number of complaints handled.

The present arrangements for this annual report are that Australian Health Ethics Committee (AHEC) of the NHMRC provides each HREC with a questionnaire for completion.

The process is regularly under review. HRECs are notified in advance of any additional information to be sought.

3. MULTI-CENTRE RESEARCH

For further detailed discussion, see the Research Ethics Collection, ‘Multi-centre research’ page E111.

**NS 3.1**

Multi-centre research may include:

(a) a research project conducted at more than one institution or organisation either by the same or different researchers, eg. a clinical drug trial;

(b) a research project conducted jointly by researchers affiliated with different institutions or organisations; and

(c) a research project being conducted by a researcher who changes affiliation from one institution or organisation to another.

It is important to recognise that there can be a great range of variation in the scale of a multi-centre research proposal. Multi-centre research ranges from large, internationally supported clinical trials involving many researchers and supported by vast resources to a PhD student in a three-year course wishing to administer a questionnaire to students in several universities. This is as much multi-centre research as is the large clinical trial. However, the PhD student may have limited resources and time and HRECs need to be aware of these limitations.

**NS 3.2**

A research proposal that involves multi-centre research will have additional implications for both review and monitoring by a Human Research Ethics Committee (HREC).

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**REVIEW**

**NS 3.3**

In order to minimise unnecessary duplication in review of multi-centre research, HRECs are encouraged to ascertain whether the same protocol has been reviewed by another HREC, including reviews conducted overseas.

HRECs should ask for information, within the format of their application form, on the identity of other HRECs that have been, are being, or will be asked to consider the research protocol (or one very similar in content) that is being submitted. They are entitled to rely on the obligation of researchers to provide this information (see NS 3.7).
NS 3.4

With a view to prompt and efficient consideration of multi-centre research protocols an individual HREC may:

(a) communicate with, and give advice to or receive advice from, any other HREC;
(b) accept a scientific/technical assessment of the research by another institution or organisation;
(c) review and, where the same research project is conducted at two or more institutions or organisations, adopt the reasons for ethical approval or disapproval of another HREC in reaching its own decision; or
(d) adopt other administrative procedures to accelerate timely consideration and avoid unnecessary duplication.

3.4 (a)

HRECs may be helped by previous acquaintance with members of other HRECs to which proposals have been submitted. Geographic groups of committees likely to share multi-centre research proposals could establish liaison processes. These might include meetings to discuss topics of mutual concern and regular contact between HREC executive officers. Greater familiarity with the resources of neighbouring HRECs (for example, an awareness of the scientific or legal expertise available to them) could also help cooperation.

Common submission forms, in whole or part, could be another outcome of interaction between HRECs. Models for successful cooperation between HRECs for the effective review of multi-centre research are likely to emerge from small-scale exercises of cooperation.

3.4 (b)

A common scientific/technical assessment of a multi-centre research proposal may be simpler to achieve than acceptance of a common ethical assessment. When presented with a multi-centre proposal, it could be advantageous if the HRECs involved decide on one HREC to undertake the scientific assessment.

A common scientific assessment could be produced by qualified members of a number of HRECs involved or by an HREC that has accepted that role. Alternatively (and subject to available resources), HRECs may agree to commission an assessment on their behalf. In some proposals, especially those relating to clinical trials, it may be appropriate for the HREC or commissioned assessors to evaluate a scientific assessment previously prepared, perhaps overseas in the case of a multi-national trial.

3.4 (c)

It may be unrealistic and unreasonable to expect that HRECs will agree in every detail with the decisions (and reasons on which they are based) of another HREC. Nevertheless, it may be possible to accommodate individual institutional requirements with respect to some details of a proposal without jeopardising its overall acceptance by a number of committees. When this is done, all involved HRECs need to be made aware of any amendments that have been incorporated in the protocol as approved by other committees.

The HRECs could agree that the decision and reasons proposed for adoption be presented in a way that explicitly identifies each relevant ethical issue and how it has been addressed and, where necessary, resolved. This would enable each other committee, in deciding whether to
adopt this decision and reasons, to be satisfied that all relevant matters had been dealt with. The National Statement would be an appropriate source for these issues.

3.4 (d)

It is an institutional and committee responsibility to ensure timely consideration and review of research protocols.

Approaches that could be part of a committee's general operating procedures can be applicable to multi-centre research. For example, there may be scope for presentation of draft protocols to the chair or a limited number of HREC members as a way of eliminating possible obstacles to approval. Such preliminary consultation may result in rapid processing of the final form of a proposal once it is submitted to the committee as a whole.

NS 3.5

With a view to prompt and efficient consideration of multi-centre research protocols, the principal researchers may agree that the primary ethical and scientific assessment be made at one agreed institution or organisation, and copies of the approvals be sent with the protocols to the other institutions or organisations involved. Where there is such an agreement, the other HRECs may accept a scientific/technical assessment of the research by another institution, organisation or HREC and adopt the reasons for ethical approval or disapproval of the protocol by the primary HREC.

It may be that the researchers participating in a large multi-centre project are in the best position to nominate a coordinating or principal researcher who can remain in close contact with a coordinating HREC.

HRECs that agree to accept the assessment and concur with the decision of another committee should consider fully the consequences of this acceptance. They are exercising a responsibility on behalf of their institutions for the protection of the welfare of participants who are recruited through their institutions. Therefore, they must establish to their satisfaction that the assessment and decision of the other committee are scientifically and ethically sound and conform to any principles of operation of their own institutions.

An institution and its HREC should also consider the issue of indemnification of its members (see Paragraph 2.3). It will be important that the decision of accepting another HREC's decision is reached in a deliberative way, for example that it involves deciding that the other HREC's decision is ethically sound for the reasons it has given. Agreements of the type referred to in the comments to NS 3.4(c) would assist.

NS 3.6

Where an HREC is satisfied that there has been full and thorough consideration of the protocol (by another HREC under 3.4 or by a primary HREC under 3.5) the HREC may, after tabling of the protocol, accept the decision of another institution, organisation or HREC in relation to multi-centre research. The HREC may still give further consideration to ethical and administrative aspects of the research which are specific to its own institution or organisation.
The extent to which one HREC can introduce modifications applicable only to its own institution into a research protocol that has been considered and approved by a number of other HRECs will be a matter for specific consideration for any protocol.

For example, if an institution makes modifications that are likely to compromise statistical comparison of data collected in different institutions, the researcher(s) may decide not to include that institution in their study. On the other hand, minor variations, such as changing the format or content of an information sheet for prospective participants, either to conform with institutional style or to cater for a group of participants with specific linguistic requirements, may not raise difficulties.

**NS 3.7**

The principal researcher shall:

(a) inform each HREC of all other Australian sites at which the research is being proposed or conducted, at the time of submission of the research project;

(b) disclose to each HREC any previous decisions regarding the research made by another HREC; and

(c) inform each HREC of whether the protocol is presently before another HREC.

These responsibilities of principal researchers in a multi-centre study should be drawn to their attention by being included in an institutional application form for ethics approval.

**MONITORING**

**NS 3.8**

An HREC must determine how the conduct of multi-centre research will be monitored and what roles each of the institutions or organisations and their HRECs will have. Consultation and agreement between and among HRECs and the institutions or organisations involved will be essential to ensure that the research is monitored and that each institution or organisation fulfils its obligations under this Statement.

Institutions and HRECs have joint responsibility to monitor the conduct of approved research (see also NS 2.33). Accordingly, monitoring procedures should be resolved at an early stage, preferably at the time of approval of the proposal by all of the HRECs involved. It may be advantageous in monitoring a large-scale multi-centre research project, such as a clinical trial, for all HRECs to delegate this function to a single authority in order that a uniform standard can be achieved.
4. RESEARCH INVOLVING CHILDREN AND YOUNG PEOPLE

NS 4.1

Research is essential to advance knowledge about children’s and young peoples’ wellbeing, but research involving children and young people (see Appendix 3 for definitions) should only be conducted where:

(a) the research question posed is important to the health and wellbeing of children or young people;
(b) the participation of children or young people is indispensable because information available from research on other individuals cannot answer the question posed in relation to children or young people;
(c) the study method is appropriate for children or young people; and
(d) the circumstances in which the research is conducted provide for the physical, emotional and psychological safety of the child or young person.

4.1 (a), (b) and (c)

A proposed study involving children or young people should only be approved if information available from studies involving individuals at other life stages cannot answer the question posed. Some childhood disorders do not occur in adults and therefore cannot be studied in the adult population. In addition, findings from research involving adults cannot always be assumed to apply to children, because (in biomedical research) normal values or ranges for biological variables (for example, lung capacity, weight, height) may differ between children and adults. They may also differ between children of different ages and stages of development. It is often necessary, therefore, for this kind of research to involve children or young people of a certain age.

Similar considerations apply to educational and psychological research. Some research, for example on language development, needs children as participants but is not designed specifically to benefit them. HRECs need to be satisfied that there is sufficient justification for the research and that participation of children is indispensable, in addition to the other matters set out in paragraphs 4.1–4.4.

An HREC should give particular scrutiny to the proposed study method and the circumstances in which the study is to be conducted. The proposed research question must be based on sound scientific principles. It should be reasonably likely to result in a valid conclusion and subsequent publication of new information important to the health and wellbeing of children and/or young people.

Study methods must be considered carefully because children are more susceptible to some types of harm that may arise from research. For instance, the potential for interference with growth in height is irrelevant to adults but important to children. Other aspects of childhood and adolescence might also be compromised, including psychological, social and sexual development.
4.1 (d)

In approving a research protocol, HRECs should also be aware of any other research that the child or young person is or has been involved in. This is often a problem encountered with children or young people suffering from a chronic illness, for example asthma or cancer. The parents and their child may be very keen to cooperate in the hope of finding an improved treatment or cure, but this willingness might be a burden on the child.

As a general rule, the participant should only be included in one study at a time and the number of consecutive studies should be limited. However, in deciding on this, the HREC may consider the nature and extent of the current and/or previous research that the child or young person has been involved in. For instance, an HREC may conclude that the safety of a diabetic child would not be prejudiced by his or her participation in a clinical drug/device trial at the same time as a survey or other non-intrusive, non-clinical research.

Fuller discussions can be found in the Research Ethics Collection, ‘Children and young people, research involving’, page E5, and ‘Children, clinical trials involving’, page E9.

NS 4.2

Consent to a child’s or young person’s participation in research must be obtained from:

(a) the child or young person whenever he or she has sufficient competence to make this decision; and either

(b) the parents/guardian in all but exceptional circumstances; or

(c) any organisation or person required by law.

In most jurisdictions, ‘age of majority legislation’ holds that a person under the age of 18 is considered a child. Beyond that age, people can make their own medical decisions in the same ways as any other adult. In New South Wales and South Australia, the ages for making medical decisions are 14 and 16 respectively.

HRECs should be aware that there are, at present, no clear statutory or common law requirements in Australia about a child or young person’s ability to consent to, or refuse, participation in a research project. A child or young person’s consent can be given whenever that person or child has sufficient competence to make a decision about participating in the research. Similarly, a child or young person can withdraw consent or refuse to participate (see also NS 1.7 and 1.8).

For further discussion, see the Research Law Collection. ‘Children and young people, research involving’, page L1.

NS 4.3

An HREC must not approve, and consent cannot be given for, research which is contrary to the child’s or young person’s best interests.

Evaluation of a child’s or young person’s best interests can be a complex process. If it is possible that the participant may benefit from a clinical trial, then participation may be considered to be in the child’s best interests—provided that potential harm does not
outweigh potential benefit. But this may still be difficult to judge, and decisions will vary with circumstances. For example, in the case of a child in danger of death or major damage to health, a potential risk that would be considered unacceptable under less serious circumstances might be judged acceptable.

This task is even more complex in non-therapeutic research, where participants cannot expect any direct or immediate benefit from the outcome of the project in the specific research context. It may be necessary to decide, for example, if a modest degree of inconvenience, some transient embarrassment, or low-level discomfort will render the research contrary to that child’s best interests.

**NS 4.4**

**A child’s or young person’s refusal to participate in a research project must be respected.**

A child’s or young person’s refusal to participate must be respected and cannot be overridden. See also NS 6.1–6.10.

**Points to consider NS 4.1-4.4**

- Is the research proposal important to the health and wellbeing of children or young people?
- Is the involvement of children or young people as research participants essential to this study?
- Is the methodology appropriate for research with this group of participants?
- Will the study be carried out in circumstances ensuring the physical, emotional and psychological safety of participants?
- Has consent been given, or refused, by a parent or guardian, as well as the child or young person to the extent that she or he is able to make a decision? Have all the requirements of the National Statement been met with regard to adequately informed consent?
- If a child or young person refuses to participate in the research project, will this be respected?
- Will a clear and full explanation of the research procedure be given to participants? Will it be given in a manner appropriate to a participant’s level of comprehension?
- Does the HREC need to obtain expert advice about the particular susceptibility of children and young people to physical, emotional or other types of harm?
- Is participation of a child or young person in a particular research project contrary to that participant’s best interests?
- Is additional care during the process of obtaining consent necessary because lines of communication are more complex than usual? An example might be when a researcher is planning to recruit participants from a ‘captive population’, such as children attending a school, kindergarten, recreation or sporting facility. Does the research protocol make it clear that information or contact details about individuals connected with that institution can only be provided to researchers with the prior consent of the people concerned?
- Has the HREC assessed whether or not a project involving sensitive personal questions constitutes an undue invasion of privacy?
Commentary on the National Statement

- If a project involving sensitive personal questions is approved, are adequate risk management strategies included in the protocol in the event of participants becoming distressed in response to these questions?

- Are HREC members clear about the difference between treatment and (non-therapeutic) research in relation to the degree of intervention that may be ethically justified?

- Are all relevant regulatory requirements satisfied, for example consent from education departments and school principals, and clearances on researchers?
5. RESEARCH INVOLVING PERSON WITH AN INTELLECTUAL OR MENTAL IMPAIRMENT

NS 5.1

When considering approval of research involving persons with an intellectual or mental impairment, an HREC should weigh the potential benefits against risks and undue burden.

Those who advocate participation in research by people with intellectual or mental impairments support an inclusive and non-discriminatory ethic for human research. Those who oppose it emphasise the vulnerability of these people and the difficulties they might experience in making an ethically sound choice. Accordingly, HRECs may be faced with arguments that such people are entitled to participate and that researchers should consider including such populations in any research. Committees need also to bear in mind that there is a wide range of impairments, so it will be important to understand precisely what impairments potential participants have.

Protection against undue burden of participation in research

One approach to protecting people with impaired decision-making capacity from bearing an undue burden from research is to ensure that projects involving them are directly related to their health problem. HRECs might also consider declining to approve research involving this group of participants when that research can be carried out with people not impaired in this way. However, advocates of inclusive ethic would be likely to oppose this.

HRECs need to assess carefully each protocol without presumptions for or against participation, and identify and weigh the benefits, burdens and risks of participation to these participants.


NS 5.2

Consent to participation in research by a person with an intellectual or mental impairment must be obtained from:

(a) the person with the intellectual or mental impairment whenever the person is of sufficient competence and, where the impairment is temporary or recurrent, at a time when the impairment does not prevent the person giving or refusing consent; or, failing that,

(b) the person’s guardian, or an authority or other organisation or person having that responsibility at law.
5.2(b)
A central issue in research involving people with intellectual impairment is their ability to decide whether or not to participate in research projects. To protect those people who lack decision-making capacity, legal measures have been implemented in all Australian jurisdictions. These provide for the appointment of third party decision-makers, including guardians and agents.

It is important to note that, in general, the potential research participant’s next-of-kin cannot give a legally valid consent, unless specifically authorised to undertake that role.

See the Research Law Collection, ‘Intellectual or mental impairment, consent and’, page L39 for a detailed discussion of the legal aspects of this issue.

NS 5.3
A Human Research Ethics Committee (HREC) must not approve, and consent cannot be given for, research which is contrary to the best interests of the person with the intellectual or mental impairment.

NS 5.4
Refusal by a person with an intellectual or mental impairment to participate in research must be respected.

A person with an intellectual or mental impairment can refuse to participate in research and that refusal must be respected and acted upon. The paragraph does not require that the refusal be made when the person is competent, by contrast with NS 5.2(a): a clear indication of refusal will be sufficient. Further, the person’s refusal cannot be overridden.

Points to consider NS 5.1-5.4

• Does the proposed research bear a direct relationship to the health problem(s) of people with intellectual or mental impairment?

• Are the proposed procedures for evaluating the decision-making capacity of potential research participants appropriate both in terms of the potential participants themselves and the nature of the proposed research? Will assessment of the potential participant’s capacity to decide whether or not to participate in research be undertaken by a competent expert who is independent of the research team?

• Do the procedures safeguard the interests and dignity of impaired people, including the appointment of legally authorised decision-makers who can consent to, or refuse, participation in a research project? Will the research be carried out in a setting in which the potential participant would feel safe and secure?
• Has provision been made for employing the appropriate method of communication with the potential research participant? If necessary, will a health carer with the appropriate skills, and with whom the potential participant is comfortable, be involved?

• Are there any conflicts of interests that would prevent a legally appointed representative from acting in the best interests of the impaired person?

• Will the refusal of an impaired person be respected?

• Should an independent advocate be engaged in order to ensure an informed choice by the impaired person?

• Are HREC members familiar with relevant legal requirements relating to consent on behalf of impaired people?

6. RESEARCH INVOLVING PERSONS HIGHLY DEPENDENT ON MEDICAL CARE

This section of the National Statement first identifies several ethically relevant features of all persons highly dependent on medical care, and then identifies specific ethical factors in relation to identified categories of such persons (NS 6.1 to 6.8).

Further discussion of these issues can be found in the Research Ethics Collection, ‘Highly dependent on medical care, persons, research involving’, page E55.

The involvement in research of people who are highly dependent on medical care raises ethical issues that deserve special attention. The gravity of their medical condition may require more invasive measures carrying increased risk. For those carrying out such research, there is a need to acknowledge that the giving of free and informed consent can be compromised by the effect of the medical condition on the person’s capacity to form and express an opinion or to communicate. Additionally, there may be a perception of coercion if a person is reluctant to refuse consent in fear that it may compromise his or her medical treatment. Researchers may also need to consider whether an unfair burden of participation (see paragraph 1.5) is being imposed on such groups as are referred to below.

Each type of research raises significant ethical concerns.

NS 6.1–6.8 are intended to provide illustrations of circumstances in which the need for additional ethical scrutiny arises when using the decision-making criteria in NS 6.9. In reaching such a decision, HRECs will also need to be satisfied that the proposed research can be conducted lawfully.

EMERGENCY CARE RESEARCH

NS 6.1

The distinguishing feature of emergency care research is that consent for entry into a project usually has to be obtained rapidly, when the vulnerability of patients and families is likely to be greatest. Moreover, the circumstances surrounding emergency care research are such that it may not always be possible to obtain consent for inclusion from either the patient or next of kin without delaying the initiation of treatment, and so risking a reduction of potential benefits.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.
INTENSIVE CARE RESEARCH

NS 6.2

The distinguishing features of intensive care research are the difficulty in communicating with patients receiving ventilatory assistance and the impairment of cognition in heavily sedated individuals.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

NS 6.3

Whenever possible, information about and consent to intensive care research should be given to and sought from potential participants before admission to that care.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

NEONATAL INTENSIVE CARE RESEARCH

NS 6.4

Research involving infants receiving neonatal intensive care should only be conducted in accordance with the principles in NS 4. ‘Research involving children and young people’. Those principles do not permit research that is contrary to the child’s best interests.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

NS 6.5

The very small size and vulnerability to harm of some infants is a unique feature of this research which renders all but minimal intrusion likely to be contrary to the child’s best interests. The collection of even small blood samples additional to those required for diagnostic purposes or handling of a low birth weight infant to make observations will demand careful scrutiny.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.
TERMINAL CARE RESEARCH

NS 6.6

Research in terminal care is distinguished by the short remaining life expectancy of participants and their potential vulnerability to unrealistic expectations of benefits.

Researchers must take care that the prospect of benefit from research participation is neither exaggerated nor used to justify a higher risk than that involved in the patient’s current treatment.

Researchers must respect the needs and wishes of participants to spend time as they choose, particularly with family members.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

RESEARCH INVOLVING PERSONS WITH IMPAIRED CAPACITY FOR COMMUNICATION

NS 6.7

The distinguishing features of research involving persons with impaired capacity for communication include situations where the impairment is an acute state requiring dependence on medical care as well as non-acute states. In the former, the condition and medical care can mask their degree of cognition and require different means to express known wishes. In the latter, the condition may be such as to prevent the person expressing wishes.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

RESEARCH INVOLVING UNCONSCIOUS PERSONS

NS 6.8

The distinguishing feature of research with unconscious persons is that, due to their incapacity for cognition or communication, it is impossible for them to be informed about the research or to determine their wishes about it. Consent for participation in research by an unconscious person must be given by others, including relevant statutory authorities, on that person’s behalf. Because of their extreme vulnerability such persons should be excluded from all but the most minimally invasive observational research.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.
HREC CONSIDERATION OF RESEARCH PROPOSALS INVOLVING PERSONS HIGHLY DEPENDENT ON MEDICAL CARE

NS 6.9

When the nature of the research procedure is such that conformity to the principle of consent [see Paragraph 1.7] is not feasible, and neither the individual nor the individual’s representative can consider the proposal and give consent in advance, a Human Research Ethics Committee (HREC) may approve a research project without prior consent provided it is satisfied that:

(a) inclusion in the research project is not contrary to the interests of the patient; and

(b) the research is intended to be therapeutic and the research intervention poses no more of a risk than that which is inherent in the patient’s condition and alternative methods of treatment; and

(c) the research is based on valid scientific hypotheses which support a reasonable possibility of benefit over standard care; and

(d) as soon as reasonably possible, the patient and/or the patient’s relatives or legal representatives will be informed of the patient’s inclusion in the research and of the option to withdraw from the research without any reduction in quality of care.

NS 6.10

In the case of research proposals in which it is practicable to approach the patient and/or the patient’s relative or legal representative to obtain consent before inclusion in the research, an HREC should also be satisfied that:

(a) adequate provision will be made for informing patients and their relatives about the research to ensure that stress or other emotional factors do not impair their understanding of it; and

(b) the dependency of patients and their relatives on the medical personnel providing treatment does not affect any decision to participate.

In these types of situations, where conformity to the principle of consent is not possible, a research project may be approved by an HREC if the committee is satisfied as to the matters listed.

As to paragraph 6.9(c), the study needs to be scientifically sound and the research question should be answerable by the proposed methodology and analysis of results. However, HRECs should be aware that this last requirement is often unachievable in emergency and intensive care settings. This is typically due to the small numbers of participants available for recruitment, a lack of homogeneity of the population being studied, and a significant risk of contamination in supposedly randomised trials, where sicker patients are often given the benefit of the trial therapy in a non-random manner.
As a result, several commentators have called for centralised review of the scientific merit of studies involving individuals highly dependent on medical care.20

In addition, HRECs should also consider the following issues when assessing research proposals of this type:

- Many people involved in intensive care research are facing death at the time of enrolment in research studies. Death is a common outcome measure in such studies and death rates may be very high. Whether such people should be exposed to greater or lesser research-related risk is a contentious issue.21
- If a therapeutic intent is apparent, is there a likelihood that the individual participant will benefit, or is it intended that individuals afflicted by the same condition might benefit in the future? If the latter, are the risks minimal?
- Although research participants are given the opportunity to withdraw from the research study at any time, HRECs should consider how achievable this would be in view of the participants' situation and their reduced cognitive capacity. Therefore, the research proposal should include specific measures for optimising the participant's opportunities to take advantage of this option.

Points to consider NS 6.1–6.10

- Is the study ‘emergency care’ (see NS 6.1) or ‘intensive care’ (see NS 6.2)?
- Is consent from a legal representative possible prior to enrolment?
- Should the scientific merit of the study be determined by an expert group with experience in the treatment of people highly dependent on medical care?
- Have the NHMRC requirements for obtaining informed consent in research involving people highly dependent on medical care been met? Is there a request for waiver of informed consent?
- Are all the burdens that will be imposed on the research participant patient clearly stated? Are these potential research participants being allocated an unfair burden of participation in research?
- Are the terms ‘minimal risk’ and ‘minimal burden’ clearly defined?
- Is the likely prognosis of the patient, regardless of treatment interventions, stated?
- Is the potential research participant free of coercion, in terms of a high level of dependency on health care staff, with regard to giving, or refusing, consent? Is the research participant free of such coercion with regard to withdrawing from the project at any time?
- Is there a therapeutic intent, and if so, to whom?
- How is the participant given the opportunity to withdraw?
- If the proposal involves terminally ill people, is it essential that these people be involved in the project in order to achieve its objective?
- Do terminally ill research participants possess adequate information about their disease and prognosis?
- If initiating a novel treatment, is the level of evidence of effectiveness made clear in the research proposal, and to potential research participants?

In studies comparing methods of symptom control for people with a terminal illness, what provision is made for rescue doses ('break-through') for symptom relief which would not interfere with the validity of comparison? If a placebo arm is considered for a study for symptom control, how is this justified?
7. RESEARCH INVOLVING PERSONS IN DEPENDENT OR UNEQUAL RELATIONSHIPS

NS 7.1

It is not possible to define exhaustively all types of dependent relationships, but they include situations where unequal power relationships exist between participants and researchers or where participants occupy junior or subordinate positions in hierarchically structured groups. Examples include:

- persons with chronic conditions or disabilities and their carers;
- patients and health care professionals;
- students and teachers;
- prisoners and prison authorities; and
- employees (including members of the police force, defence forces and hospital and laboratory staff) and their employers or supervisors.

When assessing research proposals involving dependent populations, HRECs should obtain relevant expert opinion about the particular problems that these people face. Committees should also consider involving members of the relevant population and/or a relevant advocacy group in the research proposal assessment process.

NS 7.2

Where it is proposed to involve persons in dependent or unequal relationships in research, the possibility that their relationship may impair their consent requires additional attention from the Human Research Ethics Committee (HREC) in order for the HREC to be satisfied that their consent is both adequately informed and voluntary.

HRECs must be satisfied that consent will be given voluntarily. To be voluntary, consent must not be obtained through the use of coercion or inducements. Even if permission from authorities or caregivers has been given, people in dependent relationships should never be compelled to take part in a research project.

A person is being coerced when he or she agrees to participate in a research project in response to a threat from an authority figure. The threat may take the form of physical danger or the withholding of a benefit. Potential research participants may also believe that participating in a specific research project will place them in good favour with relevant authority figures, or that failure to participate will compromise their relationship. In coming to a decision, an HREC will need to examine the proposed consent form and/or the manner in which consent will be obtained.
However, in some situations coercion can be implicit or unintentional, and the HREC may need to look beyond the consent form. For example, employees of an organisation conducting research may feel they will be disadvantaged in terms of career advancement by not participating in a study. Once again, ensuring that the HREC has access to expert opinion or the advice of interested parties can help to overcome these types of problems.

Because people in dependent relationships are vulnerable to abuse of power, whether unintentional or intentional, HRECs could consider requiring that they be provided with independent advocacy services to ensure that their consent to participate in research projects is informed and voluntary.

Also, as members of some dependent populations may be educationally disadvantaged or suffer from cognitive impairment, special measures may be needed to ensure they understand research process sufficiently. It may be necessary for the relevant statutory authority to act on behalf of the potential research participant with regard to consent to take part in a particular project. See also NS 5.1 to 5.4.

Further information can be found in NS 1.10 and Commentary and in the Research Ethics Collection, ‘Consent’, page E29.

**NS 7.3**

Where research involves persons in dependent or unequal relationships the researcher must give an assurance that refusal to participate in, or a decision to withdraw from, the research will not result in any discrimination, reduction in the level of care or any other penalty.

People in dependent groups are particularly vulnerable to harm because of their increased accessibility as research participants. Clearly, these people should not bear a disproportionate burden of research activity (see also NS. 5.1 about undue burden and people with intellectual or mental impairments). Measuring what would be an undue burden will not be a simple task and will involve considering the frequency, the requirements and the significance of research participation as well as the degree of intrusiveness of the research project.

Breaches of confidentiality are more likely when research participants are living in institutions, attend schools or universities or occupy shared working environments. As the research process may reveal sensitive information about a person's family, their mental health, sexual activity or drug use, research proposals should include an account of strategies that will maximise confidentiality (see NS 18 and NS Appendix 2).

**Points to consider NS 7.1–7.3**

- Is the ethics committee appropriately constituted to review research involving the dependent population in question?
- Are the potential research participants taking part in an excessive number of studies? How many studies have these people taken part in during the past 12 months?
- What steps have been taken to ensure that a person’s consent to participation in a research project is voluntary, that is, free of coercion or undue inducement?
- Is it necessary to involve an independent advocate to support the potential research participant during the consent, or refusal, process? Is it necessary to
involve a legal guardian if the person is not capable of making a considered decision with regard to consent or refusal?

- Does the proposed research project expose participants to a level of risk of harm that is ethically unacceptable?
- Is there an equitable complaints procedure in place and will research participants be made aware of, and have easy access to, this process?
- What steps have been taken to ensure that information about research participants remains confidential, particularly for those people living in institutional settings?

Further discussion can be found in the Research Ethics Collection on ethical issues arising for specific groups of people, including students page E159, prisoners page E121, employees page E37 and patients where research is conducted in general practice page E47.
8. RESEARCH INVOLVING COLLECTIVITIES

Collectivities are distinct human groups with their own social structures that link members with a common identity, with common customs and with designated leaders or other persons who represent collective interests in dealing with researchers. Examples of collectivities may include cultural or ethnic groups, and indigenous communities.

The following is likely to be relevant in relation to some aspects of research involving Aboriginal and Torres Strait Islander peoples. However there are separate guidelines (referred to in NS 9. Research involving Aboriginal and Torres Strait Islander Peoples) which deal with these issues specifically when they involve health and medical research or when researchers have applied for funds to specific bodies such as the Australian Institute of Aboriginal and Torres Strait Islander Studies (AIATSIS).

NS 8.1

Collectivities are distinguished by:

(a) recognition of common beliefs, values, social structures or other enduring features that identify them as a separate group;

(b) customary collective decision making in accordance with tradition and beliefs;

(c) it being customary for leaders or identified members of the collectivity to express a collective view; and

(d) members of the collectivity being aware of their common activities and common interests with other members.

Four criteria are used to determine which communities or groups are covered by the category ‘collectivities’. Use of the term has been a matter of controversy, but it has been used to address some ethical issues that arise at a group and not an individual level.

NS 8.2

Researchers must seek Human Research Ethics Committee (HREC) approval for research involving a collectivity. Before approving such research, an HREC must be satisfied that the following matters have been addressed in the research protocol:

(a) whether, in addition to individual consent, collectivity leaders should be consulted for approval;

(b) whether arrangements to address issues identified in this paragraph have followed a process of negotiation;

(c) issues of consent, privacy, confidentiality and harms within the collectivity, to either individuals or the collectivity;
(d) the ownership of data and the manner of dissemination of research findings; and
(e) the manner in which disagreements between the researcher and the collectivity will be resolved.

8.2 (a)
The process by which consent will be obtained, and the manner in which it will be given, should be made clear to the HREC. The source of consent must be consistent with the collectivity's values, customs and practices. In addition to individual consent, either the consent of the leader(s) or the group as a whole will usually need to be obtained, depending on the collectivity's decision-making process, before the research can proceed.

8.2 (b)
The research protocol should indicate that the process to be followed was arrived at in keeping with the collectivity's decision-making procedures, and that sufficient time was allowed for decision-making by the group. A schedule for ongoing liaison and consultation throughout the course of the study, often involving a nominated individual or a reference group, will often be required.

8.2 (c)
The HREC will need to be satisfied that the concepts of privacy, confidentiality and harm have been understood within the context of the collectivity. What could amount to harm within a collectivity may be different from harm outside the collectivity.

8.2 (d)
When considering arrangements for dissemination of results, the HREC will need to recognise that clues to the identity of the collectivity may be difficult to avoid in reports on the study. The collectivity should frequently be given the opportunity to view the study report before any public presentations or publication. The protocol should provide evidence that this potential problem has been recognised, discussed and an agreement reached with the collectivity.

HRECs should ensure that researchers have considered issues concerning the ownership of data and, where possible, have a procedure for the dissemination of results. These matters should be negotiated and agreed on before the study begins.

8.2 (e)
Disagreements may arise between the researcher and the collectivity. Means of resolving disputes should be documented as part of ongoing liaison and consultation between the parties.

Finally, HRECs must normally be satisfied that the research will be of benefit or potential benefit to either individuals within the collectivity or the collectivity as a whole. These benefits must be weighed against the possible risks that conducting the research might generate for the collectivity and individuals within the group.

In determining whether the proposed research is sensitive to and consistent with the collectivity’s values, needs and customs, the HREC may wish to seek the advice of an appropriate external expert.
9. RESEARCH INVOLVING ABORIGINAL AND TORRES STRAIT ISLANDER PEOPLES

Researchers conducting research which involves Aboriginal and Torres Strait Islander individuals, communities or groups and Human Research Ethics Committees assessing research proposals for such research should consult the NHMRC Guidelines on Ethical Matters in Aboriginal and Torres Strait Islander Health Research (Interim, 1991). These guidelines will be revised by a working group which includes indigenous representatives.

Research funded by the Australian Institute of Aboriginal and Torres Strait Islander Studies (AIATSIS) is required to comply with specific AIATSIS guidelines.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

The revision of the Interim Guidelines referred to in this section is not yet complete. This Handbook will be updated to include this material when it is complete.
10. RESEARCH INVOLVING IONISING RADIATION

Researchers conducting projects which may involve exposure to ionising radiation and Human Research Ethics Committees (HRECs) assessing research proposals of these projects must follow relevant State and Territory legislation and should consult the NHMRC Recommendations for Limiting Exposure to Ionising Radiation. Advice should be sought from the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) regarding legislative requirements, including circumstances in which licensing, notification or approval, in addition to that of an HREC is required.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

For a discussion of issues in this area of research, see the Research Ethics Collection, ‘Radiation, research involving’, page E135, and the NHMRC Recommendations for Limiting Exposure to Ionising Radiation.
11. RESEARCH INVOLVING ASSISTED REPRODUCTIVE TECHNOLOGY

Research involving assisted reproductive technology is governed by specific legislation in Victoria, South Australia and Western Australia. In other States and Territories those undertaking such research should consult the NHMRC Ethical Guidelines on Assisted Reproductive Technology (1996).

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

12. CLINICAL TRIALS

A clinical trial is a study involving humans to find out whether an intervention, including treatments or diagnostic procedures, which it is believed may improve a person’s health, actually does so. A clinical trial can involve testing a drug, surgical or other therapeutic or preventive procedure, or a therapeutic, preventive or diagnostic device or service. Any intervention, including so-called ‘natural’ therapies and other forms of complementary medicines, can be tested in this way. Other related disciplines also conduct research which involves similar ethical considerations to those raised in clinical trials.

In pharmaceutical and medical device trials there are established codes of good clinical research practice which define clearly what is meant by a clinical trial for those purposes. 12. Clinical Trials has principal application in the context of biomedical clinical trials but should also apply to any other intervention claiming therapeutic benefit, wherever provided or conducted.

Reference could be made to the Research Ethics Collection, ‘Clinical trials’, page E11, for a detailed discussion of types of drug trials. Appendix 2 of this Handbook contains a detailed account of the Australian system of regulation of access to unregistered therapeutic goods. It contains a full description of the approval processes for both the Clinical Trial Exemption (CTX) and Clinical Trial Notification (CTN) schemes, including the role and responsibilities of HRECs.

When a clinical trial is being conducted at multiple locations, it will be reviewed by more than one HREC. In this case, one HREC may itself undertake (or commission) a detailed scientific assessment of the proposed trial, on the understanding that other HRECs will adopt that assessment when considering the ethical aspects of the trial. Further reference should be made to NS 3.1 to 3.8 and the Research Ethics Collection, ‘Multi-centre research’, page E11.

NS 12.1

The aims of every trial must be precisely stated in a protocol presented to and approved by a Human Research Ethics Committee (HREC) and every trial must be conducted by researchers with suitable experience, qualifications and competence and, where applicable, adequate training in relevant procedures including the use of any device being trialled.

The proposal should provide a comprehensive overview of the purpose of the trial and how each step is to be conducted. It should contain clear, precise information, including the specific aims, the experimental design and the details of the proposed intervention. Adequate information should be provided about the methods of drug use and therapeutic or diagnostic devices, the benefits and risks expected from such use, and procedures to be adopted in order to assess safety. Where new drugs or devices are involved, full investigational profiles of the products should be included.
In the case of drug trials, precise information about dosage, formulation and frequency of administration are necessary. An HREC may want assurance that the protocols for such trials have been prepared with the assistance of a pharmacologist. In the case of trials involving therapeutic or diagnostic devices, the HREC should also consider whether persons suitably qualified to assess the technical and clinical aspects of the device have been involved in preparing the protocol.

When assessing protocols for clinical trials involving the use of unregistered medicines, an HREC should consider the mechanisms proposed, if any, for access to continued treatment with those medicinal products by patients/participants for whom treatment has been found to be effective, and where long-term therapy would be appropriate following completion of the trial. The advisability of including a post-study supply component within the research protocol may also be examined.

**NS 12.2**

An HREC must consider all aspects of the design of a clinical trial and be satisfied that:

(a) the trial is directed to answering a specific question or questions;

(b) there is a scientifically valid hypothesis being tested which offers a realistic possibility that the interventions being studied will be at least as effective as standard treatment;

(c) where the research is therapeutic, and is therefore intended and likely to be of direct benefit to participants, there is an acceptable balance between the risks and benefits of the trial;

(d) the methodology provides:
   (i) a rationale for the selection of appropriate participants;
   (ii) an appropriate method of recruitment;
   (iii) adequate, understandable information for the purpose of obtaining participant consent;
   (iv) a clear description of the intervention and observation to be conducted; and
   (v) a sample size adequate to demonstrate clinically and statistically significant effects;

(e) it has access to adequate expertise or advice to consider the safety of the drugs, medical devices or other intervention under investigation; and

(f) it is familiar with the requirements of the Therapeutic Goods Administration (TGA) in relation to unregistered drugs and devices, particularly the Clinical Trial Notification (CTN) and Clinical Trial Exemption (CTX) schemes, where relevant.

**12.2(a)**

The complexity of design in some clinical trials does not relieve an HREC of the need to be satisfied that a research question is identified and set out clearly in information sheets for participants.
12.2(b)
The study design should be appropriate to the clinical question being asked. The commonly used designs, the nature and importance of endpoints and outcome measures, and an analysis of results and issues arising from the testing of generic drugs in equivalence studies are discussed in the Research Ethics Collection, ‘Clinical trials’, page E11.

12.2(c)
Risks may not be confined to adverse effects on physical health but could extend to emotional, economic and other types of disadvantage. In seeking to establish whether benefits and risks associated with a trial are acceptably balanced, an HREC should consider whether such a balance is struck not only at the level of the entire participant population but also for individual participants. For instance, planning of a trial should seek to avoid situations in which the likelihood of benefits is predictably higher than average for one identifiable group of participants whilst risks are predictably higher for another.

12.2(d) (i) and (ii)
The proposal should clearly identify how the classes of participants have been selected so as to permit the best extrapolation of trial results to the patient groups to whom the new treatment, if successful, is to be administered.

For further discussion of inclusion of women and children in clinical trials, reference can be made to the Research Ethics Collection, ‘Clinical trials’, page E11.

12.2(d) (iii)
The HREC should scrutinise the participant information statement carefully. Medical terminology and abbreviations should be avoided or explained in plain language. The document should clearly explain the purpose of the trial and give a detailed account of the nature of interventions and procedures to be employed, as well as any risks involved. The latter include possible effects of drugs, medical devices or any changes to existing therapies, as well as the interventions to be used in assessing these effects.

Where applicable, it should be stated that interventions will be randomly assigned and that participants may receive inactive or unproven interventions. Special care should be taken with vulnerable participants, such as those with incurable diseases, who may be particularly disposed to try new therapies, as well as those with whom communication is difficult. Potential participants should be informed about available alternative treatments and advised that they may discontinue participation in the study at any time without prejudice to their ongoing medical treatment.

The HREC should also consider the ongoing availability of a drug that is proposed for incorporation in a clinical trial. It would be reasonable for the HREC to seek assurances from the sponsor that, in the absence of observation of detrimental side effects or of inefficacy, the drug will remain available until the trial is completed.

Details should also be provided about:

- compensation and treatment available in the event of trial-related injury to the participant;
- issues of confidentiality;
- contact details in case of emergency; and
- the name of an independent person with whom concerns about the study could be discussed.
12.2(d) (iv)
It should be clear to an HREC precisely what the amounts and frequency of dosages of the drug will be, and the kinds and frequency of tests or monitoring involving hospital or clinic attendance that will be required.

Dosages of unmarketed drugs should be based upon pre-clinical and early phase clinical trial data. Care should be taken to ensure that these are consistent with earlier studies. Often, the duration of therapy is much longer in later phase studies than in earlier ones. If the proposed treatment period is significantly longer than those for which data exist, interim safety reports will be necessary and should be built into the study design.

12.2(d)(v)
A justification of the proposed sample size, based on the primary endpoint of the study, should be provided. Details should be given about expected clinically important differences between the test and control therapies and the expected variability of the outcome variables. Calculations of the required sample size based on such information are referred to as ‘power calculations’. The sample size required for the conduct of any comparative study is directly proportional to the ‘power’ of the study and the natural variation in the outcome of interest in the population, and inversely proportional to the size of the difference the researcher wishes to detect.

An ethics committee should be satisfied, usually on the basis of expert opinion, that a clinical trial design indicates that the trial can reliably show a reasonable comparative benefit in relation to the new drug or device simply because sufficient participants are to be studied.

12.2(e)
HRECs need to receive competent advice about the scientific details of a proposed project. This includes all of the items listed in NS 12.2(d), that is, the protocol, study design, inclusion and exclusion criteria, endpoints and outcome measures, sample size, dosages and duration of therapy, and methods for analysing results. When seeking advice from non-members, an HREC should ensure that confidentiality about all aspects of the proposal is preserved and that the intellectual property of the sponsor is not jeopardised (see also NS 2.19–2.20 on the avoidance of conflicts of interest).

12.2(f)

NS 12.3
An HREC, before granting approval to a clinical trial, must be satisfied that the protocol conforms to:
(a) this Statement;
(b) the World Medical Association Declaration of Helsinki;
(c) where relevant, the CPMP/ICH Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95) and the ISO 14155 Clinical Investigation of Medical Devices and the requirements of the TGA; and
(d) any requirements of relevant Commonwealth or State/Territory laws.
This paragraph is regarded as sufficiently clear, and so no commentary has been added.

The Declaration of Helsinki is available at http://www.wma.net/e/approvedhelsinki.htm.

**NS 12.4**

The use of a placebo alone or the incorporation of a non-treatment control group is ethically unacceptable in a controlled trial where:

(a) other available treatment has already been clearly shown to be effective; and

(b) there is risk of significant harm in the absence of treatment.

If there is genuine uncertainty about the net clinical benefit of treatment, a placebo controlled trial or a trial with a no-treatment arm may be considered.

If it is considered appropriate to include a placebo group in a trial, some additional considerations may arise as the trial progresses. Participants receiving placebo treatment may drop out of the study because it is not effective, thereby diminishing the apparent effectiveness of the test treatment. On the other hand, participants may drop out of the test group because of adverse effects, thereby reducing the apparent difference in adverse effects between test and control treatments. Studies should be scrutinised carefully to ensure that these questions have been adequately addressed. An HREC may need to seek expert advice in order to assess the validity of a study design. The requirements that are specified by the HREC for follow-up of the project should also take account of these factors.

Sometimes the study design involves withdrawal of current therapy with a placebo ‘run-in period’ followed by random allocation of participants to active drug or placebo. In this situation, the duration of placebo therapy and the frequency with which participants are followed up to ensure that adverse effects are not occurring are major issues. An example of potentially risky circumstances resulting from this approach might be some hypertension studies where cessation of therapy may result in a participant’s blood pressure rising to unacceptable levels. HREC members should ask whether cessation or withdrawal of usual and effective therapy in order to test the proposed intervention is justifiable and safe.

There is continuing debate over the scientific and ethical justifications for the use of placebos in pharmaceutical drug trials and over the position reflected in this paragraph and in clause 29 of the Declaration of Helsinki,22 http://www.wma.net/e/approvedhelsinki.html.

**NS 12.5**

A researcher must inform an HREC of any business or other similar association which may exist between a researcher and the supplier of a drug or surgical or other device to be used in the trial.

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22 The Declaration of Helsinki was amended in October 2000. Where there are differences between the Declaration of Helsinki and the National Statement, conformity with the National Statement, in particular 12.4, will presently satisfy all requirements.
A business association between a researcher and a sponsor or supplier of a product, could affect the researcher’s objectivity in determining whether a participant should be enrolled in a trial. Associations may include a direct financial interest, such as shareholdings, or prior associations, such as consultancies. For trials where the researcher is also the sponsor of the product, it is important that the HREC considers the potential for future commercial gain for the researcher or sponsor, such as the possibility of patents or royalties from future commercialisation.

**NS 12.6**

An HREC must examine those aspects of the budgets of clinical trials which raise ethical issues, including capitation fees, payments to researchers, institutions or organisations involved in the research, current and consequential institutional or organisational costs and costs which may be incurred by participants. It should be satisfied that:

(a) payment in money or kind would not cause researchers to apply pressure to individuals so as to obtain their consent to participate;

(b) payment in money or kind could not influence the findings of the research;

(c) there will be disclosure to the research participants of relevant aspects of those budgets; and

(d) funding is sufficient to conduct and complete the trial so that participants are not disadvantaged by premature cessation.

**12.6(a)-(d)**

HRECs should identify specifically the proposed arrangements for payments to researchers. Capitation payments, that is, payments tied to the number of participants recruited, should be carefully considered.

It is essential that payment in money, or kind, does not influence the findings of the research in any way. For example, it would be inappropriate for payment to be related to the outcomes of the study, or that results would be published only if positive in favour of the experimental drug.

Decisions about what information to disclose to prospective participants should be taken with care. The responsibility of HRECs to guard the rights and welfare of participants coupled with the risk of conflict of interests should be the justification for deciding that disclosure should take place. Accordingly, where financial or business arrangements exist but have been structured so that they are unrelated to the conduct of the research, there may be less justification for insisting on disclosure. A typical example of justified disclosure would be the personal financial rewards being received by researchers related directly to the number of participants recruited (the situation referred to in paragraph 12.6(a)). Knowing the arrangements before deciding whether to participate or not will largely prevent subsequent questioning about the soundness of the consent process.

**Resource requirements and duality of interest**

It is important that studies are adequately resourced so that they can be completed appropriately. Information provided to the HREC should include details of any proposed payments to volunteers, costs to the host institution and financial or other rewards being
offered to researchers. The committee will need to assess whether the researcher has access to adequate numbers of qualified staff, as well as adequate facilities, for the projected duration of the trial. This should include an assessment of the ability of the institution or organisation to provide adequate medical care to participants if any adverse events result from the conduct of the trial.

**NS 12.7**

An HREC must be satisfied, before approving a clinical trial, that arrangements exist to ensure adequate compensation to participants for any injury suffered as a result of participation in the trial.

HRECs should arrange for indemnity statements to be assessed to verify that they adequately protect the interests of the participants as well as those of the institution where the study is to be conducted. A standard indemnity agreement has been developed by the Australian Pharmaceutical Manufacturers’ Association. HRECs need to be satisfied that the scope of this indemnity is adequate. The terms of the indemnity and the extent of any compensation that might be available in the event of injury should be explained to prospective participants. Ethics committee members should be familiar with the contents of the NHMRC Report on Compensation, Insurance and Indemnity Arrangements for Institutional Ethics Committees.\(^{23}\) http://www.nhmrc.gov.au/publications/synopses/e25syn.htm

Because of concerns about legal liability arising from the approval of clinical trials, it is essential that relationships involving sponsors, researchers and organisations be clearly defined by legal agreements. Such agreements will need to cover responsibilities for compensation and treatment in the case of injury or death, as well as for any insurance or indemnity to cover the liability of each of the parties involved. HRECs may need to seek clarification of legal agreements that exist between sponsor and researcher. This will be important where the investigator is also the sponsor. Here, the source of adequate indemnity may be an extension of existing professional indemnity insurance or a fresh contract set up for the project.

**NS 12.8**

An institution or organisation and its HREC must require the researcher:

(a) to conduct the trial in compliance with the approved protocol;

(b) to provide reports of the progress of the trial to the HREC at a frequency directed by the HREC that is related to the degree of risk to participants, but at least annually;

(c) to inform the HREC of, and seek its approval of, amendments to the protocol including any:

(i) proposed or undertaken in order to eliminate immediate hazards to participants;

(ii) that may increase the risks to participants; or

(iii) that significantly affect the conduct of the trial;

(d) to inform the HREC and the TGA of all serious or unexpected adverse events that occur during the trial and may affect the conduct of the trial or the safety of the participants or their willingness to continue participation in the trial;

(e) to inform the HREC as soon as possible of any new information from other published or unpublished studies which may have an impact on the continued ethical acceptability of the trial or which may indicate the need for amendments to the trial protocol;

(f) to inform the HREC, giving reasons, if the trial is discontinued before the expected date of completion; and

(g) in relation to trials with implantable medical devices, to confirm the existence of or establish a system for tracking the participant, with consent, for the lifetime of the device, and to report any device incidents to the TGA.

12.8(b)

An HREC should be aware of other processes within the trial for such reports and use these so as to reduce duplication. A comprehensive report of the outcomes of the trial, of their correspondence or otherwise with the initial aims and of any deviations from the approved protocol should be provided promptly to the HREC when the trial is completed.

12.8(c)

It is in the nature of large clinical trials that events occur prompting changes of the protocol. Many of these changes are administrative, but some can directly affect participants.

HRECs need to establish procedures to assess these changes and determine whether their approval requires a full meeting of the HREC or, in cases where they can be regarded as of minimal risk, by some other arrangement. HRECs may need to decide whether these reports indicate that changes should be made to participant information sheets or consent forms.

12.8(d)

A ‘serious adverse event’ is defined in Appendix 3 to the National Statement. An event should be considered ‘unexpected’ if it is not documented in the current Australian Product Information in the case of a marketed drug, or in the investigator’s brochure for unregistered drugs.

Every serious and unexpected event occurring in relation to a trial should be reported to all HRECs from which approval for the conduct of the study was obtained. Where such an event occurs at the institution at which the HREC is located, the event should be considered in detail within the context of both the treatment/intervention and the underlying disease process for that participant. In some situations, such as studies involving terminal illness, the outcome may be clearly disease-related. In other situations, the possibility of a treatment/intervention-related event should be examined. Where this seems likely, the need for further action should be carefully considered. Such action could include changing the conditions of the study, requiring an addition to the participant information statement, or withdrawing support for the continuation of the study.
Adverse effects reported in early-phase development of a drug need to be scrutinised with particular care. The number of participants exposed to the drug should be noted, as well as the duration of the exposure. Frequently, Phase II-III trials involve much longer exposures than early-phase studies and this should be taken into account in weighing up the safety of a trial. Similarly, the dosage range in early-phase studies should be analysed in comparison with that proposed in the study under consideration. Sometimes higher doses may be used than in earlier studies in an attempt to identify doses that are optimal.

12.8(e)

Researchers need to recognise that they are to report if any new information from other published, or unpublished, studies becomes available that may have an impact on the ethical acceptability of the trial, or indicate the need for amendments to the protocol. For example, following the commencement of a study, evidence may become available from other studies of previously unexpected adverse effects. In this situation, the researchers should advise the HREC and explain the implications, if any, of this information for their own project.

12.8(f)

If the trial is prematurely terminated, an HREC should ensure that adequate and accurate information about the reasons for this, and any consequences, will be provided to participants. When entry into a trial, which is subsequently terminated prematurely, has entailed changes in the pre-existing clinical management of participants, the HREC must ensure that the researcher and trial sponsor can provide for the resumption of earlier management procedures.

12.8(g)

In the case of implantable medical devices, research participants need to be protected beyond the end of the trial. Researchers should establish a system for tracking participants for the lifetime of devices to detect any relevant adverse events and to enable remedial action if a significant defect is identified.

NS 12.9

The institution or organisation and its HREC must determine the type and frequency of review appropriate to the drug or device being investigated and to the degree of risk to participants provided that the review occurs at least once a year.

HRECs and institutions are responsible for monitoring the progress and conduct of trials that HRECs approve. In addition, a committee has a responsibility to withdraw approval of a clinical trial if that committee becomes aware of a serious risk to participant safety, a breach of good clinical practice, or a breach of Australian regulatory requirements. (See NS 2.44.) If a committee is not confident about its ability to monitor a particular trial, it may appoint a monitor who is independent of both the researcher and the sponsor.

However, an HREC may review, or commission a review of, the progress of a clinical trial at any time. Additional monitoring mechanisms available to HRECs include random inspections of research sites, case record forms and signed consent forms, as well as interviewing research participants (with prior consent). The range of issues raised by, and the requirements associated with, the monitoring of research projects in general are discussed in this Handbook at NS 2.33–2.38 and in the Research Ethics Collection.
‘Monitoring Research’, page E109. Advice and assistance about monitoring of clinical trials can be obtained from the Therapeutic Goods Administration.

HRECs should know of processes for monitoring safety included in a clinical trial design. This commonly takes the form of a Data and Safety Monitoring Board, which is usually independent of both the researchers and the sponsors of the study. The Board commonly has regular access to ‘unblinded’ study data and the authority to stop the study if data become available that suggest it is unsafe to continue, or if ‘stopping rules’ about benefit or adverse effects of the drug are met.

**NS 12.10**

It may be unethical for a researcher to continue a trial if:

(a) there are or have been substantial deviations from the trial protocol;
(b) side effects of unexpected type, severity, or frequency are encountered; or
(c) as the trial progresses, one of several treatments or procedures being compared proves to be so much better, or worse, than other(s) that continuation of the trial would disadvantage some of the participants.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**NS 12.11**

In a clinical trial, data must be accurately recorded in a durable and appropriately referenced form and:

(a) data management should comply with relevant privacy requirements, including the Standards Australia Personal Privacy Protection in Health Care Information Systems (AS4400-1995);
(b) if data are of a confidential nature, confidentiality must be observed;
(c) data and records must be preserved for such periods and in such manner as prescribed by laws of the Commonwealth, the relevant State or Territory or national policies or guidelines; and
(d) where materials of biological origin are being used in a trial, records should be preserved for such periods as will enable participants to be traced in the event that evidence of late or long-term effects emerge.

12.11(b)

To ensure proper conduct of the clinical trial, drug companies may require access to participants’ medical records. Prospective participants in a clinical trial should be advised of the possibility of this. The primary researcher should assume responsibility for supervising such access and for promptly re-establishing contact with participants if information that is potentially important for their health becomes available.
NS 12.12

In trials of therapeutic goods, including pharmaceuticals and biological substances, the HREC must follow the requirements of the TGA and the CPMP/ICH Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95).

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

NS 12.13

In medical device trials, the HREC and the researcher must follow the requirements of the TGA (Australian Device Requirement Version 4, DR4, May 1998) and the ISO 14155 Clinical Investigation of Medical Devices on Human Subjects.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

Points to consider NS 12.1-12.13

- Does the study fall within the Clinical Trial Notification (CTN) or Clinical Trial Exemption (CTX) Schemes? If the former, has all the relevant documentation been provided? If the latter, has the Therapeutic Goods Administration provided a report allowing the HREC to carry out its own assessment?
- Is the HREC satisfied that the trial proposed as a CTN should proceed as a CTN trial?
- What is known from previous studies about the safety and efficacy of the proposed intervention? What further information is required? How should potential risks and benefits be assessed and what relative weight should be given to each?
- Is the design of the study appropriate to the study's aims and objectives? Is the study likely to provide an answer to the questions being asked? Is the inclusion of a placebo arm justified in view of what is known about existing therapies? Are doses and durations of therapy consistent with those used in previous applications of the drug? Is expert review of the study design required?
- Does the protocol include a clear statement of the number of participants to be enrolled in the study and the proposed method of recruitment and selection of participants? Are the inclusion and exclusion criteria appropriate to the aims of the study?
- Do pre-clinical and clinical data indicate that the risks associated with the proposed use of the drug or device are acceptable? Has an expert opinion on the safety aspects of the drug and its pharmacology been obtained? What procedures are proposed for monitoring safety? What are the criteria according to which the trial is to be stopped in the event of new data regarding safety or efficacy becoming available? Is there a need for an independent Data and Safety Monitoring Board?
- How is consent to be obtained? Have special provisions been made for the protection of vulnerable groups or individuals? Does the participant information statement explain in sufficient detail, and with sufficient clarity, the existing knowledge about the drug or device and the risks posed by its use within the
context of the study? Will participants be adequately informed about the implications for existing treatments that they might be receiving?

• Is an indemnity statement provided? Are participants to be advised about the terms of this indemnity?

• Are there any resource issues that may affect the conduct of the trial or its outcomes? Do researchers face potential conflicts of interest that should be disclosed?

• What reports are to be provided to the HREC regarding the conduct of the trial and any adverse effects that might arise in connection with it?

• Are the financial arrangements between the drug company and the researcher likely to lead to a conflict between the responsibilities of the clinician and that of the researcher? Have such arrangements been appropriately acknowledged to potential participants? Are any other clinical values likely to be compromised?

• Does the proposed study have sufficient scientific merit to justify the contributions of both researchers and participants? Will the researchers be free to pursue publication after the completion of the study?
13. INNOVATIVE THERAPY OR INTERVENTION

Clinical research is defined in the Declaration of Helsinki as ‘medical research combined with professional care’. This can occur in a number of settings, including public and private hospitals and clinics, other institutions or organisations, community settings, and in general or specialist medical practices.

Clinical research must conform to the requirements of this Statement.

Innovations in clinical practice include the wide range of new diagnostic or therapeutic methods which are aimed at improving health outcomes beyond those of existing methods, but which have not yet been fully assessed for safety and/or efficacy. The spectrum of innovations ranges widely from minor variations of existing methods, or extension of existing methods to new indications, through to completely novel technologies. Whether a change in an individual’s investigation or treatment represents such an innovation or whether it constitutes clinical research is a matter for the responsible clinician’s judgement.

At the stage at which a specific form of innovative therapy becomes subject to systematic investigation to determine its efficacy and safety in order to decide whether its introduction should be recommended, it should be treated as clinical research requiring formal consideration by a Human Research Ethics Committee.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.
14. EPIDEMIOLOGICAL RESEARCH

Epidemiological research is concerned with the description of health and welfare in populations through the collection of data related to health and the frequency, distribution and determinants of disease in populations, with the goal of improving health. Some epidemiological research may require whole of population studies and be beyond an individual institution or organisation.

Epidemiological research is part of wider public health and health services research concerned with improvements of health and welfare in human populations and with improving the efficiency and performance of human health services. Public health and health services research are usually or often carried out with human participants, or data or biological samples from them, and provide important new knowledge that is not readily obtainable in other ways.

Public health surveillance should be distinguished from public health and epidemiological research. Its role is to monitor the health status of the community, known risk factors and emerging threats to community health. Its purpose is to facilitate a prompt, effective and corrective response. It may be carried out for reasons of disease surveillance, provision of information to government health services or to inform the development of health policy. Public health agencies generally are required or authorised by law to conduct health surveillance.

In epidemiological research, medically relevant information about individuals and groups is accumulated so those features of groups of persons may be investigated whether the information was or was not originally obtained for research purposes.

CATEGORIES OF PERSONAL INFORMATION

Epidemiological research includes the use of the following types of data:

Identified

Data that allow the identification of a specific individual are referred to as ‘identified data’. Examples of identifiers may include the individual’s name, date of birth or address. In particularly small sets of data even information such as a postcode may be an identifier.

Potentially identifiable (coded, re-identifiable)

Data may have identifiers removed and replaced by a code. In such cases it is possible to use the code to re-identify the person to whom the data relate so that the process of de-identification is reversible. In these cases the data are referred to as ‘potentially identifiable’.

De-identified (not re-identifiable, anonymous)

The process of de-identification can be irreversible if the identifiers have been removed permanently or if the data have never been identified. These data are referred to as ‘de-identified’. It should be recognised that the term ‘de-identified’ is used frequently, in documents other than this Statement, to refer to sets of data from which only names have been removed. Such data may remain ‘potentially identifiable’.
Epidemiological studies may require participants to fill in questionnaires or undergo a medical examination or laboratory tests, or they may simply require the examination of medical records.

Reference could be made to the Research Ethics Collection, ‘Epidemiology research’ page E39 for a discussion of the issues.

**NS 14.1**

All epidemiological research must be approved by a Human Research Ethics Committee (HREC) and should be conducted according to written protocols that state the aims of the study, the data needed and the way in which the data will be collected, used and protected.

HRECs need to establish precisely what data are to be collected and used, whether they will be identifiable, potentially identifiable or de-identified and how they will be collected, used and stored.24

**NS 14.2**

When an HREC considers a protocol for epidemiological research it must be satisfied that:

(a) the research complies with any relevant Commonwealth and State/Territory legislation or policies dealing with the privacy and confidentiality of data held by Government authorities;

(b) researchers have the necessary skills in epidemiology and facilities for the research;

(c) access to medical or other records for research should be restricted to properly qualified researchers and research associates responsible to them; and

(d) there is a scientifically acceptable process for the disclosure of information and communication of research results and, where there is to be selective disclosure of information, that there are scientifically justifiable reasons for so doing.

14.2(a)

The relevant Commonwealth legislation is the Privacy Act 1988 (Cth). Guidelines for the use and disclosure of Commonwealth information are ‘Guidelines under Section 95 of the Privacy Act 1988 (Cth).


See also NS 18.1–18.5.

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14.2(b)
HRECs should assess the qualifications of the researcher in relation to the type of study to be conducted, the research population involved, the methodology to be used and the supervisory or support resources to be made available to the researcher.

14.2(c)
This is a major area of ethical concern in epidemiological research. Such research may involve collecting and storing data relating to individuals and groups. Such data, if disclosed to third parties, may result in harm or distress for the participant/s. Consequently, researchers should make arrangements for protecting the confidentiality of such data by omitting information that might lead to the identification of individual participants, or limiting access to data by other means.

One means of minimising the risks to privacy and confidentiality is to confine access to personal information only to those whose access is essential to the research. HRECs need to be satisfied that such restrictions exist and will be effective.

Identifiable data should not be used when a study can be carried out without personal identification of participants. When personal identifiers remain on records used for a particular study, researchers should explain to the HREC why this is necessary and how confidentiality will be protected. Further discussion can be found in the Research Law Collection on ‘Privacy’, page L43 and ‘Confidentiality’, page L7.

NS 14.3

Consent of participants should generally be obtained for the use of identified or potentially identifiable data for epidemiological research.

HRECs need to be alert to the correct classification of the data in each research proposal so they can be satisfied that consent will be sought for use of identified or potentially identifiable data.

NS 14.4

An HREC may approve access to identified or potentially identifiable data without consent of those the data identifies where the HREC is satisfied that:

(a) either

the procedures required to obtain consent are likely either to cause unnecessary anxiety for those whose consent would be sought or to prejudice the scientific value of the research and there will be no disadvantage to the participants or their relatives or to any collectivity involved

or

it is impossible in practice, due to the quantity, age or accessibility of the records to be studied, to obtain consent;

AND

25 ibid. At vol. 24.17.
(b) the public interest in the research outweighs to a substantial degree the public interest in privacy.

A researcher who proposes not to seek informed consent has an obligation to provide the HREC with adequate justification for this decision, as well as an explanation of how the study could still be considered ethical in the absence of such informed consent.

An example of a situation involving ‘unnecessary anxiety’ might be the effect on a person of consent being sought for access to information in order to conduct research on risk factors for a serious illness. The person may be a member of a population relevant to the research because of age, geography, demography, gender or a range of socioeconomic factors. The effect of disclosing the disease that is the focus of the research may be to cause the kind of anxiety referred to. Even if the research does disclose information of clinical relevance, paragraph 14.13 is designed to address the protection of such persons.

The expression ‘disadvantage’ should be given a broad meaning.

An example of a situation where seeking consent could prejudice the scientific validity of the research might be where disclosing relevant information may result in changes to participant behaviour that the study proposes to examine.

An example of a situation of impossibility in practice might be where there has been a significant increase in medical practitioner reports of a side-effect from a particular drug. The Government organisation responsible may decide to release this information to researchers so that the cause of the increase can be identified. However, in order to do this the researchers would need to compare the above-mentioned reports with the medical records of individuals who had taken the drug but had not developed the side effect. This would necessarily involve the examination of thousands of medical records. Therefore, it would be impossible to obtain consent from each individual before accessing their record.

See also ‘Guidelines under Section 95 of the Privacy Act 1988 (Cth).’

NS 14.5

Where an HREC approves the use of potentially identifiable data that has been coded, the HREC should decide whether an independent person should hold the code.

HRECs will need to assess what constitutes an ‘independent person’ in order to protect the privacy of participants.

NS 14.6

Where the research involves a collectivity, the HREC should be satisfied that the requirements of 8. ‘Research involving collectivities’ have been fulfilled.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.
NS 14.7

Where identified or potentially identifiable data are used in the research, an HREC must be satisfied that the information:

(a) will be collected, dealt with and stored in accordance with the Information Privacy Principles of the Privacy Act 1988 (Cth) (see Appendix 2) and the Standards Australia Personal Privacy Protection in Health Care Information Systems (AS4400-1995); and

(b) will not be used so as to cause material, emotional or other disadvantage to any participant; and

(c) will not be used for any purposes other than those specified in the approved protocol.

HRECs need to:

• clearly understand how the personal information is to be used in the research, and that its use will not harm participants; and

• be satisfied that controls are in place to confine its use to the research.

The Privacy Act 1988 (Cth) is available at http://scaleplus.law.gov.au

NS 14.8

Where research involves linkage of data sets, an HREC may approve the use of identifiers to ensure that the linkage is accurate, but once linkage has been completed the HREC should require that the resulting data be coded or de-identified.

Some epidemiological research involves linking sets of data about individuals. Once the sets are linked so that individual data are matched, the research can often proceed without the need for identifying data. Accordingly, the conversion to coded or de-identified forms at that time will not obstruct the research and will better protect participants.

NS 14.9

If identified or potentially identifiable data are to be used for any research purposes or by any persons other than those specified in the approved protocol, a new protocol must be presented to an HREC for approval.

Epidemiological research projects frequently accumulate data that can be used for different purposes or be subjected to analysis for correlation of different factors, either by the same researchers or by others. Every such new use or analysis is a research proposal to be reviewed by an HREC before proceeding.
**NS 14.10**

Information arising from both long and short-term epidemiological research must be securely stored.

Epidemiological research will often accumulate quantities of personal information in electronic, sound, print or other forms. HRECs need to be satisfied that appropriate and secure storage arrangements will be provided. The duration for which the data need to be stored may affect the form that is used.

**NS 14.11**

When consolidating data for statistical analysis and the preparation of results, researchers must preserve the confidentiality of information about participants.

HRECs need to understand the processes to be used when individual data are aggregated either for statistical analysis or the presentation of results of the research. They need to be satisfied that confidentiality of personal information is protected.

**NS 14.12**

Results of research must not be published in a form that permits identification of individual participants and must be published in a form which gives due regard to cultural or other sensitivities.

HRECs need to understand clearly how the results of the research will be published.

Both researchers and ethics committees should be aware that some studies can involve a risk of harm for participants in indirect ways. For example, when scarce health care personnel are taken from routine duties in order to meet the needs of a study, or when, unknown to a community, health care priorities are changed. Other instances of harm include the effects of damaging publicity, disruption of social mores, and insensitivity to specific cultural values when researchers are investigating cultures other than their own.

HREC review should also include assessment of the risks for participants or groups already suffering from stigmatisation, prejudice, loss of prestige or self-esteem, or economic disadvantage. Researchers should inform the ethics committee and potential participants of any such risks, as well as the strategies devised to prevent or minimise these. Researchers should be able to demonstrate that the benefits of the study outweigh the risks for both individuals and groups.
**NS 14.13**

If in the course of epidemiological research new knowledge of clinical relevance is obtained, or existing treatment is thought to need alteration, that knowledge should be disclosed to the appropriate health authorities and, wherever possible, participants and their usual medical attendants should be informed.

Part of the benefit that communities, groups and individuals may reasonably expect from epidemiological studies is that they will be told about findings relevant to their health and welfare. Where findings could be applied to public health measures, communication to the relevant health authorities would be appropriate. Research proposals should include provision for communicating findings to communities and individuals.

HRECs should be aware that it may not always be possible to inform individual participants about research findings. Where this is so, potential participants should be advised. For example, it may not always be possible to extract information about individuals and their families from pooled findings. In this situation, when findings indicate a need for health care, all participants should be advised to obtain an individual diagnosis and individual advice.

When data are unlinked, and participants therefore cannot be advised as above, researchers should provide the communities involved with the relevant health care advice, with appropriate protections for individual privacy.

**Points to consider NS 14.1–14.13**

- Does the research proposal comply with relevant Federal and State or Territory legislation and policies dealing with confidentiality of data held by government authorities?
- Is access to medical or other records restricted to appropriately qualified researchers and their research associates?
- Are data securely stored?
- If access to identified, or potentially identifiable, data without the consent of the people concerned is to be approved, is this decision justifiable in terms of the exceptions allowed by the National Statement?
- Are there adequate plans in the research proposal to protect participants from risks of breach of confidentiality and invasion of privacy?
- If there are burdens of privacy invasion involved in the research, are these ethically acceptable?
- Are there alternative, less intrusive, methods of carrying out this research project?
15. USE OF HUMAN TISSUE SAMPLES

Samples of tissue, including blood and other body fluids, are collected from persons in hospitals and other health care institutions in a variety of circumstances. Samples collected for diagnostic purposes in the course of treatment may also be used for teaching or quality assurance activities and for research. Directors of Pathology have traditionally exercised, and should continue to exercise, discretion in the use of clinical samples in the interpretation and development of laboratory procedures. After the original purpose for which samples were collected has been achieved, the residual tissue may be discarded. Hospitals and pathology laboratories are required by law to retain archival samples for diagnostic or forensic purposes. Accordingly, most hospitals have collections of stored samples, the use of which in research may lead to important advances in the understanding and treatment of disease.

The principles of ethical conduct and review described in 1. 'Principles of ethical conduct', and 2. 'Human Research Ethics Committees' of this Statement should govern all such research.

This Statement refers to such tissue samples as are referred to above but excludes fetal tissue, reproductive tissue and tissue from autopsy to which additional guidelines or legislation may apply.

Where human tissue is to be used in any research, researchers and Human Research Ethics Committees (HRECs) need to be satisfied that the research proposal conforms to the guidelines below. The additional ethical issues that arise in genetic research that uses human tissue need to be addressed in conformity with 16. 'Human Genetic Research'.

Appendix 3 to the National Statement defines 'human tissue' as including the substance, structure, and texture of which the human body or any part or organ of it is composed that is removed or separated from living human beings. This also includes blood, blood components and waste products.

RESPECT FOR PERSONS

NS 15.1

The fundamental ethical principle to be observed in the use of human tissue samples for research is respect for the person and this is reflected in:

(a) the provision to the donor of full information about the purposes of the sampling, and/or the plan of the research proposal;
(b) consent by the donor to the use of the sample;
(c) the professional removal of samples to be used;
(d) provision for appropriate and secure storage of tissue samples;
(e) provision and maintenance of appropriate and secure systems to ensure confidentiality and privacy in the recording, storage and release of data; and
(f) accountability in the care and usage of such samples.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**NS 15.2**

It is important for institutions or organisations in conjunction with their HRECs to determine when consent should be sought for the use of tissue in research or when a waiver of the requirement for consent may be considered.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**INSTITUTIONAL RESPONSIBILITY**

**NS 15.3**

Institutions or organisations at which research involving the use of human tissue samples is conducted, should develop policies about the conduct and ethical approval of such research which conform to relevant legislation and are consistent with this Statement. Those policies need to provide guidance to researchers and HRECs in relation to soliciting or accepting voluntary donations of, and specifying conditions for, the use of human tissue samples in research. In their development, relevant considerations include:

(a) the source, nature and cultural or religious sensitivity of the sample;
(b) the original reason for its collection; and
(c) the purpose of the research.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**WHERE CONSENT WOULD BE REQUIRED**

**NS 15.4**

Where human tissue samples are collected for purposes including research, consent for their use in research is generally required.
Except where the requirement for consent is waived by a Human Research Ethics Committee (HREC) under Paragraph 15.8, persons who have tissue removed from them should be given the opportunity to agree or object to their tissue being used in research, or even to opt for its disposal.

For more information on statutory provisions relating to donation, see the Research Ethics Collection page E89 and the Research Law Collection page L35.

**NS 15.5**

Consent should:

(a) be voluntary; and

(b) be specific to the purpose for which the tissue is to be used; and

(c) follow the provision of full information about the project, including advice as to whether, after completion of the research for which consent is given, tissue samples are to be stored.

**15.5(b)**

This is an important element of the way that consent in this type of research is expressed. HRECs need to be satisfied that there is sufficient detail about the purpose of the research for which the tissue is sought.

**15.5(c)**

HRECs should be satisfied that those responsible for obtaining consent provide potential donors, or authorised third parties, with full information about:

- the purpose(s) of the research;
- the type and amount of tissue to be taken, as well as the (bodily) location that the tissue is to be taken from;
- the manner in which tissue will be taken and the safety and invasiveness of acquisition;
- the duration and conditions of preservation of the tissue;
- the potential uses for the tissue, including any commercial uses;
- the safeguards in place to ensure protection of the donor's, and the donor's family's, privacy and confidentiality;
- identifying information to be attached to the tissue and whether it will render the donor of the tissue potentially identifiable;
- how use of the tissue could affect the donor's privacy; and
- what will happen to any remaining tissue when the research has been completed.

**NS 15.6**

Where it is proposed that human tissue samples previously collected and stored with consent for research be used for a research purpose different from that of the previously approved research, consent for the use of the tissue samples in the new
research should generally be obtained. An HREC may waive the requirement for consent in conformity with paragraph 15.8.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**NS 15.7**

Where it is proposed to use tissue samples which have been:

- obtained for or held in storage following, or in association with, clinical investigations;
- held in archives or banks; or
- removed in the course of a clinical procedure and not required for any clinical purpose, in research that may be lead to harm, benefit or injustice to a donor of such tissue, consent of those donors should normally be obtained.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**WHERE THE REQUIREMENT FOR CONSENT COULD BE WAIVED**

**NS 15.8**

An HREC may sometimes waive, with or without conditions, the requirement for consent. In determining whether consent may be waived or waived subject to conditions, an HREC may take into account:

- the nature of any existing consent relating to the collection and storage of the sample;
- the justification presented for seeking waiver of consent including the extent to which it is impossible or difficult or intrusive to obtain specific consent;
- the proposed arrangements to protect privacy including the extent to which it is possible to de-identify the sample;
- the extent to which the proposed research poses a risk to the privacy or wellbeing of the individual;
- whether the research proposal is an extension of, or closely related to, a previously approved research project;
- the possibility of commercial exploitation of derivatives of the sample; and
- relevant statutory provisions.
CONFIDENTIALITY

NS 15.9

Wherever human tissue samples or related information are gathered in the course of a professional relationship, professional confidentiality must be observed. Identification of samples must be limited to the minimum necessary to achieve the stated objectives of the study. If the study may produce information relevant to the health and well being of the person from which it was derived, the HREC may require procedures to allow participants to be identified to facilitate appropriate follow-up.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

Points to consider NS 15.1-15.9

- Does the research have a therapeutic intention that justifies collecting tissue in a way that may otherwise be considered lacking in respect for the integrity of the human body, living or dead?
- Is the tissue ‘previously collected’ or is it to be collected for the purposes of the proposed research?
- Is the consent of individual providers required? What arrangements are proposed for obtaining consent? Are they appropriate in the circumstances of the tissue collection and the proposed research?
- If the tissue for research is identifiable or potentially traceable to the tissue donor, has the researcher provided protocols for ensuring that the privacy and confidentiality of tissue providers will be protected?
- Does the research have the potential to reveal information about future health risks for the tissue donor or her or his family? Has the researcher provided a protocol for informing tissue providers and/or their families of research results?
16. HUMAN GENETIC RESEARCH

Genetic research enhances our understanding of how genes and environmental factors interact to influence the health of individuals and populations and in doing so, generates knowledge with the potential to improve individual and community health.

Genetic research can reveal information about an individual’s susceptibility to disease and hence about the individual’s future health. Such information may be of interest and benefit to research participants, especially if preventive strategies exist.

In addition to ethical considerations which apply to all research involving humans there are ethical issues unique to genetic research. These arise from the nature of genes and genetic information which, though personal, are also shared with other family members and with unrelated individuals in the population.

Participation of families rather than individuals is required for many genetic research studies. Research results and genetic material and information collected for research may be of significance to the health of blood relatives, including some who have not participated in the research. These family members may have an interest in their relative’s genetic material or in information which the research generates, because testing that material or acquiring that information may create new options for life decisions, including those with potential to improve health. However, some family members may prefer not to be given information which may provide knowledge of future health or health risks. In addition, other family members who are not blood relatives, such as partners and spouses, may have an interest because of concerns about the health of offspring.

There is potential for harm to participants arising from the use of genetic information, including stigmatisation or unfair discrimination, and researchers should recognise that special care must be taken to protect the privacy and confidentiality of this information. The results of genetic tests, particularly those which provide information about future health, could potentially be used by third parties such as insurance companies and employers to assist with decisions concerning research participants and their families. By participating in genetic research people should not be put at risk of being deprived of benefits that are available to other members of the community.

All genetic research is subject to the ethical considerations and constraints common to any other research involving human participants. However, there are some issues specific to genetic research. This is because genetic information is shared among blood relations and so may have implications for persons other than those participating in a research project. The results of genetic research may have implications for the future health of the individuals being studied and their descendants. It may also affect decisions concerning social relationships, reproduction, employment and insurance.
SOCIAL SIGNIFICANCE AND CONSEQUENCES OF GENETIC RESEARCH

NS 16.1

Researchers should consider the social and cultural significance of their research, particularly in the areas of complex socially significant characteristics and the genetic characteristics of collectivities. When such characteristics are the subject of research, Human Research Ethics Committees (HRECs) should satisfy themselves that no contestable or dubious ethical values are assumed by the research protocol.

An example of such might be studies of the genetic basis of complex socially significant characteristics such as intelligence, personality, sexuality or the genetic differences between population groups. These studies may have the potential to be applied in an adverse or discriminatory manner, so potentially negative consequences need to be carefully considered in relation to potential benefits.

NS 16.2

When assessing proposals of this type, HRECs should consider the balance between the contribution to knowledge and the potential for harm to individuals or collectivities.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

PRIVACY AND CONFIDENTIALITY

NS 16.3

Researchers must ensure the confidentiality and privacy of stored genetic information or research results relating to identified or potentially identifiable participants.

Reference should be made to the Guidelines for Genetic Registers and Associated Genetic Material, (NHMRC 1999).

NS 16.4

Researchers must keep information provided by participants about family members confidential. Such confidential information must not be revealed either to family members or persons who are not family members.
HRECs need to pay particular attention to the ways in which information is obtained and data stored. Researchers will often be provided with medical information about relatives of research participants that is of questionable accuracy or incomplete and, in relation to which, at the time the information is provided, the relatives will not have given consent.

Researchers need to ensure that information obtained under these circumstances is treated with great care and must take precautions to prevent its inappropriate dissemination.

**NS 16.5**

The research protocol must specify whether genetic information or genetic material, and any information derived from studying the genetic material, will be stored in identified, potentially identifiable (coded) or de-identified (not identifiable, anonymous) form. (See the introduction to 14. 'Epidemiological research'). Researchers should be aware that the rarity of some genetic disorders might allow certain families to be identified by other researchers, and in some cases by members of the community, even if information is communicated to others in de-identified form.

The decision made about the labelling of specimens, and its implications, should be presented to prospective participants when their consent is being sought.

HRECs should be aware that certain genetic material, such as that stored as a legal requirement or for potential clinical use in addition to research use, cannot be de-identified and must retain its identifiers. It may be possible to use part of the stored sample in coded or de-identified form for research, while retaining part in identified form for the primary purpose for which it has been stored.

**NS 16.6**

Researchers should consider carefully the consequences of storing information and material in de-identified form for the proposed research, for future research and for communication of research results to participants.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**NS 16.7**

Identifying genetic information must not be released to others, including family members, without the written consent of the individual to whom the information relates, or a person or institution which may legally provide consent for that person.
The family context in which genetic information is usually derived may suggest that another family member has a right to some information. However, where disclosing that information will identify another member, their consent should be sought.

Recognition of the principle is an important element in informing people before they decide whether or not to undertake a genetic test. Further discussion can be found in NS 16.10(e) and (g) and commentary and in Ethical Aspects of Human Genetic Testing: an Information Paper (NHMRC 2000).

**NS 16.8**

_**A researcher must not transfer genetic material and related information to another research group unless:**_

- the researcher and the other research group are collaborating on research which has been approved by an HREC; and
- the genetic material and information is provided in a form which ensures that participants cannot be identified. However, an HREC may approve transfer of genetic material and information which is identified, or potentially identifiable, in certain circumstances (eg. see paragraph 14.8). If this occurs, the other research group must undertake to hold the material and related information in such a manner that there is no reduction in the protection of the privacy of the participants or of the confidentiality of the information.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**CONSENT**

**NS 16.9**

_**Consent from participants (and/or other appropriate person or organisation as specified in guidelines 4, 5, 6, 7 and 8 of this Statement) must be obtained for human genetic research unless an HREC waives the requirement for consent (paragraph 16.13).**_

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**NS 16.10**

_When consent is being sought from individuals for prospective collection of genetic material and information they should be informed:_

(a) that they are free to refuse consent without giving reasons. Researchers should be aware that for some genetic research, an individual’s participation may be requested by, and may
primarily serve the interests of, other family members and the individual may agree to participate out of a sense of obligation;

(b) about arrangements to ensure the privacy and confidentiality of their genetic information both with regard to other family members and persons who are not family members. Participants should be informed whether their genetic material and information will be used in an identified, potentially identifiable, or de-identified form and, if their material or information is to be de-identified, that it will not be possible to provide them with personal research results;

(c) if the research may reveal information of potential importance to the future health of an identified or potentially identifiable participant or the participant's offspring;

(d) that the researchers will endeavour to provide information about the outcome of the research. Participants should be advised when it is not intended to provide feedback. If relevant, participants should be asked whether they wish to be notified of research results which relate to them as individuals. A decision not to be notified should be respected;

(e) that if the research generates information about participants which may be of relevance to the health of other family members, the consent of participants will be sought before offering to disclose such information to the family members concerned;

(f) if information about family members, in addition to that provided by participants, is required for the research;

(g) if it is proposed to approach relatives, consent to do so will first be obtained from the participant. In coming to a decision to recruit relatives, researchers must consider the privacy and any known sensitivities of the relatives, accepted habits of communication within the family, and the balance of potential benefits and harms which might result from participation in the research;

(h) if the research has the potential to detect non-paternity or non-maternity;

(i) that genetic material and information may have uses unrelated to HREC approved research. Participants should be advised that their material and information will not be released for other uses without consent, unless required by law;

(j) about any intention to store their genetic material and information because it could potentially be useful for as yet unspecified future research conducted in accordance with paragraphs 16.12 and 16.16 below. If consent is given, the duration of storage should be specified. If consent for future research use is refused, the genetic material and information should be disposed of at the end of the research, once the sample storage and record keeping requirements of good research practice have been met;

(k) if their genetic material is to be disposed of on completion of the research or after a further period of storage. Some
participants or collectivities will have sensitivities regarding disposal of their genetic material. These should be established and recorded at the start of the research and account taken of them at the time of disposal; and

(l) that they are free to withdraw from the research at any time. This may involve a request that their genetic material and information be disposed of, provided the samples can be identified. Alternatively samples and information may be retained provided they are de-identified, depending on the wishes of the participants.

16.10(a)
HRECs should recognise that some family members may feel that they should participate in a research project out of a sense of obligation to the rest of the family. Particular attention should be paid to this possibility if the research is burdensome or carries risks, such as the possibility of revealing information that might be predictive of future illness.

16.10(b)
This paragraph is regarded as sufficiently clear, and so no commentary has been added.

16.10(c)
Individual participants should be asked if they wish to be given information relevant to their health where research carried out using identified or coded genetic information and material could provide it. In addition, information relevant to their future health, or about any risk to the health of their children or descendants, should be provided in conjunction with counselling from genetic counsellors or health professionals.

When designing their research protocols, researchers should consider whether the research has the potential to reveal predictive genetic information about individuals or carrier status that will affect a participant’s chance of having affected children. Participants should be informed when these situations could arise, as they may be a significant factor in the decision whether or not to participate.


16.10(d)
It is essential that potential participants are aware at the time of giving consent and donating their genetic information and material that no feedback will be possible, and that consent is given on that basis.

16.10(e)
Where consent is given, the participant’s advice should be sought about the most appropriate method of communication with the family members. Researchers may not have the skills needed to discuss clinically relevant information with research participants or their families. Consideration should be given to forming a liaison with a clinical group that includes suitably trained counsellors who can undertake this task. The possibility that family members may not wish to know such information should be considered.
On occasions, a research participant may refuse permission to disclose his or her genetic information to family members. If this occurs in a situation where there may be a threat to the health of those family members, the researcher should consider whether the threat is serious enough to warrant disclosure without the participant’s consent. In these situations, researchers should seek the advice of an HREC before proceeding.

As a possible solution to this problem, an HREC may decide it best to exclude participants who indicate that they would withhold crucial information from family members.

16.10(f)
Genetic research often involves gathering information about a participant’s family members as well as the participant. The participant may have identified a family member to the researchers, expressed the view that the family member has or does not have a particular disorder, and may have provided some clinical information about the family member.

16.10(g)
The recruitment of family members identified by a participant should only be undertaken if the participant agrees, and the method of approach to the relatives should be discussed with him or her. If willing, the participant should approach the relevant family members to seek permission for the researchers to contact them. If the family members agree, the researchers can then make contact in order to explain the research proposal and seek consent.

16.10(h)
Non-paternity or non-maternity should only be revealed by, or with the assistance of, an experienced health professional. It may also be helpful to enlist the support of the participant’s general practitioner if an established relationship exists.

16.10(i)
Researchers must specify the procedure to be followed in response to a request for access to stored genetic material, or information generated by the research.

16.10(j)
Consent should normally be specific. However, the nature of genetic research may make it difficult to be specific at the time of collection. It is appropriate to ask potential research participants to consent to storage of genetic material for unspecified future use, on the basis that consent will be sought at the time a specific research project is identified. People should be given the opportunity to refuse permission for storage. If they do refuse, the genetic material and information should not be used for future research and should be disposed of after a specified period following the completion of the current project. However, it should be noted that participants who do not wish their genetic information and genetic material to be used for future research in identified or coded form may consent to its use in de-identified form.

16.10(k)
This should be done at the time of collecting the samples, but if this has not been done, the views of the group should be obtained when the time for disposal arrives and prior to disposal.
16.10(l)
In research involving genetic material, withdrawal may affect not only the research participant, but also her or his blood relations. One example of this would be where the research sample is unique and potentially useful to the clinical needs of other family members. In such situations, there may be ways of meeting the wish of the participant to withdraw from the project while at the same time preserving the clinical potential of the genetic information and material for the rest of the family.

NS 16.11
When researchers propose to collect genetic material and information from individuals chosen by virtue of their membership of a particular collectivity, consent should be sought from appropriate collectivity representatives as well as from the individuals concerned, in accordance with Section 8: ‘Research involving collectivities’.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

WHERE THE REQUIREMENT FOR CONSENT COULD BE WAIVED

NS 16.12
As a general principle, where a researcher proposes to conduct research using stored genetic material or genetic information, the consent of the person from whom the material was derived, or to whom the information relates, is required.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

NS 16.13
An HREC may sometimes waive, with or without conditions, the requirement for consent. In determining whether consent may be waived or waived subject to conditions, an HREC may take into account:

• the nature of any existing consent relating to the collection and storage of the genetic material and genetic information;
• the justification presented for seeking waiver of consent including the extent to which it is impossible or difficult or intrusive to obtain specific consent;
• the proposed arrangements to protect privacy, including the extent to which it is possible to de-identify the genetic material and genetic information;
• the extent to which the proposed research poses a risk to the privacy and wellbeing of the individual;
• whether the research proposal is an extension of, or closely related to, a previously approved research project;

• the possibility of commercial exploitation of derivatives of the sample; and

• relevant statutory provisions.

When an HREC waives the requirement for consent about stored genetic information or genetic material, it needs to decide whether the data will be used in potentially identified (coded) or de-identified form. If in potentially identified (coded) form, the committee will need to decide whether the code that links the information and material to the identifiers should be held by the researchers or by a third party. Careful consideration should be given to the relative benefits and disadvantages of de-identifying specimens.

**NS 16.14**

Institutions or organisations wishing to conduct research on genetic material and information collected for non-research purposes, should develop and disseminate a general policy which informs patients that such material and information may be used for future research following HREC approval, subject to the issues raised in paragraphs 16.12 and 16.13. Patients of such institutions or organisations should be informed that this policy exists, and that their privacy and confidentiality will be protected. They should be given the opportunity to refuse consent to use of their material and information for such research.

This paragraph is regarded as sufficiently clear, and so no commentary has been added.

**GENETIC COUNSELLING**

**NS 16.15**

When research may reveal information of potential importance to the future health of an identified or potentially identifiable participant’s future health or the participant’s offspring, the research protocol must provide for consent procedures, counselling, support, test quality and test result confidentiality as would apply if the participant sought such information in a clinical setting. Otherwise such research may only be performed if the genetic material has been de-identified. Counselling and provision of information arising from the research must be provided by health professionals with appropriate training, skills and experience.

It is important to recognise that the implications of research results may not be fully understood by participants at the time that the research is carried out and that very sensitive issues may be raised later. Therefore, specialist genetic counselling services should be made available as needed.
Details of the standard of care required and who should provide it may be found in Ethical Aspects of Human Genetic Testing: an Information Paper (NHMRC 2000).

**NS 16.16**

If asked to consent to the use of their genetic material and information for future research, participants should be provided with information and counselling about the possible consequences of doing so. In general, their genetic material and information will be used for future research in de-identified form and feedback will not be possible. However, the HREC may direct the researchers to use the genetic material and information in potentially identifiable (coded) form. In such instances, the views of participants regarding the feedback of information of potential significance to their own or their relatives’ future health should be established, recorded and respected. If feedback is requested, the participant should receive information and counselling about the implications of receiving that information; this can be provided at the time of obtaining consent or, in the future, prior to the provision of the feedback.

Researchers should discuss with participants any foreseeable potential consequences from participation. For example, research that currently seeks to identify mutations in known dominant breast cancer genes, with a specific set of consequences for participants if a mutation is found, may ultimately progress to research on the polygenic basis of susceptibility to breast cancer and the interaction of susceptibility genes with environmental factors. This could have a different set of potential consequences for participants.

**Points to consider NS 16.1-16.16**

- What kind of genetic research is involved?
- Will the research participants be individuals, families or populations?
- Does the research involve pre-symptomatic, susceptibility or carrier testing?
- Does the research require the collection of genetic material from participants?
- Is the research narrow in focus or broad ranging?
- Is it gene therapy research? (See relevant NHMRC guidelines)
- Does the research involve studies on embryos? (See relevant NHMRC guidelines)
- Does the research raise issues of cultural or social sensitivity? If so, these should be taken into account. Special safeguards may be necessary to protect vulnerable groups. If the research involves a collectivity, does the project have the support of the collectivity as well as individual participants?
- Will the project require approaches to research participants' relatives? If so who is the most appropriate person to make this approach and how will the project be presented to these relatives?

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26 A polygenic disorder is one where the presence of variants in two or more genes results in disease, increasing the risk of developing disease or modifies disease severity. It will often be the case that individually, the variations in these genes will have a similar functional effect on the gene product and less predictable effects on health; it is their combined effect that is important. Examples include many of the common birth defects such as cleft lip and palate and congenital heart malformations.
• How are the data collected in the course of the research to be stored? Who will have access to this data and in what form will it be disseminated? If material is to be stored in a genetic register, who will be responsible for supervision of the register and what safeguards have been developed to regulate access to it?

• Will the proposed research involve identified, potentially identifiable (coded) or de-identified information and material? If the first situation, what safeguards are in place to ensure that the privacy and confidentiality of personal information is protected, both in general and within the family? In the second situation, who has access to the codes and what procedures have been developed to ensure that these codes are secure?

• How is informed consent to be obtained? Do the consent form and information leaflet address all relevant issues? In particular, will participants be informed if the research has the potential to generate significant information about their personal health or that of their children, or their future children? Will participants be advised if the research has the potential to generate information of social significance, for example non-paternity or information that may influence access to insurance?

• Does the research involve storage of genetic information and material? If so, will consent for storage be obtained? Has the duration of storage of the information and material, its future research uses and its disposal, been addressed?

• If the research involves the use of samples collected for previous research or clinical purposes and stored, will consent be obtained from each of the donors with regard to the proposed project? If not, has the researcher provided adequate justification for the HREC to waive the requirement for consent? If the research will involve use of genetic material stored as a legal requirement or for potential clinical use (for an individual or for a family), has provision been made to ensure that sufficient material is retained for the original purpose?

• Will research participants be advised of project results? If so, will this information be grouped data or relate to each individual participant? If the latter, how are the research and clinical issues to be separated? Are quality controls on the research procedures sufficient to justify clinical inferences and are appropriate counselling facilities available?
17. RESEARCH INVOLVING DECEPTION OF PARTICIPANTS, CONCEALMENT OR COVERT OBSERVATION

NS 17.1

As a general principle, deception of, concealment of the purposes of a study from, or covert observation of, identifiable participants are not considered ethical because they are contrary to the principle of respect for persons in that free and fully informed consent cannot be given.

Further reference should be made to the Research Ethics Collection, ‘Deception, research involving’, page E35.

NS 17.2

In some fields of research, for example the study of human behaviour, there may be exceptional circumstances where studies cannot be conducted without deception, concealment or covert observation of participants. Before approving a research proposal which involves any degree of deception, concealment or covert observation, a Human Research Ethics Committee (HREC) must be satisfied that:

(a) the provision of detailed information to prospective participants about the purpose, methods and procedures of the research would compromise the scientific validity of the outcome of that research;

(b) the precise extent of deception, concealment or covert observation is defined;

(c) there are no suitable alternative methods, not involving deception, concealment or covert observation, by which the desired information can be obtained;

(d) participants are not exposed to an increased risk of harm as a result of the deception, concealment or covert observation;

(e) adequate and prompt disclosure is made and de-briefing provided to each participant as soon as practicable after the participant’s participation is completed;

(f) participants will be able to withdraw data obtained from them during the research without their knowledge or consent; and

(g) such activities will not corrupt the relationship between researchers and research in general with the community at large.
17.2(a)
In order to assess such a justification, the HREC will need to be fully aware of the scientific basis on which the research is based and, for this purpose, may need to draw on expert advice (see NS 2.19). The assessment will need to identify the degree of detail that would fulfil the obligation (NS 1.7) to provide information, given the nature of the research and the intended participants.

17.2(b)
This paragraph is regarded as sufficiently clear, and so no commentary has been added.

17.2(c)
An HREC will need to understand not only the goals of the research but also the methods that are normal in the relevant discipline.

17.2(d)
HRECs need to distinguish the risk of harm of participation in the research from the risk of harm posed by the intended deception, adopting a broad concept of harm, as indicated by the definition in Appendix 3 to the National Statement.

17.2(e)
The feasibility of adequate de-briefing should be regarded by an HREC as an essential feature of such protocols. It cannot be automatically assumed that debriefing will necessarily reverse any harm or remove the memory of embarrassment produced by the earlier deception. Doubts about the efficacy of de-briefing may require that an HREC asks a researcher to modify the preceding deception.

An HREC also needs to consider if an adverse impact on participants of research involving deception may be caused by subsequent disclosure of the deception to participants. HRECs may also need to consider whether counselling should be made available to such participants.

17.2(f)
HRECs should be satisfied that researchers have made provision in their research design for the possibility that participants may choose to withdraw any information obtained from them through deceptive means.

17.2(g)
The attitudes of the community at large to research in general may be adversely affected if examples of research are perceived to be tainted with untruth. An HREC will need to consider carefully how knowledge of research involving any deception will be disclosed either through its reported results or in other ways.

For a brief outline of legal issues in this area, see the Research Law Collection, 'Deception, research involving', page L21.

For an extended discussion of this issue and examples, see also the Research Ethics Collection, 'Deception, research involving', page E33.
18. PRIVACY OF INFORMATION

Privacy is a complex concept that stems from a core idea that individuals have a sphere of life from which they should be able to exclude any intrusion. Privacy can refer to the reasons on which individuals rely in reaching decisions about participation in research or in health care, the protection from interventions in the lives of persons who cannot make decisions or the freedom of individuals from observation or surveillance.

A major application of the concept of privacy is information privacy: the interest of a person in controlling access to and use of any information personal to that person. It is this application of privacy that is considered below.

CONFIDENTIALITY AND PRIVACY

Confidentiality refers to the legal and ethical obligation that arises from a relationship in which a person receives information from or about another. The recipient has an obligation not to use that information for any purpose other than that for which it was given. Traditional examples of relationships in which that obligation arises are those between doctors and patients and priests and penitents. However, the obligation can be created by contract.

Privacy is a broader concept. A person’s interest in keeping personal information private relates to anyone who might have access to that information, whether through a relationship or otherwise.

LEGAL REGULATION

At the Commonwealth level, the collection, storage, use and disclosure of personal information by Commonwealth agencies is regulated by the Privacy Act 1988 (Cth). There is regulation at State and Territory level in the form of legislation related to privacy generally or the administration of agencies, or administrative codes of practice. Others have included more limited controls as part of the administrative structure of health departments and agencies.

INFORMATION PRIVACY PRINCIPLES

The Privacy Act 1988 (Cth) requires Commonwealth agencies to conform to the Information Privacy Principles (IPPs) in dealing with personal information. These principles, adapted from international standards, form a code of conduct that balances the public need for information with the interests of individuals in their privacy. The IPPs are included in Appendix 2 to this Statement.

INFORMATION PRIVACY PRINCIPLES AND MEDICAL RESEARCH

The use of personal information for research is not exempt from the IPPs. However, a balance between the public interest in medical research and in the protection of privacy is reflected in section 95 of the Privacy Act 1988 (Cth). This provides that a Commonwealth agency may, in relation to medical research, deal with personal information in ways that may infringe the IPPs if that research conforms with guidelines devised by the National Health and
Medical Research Council (NHMRC) and approved by the Privacy Commissioner.

Reference should be made to the Research Law Collection for a discussion of legal issues in protection of privacy, page L43.

The Privacy Act 1988 (Cth) is available at: http://scaleplus.law.gov.au

**NS 18.1**

An HREC must be satisfied that a research proposal conforms to all relevant Commonwealth, State or Territory privacy legislation or codes of practice.

The statutory and policy regulation of privacy varies across Australia, so Human Research Ethics Committees (HRECs) in each State need to be aware of local legal controls. These will include controls on access to and use of data held by government agencies and also data held or gained in the private sector.

**NS 18.2**

An HREC must be satisfied that, where a research proposal involves the collection, storage, disclosure or other use of personal information, the privacy of persons to whom that information relates is protected. In most situations, conformity to the IPPs provides an acceptable standard of protection.

The research unit conducting an investigative project is required to establish procedures for the retention of data and for maintaining adequate records of data held. Researchers are responsible for ensuring the security of confidential material, including that held in computer systems.

Two issues arise in relation to the storage of data. On the one hand, data should be held for reference purposes. This allows for review and verification should this become necessary, or, in the case of drug trials, for assessment of possible adverse effects. On the other hand, the protection of research participants’ privacy may involve requests that identifying information should be destroyed after a specified period.

Research participants and ethics committees should be clearly advised by researchers on plans for storage and disposal of data: where the data will be kept and who will have access. Where long-term storage of data is envisaged, it may be necessary to consider the arrangements adopted by host institutions for the continuity of secure storage, as well as the procedures that would be adopted in the event of staff changes.

**NS 18.3**

Where a proposal for medical research may involve a breach of the Information Privacy Principles, the HREC must follow the guidelines contained in Aspects of Privacy in Medical Research (1995) [Under review].
The NHMRC Guidelines under Section 95 of the Privacy Act 1988 (2000) (Cth) http://www.nhmrc.gov.au/publications/synopses/e26syn.htm have a limited scope: they apply only to access to and use, for the purpose of medical research, of personal information held by Commonwealth agencies.

**NS 18.4**

*Generally the consent of participants in research should be obtained for the use of their personal information where:*

(a) the information is to be held on registers for use by researchers in future research projects; or

(b) the information is to be disclosed to other persons for use in future research projects.

A typical arrangement will be that consent is given by those people to access to their information on the register by researchers from an identified institution or institutions for the purpose of identifying, and then contacting and seeking their consent to participation in research projects. In such an arrangement, consent to inclusion on the register needs to be distinct from consent to participation in late research.

Genetic registers should be established and conducted in accordance with the Guidelines for Genetic Registers and Associated Genetic Material (NHMRC 1999). http://www.health.gov.au/nhmrc/publicat/synopses/e14syn.htm

**NS 18.5**

*In research based on linkages between records, an HREC may permit personal information to be used to enable the record linkage without consent if it is satisfied that:*

(a) the identity of participants is not disclosed except for the purposes of record linkage and is not retained once record linkage has been completed;

(b) identifying information is used with sufficient security; and

(c) the research has public benefit.

Some research is conducted by using linked sets of data (see NS 14.8) containing personal information about individuals. Once the sets have been linked and individual information matched, the research can be conducted without needing to use personal information that identifies any individual.

The requirement that the research has a public benefit is a simpler test to satisfy than that used in the Guidelines under Section 95 of the Privacy Act 1988 (Cth) http://scaleplus.law.gov.au] and Paragraph 14.4 of the National Statement.

**Points to consider NS 18.1-18.5**

- Where will the data be stored? Who will have access to it? What precautions will be taken to ensure that storage will be secure?
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- For how long is it envisaged that data will be stored in identifiable, or potentially identifiable, form?
- Does the research project involve drugs or medical interventions? If so, will the storage period be sufficient to allow reasonable review of possible associations with adverse events?
- What will happen to the data at the expiration of the prescribed storage period?
- What contingencies exist for maintenance of security of storage in the event of staff changes?

From December 2001, the application of the Privacy Act 1988 (Cth) will extend to collection, storage, use and disclosure of personal information in the private sector. Guidelines are being developed about the non-consensual use of personal information in research, analysis and compilation of statistics in the interests of public health and safety, and the management of health services, including funding and monitoring.
19. INTELLECTUAL PROPERTY

Some research involving humans may be intended for, or later directed towards, purposes of commercial exploitation. As a general principle disclosure of interests by researchers should be made to the Human Research Ethics Committee (see paragraph 2.21) and the consent of participants obtained (paragraphs 1.2 and 1.7).

The Joint NHMRC/AVCC Statement and Guidelines on Research Practice and the Australian Vice-Chancellors’ Committee (AVCC) discussion paper, Ownership of Intellectual Property in Higher Educational Institutions, provide useful points of reference for addressing issues of intellectual property, disclosure or commercial-in-confidence undertakings.

Reference should be made to the Research Law Collection for a discussion of legal issues relating to intellectual property, page L41.


A RESEARCH ETHICS COLLECTION

EXPLANATORY NOTE

This is a collection of opinions on recurrent issues of ethics relevant to research involving humans. It is not an exhaustive collection and suggestions for additional topics are welcome. The opinions have been written by some of the contributors, who are listed at the front of this Handbook, and the views they express are not all necessarily shared by NHMRC. Nonetheless, they do serve the purpose of fostering an open and reflective discourse in ethics relating to research involving humans.

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AUTONOMY

Personal autonomy has been variously characterised as the capacity for individual self-determination, as freedom from coercion, undue influence and external restraint in decision-making, and as the capacity for deciding and acting in accordance with one’s own values. Political autonomy is the idea of a people's self-governance and self-determination and is contrasted with political subordination and domination.

In the context of research involving humans, reference to autonomy usually involves personal autonomy and is often closely identified with the requirements for informed consent, protection of confidentiality and protection against undue influences that may limit a person's ability to voluntarily choose whether to participate or continue participation in research. Personal autonomy extends beyond mere free, informed choice, however, to include recognition of the contexts of personal choice and the development of the capacity for personal autonomy (footnote: S. Sherwin, ‘A Relational Approach to Autonomy in Health Care’, The Politics of Women’s Health: Exploring Agency and Autonomy The Feminist Health Care Ethics Research Network, coordinator Susan Sherwin, Philadelphia, Temple University Press, 1998; S. Dodds, ‘Choice and Control in Bioethics’, Catriona Mackenzie and Natalie Stoljar (eds), Relational Autonomy in Context: Feminist Perspectives on Autonomy, Agency and the Social Self, Oxford University Press, New York, 2000, pp. 213-235).

In research involving collectivities, respect for both personal and political autonomy may be required, and they may conflict. For example, a collectivity, as a matter of collective self-determination may seek to control researchers’ access to participants from among the collectivity in a manner that could limit the personal autonomy of collectivity members. Ethics committees will have to assess the relative significance of the two distinct expressions of autonomy in assessing whether respect for the interests of the collectivity (an its constituent members) in self-determination outweigh the interests of individual members of the collectivity in being able to make individual autonomous decisions whether to participate in the research.

See also the discussion of ‘Respect for persons’, page E153.
BENEFICENCE

[NS 1.3 and Commentary]

The focus of NS 1.3 is on the reduction of harm. However, the principles of beneficence can include other ideas, particularly the idea of benefits to society as a whole flowing from the results of the research enterprise.¹ The inclusiveness of this view has been challenged.

In many of the codes of ethics for research, there is an assumption that the interests of science coincide with the interests of society. …However, the assumption is open to question. Hans Jonas, an early philosopher to write on the ethics of human experimentation, challenged the view that ‘science benefits society’…implicit is an assumption that the benefits of research are experienced by the whole of society whereas the burdens are suffered by individual subjects. …It is not society as a whole, but some individuals who may benefit from research into particular diseases. The issue then is the conflict between the search for potential benefits for individual sufferers of a disease as against the potential harms, or the risk of harm, to individual subjects of research.²

While ethics committees need to engage in an assessment of the risks of harm associated with research proposals, there may be some difficulty in establishing exactly what these are. ‘Harm’ has been defined as the defeating of an interest, where an individual’s interests are understood to be the range of things in which that individual has a stake.³ Understanding ‘harm’ in this way means that a person can be harmed not only by direct damage to their wellbeing, such as a physical wound, but also, for example, by loss of access to needed social services. Therefore, although ‘harm’ is most frequently understood in physical terms, it can also include psychological distress, discomfort, social disadvantage, invasion of privacy and infringement of rights (See NS Preamble p.4 and 1.14, 1.19 and 1.20). See ‘Risk’ in this Collection, page E155, for a detailed discussion of defining and assessing risks to research participants.

The term ‘risk’ refers to both the probability of a harm occurring and the magnitude or severity of that harm. Assessments of the risks associated with a research project frequently incorporate the combined probabilities and magnitudes of several potential harms. Many kinds of possible harms need to be taken into account when considering risks to participants:

• physical harms, such as pain, discomfort, injury or side-effects of drugs;
• psychological harms, such as depression, anxiety, confusion, stress, guilt, embarrassment and loss of self-esteem;
• harms associated with infringements of privacy and breaches of confidentiality;
• social harms, such as ‘labelling’, stigmatisation or discrimination in employment; and
• economic harms, such as actual financial costs of participation.

HOW CAN RISKS BE MINIMISED?

Given that it is not possible to remove all risks from the research process, the task for ethics committees is to:

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• consider whether a risk to participants is reasonable in relation to the potential for the particular research project to benefit relevant others in the future;

• be satisfied that risks to participants are minimised where possible;

• consider rejecting, or requesting amendment of, those proposals that appear to involve an unacceptably high degree of risk to participants; and

• be satisfied that those who volunteer to take part in research clearly understand the nature of the risks involved.

Researchers may adopt, and HRECs may require that researchers adopt, risk minimisation strategies. Such strategies may include:

• frequent monitoring of participants;

• the presence of trained personnel who can respond to emergencies;

• coding of data to protect confidentiality;

• ‘debriefing’ for participants;

• continuing review and monitoring of data to ensure that the study does not continue after the emergence of reliable evidence of reduced efficacy and/or safety, or actual harm to participants;

• exclusion of vulnerable individuals or groups from participating in research where necessary and justified; and

• consideration of whether alternative means for answering the research question are available, and whether participation by humans is really necessary.
The following discussion deals with considerations that apply either to children or young people exclusively, or to children and young people in comparison with adults. While it is generally agreed that research is necessary in order to advance knowledge about the health and wellbeing of these two groups, the National Statement requires that such research should only be conducted where certain criteria are met. The proposed research question should be important to the health and wellbeing of children or young people and the study method should be appropriate for these age groups. Research should only be undertaken if information available from studies involving individuals at other life stages cannot answer the question posed; and the circumstances in which the research is to be conducted should provide for the physical, emotional and psychological safety of research participants (NS 4.1).

The National Statement also requires that consent to a child's or young person's participation in research should be obtained from the child or young person whenever she or he is capable of making this decision, as well as from either parents or guardian, or any organisation or person required by law (NS 4.2). (Note that the National Statement refers to ‘the parents/guardian…’ However, HRECs should be aware that there could be many instances in which the implied ‘both parents’ simply would not be accessible and it may only be possible to obtain consent from one parent.) In addition, a child’s or young person’s refusal to participate in a research project should always be respected. Finally, an HREC should not approve, and consent cannot be given for, research that is contrary to the child's or young person’s best interests (NS 4.3; 4.4).

The above requirements stem from a consideration of the essential differences between children, or young people, and adults. These include:

- Findings from research involving adults cannot always be assumed to apply to children. Some childhood disorders do not occur in adults and therefore cannot be studied in the adult population.
- With regard to biomedical research, normal values or ranges for biological variables may differ between children and adults and between children of different ages and stages of growth and development.
- Activities unique to children may impose additional risks. For example, research involving a school or classroom population may carry a risk of invasion of privacy for research participants. This is discussed in more detail below.

**CONSENT**

The situation of the child research participant differs from that of the adult most strikingly in that consent is sought from a person, or persons, other than the potential participant. Nevertheless, the National Statement requires that the child's consent also be sought if he or she is able to make a decision. This raises a number of issues.

HRECs should be aware that there are, at present, no clear statutory or common law requirements in Australia with regard to a child's ability to consent to, or refuse, participation in a research project. While the Research Law Collection provides an account of the legal aspects of consent, including competence, in relation to children, it should be pointed out that this discussion involves the law about consent to medical treatment. While this may provide some guidance for research, it is essential to understand that the law allows for greater intervention in treatment because such intervention is considered to be in the child's immediate best interests. This degree of intervention cannot be justified in (non-therapeutic) biomedical research, where such
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The research intervention aims at benefiting other children sometime in the future. Therefore, ethics committees may be required to resolve certain inevitable ethical ambiguities in the matter of consent, or refusal, when assessing research proposals involving children as potential participants.

However, statutory requirements around the age of consent for participation in research can be taken from age of majority legislation in the relevant jurisdiction. In most Australian jurisdictions, this is 18 years. (See the Research Law Collection, page L1 for a more detailed discussion.) The ethical importance of this for all types of research is demonstrated by a project conducted within a psychology department of an Australian university, where a survey of the experiences of 12-year-old children in relation to puberty was carried out without obtaining parental consent. The outcome was distressed children and angry parents.4

In addition, HRECs need to be aware that parents may, in certain circumstances, find themselves in painful conflicts of interest. For example, parents may wish to enrol their healthy child in a trial involving transfer or transplant of tissue because of potential benefit to that child’s gravely ill sibling. The difficulty is that parents in this type of situation are unlikely to be able to make a reasonable and considered decision about the best interests of their healthy child. Depending on the particular legal jurisdiction, an HREC may need to consider applying to a Guardianship Board for a decision on what course of action is in the healthy child’s best interests.

CONSENT PROCESS

Wherever appropriate, researchers should carefully explain to the participant:

• the purpose of the research;
• the likely benefits of the research for the participant;
• any risks associated with the research;
• the procedures to be undertaken and their duration;
• the arrangements for the protection of confidentiality and privacy throughout the research activity.
• the likelihood of any complications from the research, including pain; and
• that participation in the research is voluntary and that the participant may withdraw consent at any time.5

Children of appropriate maturity and capacity should have these things explained to them in a manner and language that they can understand. Adequate time must be allowed for the child/young person and his/her family to ask questions about the research and to receive answers.

If possible and age-appropriate, the child or young person’s consent should be obtained in writing.

The parents/guardian of the child or young person should be approached before the potential participant is approached.

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4 Herald Sun, 30 June, 1999, p.18.
5 Division of Paediatricians Policy Statement; Ethics of Research in Children, Royal Australasian College of Physicians, May 1998
In addition to the research details mentioned above, the researcher should particularly advise the parents/guardian of the following when seeking consent:

- any costs likely to be incurred;
- the fact that non-participation in, or subsequent withdrawal from, the research will not alter the care and treatment that the child would otherwise have received; and
- any likelihood that the research will result in the pre-symptomatic diagnosis of a disease. This should be explained beforehand to the family and provision made for adequate support and counselling in the event that a positive result of such a diagnostic test is found. It is important that current knowledge on the potential advantages or disadvantages of pre-symptomatic diagnosis be discussed with the family and, where appropriate, with the child.

Again, the researcher should ensure that this information is given in an appropriate manner taking into account cultural sensitivities (if any) and allowing time for the parents/guardian to ask questions.

If consent is obtained, and the child has sufficient competence to make a decision, the researcher can then approach the child to seek his or her consent.

Consent for a child or young person’s participation in research may also be needed from an organisation or individual who has a legal duty of care involving the child or young person. An example of this would be where the potential participant is in a detention facility. In this situation, consent would be needed from the facility’s management, in addition to the child or young person and their parents.

Some research proposals may involve school children as participants. This raises a number of ethical issues. Lines of communication are often more complex here than is usual with research involving other groups. Projects may involve the child in the classroom, the child’s parents, the class teacher, the school principal, the relevant department of education and the researcher. An HREC should be particularly careful to ensure that the requirements of NS 4.2 (about consent) are not compromised by circumstances such as these. See also ‘Schools, research in’ page E157, in this Collection.

Note also that school personnel cannot give consent on behalf of students or parents, nor can they disclose information for research purposes about these groups without the prior knowledge and consent of the persons affected.

**RISKS, BENEFITS AND THE RESEARCH PARTICIPANTS’ BEST INTERESTS**

Each HREC will need to weigh up the risks and benefits involved in specific research projects involving children, keeping in mind that the committee’s primary purpose is to protect the welfare and rights of all research participants (NS 2.5). (See the Commentary on NS 1.4 and this Collection on page E155 for a general discussion of weighing up risks and benefits.)

The greater susceptibility of children to some types of harm deserves emphasis. For example, the potential for interference with growth in height is irrelevant to adults but important to children. The same applies to other aspects of childhood and adolescence, including psychological, social and sexual development. Therefore, an ethics committee should be satisfied that the circumstances in which the research is to be conducted ensure optimal physical, emotional and psychological safety for research participants. In order to do so, it is essential that every HREC considering research proposals involving children as potential participants has access to expert advice on these matters, thereby ensuring that children as research participants are protected from harm.
However, even with such advice, evaluation of a child’s or young person’s best interests can still be a complex process. This is less difficult when, for example, a trial of treatment intended to directly benefit the research participant (therapeutic research) is being considered. If it is possible that the participant may benefit from a trial of treatment, then participation may be considered to be in the child’s best interests provided that potential harm does not outweigh potential benefit. Nevertheless, this may still be difficult to judge, and appropriate decisions will vary with the particular circumstances. For example, in the case of a child in danger of death or major damage to health, a potential risk that would be considered unacceptable under less serious circumstances might be judged acceptable. This task is even more complex in relation to non-therapeutic research (the majority of research), in which participants cannot expect any direct or immediate benefit from the outcome of the project in the specific research context. It will be necessary to decide, for example, if a modest degree of inconvenience, some transient embarrassment or low-level discomfort can be justified.

Where a research proposal includes questions that may be sensitive for a child or young person to answer, an HREC will need to decide whether or not the questions are acceptable given the level of invasion of privacy involved. Sensitive questions might include those dealing with abuse, sexual development or activity and physical development, for example. If sensitive questions are approved, the committee will need to be assured that the researchers are sufficiently qualified and experienced to minimise risk to participants. The committee should also see evidence of appropriate risk management strategies to deal with any distress caused.

Above all, it is the duty of HRECs to ensure that researchers have provided the highest level of safety for research participants. To help them do so, it is essential that every HREC assessing research proposals involving children or young people as potential research participants have access to expert advice. Advice might be sought from paediatricians, social workers, nurses, psychologists or other health professionals, depending on the nature of the research.

UNITED STATES GUIDELINES

Recently, the United States National Institutes of Health (NIH) released its Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects http://grants.nih.gov/grants/funding/children/pol_children_qa.htm, which states that:

…It is the policy of NIH that children (i.e. individuals under the age of 21) must be included in all human participants research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them…therefore, proposals for research involving human subjects must include a description of plans for including children. If children will be excluded from the research, the application or proposal must present an acceptable justification for the exclusion.6

CHILDREN, CLINICAL TRIALS INVOLVING

Historically, data related to children have often been omitted in applications to register new drugs. This has significantly disadvantaged children because it has led to non-availability of paediatric formulations of drugs, as well as a lack of information on which paediatric dosages could be based. Therefore, it is important that clinical trials are conducted involving children, although participation by children in clinical trials should only be approved where it is indispensable ‘because information available from research on other individuals cannot answer the question posed in relation to children’ (NS 4.1(b)). While such clinical trials are generally subject to the same considerations as those involving adults, particular attention should be paid to the following points.

- Trials should be designed to include the minimum number of participants required to achieve adequate statistical power.
- Where possible, non-invasive methods of collecting samples should be employed, for example, collecting urine rather than blood samples.
- Attention should be given to the possibility of heterogeneity in study populations with respect to the state of maturity, height, weight, body surface area and other factors such as nutritional status.
- Particular care should be taken with drug dosages, since these can vary from those predicted on the basis of adult studies. This variation results from differences between adults and children in drug metabolism, vulnerability to toxic effects and other factors.
- Different criteria may be appropriate for breaking codes of blinded studies in the event of possible dangers to participant safety.
Clinical Trials

[NS 12.1–12.13 and Commentary]

Drug Trials

Clinical trials of drugs are generally classified according to the stage of drug development.

1. Phase I studies involve the first administration of the drug to humans. Their purpose is to determine the safety of the drug, its pharmacological activity, how it is handled by the body and how well it is tolerated.

2. Phase II studies are the first trials of the drug involving participants suffering from the disorder that the drug is intended to treat. The principal aim of these studies is to determine efficacy (effectiveness) and safety.

3. Phase III studies involve greater numbers of participants and aim to determine whether the drug provides clinical benefit in relation to the disease/s for which effectiveness was demonstrated in Phase II studies, and whether the incidence and nature of adverse effects are acceptable.

4. Phase IV studies are undertaken after the drug has been marketed for the treatment of a particular disease. These studies include those that aim to compare the drug to a wider range of drug investigations and therapies in normal clinical settings.

Clinical trials of drugs and devices conducted in Australia are subject to government regulations administered by the Therapeutic Goods Administration (TGA). There are two schemes under which clinical trials may be conducted: the Clinical Trial Exemption Scheme (CTX) and the Clinical Trial Notification Scheme (CTN). These Schemes apply to the testing of any drug or device not entered on the Australian Register of Therapeutic Goods, including any new formulation of an existing product or any new route of administration, as well as the use of marketed drugs and devices that extends beyond the conditions of existing marketing approval. This includes new indications extending the use of the product to a new population group, as well as the extension of doses, or duration of treatments, outside the approved range. Studies in which marketed drugs and devices are used within their approved indications/doses may not be subject to CTN or CTX requirements but will still require assessment and approval by an HREC.

Under the CTN Scheme, the trial protocol is submitted directly to the HREC, which is then responsible for assessing the scientific validity and safety of the protocol. The TGA does not undertake any review of the project. If the HREC approves the trial, the sponsor submits a Clinical Trial Notification form, the CTN form, to the TGA.

The CTX Scheme is intended to assist HRECs when information about a drug or device is limited, or further advice is required for some other reason. Under this Scheme, a sponsor submits a package of data to the TGA for evaluation and comment. The TGA examines these data in order to assess the safety of the product, paying particular attention to its overseas status, proposed usage guidelines, pharmaceutical data sheets, details of medical device construction and principles of operation, and pre-clinical and clinical data. The TGA then decides whether or not it has any objection to the proposed usage guidelines for that product. If no objection is raised, the researcher then submits the data to the ethics committee associated with the institution or organisation where the trial is to be conducted. This committee then considers the data, together with any comments provided by the TGA, assuming responsibility for assessing, and where appropriate, approving, the proposal.
HRECs may decide whether a clinical trial should proceed by the CTX or CTN route. Under the latter Scheme, ethics committees may agree to consider trials of new indications and dosages, or new participant groups, for currently marketed drugs where certain conditions are met. This includes situations where chemistry and toxicity are well defined and where extensions to trials have been evaluated under previous CTX arrangements. It also includes situations where Phase III or IV trials of new agents (non-marketed) have been approved for marketing in the United States, the United Kingdom, Sweden, Canada and the Netherlands, or have been evaluated under the equivalent of the CTX Scheme operating in the United States or United Kingdom. Bioavailability/bioequivalence studies are also included here. Physiological studies involving drugs given for non-therapeutic purposes would also normally fall within this category. It is, however, within the discretion of individual HRECs to adopt wider or narrower sets of criteria according to which studies are to be accepted under this Scheme.

Where technical, scientific or medical data are lacking, the CTX route of approval will normally be preferred. For research proposals involving gene therapy, HRECs are required to seek the advice of the Gene and Related Therapies Research Advisory Panel (GTRAP) http://www.nhmrc.gov.au/aboutus/committees.htm, a subcommittee of the Research Committee of the National Health and Medical Research Council.

In order to decide on the appropriate classification of a trial, an ethics committee needs to have access to relevant correspondence from other regulatory bodies, together with information confirming that the dose, duration of therapy and participant groups to be studied are similar to those approved by the overseas agency. When studies that have not been approved by other regulatory agents are proposed under the CTN Scheme, and occasionally when they have been approved but other issues have subsequently arisen or substantive concerns have been identified, the committee may request commission of a review of the available data. This is normally carried out at the expense of the researchers or the sponsoring company.

Further reference should be made to Appendix 2 to this Collection, ‘Human-Research Ethics Committees and the Therapeutic Goods Legislation’ which is also available at www.health.gov.au/tga/docs/html/hrec.htm.

**PROTOCOL AND STUDY DESIGN**

When assessing protocols for clinical trials involving the use of unregistered medicines, an HREC should consider the mechanisms proposed, if any, for access to continued treatment with those medicinal products by patients/participants for whom treatment has been found to be effective, and where long-term therapy would be appropriate following completion of the trial. The possibility of including a post-study supply component within the research protocol may also be examined. Trials of ‘natural remedies’ should be undertaken with the same rigour as is applied to prescription pharmaceuticals and devices, and should be subject to a similar level of surveillance by HRECs.

The most common clinical trial design is that of the parallel group, in which participants are divided into two or more groups and the effects of a test treatment are compared against those of placebo or active control treatments. Another commonly employed design is that of the ‘cross-over’, in which each participant serves as his or her own control by receiving both the test and control treatments, separated by a ‘washout period’. The main issue here is whether the washout period is adequate to ensure that a carry-over effect from the preceding treatment does not occur.

The random allocation of participants to the test and control arms of the study is an important protection against bias in the study design. A further protection involves ‘double-blinding’, where neither researchers nor participants are aware of the type of
treatment the latter are receiving. A ‘single-blind’ study is one where participants are not aware of actual treatments but the researchers are. HREC members should assess the merits of ‘double-blinding’ or ‘single-blind’ procedures in a clinical trial protocol.

**INCLUSION AND EXCLUSION CRITERIA**

A drug or medical device being tested for registration should be tested in the population of people for whom its use is intended. Generally, in the early phases of a drug’s development, healthy volunteers are studied, followed by patients with the condition of interest but without other illness. Following registration and marketing a much broader cross-section of the community will be exposed to the new drug, including people of various ages with multiple illnesses who are taking a wide range of medications. The trial methodology should contain a clear rationale for the selection of appropriate participants and ethics committees should assess the merits of the proposed inclusion and exclusion criteria. For example, concerns may be raised if the proposed participants are to be under the age of 65 for a Phase III study of a drug that is potentially useful for a condition found more often in older people.

**STUDY ENDPOINTS AND OUTCOME MEASURES**

It is important that a clinical trial has a primary, or main, outcome measurement. This should be appropriate to the clinical question being asked. Where possible it should also represent a significant health outcome, such as the occurrence of dementia, the level of pain, mortality or the quality of an individual’s life. Trials with clinical endpoints of this sort, however, often have a long duration and are expensive to conduct. In order to overcome these problems, many clinical studies seek to use alternative outcomes, so-called ‘surrogate endpoints’. A surrogate endpoint must be a correlate of the true clinical outcome it seeks to reflect and it must fully capture the net effect of treatment on the clinical outcome. Examples include blood cholesterol concentrations, HIV levels, blood pressure and bone density.

Where the researcher wishes to use a surrogate endpoint, the ethics committee needs to assess whether the validity of that endpoint has been rigorously established. This assessment should take into account the stage of development of the proposed intervention, the sample size being studied and the duration of therapy. For example, a mortality study cannot be performed with low numbers of participants or therapy of short duration, while, conversely, exposing large numbers of participants to long-term therapy using surrogate endpoints without prospectively examining clinical outcomes may result in exposure to therapies with unknown risks for excessive periods.

**ANALYSIS OF RESULTS**

Researchers need to specify what analyses they propose to carry out with the data gathered from the study. This is necessary to protect against ‘sub-set’ analysis, sometimes called ‘data-dredging’. The more analyses performed on a set of data the more likely a statistically significant difference will be observed, which could be misinterpreted as an important result. For example, a process of sub-set analysis may find that a treatment is superior to the control treatment in women over the age of 70 when there is no
difference in the sample as a whole. Unless a stated aim of the study was to extract the sub-set of women over the age of 70 for separate analysis, such an analysis can only be considered an indication of what may be the truth. A further study would be required to prove the point.

Data should also, where possible, be analysed under the ‘intention-to-treat’ principle. That is, if the intention was to treat a participant in a clinical trial with a particular therapy, then the results from that participant should be analysed accordingly, irrespective of whether or not the participant completed the study. Restricting the analysis to data from participants who reach the end of the study can be misleading with respect to the actual efficacy, or toxicity, of a new drug.

**TESTING ‘GENERIC’ DRUGS AND MARKETING DISGUISED AS RESEARCH**

An HREC needs to pay particular attention to the aims of a clinical trial to ensure that a proposal that is not original and scientifically valid (for example, a promotional exercise) is not purported to be a genuine trial. Clinical trials will be scrutinised for this purpose more frequently than other types of research.

Some research proposals, often called equivalence studies, simply involve testing whether a new formulation of a particular drug is equivalent to a standard marketed brand. Often this involves the study of a generic or copy product in healthy volunteers. The rationale can be mainly commercial in that data are required to register the new formulation of the drug. HRECs need to be satisfied that the proposal meets the conditions of NS 12.2.

Some drug studies have been marketing exercises rather than scientific endeavours. These studies aimed to achieve exposure for a new drug or for a new indication for an old drug, or to promote familiarity with a drug’s use among clinicians. HRECs should carefully examine the hypotheses the trial is designed to test and the level of relevant existing knowledge. The committee should also determine whether there have been previous studies.

**SAFETY ISSUES**

HRECs should be satisfied that any proposed treatments are safe for research participants. This requires assessment of data obtained from previous experience, including pre-clinical, clinical and mutagenicity studies. In general, a formal opinion should be sought from a pharmacologist external to the committee if one is not included among committee members. Pre-clinical testing is generally used to show that the drug does not produce serious adverse effects in a variety of species of animals at, or above, doses equivalent to those to be used in the proposed studies. Organ-specific and generalised diseases, as well as adverse reactions to high drug doses, may vary between species. Accordingly, it is particularly important to consider whether an adverse effect has emerged within a particular species or whether a common reaction pattern has emerged across species.

There may be situations in which a doctor’s primary ethical responsibility to their patient is in conflict with double-blinding and with random allocation. There are situations in which the best scientific approach is incompatible with the best ethical approach. For example, if one of the two treatments that are to be compared increases risk of harm to the health of an identifiable subgroup within the participants, it would be unethical to allocate individuals in that subgroup to receive that treatment. However, deliberately to allocate them to the safer treatment group would spoil the trial. It may be possible to plan exclusion criteria when designing the trial to avoid this situation. In some situations it may not be feasible to design a trial that is both ethical (or beneficient, in that the risks are minimised) and scientifically
sound. What remains important is that potential participants are fully informed of the risks of participating before making their choice.

Another important issue is that the intimate relationship of caring professionals with dependent, aged and vulnerable patients may make it difficult for individuals to make an independent decision about whether or not to participate in a study. This close relationship may lead clinicians to protect their patients too closely against what they consider an undesirable intrusion (See NS 7.1-7.3 and Commentary).

**Suggested reading**


**See also:**

Children, clinical trials involving, page E9, and Women, clinical trials involving, page E165.
COMPLAINTS

Those most likely to be aware of problems as they arise during the research process are the researchers themselves, their assistants and research participants. It makes sense, therefore, to provide these people with an avenue for reporting any problems or concerns. The following deals with such complaints. Note that there may also be complaints concerning the ethics committee review process itself.

Possible complaints cover a broad spectrum from ‘inadvertent technical deviations’ from established protocols to allegations of scientific misconduct or fraud. The primary concern in response to any complaint is the extent to which research participants are endangered. There may also be concerns about the degree to which researchers are fulfilling their responsibilities and, in some situations, questions about culpability for misconduct. There may also be concerns about misleading reports having been published by a researcher accused of misconduct or fraud. An HREC will often be the most appropriate body to consider complaints in the first instance, although ultimately, this is the responsibility of the relevant institution (NS 2.39–2.43).

PUBLISHED PROCEDURES

NS 2.43 requires institutions to establish procedures to receive and deal with complaints about research involving humans. These procedures could be part of an institution’s established reporting system in relation to research findings, deviations from approved research proposals and any concerns about the conduct of research projects.

A COOPERATIVE CLIMATE

It should be emphasised that, while transparent and fair procedures for dealing with complaints and appeals are necessary, the majority of matters dealt with by HRECs are considered in a cooperative and constructive manner. This should always be the intention and the underlying guiding principle of ethics committees, institutions and researchers.

RECEIVING COMPLAINTS ABOUT THE CONDUCT OF RESEARCH

HRECs should provide adequate opportunity for research participants, research assistants and researchers to express any concerns that might arise during the research process, particularly about situations where the welfare of participants may be jeopardised. Therefore, before a project begins, all parties to the research process should be advised of the name and contact details of the person nominated by the ethics committee to deal with complaints (NS 2.40).

Complaints and grievances about research involving humans are best dealt with by using a common set of procedures. These procedures would ideally constitute part of an institution’s established system for reporting research findings, deviations from approved research proposals and any concerns about the conduct of research projects. Herman Wigodsky suggests that institutions use ‘existing channels of communication, supplementing them as needed to make them more effective’.9

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8 Where a researcher has been accused of fraud and has published misleading or false reports, it may be necessary to publish reports which draw attention to the misleading information.

9 Wigodsky, op.cit., pp.70, 76.
RESPONDING TO COMPLAINTS ABOUT THE CONDUCT OF RESEARCH

The elements of an effective system for dealing with complaints, as suggested by Wigodsky, are:

…readily available; have easy entry; provide for anonymity if necessary; be capable of determining facts quickly and of responding very promptly when necessary; have immediate access to the highest administrative authority of the institution; be effective in resolving problems on a factual basis; provide feedback to those who report, including whistleblowers; and, above all else, provide immediate protection to the human research subject concerned. If such a system functions properly, it also will protect the investigator(s) and institution from unjust embarrassment or harassment. The system also should include an appeals system that provides for due process.10

At least one person should be designated to receive complaints, although two people may be necessary to carry out the investigation. The complaints officer should be easily contactable, be seen to be easily approachable and have the authority to act promptly and appropriately. They should also be capable of dealing sympathetically with any concern that arises and be prepared to take action to resolve the complaint. Complaints may be written or verbal, and the complainants should identify themselves.

All details related to this process, including relevant names and contact information, should be given to all research participants as part of the information package provided on entering a study, as well as to collaborating researchers and research assistants (NS 2.42). These details should also be widely advertised throughout an institution and forwarded to any associated research bodies. Adequate resources should be provided to allow complaints officers to carry out their functions.

PROCEDURES FOR RESPONDING TO COMPLAINTS

Complaints officers should respond urgently when there is any suggestion of harm to research participants, researchers or any other person. In extreme circumstances, an immediate demand to suspend a research program may be necessary while concerns are adequately investigated. In other cases, prompt action may be required to rectify or remove the cause of concern. Having determined the urgency of the need for action, the complaints officer should take any, and possibly all, of the following steps according to the circumstances:

• make a clear and full written record of the complaint;
• seek further information from all relevant parties;
• convene an urgent meeting of the ethics committee; and
• if necessary, confer with the highest level of management and authority within the relevant institution.

PROCEDURES FOR INVESTIGATING COMPLAINTS

Where initial investigations reveal a situation that requires further investigation and review, the following procedures are recommended:

• Invite the researcher(s) to explain the situation to the committee and to demonstrate why the project should not be discontinued and ethical approval withdrawn.

10 Ibid., p.61.
• Advise researcher(s) that they may be accompanied by one or more colleagues.

• Reconsider the original research proposal and seek additional information from the researcher(s) in relation to the conduct of the study, or any other relevant factors, before making a final decision whether to revise or reconfirm the original decision to approve the project.

Having considered the matter, the committee may:

• withdraw approval and stop the project, although in many situations this will require endorsement from the institution unless the HREC has previously been given authority to act in this capacity;

• require amendments to the original research proposal or to the conduct of the research; or

• allow the project to continue without amendment.

Principles of natural justice suggest that an HREC should provide the researcher(s) with an explanation of the reasons for withdrawing approval, amending the research proposal or amending the way in which the project is conducted.

In addition, it may be necessary to inform research participants that the research they have been participating in has been modified or discontinued. The institution may take advice from the researcher(s) about the wording of the notice to participants.

If funding has been provided for a research project from which an HREC subsequently-withholds or withdraws approval, the return of funds becomes an issue. Ideally, the HREC will consider the matter and advise the institution on a just outcome. Obviously, the terms and conditions of the grant will have an important bearing on the situation. Other relevant information includes the extent and nature of expenditure already made, the funds remaining and the means at the disposal of the researchers to reimburse their sponsors.

Having made a preliminary report to the institution, it is advisable that the institution’s responsible officers then deal with the matter. The institution will need to determine the appropriate action and will in many cases, depending on the nature of the grant, be obliged to report to the funding body that approval for the study has been withdrawn by the HREC and that the researchers have been requested to stop the project. It may or may not be necessary to advise the funding body of the reasons for withdrawal of approval.

ALLEGATIONS AND COMPLAINTS OF SERIOUS RESEARCH MISCONDUCT

While this Collection recommends a common set of procedures, special provisions may be needed for responding to complaints or allegations of serious research misconduct. Imogen Evans has defined such misconduct as:

...fabrication, falsification, plagiarism, or deception in proposing, carrying out, or reporting results of research and deliberate, dangerous, or negligent deviations from accepted practice in carrying out research. It includes failure to follow established protocols if this results in unreasonable risk or harm to human beings, other vertebrates, or the environment and also the facilitating of misconduct by collusion in, or concealment of, such actions by others. Misconduct does not include honest error or honest differences in the design, execution, interpretation, judgment in

evaluating research methods or results of misconduct (including gross misconduct) unrelated to the research process.12

Where there has been an allegation of serious misconduct, an institution should have recourse to existing procedures designed to achieve the following objectives:

• protection of participants;
• appropriate confidentiality (in case the allegation proves to be groundless);
• protection of ‘whistleblowers’; and
• natural justice for those who are the subject of any allegations or complaints.

Confidentiality, protection for complainants and natural justice for the person complained about could be dealt with by a review process summarised as follows.

1. Determine whether the allegation falls within the above definition of scientific misconduct.
2. Determine whether there is prima facie evidence of scientific misconduct.
3. Institute a formal investigation to evaluate all relevant facts to determine whether scientific misconduct has been committed and, if so, by whom, as well as the seriousness of the misconduct. The integrity of the research data must be evaluated and all appropriate groups advised if inaccurate, misleading or invalid data have been published or submitted to other agencies.13
4. If appropriate, make a decision about the imposition of sanctions.
5. Provide an appeal process. If the appropriate institutional authority decides that the allegations have substance, and that the consequences are of a serious nature, then the circumstances leading to the complaint, the allegations, and the eventual decision taken following an investigation, along with the reasons for the decision and subsequent action, should be reported to the research funding authority and any other relevant government bodies. If it is found that an allegation is not substantiated, or that an error was made of an unintentional nature and did not lead to any harmful consequences, then this should be communicated to both parties and protection against unfair retaliation continued. If the finding is that the complaint has no substance and that the complainant was motivated by malice then the institution should respond appropriately.14

People who make complaints of a more serious nature are known worldwide as ‘whistleblowers’.15 This term is used to describe someone within an institution who reports on their observations of mismanagement, corruption or dangerous practices taking place within

13 Ibid.
14 Adapted from Wigodsky, op.cit., pp.66–68.
that institution. Typically, whistleblowers within institutions fare badly.\textsuperscript{16} Most are motivated by a concern for the welfare of other people and believe that those in authority will act to rectify the problem.

Regrettably, the record shows that most institutions turn on the whistleblower and attempt to cover up the problem.\textsuperscript{17} Another difficulty is that whistleblowing is seen by members of the scientific community as violating the obligation of loyalty to the community and as undermining the community’s autonomy and self-regulation.\textsuperscript{18} For these reasons it is important for institutions and HRECs to develop policies for dealing fairly with the substance of complaints rather than reacting either adversely, or defensively, to the fact that a complaint has been made.

**Natural Justice and Due Process**

Most complainants act out of goodwill. However, some people may make allegations out of malice or the desire to harass or embarrass. Natural justice demands that the complaint be fairly investigated, that all interested parties be given a fair hearing, and that the complainant, and the person complained about, be protected from any form of harassment while this investigation is being conducted.\textsuperscript{19}

In addition, it should be possible to appeal against a decision, with those considering an appeal being independent of the parties who made the original decision. Decisions should be based on sound reasons and both the decision and reasons for that decision should be recorded. While not all HREC processes are subject to the requirements of administrative law and the principles of natural justice, it would be prudent, and not impractical, to ensure that these principles are satisfied.

**Complaints Concerning Human Research Ethics Committee Review Processes**

Most complaints received by HRECs concern the review process itself or the manner in which researchers and their projects have been considered and dealt with. For example, researchers may complain when an ethics committee has rejected a proposed project, when a committee is perceived to be taking undue time considering a proposal, or when conflict has arisen between a committee and researchers. While the majority of complaints are from researchers, all parties to the research process are free to take such action.

In many situations the problem may simply be one of inadequate communication between the committee, its officers, and the complainant(s). This may be dealt with by hearing the concern or complaint and responding to the substance of the matters raised. In some circumstances an appropriate response will be to provide more information.

\textsuperscript{16} A survey of more than 200 ‘whistleblowers’ in the United States showed that 90% had been sacked or demoted, 27% faced lawsuits, many had lost homes, gone bankrupt, divorced, suffered ill health or attempted suicide. See Bill Mellor, ‘Integrity and Ruined Lives’, *Australian Time Magazine*, 21 October 1991, p.51. J.P. Swazey and S.R. Scher have said that the ‘almost universal experience of whistleblowers...is that their actions generate a vehement, angry, and often punitive response by colleagues and superordinates.’ See Judith P. Swazey and Stephen R. Scher, ‘The Whistleblower as a Deviant Professional: Professional Norms and Responses to Fraud in Clinical Research’ in *Whistleblowing in Biomedical Research: Policies and Procedures for Responding to Reports of Misconduct*, op.cit. p.187.

\textsuperscript{17} Glantz has said in relation to research fraud: ‘institutions rightly feel that disclosing a research fraud will affect their future reputation and quite possibly their further eligibility for grants...’ See Leonard H. Glantz, ‘Commentary: The Role of the IRB in Monitoring Research’ in *Whistleblowing in Biomedical Research: Policies and Procedures for Responding to Reports of Misconduct*, op.cit., p.77.

\textsuperscript{18} Swazey and Scher, op.cit., p.184.

\textsuperscript{19} Ibid., pp.66; 70
However, some complaints might require HREC acknowledgement of a mistake and modification of subsequent responses. For example, a committee that takes far too long to respond to researchers’ applications may need to acknowledge this shortcoming and rectify it. Those complaints that cannot be resolved in this way will require further consideration and may become the subject of an appeal and mediation as outlined below.

SANCTIONS

Except in relation to clinical trials, there are few sanctions available in a legal sense. However, an ethics committee possesses a powerful sanction in terms of its ability to withhold approval of a research project and to advise an institution that a particular project should be discontinued (NS 2.13). Such sanctions are likely to result in serious negative consequences for researchers in terms of their ability to publish articles and obtain further funding for research. There may also be financial consequences if grants have to be returned to funding bodies. Other sanctions might include notifying professional registration boards of decisions taken in relation to unsatisfactory performance of research.

Institutions should provide a clear account of circumstances in which research projects might be discontinued. These should include serious misconduct by researchers, projects found to be jeopardising the wellbeing of research participants, and situations where researchers appear to have let a study lapse and have failed to meet the HREC’s reasonable requests to complete their study within specified time frames.

The Therapeutic Goods Act 1989 (Cth) now contains offences for intentionally acting or omitting to act or being reckless as to whether an act would breach a condition of approval for use of unregistered goods. These conditions now include compliance with the National Statement. Further reference should be made to Appendix 2 to this Collection.

APPEALS AND REVIEW OF HUMAN RESEARCH ETHICS COMMITTEE DECISIONS

If complainants have a concern about any ethics committee action in relation to a program of research, they should contact the complaints officer and attempt to resolve the issue.

Where the complaint is about a decision or action of the committee, the complainants should be provided with information about the reasons for the decision. If the matter is not thereby resolved to the satisfaction of the complainant, they may take further steps, including an appeal against the decision. These steps may include the following.

- The ethics committee or the researcher may contact the Australian Health Ethics Committee for advice on interpreting NHMRC Guidelines, or this Handbook, in order to reach an appropriate decision or to help a complainant understand the reasons for the committee’s decision.

- If the complainant(s) are still not satisfied, they may seek a meeting with the chairperson and the complaints officer of the ethics committee for further clarification. The complainant(s) may be accompanied by one or more support persons, or, in the case of researchers, one or more colleagues. A record of any such meeting should be kept.

- The institution and the complainant(s) may agree on a person who can take the role of mediator, not necessarily a professional mediator, in an attempt to resolve the dispute. The institution should bear the costs of such mediation.
• The mediator should consider the complaint, the reason(s) for the committee's original decision (from the minutes of the relevant meeting), the advice, if any, provided by the Australian Health Ethics Committee and the record of the meeting with the chairperson and the complaints officer, as above. Having considered this material, the mediator should then meet with the parties, attempt to facilitate a resolution of outstanding issues and provide a report of the results of that meeting to the institution.

• If the matter remains unresolved despite such steps being taken, the final decision rests with the relevant institution. In some circumstances it may be open to a complainant to seek judicial review.
CONFLICTS OF INTEREST

[NS 2.19–2.21, 12.6 and Commentary]

CONFLICTS OF INTEREST AND HUMAN RESEARCH ETHICS COMMITTEE MEMBERS

No member of an ethics committee should adjudicate on research in which he or she has any conflict of interest, including any personal involvement or participation in the research, financial interest in the outcome, involvement in competing research, or an interest as an academic supervisor of a student researcher (NS 2.20). Such a conflict of interest is most likely to arise when a member's own project is being reviewed. However, a conflict of interest also arises when a member is involved in competing research, or has any financial interest in the outcome of the review process.

When a committee member has a conflict of interest in relation to a project under review, or could be seen to have a conflict of interest, that member should withdraw from the meeting. The absence of the member concerned should be recorded in the minutes. In addition, a committee member in this situation should refrain from discussing the project with other committee members, or attempting to influence the committee in any way. HRECs relying on the advice of subcommittees or advisory bodies should also seek assurance that members of these groups will declare any conflict of interest.

CONFLICTS OF INTEREST AND THE RESEARCHER

The expression 'conflicts of interest', used in an ethical sense, refers to conflicting obligations or influences confronting an individual in the course of a relationship or activity that has some moral content. Conflicts of interest may or may not involve explicitly recognisable dilemmas; they may or may not involve financial or monetary interests. Some have tried to define the nature of an ‘interest’ and the conditions for a ‘conflict’ more precisely, while others have sought to distinguish conflicts of interest from conflicts of loyalties or obligations.20 The central issue, however, is that individuals engaging in conduct that has ethical dimensions are drawn in two directions at once in such a manner that their judgment may be affected, or their motives may be open to question.

Conflicts of interest can, and do, arise in the research context. Conflicts frequently occur between the roles of clinician and scientist in a biomedical context. The obligations of a researcher to answer a question, to clarify mechanisms or to understand a process may be at odds with the primary interest of a sponsor in achieving financial gain, or the interest of the researcher in achieving personal success or recognition. Academic supervisors of student research projects may also face conflicts of interests between the needs of students to complete their project to a required timetable and the interests of potential research participants, and the general community, in ensuring that all research involving humans is ethically conducted.

Conflicts of interest are not usually the result of malign motivations of particular individuals but most often arise out of the structural features of relationships or practices. In many situations, therefore, it is impossible to eliminate conflicts of interest. Rather, these should be identified where they exist and steps taken to disclose them openly and control their impact.

It may be, for example, that increasing economic pressures from government have intensified conflict situations within research practice. The intensification of an entrepreneurial spirit within the biomedical research environment may well increase the gap between professional and personal interests of practitioners. Similarly, reductions in funding for research and universities may distort the choices researchers make and, contrary to the wider public interest, researchers may favour projects that deliver immediate economic returns rather than new basic insights that will foster future innovative work.

HRECs play a key role in assessing and clarifying conflicts of interest in the research setting and in limiting any possible adverse consequences. An ethics committee may need to ask a few fundamental questions about the nature, funding and institutional structures involved in the research project in order to develop procedures for dealing with the most common conflicts. For example, it is important to ask whether a particular research proposal has a primary commercial purpose, or seeks to answer genuine research questions. It is also important to ask whether the combined roles of clinician and scientist are likely to influence either the appropriate treatment of patients or the ethical conduct of the project, and whether sponsorship from industry will limit scientific communication in order to protect proprietary information. When the committee is discussing a project, members with personal interests in the study should absent themselves. On occasion, it may be necessary to seek specific advice from disinterested parties.

Similarly, with regard to the actual conduct of the research, a clinician may be advised to ask a fellow researcher to take responsibility for approaching his or her patients about the possibility of participating in the study. In addition, an independent review committee may be necessary to ensure that adverse events are properly scrutinised and the trial stopped if risks to participants become unacceptable.

In summary, conflicts of interest arise in many ways in relation to research involving humans, and both HRECs and researchers should be sensitive to the potential impact these may have. Rigorous disclosure of opposing interests will help avoid problems, or facilitate their resolution if they should arise. Specific questions, however, need to be considered within the contexts of particular types of research.

Points to consider

• What parties have interests in the specific research setting and exactly what are their interests?
• Is the primary purpose of the research project a commercial or a scientific one?
• Does a researcher face a conflict of interest with regard to the obligations of, or pressures involved in, having more than one professional role in relation to a specific research project?
• Is sponsorship from industry likely to limit scientific communication in order to protect proprietary information?
• Have researchers fully disclosed any financial interests relating to the research project? Is any payment to researchers fair and not excessive?

Suggested reading


CONSENT

[NS 1.7–1.12, 15.4–15.8, 16.9–16.14 and Commentary. ‘Consent’ is also discussed in other relevant sections of the Commentary.]

TRUST

Consent is widely believed to affirm the autonomous decision-making rights of prospective research participants, and their capacity to protect their own interests. However, this belief can also be seen as simplistic, for it can seem to ignore the wrongness even of asking people to consent to some proposals (for example, to becoming enslaved).21 In biomedical research, for example, many research participants who are also patients trust their physician, who is also the researcher, to guide them through this decision-making process.22

A ‘Subject Interview Study’ conducted by the United States Advisory Committee on Human Radiation Experiments found, not surprisingly, that many factors influenced patients’ decisions to participate.23 What is striking about this research, and other studies,24 is the profound trust that participants placed in researchers and the research enterprise. However, while it is no doubt true, as E.D. Pellegrino has suggested, that trust is essential to all human relationships25 and that this is a critical aspect of the relationship under discussion, trust does not necessarily protect the vulnerable party to a relationship from being harmed.26 Taking advantage of participants’ vulnerabilities is a serious abuse of trust and HRECs must safeguard research participants against this.

FORMS OF CONSENT

Consent to participation in research should normally be provided by participants themselves. However, there may be circumstances where other forms of consent are acceptable:

- Deferred consent is where the subject is entered into a research study and consent is gained from surrogates after a specified period of time for continuation of the subject’s inclusion in the trial. This form gained popularity in the research community in the 1980s but was abandoned by the US Department of Health and Human Services on legal advice in 1993.

- Prospective informed consent represents an attempt to canvass support in advance from a population considered at risk of developing a serious illness. This approach suffers from all the weaknesses associated with advance directives, and is rarely applicable to the conditions relevant to emergency research, such as sudden cardiac arrest or motor vehicle trauma.

- Surrogate consent (ideally a substituted judgement made by a person responsible for health care decision-making for a particular patient under the relevant legislation) has been questioned, but remains the standard for autonomous health

care decisions in incompetent patients. This form of consent remains relevant in all but the most emergency situations, and offers some reassurance that the requirements described above have been considered.

CONSENT AND INDUCEMENT

Inducement involves the offer of excessive and inappropriate reward in order to obtain compliance from potential research participants. Examples of inducements may include payment for research participation, offers of subject credits to students, or promises of leniency to prisoners.

Inducements compromise the ability of the potential participant to make a free choice. However, exactly what constitutes excessive or inappropriate reward can be difficult for an HREC to determine. Monetary compensation appropriate for volunteers of a medium socioeconomic group (or for a member of an HREC), could well constitute an inducement for volunteers of a lower socioeconomic group. Economic disadvantage and/or low self-esteem may be found among certain dependent groups. Both these factors make exploitation by way of inducement far more likely. But equally, people in dependent relationships should not be exploited by denying them due reward for taking part in research projects.

Payment may induce the participation of those who are most vulnerable, leading to exploitation of the poor as research participants for the primary benefit of the rich. Indeed, there is some evidence to support this view. However, at the same time, a certain level of payment may constitute fair recognition of the contribution that participants make to research. In assessing whether a payment constitutes an inducement, as opposed to appropriate recompense, HRECs need to evaluate each research proposal within its specific context. Committees will need to weigh the risks associated with participation, the relative freedom of potential participants to refuse to take part uninfluenced by an offer of payment, and the degree of the participant population’s vulnerability to exploitative offers.

Further reference should be made to the Research Ethics Collection, ‘Prisoners, research involving’, page E121, for a more detailed discussion of these issues, and to the Research Law Collection, ‘Consent’, page L13, for a discussion of legal issues.

CONSENT, REFUSAL AND WITHDRAWAL

Withdrawal of consent to further participation needs to be distinguished from removal of all data related to the participant who withdraws. In some cases, where all data about the participant are identifiable, withdrawal of consent can be accompanied by withdrawal or destruction of data relating to that participant. In other cases it may be practically impossible to withdraw information specific to a particular participant, or it may be that the research would be undermined were such withdrawal to take place.

It is important to distinguish between ‘identifiable’, ‘potentially identifiable’ and ‘de-identified’ data. If data are identifiable, they will be possible to track that data belonging to a particular individual and, in some situations, remove them from the collected research data. If data are de-identified, it cannot be identified and tracked. That is, all identifiers have been removed from the data and it is therefore impossible to retrieve or expunge information related to a particular individual. ‘Potentially identifiable’ data, though not immediately identifiable, may be re-identified via the code used to replace participant identifiers, such as the name of the participant concerned. Therefore, it may be possible to retrieve and expunge potentially identifiable data when a participant withdraws consent.

However, it may be difficult or time-consuming for the researcher to retrieve a sample. An HREC must also consider whether the validity of the study could be affected by withdrawing such a sample.

If it is initially intended that a sample or data not be withdrawn after a particular stage in the research process, then this should be made clear on any information sheet or consent form given to potential participants. A researcher should also be asked to justify the rationale for this requirement.
DECEPTION, RESEARCH INVOLVING

[NS 17.1–17.2 and Commentary]

An HREC needs to consider research involving deceptive components on a case-by-case basis. For example, a minor degree of deception may be of little significance for one class of participant but have a devastating impact on others.

Some types of participants will be especially vulnerable to deception. For example, a research project that sought to examine gender differences in the response to failing a test and which entailed deceiving a group of school children into thinking that they had failed might have adverse effects on morale, self-confidence and trust of elders that may not be smoothed away by debriefing. An identical project might have minimal impact on university students.

The use of deception to facilitate recruitment of participants for a project is invariably unethical. This may become a more pressing issue in the future, especially for HRECs that receive proposals for the controlled testing of new surgical procedures that entail the use of sham operations. Traditionally, clinical trials of any type of procedure have entailed the provision for entering participants to be randomly allocated to one of two or more groups. Participants must also be told, in ‘conventional’ trials, that some of them will receive a placebo, or the best existing form of treatment (if there is one). That is, although the participants do not know to which treatment group they have been allocated, they are not provided with incorrect information.

However, in some recent surgical trials, in which the aim has been to distinguish psychological effects occurring in the sham operated group from the effects achieved in those receiving the surgical procedure under test, it has not always been clear that all patients realise when consenting that they may subsequently be deceived. This should be of particular concern to an HREC when the medical condition for which a sham operation may be provided is so serious that the judgement of prospective participants may be warped by ‘last resort’ hopes. Researchers, and HRECs dealing with projects that involve comparison of appropriate and sham procedures for life-threatening conditions should be especially careful that they do not become complicit in varying degrees of self-deception by highly vulnerable participants. It is the responsibility of the researcher to ensure that this type of prospective participant is fully aware of the possible options that may be selected for them. It is the responsibility of an HREC to ensure that the researcher meets this requirement.

Covert observation is usually regarded as acceptable if undertaken in a public place. Some qualification to this generalisation may, however, be appropriate. For example, it is implicit in sanctioning unconsented observation of individuals in a public place that they are aware that any of their actions will be visible to anyone simultaneously present. However, in the case of an individual who is incompetent, either temporarily as a result of alcohol or other drugs, or persistently as a result of disease, it cannot be inferred that they have considered the likelihood that others may observe them and, consequently, consent to such observation. In these circumstances, an HREC may well have reservations about the ethical adequacy of the protocol. The nature of activity that is being covertly observed may also be a factor in deciding on acceptability of the protocol. An HREC may well question whether all activity undertaken in a public place is fair game for the researcher. The recording of some types of activity, including (but not limited to) illegal activity, may have harmful consequences for the individuals who are being observed. See also the Research Law Collection, ‘Illegal conduct, research involving’, page L37.
EMERGENCY AND INTENSIVE CARE RESEARCH

[NS 6.1–6.10 and Commentary]

Frequently, in the intensive care and emergency setting, informed consent cannot be obtained from potential research participants.

These people have most likely been admitted to hospital without being able to give their consent. The hospital situation is acute, non-elective and unforeseen and there is often an incompetence, a loss of decision-making rationality or a reduced capacity, rationality and comprehension to understand. In addition, even when people in these situations are capable of giving consent, they are quite likely to feel coerced into ‘cooperating’. Perhaps some degree of coercion is unavoidable in such a highly emotionally charged situation, confronted by a life-threatening illness and high dependence on the treating physician (especially where she or he is also the researcher). In these situations it is essential that an independent third party, such as a State Guardianship Board or person lawfully appointed to do so, acts on behalf of the potential participant in giving, or refusing, consent to inclusion in a research project. It is not legally valid for this decision to be taken by any other party, including the ill person’s next-of-kin. For discussion of legal aspects, see the Research Law Collection, ‘Emergency care, research and’, page L27.
EMPLOYEES, RESEARCH INVOLVING

[NS 7.1 and Commentary]

The researcher and HREC need to consider the extent to which the research will affect not only those employees who will be participants, but other employees as well. The freedom of potential participants who are employees to refuse to participate without disadvantage and the means of protecting the identity of participants and the confidentiality of information given to the researcher will require careful attention. Suitable consultation will normally be necessary with the employer.

Different place of employment and different research designs are likely to raise different issues.
EPIDEMIOLOGY RESEARCH

[NS 14.1–14.13 and Commentary]

EPIDEMIOLOGICAL STUDY DESIGNS

Epidemiological study designs can be broadly divided into observational and experimental studies. In observational studies events are simply observed, while in experimental studies an intervention takes place with the aim of bringing about a specific change. What happens following that change is then observed.

There are three types of observational studies: cross-sectional, case control, and cohort studies. Such studies generally involve participants in the completion of questionnaires or, occasionally, undergoing laboratory tests, or they may simply involve the examination of medical records.

Cross-sectional studies, or surveys, are commonly carried out on a random sample of a specific population. This may involve completion of questionnaires or interviews, a medical examination or laboratory investigations. The aim is to assess aspects of the health of a population, or to test hypotheses about possible causes of disease or suspected risk factors.

Case control studies compare individuals who have suffered from a particular disease with a control group of people who have not. These studies look for differences between the people in the two groups in an attempt to identify what may have been responsible for the development of the condition being studied. For example, the amount of smoking among people with lung cancer is likely to be greater than that in a control group of people who do not have lung cancer, because smoking is a cause of this disease. Different frequencies of past exposure to suspected risk factors between the two groups could be statistically analysed to test hypotheses about possible causes of disease or suspected risk factors.

In cohort studies, also known as longitudinal or prospective studies, individuals with differing exposure levels to suspected risk factors are identified and observed over a period of time, commonly years, and the rates of occurrence of the condition of interest are measured and compared in relation to exposure levels.

Again, participants may be requested to fill in questionnaires, or to undergo medical examinations or laboratory investigations. These studies may involve many thousands of people and therefore, while they provide similar information to a case control study, the information obtained from cohort studies is generally considered more reliable. However, because this type of study involves large numbers of participants and continues for an extended period it is expensive to conduct.

EPIDEMIOLOGICAL RESEARCH AND PUBLIC HEALTH SURVEILLANCE

Public health surveillance should be distinguished from epidemiological research. Public health agencies are required, or authorised by law, to carry out health surveillance. For example, a public health authority may observe an unusual increase in the incidence of a particular infectious disease. This authority must then take urgent action to establish the cause of the problem. Such action does not need to be approved by an HREC. Indeed, to delay action until ethical approval could be obtained would be negligent.

Researchers, however, do not have the responsibility that a public health authority has and do not need HREC approval before their proposed study can go ahead. The above distinction may not always be immediately obvious, and ethics committees need to be aware of this.
Suggested reading


**ETHICAL THEORY**

HREC members could adopt a number of approaches to assessing the ethical aspects of research proposals. They might rely on their intuitions about whether or not a proposal is morally acceptable or they might apply specific moral theories to this assessment. Such theories include ‘utilitarianism’, ‘virtue ethics’ and ‘rights-based’ moral theory. Several ethical frameworks have been applied to ethical issues in research practice and these are discussed in detail in the relevant literature.28

According to utilitarian moral theories, it is the outcomes or consequences of actions or policies that denote whether or not an action or policy is ethically acceptable. Actions or policies that promote positive outcomes, understood in terms of improving welfare and increasing happiness or the satisfaction of preferences, are ethically acceptable. Those that are likely to lead to negative consequences, understood in terms of causing harm and increasing suffering or frustrating preferences, are not. Utilitarian moral theories focus on the ‘greatest good for the greatest number’ and do not recognise individual rights as the primary ethical concern.

Those who adopt a virtue-based ethic focus on the development and exercise of sound moral character. Here, virtuous character traits, such as generosity, goodness, kindness, sympathy and care for others are valued and encouraged.

Rights-based moral theories focus on the identification of the moral rights relevant to a particular course of action, such as the right to life, the right to self-determination, the right to privacy, or the right to health care. Rights-based theories require an assessment of actions and states of affairs in terms of the identification of conflicting rights, the potential for rights violation and the protection of the individual’s rights.

An HREC member who chooses to assess research proposals in terms of moral theory would face the constant challenge of having to resolve the central conflict between utilitarian and rights-based theories. That is, the conflict would be between the ‘greatest good for the greatest number’ and the primacy of individual rights.

Another possible approach to the assessment of research proposals involves applying a set of moral principles to the circumstances of the specific proposal and assessing whether or not it is consistent with those principles. Ethical ‘principlism’, which has been central in the development of the bioethical literature, and the literature concerning research ethics in particular, seeks to avoid some of the problems associated with the application of abstract moral theories to practical ethical questions. At the same time, ‘principlism’ draws together ethical considerations grounded in different moral theories, such as concern with individual rights to autonomy, respect for persons and the promotion of social welfare and the avoidance of harm.

The National Statement refers to three key ethical principles (see NS 1.2–1.5)

- respect for persons: ‘individuals should be treated as autonomous agents and that persons with diminished autonomy are entitled to protection’;
- beneficence: ‘the obligation to maximise possible benefits and minimise possible harms. (The obligation to do no harm is referred to separately as non-maleficence.’); and
- justice: ‘addressing the resolution of the question of who ought to receive the benefits of research and bear its burdens.’

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These principles are generally relevant to the evaluation of research ethics, no matter what ethical theory or framework an HREC member adopts. Some principles may simply carry greater weight depending on the individual committee member’s ethical position. However, it should also be pointed out that this approach could, on occasion, lead to differing recommendations.

For example, an emphasis on respect for persons, understood as respect for participants’ autonomy or self-determination, can conflict with concern for beneficence or wellbeing. For instance, providing a participant with information about the outcome of tests undertaken as part of the research process might have harmful consequences for that participant.

Another example is a research project that involves taking blood samples from several members of a family. The results of the blood test might demonstrate that a particular child could not have been fathered by the man whom the participant has always accepted as her or his biological father. It could be argued, on the basis of respect for persons, that participants ought to be told of the finding, even though they might be badly affected by the news. However, it could also be argued, on the basis of beneficence, that revealing this information would be harmful to a participant and so should be withheld. In addition, this particular example is complicated by the fact that several members of the same family are involved, and so revealing this information to the participant could well affect other family members. It is the significance (or salience) of each principle in a particular context that is the key to the resolution of such conflicts.

However, regardless of the ethical position an HREC member adopts, it is essential that committee members identify and evaluate the relevant issues. This section of this Collection suggests an approach to ethics committee review that focuses on the process of identifying, assessing and balancing relevant ethical aspects of specific research projects.
GAY MEN AND LESBIANS, RESEARCH INVOLVING

Research issues relevant to gay men and lesbians are similar to those for any marginalised population. As with standard practices adopted in research involving people from religious or ethnic minorities, for instance, it is suggested that procedures protecting gay and lesbian research participants from stigmatisation or further marginalisation, either as individuals or as members of a community, should be adopted.

RELEVANT CONSIDERATIONS

When reviewing research protocols involving gay men and lesbians, HRECs should consider several specific issues. These include: community involvement; the appropriateness of the language used; the appropriateness of the methodology; confidentiality and disclosure of sexual orientation; respect for cultural difference; HIV/AIDS issues and gay men; involvement of gay male participants under the age of consent; recruitment issues; differences between gay men and lesbians; transgender issues; and research into the causation of homosexuality.

Community involvement

Research involving gay and lesbian participants should include consultation with appropriate gay and lesbian community agencies and their community representatives at the research design stage. Such community representatives are in a position to act as consultants in commenting on the research design, the appropriateness of language used in questionnaires, recruitment material and the likelihood of serious or damaging repercussions for individuals and their communities where issues of privacy may, sometimes unwittingly, be infringed by researchers.

Such consultants include, for example, lawyers with a knowledge of legal rights issues, academics with knowledge of the specific discipline, educators who have worked with gay men in AIDS Councils, or health workers who have a good knowledge of lesbian health issues. HRECs that often deal with requests to work with gay and lesbian communities should keep a resource bank of names of people who can assist with this work.

Gay and lesbian community representatives with knowledge of the violence and harassment issues that have occurred in a particular community will be the best people to predict where such problems might arise. For instance, it has been noted around the world that when details of gay or lesbian nightclubs are published or publicised, violence against those who attend them often increases. Because of the potential risks associated with some research involving gays and lesbians, many prospective participants will expect feedback processes to be established and that outcomes from the research project will be used, where appropriate, to assist in improving the position of gays and lesbians in society.

Appropriate language

Terms used in research material need to be appropriate to the target group and any particular subculture involved. Some gay men and lesbians will refer to themselves as queer, for instance, whereas others will prefer to use gay or lesbian, ‘men who have sex with men’ or even the vernacular of ‘queen’ or ‘dyke’.

The use of terms such as ‘victims’ or ‘sufferers’ when referring to people with HIV/AIDS is unacceptable in view of the connotations of helplessness and disempowerment. Similarly, the use of judgmental terms in questionnaires such as ‘sexual minorities’, when this might be used to infer inferiority of one’s sexual preference, should be avoided.
Appropriate methodology
Some research instruments that list sexual practices from ‘normal’ to ‘deviant’ or ‘way-out’, and which ask participants to tick those that they have been involved in, have been criticised for their insensitivity and judgmental undertones. Such problems could be avoided by consultation between researchers and gay men and lesbian community consultants.

Confidentiality and disclosure of sexual orientation
In addition to confidentiality provisions that apply to all research, with gays and lesbians specific permission should be obtained to disclose details of sexual orientation. This applies even where the individuals concerned may be regarded as open, or ‘out’, about their sexual orientation.

Respect for cultural difference
Attempts by researchers to compare aspects of gay culture with the mainstream, or to incorporate it into the latter, may not be in the best interests of some gay men and lesbians. For instance, a research project on beats may reach conclusions that could potentially damage the participants involved by pathologising behaviour when making comparisons with heterosexual, or even other homosexual, ‘norms’. Lack of respect for a culture can be damaging to both the individuals concerned and the community as a whole.

HIV/AIDS and gay men
While the issue of HIV/AIDS-specific research is dealt with in this Collection, issues to do with assumptions about gay men and safe sex in the age of HIV/AIDS still needs to be mentioned here.

HRECs should ensure that researchers are careful not to include their own paradigms or beliefs in the way they form questions or draw conclusions about an individual’s intentions when it comes to safe and unsafe sexual behaviours. For instance, in surveys of people’s intentions to have unsafe sex, researchers should check their own assumptions before attributing blame to behaviours and deciding on possible ‘aggressors’ and ‘victims’ in the process.

Involvement of gay male participants under the age of consent
HRECs should protect the interests of both the researcher and the research participant when individuals to be interviewed are under the age of sexual consent. Any possibility that researchers might be accused of illegal sexual activity with a minor should be avoided by the implementation of appropriate protocols establishing acceptable neutral places of interview.

Recruitment
Because of the difficulties that might be involved in recruiting gay men and lesbians for research projects, and particularly the risks involved in revealing their sexuality, recruitment methods need to be carefully detailed in the research protocol. For example, a technique called ‘snowballing’ is often used in relation to marginalised communities. This involves research participants finding further recruits for the research project. The rules for using this technique should be tightly controlled and no researcher should ask one participant to give the name and contact details of another potential recruit.

Enticements to participate in research projects also need to be monitored carefully. It has been common practice to use the classified section of gay newspapers to advertise for
gay men to participate in research projects, using catchy phrases like ‘Do you like having sex with other guys?’ without mentioning that if the individual rings this number he will be asked to participate in a research project. In general, the use of methods of recruitment that employ deception in this or any other way is inappropriate.

**Differences between gay men and lesbians**

While gay men and lesbians are often considered together because of the same-sex nature of their relationships and the similar issues that they may experience in their treatment within society, there are many research issues where they might be best studied separately. Issues to do with health, parenthood, sexuality and perceived roles and status in society, for example, are often more to do with gender than with any shared concept of a ‘gay and lesbian community’. Many issues to do with lesbians and lesbian culture will have more to do with women’s issues, and some issues to do with gay men will have more to do with the gay male subculture and with masculinity. HRECs should be sensitive to these differences and be prepared to guide researchers where appropriate.

**Transgender issues**

While some researchers may assume that people of transgender belong to the gay or lesbian community, this is not the perception of some people of transgender. For example, such people who were previously men will argue that they are now women, a fact not readily accepted by many in the women’s movement. However, some people of transgender do regard themselves as being gay or lesbian and this needs to be taken into account by researchers for whom such data might be significant.

**Research into the causation of homosexuality**

It has been argued in the relevant literature that biomedical research has failed to produce evidence for a possible cause of homosexuality and the question has been raised as to whether it is ethical to conduct research into this subject. It has been suggested that such research is unethical as it adopts a heterosexist perspective on the issue, with undertones that any difference from a heterosexual ‘norm’ is somehow inferior and should be changed or cured.29 Others argue that while researchers should not be prevented from investigating this subject, they should examine any assumptions made about the relationship between cause and effect in reaching their conclusions and should also consider whether these assumptions could also be applied to other forms of sexual expression in society.

**Points to consider**

- Will gay and lesbian community representatives be consulted before research into their communities begins, in order to check that appropriate safeguards are in place for participants, that privacy is protected, that appropriate language is used in research material, and that the researchers understand the need to protect cultural differences between gay and lesbian communities and the predominant heterosexual culture?

- If gay, lesbian and transgender groups are to be involved in research, will representatives be consulted separately to discuss specific issues related to their communities?

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• If relevant, does a research proposal include specific safeguards to protect the interests of researchers as well as research participants where the latter are under the legal age of consent?

• Does the research proposal include specific measures that will ensure that recruitment processes are ethical? Use of recruitment processes such as ‘snowballing’ can have dangerous ramifications for the protection of people’s privacy and careful attention should be given to methods of recruitment through advertising with regard to the avoidance of deception or enticement.

Suggested reading


GENERAL PRACTICE RESEARCH

General practice is the branch of medicine that provides primary care, preventive care and comprehensive continuing care to individuals and their families in a community setting.\(^30\) The primacy of the patient in the clinical encounter, the durability and continuity of the relationship between medical practitioner and patient, the importance of context and process rather than merely content, and the significance of the relationship between practitioner and patient have all been widely acknowledged as influencing outcomes.\(^31\) These factors are also defining characteristics of general practice, as well as contributors to the emerging patient-centred model of health care.

By its very nature, therefore, general practice is holistic and anti-reductionist in its approach to diagnosis and management. General practitioners see patients in their clinics, at the patient’s home, in nursing homes and in hospitals. Domiciliary care provides practitioners with privileged insights into the lives of patients and their interactions with their environment. It also provides general practitioners with an appreciation of the importance of social support systems and the significance of interdisciplinary care in maintaining the wellbeing of chronically ill people. In addition, general practitioners often see patients over very long periods of time and establish professional relationships with many different members of a family group.

This special nature of general practice raises particular ethical issues in relation to research practice. In the past, this type of research has not always been subject to assessment by ethics committees. In recent years, however, the importance of formal ethical review has become increasingly recognised and research projects are now often assessed by HRECs in hospitals and universities, or by the ethics committee of the Royal Australian College of General Practitioners.

As general practice is conceptually positioned between the biomedical and social sciences, research questions raised by general practitioners may be of either a biomedical or a social science nature and the methods employed to investigate these questions will be linked to accepted methodology in each of these fields. The major fields of general practice research are listed below, along with related examples.

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<tr>
<th>Field of research</th>
<th>Examples</th>
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<tr>
<td>1. Clinical/Epidemiological</td>
<td>Illness, disease, morbidity patterns, treatment</td>
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<tr>
<td>2. Health service</td>
<td>Medical workforce, funding, care models</td>
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<tr>
<td>3. Behavioural</td>
<td>Patient lifestyle, doctor/patient relationships, practitioner behaviour, patient education and health promotion</td>
</tr>
<tr>
<td>4. Professional</td>
<td>Education, training, inter-professional relationships, medico-legal and ethical issues</td>
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The research designs employed in these fields will vary from the experimental in the case of pharmacological or behavioural interventions, to descriptive in the case of surveys (qualitative, semi-qualitative and quantitative), to analytical in the case of epidemiological research (case control studies, cohort studies and cross-sectional studies). While each of these research fields raises ethical issues that are common to all research involving humans, there are special features that apply within the context of general practice. These can be considered under the headings of: coercion and consent, confidentiality and intrusiveness.


The Research Ethics Collection

COERCION AND CONSENT

Patients may feel obliged to participate in research projects suggested by their general practitioner in return for the care and attention they have received over the years. This places general practitioners in a potential position of power and leaves the patient potentially vulnerable. (See NS 7.1–7.2.)

HRECs should be aware of this latent power differential. It is important that the research proposal makes it clear that refusal to participate, or withdrawal during the project, will not damage their ongoing relationship with their general practitioner. Signs may be erected in practitioners’ waiting rooms pointing out that the practice is involved in a research project and inviting participation, while at the same time emphasising that failure to participate will not damage the person’s relationship with their doctor. HRECs will need to assess whether or not they consider the above measures adequate protection from coercion for patients of general practitioners.

Because the general practitioner is often one of the researchers, it is frequently helpful to involve an independent third party, such as a nurse, in the consent process, and to insist on a ‘cooling off’ period between the time when explanations about the project are given and data collection begins.

CONFIDENTIALITY

General practitioners are in a position of trust. They carry with them documented and undocumented information not only about patients but also, frequently, about their families. Often, a general practitioner will treat many members of the same family. HRECs should be satisfied that research proposals that include the collection of data from clinical records ensure protection of confidentiality, as discussed in the Research Law Collection, page L7.

Research proposals involving audiotaping or videotaping of clinical consultations pose a particular threat to the protection of confidentiality and privacy for the research participant. Particular problems can also arise in relation to research projects involving the use of patient notes, especially in a retrospective manner. In these situations, it may be difficult or impossible to contact patients, for example, where people have changed addresses or died. The ethics committee will need to consider carefully whether the potential benefits arising from the project are sufficient to justify allowing it to proceed.

INTRUSIVENESS

All research involving humans is potentially intrusive. In general practice, the process of data-gathering rarely involves collecting tissue samples or bodily fluids so that physical pain is not usually an issue. However, it does involve collecting opinions or factual information and this is time-consuming for the research participant and may provoke anxiety. In-depth interviews may last an hour or more, with the simplest questionnaire taking 15 minutes to complete. This process remains intrusive, regardless of the length of time involved. HRECs should assess whether or not a research proposal of this type will be unduly intrusive from the point of view of research participants.

In addition, questionnaires seeking to assess risk factors for cancer, cardiovascular disease or mental illness may be administered to an unselected, or randomly selected, group of patients in a waiting room. The identification of positive responses may result in significant anxiety as an unintended consequence of the research project. Effective strategies for dealing with resultant apprehension and anxiety on the part of research
participants are therefore essential. Ethics committees should ensure that research proposals include an adequate plan for managing such unintended consequences.

**Points to consider**

- Are researchers aware that all forms of research on humans, including short questionnaire surveys, require the approval of an ethics committee?
- Are ethics committee members aware of the power differential in the clinical encounter and the consequent vulnerability of patients in relation to recruitment as research participants when the request is made by their general practitioner? Does the specific research proposal provide sufficient measures to protect patients against coercion?
- Does the research proposal contain sufficient safeguards against breaches of confidentiality and invasion of privacy with regard to research participants?

**Suggested reading**


GENETIC RESEARCH

[NS 16.1-16.16 and Commentary]

Genetic research involves the study of the nature, functions and control of genes in both health and disease. Work in this area has contributed significantly to the understanding of mechanisms underlying a number of serious medical conditions. It has led to the development of methods for screening for susceptibility to certain conditions and to new methods for diagnosis and treatment. It has also produced insights into the interactions between genes and environmental factors. These achievements have already resulted in important health benefits for both individuals and populations and it is likely that many new applications for the techniques of genetic research will be developed in the future.

Human genetic research may take several forms. It may involve:

- the study of individuals and/or families in which a particular medical condition is present. The study may involve analysis of medical information and testing of genetic material. Studies of families may involve family members both with and without the disorder;
- the study of the distribution of certain genetic traits within specific groups of individuals and the relationship between these traits and particular medical conditions. For example, the gathering and comparison of such information from both a group of affected individuals and a control group; and
- the development of new treatments for genetic disorders, including gene therapy.

OVERVIEW OF ETHICAL ISSUES RAISED IN RELATION TO HUMAN GENETIC RESEARCH

Genetic research involving humans may raise issues of a social or cultural nature. For example, the research may address socially contentious issues such as the nature of intelligence or personality, or have the potential to lead to results that may be used in a culturally or socially harmful manner in relation to specific ethnic or racial groups.

Genetic research may raise special issues concerning privacy and confidentiality. As already noted, there is a need to share genetic information within families. HRECs should ensure that genetic information flow within families gives due recognition to individual privacy and confidentiality, while at the same time maximising relevant health benefits to the family as a whole. However, at times, it may be difficult to conceal the identity of specific research participants or families. (See the Research Law Collection for a detailed discussion of the legal aspects of privacy of information, page L43.)

Obtaining informed consent may be especially difficult because of the complexity of the issues involved. Particular care is required when genetic research involves children or those with mental or intellectual impairment. (See the Research Law Collection for a discussion of the legal aspects of consent to research in relation to children, page L1 and this Collection for an exploration of this issue in relation to people with mental or intellectual impairment, page E101.)

On occasion, permission may be sought to study genetic information and material previously obtained either in a clinical setting or in relation to other research projects. HRECs will need to decide, in relation to the specific research proposal, whether to waive the requirement for consent. (See the Research Law Collection for a detailed discussion of the legal aspects of consent in relation to research in general, page L13.)

Special issues may arise about the storage and future use of genetic materials and information, and there may also be issues involved in providing research participants with the results of research. As already noted, some genetic research will produce
information of significance to the future health of specific participants. Such information may raise difficult questions about the participant’s future health, wellbeing and life opportunities, as well as present and future relationships. This possibility should be identified before research commences and participants should be informed of such a possibility prior to giving consent. In addition, the mechanism for feedback of research results should be defined.

In addition, research related to gene therapy and the genetics of embryos using cloning techniques carries specific risks that should be carefully considered. These issues are addressed in detail in other NHMRC documentation on gene therapy, cloning and assisted reproductive technology.[32]

OTHER RISKS AND RESEARCH INVOLVING CHILDREN

Genetic research involving children involves special ethical obligations for HRECs. In addition to considerations of third party consent, there are special considerations involved if the research includes pre-symptomatic or carrier testing. Therefore, research involving the genetic testing of children should not normally be undertaken in the absence of possible therapeutic interventions. Children may be at particular risk of stigmatisation both within and outside their families.

RESEARCH INVOLVING GENE THERAPY OR CLONING

‘Gene therapy’ refers to innovative techniques that involve the modification of genetic material for the purposes of overcoming an inherited or acquired genetic abnormality. ‘Cloning’ refers to a range of techniques directed at asexual reproduction, or copying of cells and organisms, including the possibility of cloning human beings. Both techniques are the subject of vigorous public debate about scientific, social and ethical implications.

At present, it is generally agreed that gene alteration involving human germline cells or human embryos, and cloning directed towards the production of new human individuals, should not be carried out. However, gene alteration for therapeutic purposes involving somatic[33] cells only may be legitimately pursued. Even so, both the scientific and ethical issues are complex and difficult.[34] For example, the potential adverse consequences of somatic gene therapy, including negative effects of interruption of a normal host gene and only partial correction of the disease, remain to be quantified. Therefore, at present, applications to consider research involving human participants employing such innovative techniques should be considered with extreme caution and individuals with appropriate expertise should be consulted.[35]

RESEARCH INVOLVING STORED MATERIAL

Some research projects may involve the use of genetic material or information that has been stored for other purposes, either clinical or research. Where possible, consent should be sought from the original donors. However, in some situations this will not be possible. Such situations include those where samples have been stored for a long time.

[33] Somatic cells are all the cells of the body except the reproductive cells.
[35] Ibid.
and the donors are untraceable or have died, or where it would be excessively difficult to trace donors. In these circumstances, an HREC may approve the use of these samples in either a coded or de-identified form. Where it is technically impossible to de-identify stored genetic material that is to be used for such purposes, HRECS should give particular attention to protection of the codes. However, where a donor has refused consent for his or her tissues to be used in this fashion, HRECS should give no such consent.

When relatives are to be approached for verification of the accuracy of information provided by others, or the gathering of additional medical information, it is generally appropriate for the researcher to seek the participant’s permission to do so and to ask that participant to make the initial contact. Where the research participant chooses not to approach a family member, it may be appropriate to seek the assistance of another member of that family or a health professional, such as a general practitioner, who may have an existing relationship with the person concerned.

In some situations, validation of family information provided by research participants may be achieved by simply consulting public records, such as those concerning births, deaths and marriages. In other circumstances, such as epidemiological studies, an HREC may decide that it is appropriate to validate the information obtained without the consent of the individuals to whom the information relates, provided that no additional information is obtained. For example, the committee may authorise access to computerised data sets or medical records to verify diagnoses.

**Suggested reading**

HIGHLY DEPENDENT ON MEDICAL CARE, PERSONS, RESEARCH INVOLVING

[NS 6.1–6.10 and Commentary]

There are several ethical dilemmas to be considered in research involving people highly dependent on medical care. The gravity of the person’s medical condition may mean that research interventions are particularly invasive and therefore pose increased risks. Free and informed consent is likely to be compromised due to the person’s medical condition and their reduced capacity to form, express and communicate an opinion.

There may also be a perception of coercion if a person is reluctant to refuse consent out of fear of compromising her or his medical treatment. Researchers may also need to consider whether an unfair burden of participation in research is being imposed on people in this situation. According to the National Statement, this includes people in emergency care, people in intensive care, neonates in intensive care, terminally ill people, people with impaired capacity for communication and people receiving medical care who are unconscious (NS 6.1–6.8). The primary ethical issue facing research involving people in emergency and intensive care areas is simple to state: informed consent from the participant at the time of enrolment in the study cannot be obtained; and yet clinical research in these areas offers much promise of community benefit.

All proposed solutions to this dilemma are problematic, and researchers are aware of this. There is considerable evidence from other countries that HRECs are frequently by-passed by researchers in both emergency care and intensive care departments, and even in university-affiliated hospitals with a properly constituted HREC. This is unacceptable, given that the critically ill person is uniquely vulnerable as a research participant (NS Preamble, page 6) and bad research is common in such patient groups.

RELEVANT INTERNATIONAL STANDARDS

On consent, the Nuremberg Code is uncompromising: ‘The voluntary consent of the human subject is absolutely essential’. No consent means no research. This was an important doctrine in the political context in which it was written, and remains the most philosophically tenable. However, it fails to address the above dilemma.

The Revised Declaration of Helsinki (2000) allows surrogate consent in relation to incompetent patients from the ‘legal guardian in accordance with national legislation’ (Rule 1.11). Regarding the potential for coercion, another rule (1.10) urges caution by a researching and treating doctor ‘if the subject is in a dependent relationship to him or her or may consent under duress’, recommending an independent doctor to obtain consent if this is considered likely. Recent legal commentary suggests that this may indeed be necessary in intensive care settings. Also introduced is the idea that recruitment of incompetent subjects is allowable ‘only to the extent that medical research is justifiable by its potential diagnostic or therapeutic value for the patient’. The implication here is that the research must have the potential for direct benefit to the individual participant: an impossible hurdle for a truly innovative form of therapy or for control subjects in a placebo-controlled trial.

53 World Medical Assembly 2000, accessible at http://www.wma.net/e/approvedhelsinki.htm
The European Convention on Human Rights and Biomedicine\textsuperscript{41} reiterates this in 17.1.ii, in allowing research in persons not able to consent only when 'The results of the research have the potential to produce direct benefits to his or her health', but allows in 17.2, where this criterion cannot be met, 'under protective conditions prescribed by law', research with 'the aim of contributing through significant improvement in the scientific understanding of the individual's condition, disease or disorder, to the ultimate attainment of results capable of conferring benefit to the person concerned or to other persons in the same age category or afflicted with the same disease or disorder or having the same condition'. The same section (17.2.ii) further stipulates that 'the research entails only minimal risk and minimal burden for the individual concerned'.

The US Food and Drug Administration introduced its own rules for the waiver of informed consent in emergency research\textsuperscript{42} imposing similar restrictions on researchers (and considerable burdens on HRECs), adding new criteria for community consultation and public disclosure. The addition of these new criteria has resulted in controversy, as well as a significant increase in the time that HRECs spend in considering research proposals.\textsuperscript{43} It is too early yet to gauge the ultimate result.

Current outcomes of this evolving process appear to be:

- The absolutist ethical position enshrined in the Nuremburg Code has given way to a more pluralist benefits v. burdens model. This is an ethically difficult stance and puts great burdens on HRECs.
- There is still a role for decision-making by representatives in non-emergency situations.
- Where no form of consent can be obtained (an emergency), a waiver of informed consent may be granted by the HREC subject to the conditions referred to above.

**Suggested reading**


\textsuperscript{41} Convention for the protection of human rights and dignity of the human being with regard to the applications of biology and medicine. Convention on Human Rights and Biomedicine by the Council of Europe, 6 Jun 1996.

\textsuperscript{42} Waiver of informed consent requirements in emergency research (CFR 45 CSR part 46) Federal Register, October 2 1996, 61, pp.51531–33.

HIV/AIDS

RESEARCH INVOLVING HIV/AIDS

Australia has an excellent record in HIV/AIDS research. For more than a decade researchers from government-funded research organisations like the three National Centres in HIV Research (Virology, Epidemiology and Clinical, and Social), as well as researchers working in other locations, have made important contributions to the world’s understanding and knowledge of the virus, its treatments and those it affects. While most research has been done in the area of medical science, increasing attention has also been made in recent years to research in fields of allied health (for example, nursing, occupational therapy, physiotherapy, social work) and in social research.

Detailed analysis of all these areas is not possible here and attention has largely been given to areas of research with the most potential to do harm to research subjects (that is, clinical trials). However, general ethical considerations that should be observed in HIV-related research are discussed below. They are:

Confidentiality

The need to take utmost care with patient confidentiality is a paramount consideration in HIV-related research. Because of the potential for serious discrimination, stigmatisation and general distress to occur if details of a subject’s HIV status was to be revealed to others, researchers must take great care to ensure that all personal details divulged are secure and that no identifiers are used on any publicly available material. Mail should not be sent to an individual’s address or phone calls made that could identify them as possibly being HIV-positive, as it is quite possible that people will have withheld this information from friends, flatmates or family members.

Particular consideration needs to be given to confidentiality because HIV is mainly transmitted through sexual or injecting practices, some of which may be stigmatised or illegal. Therefore the significant public health benefits arising from research on illegal behaviours must be weighed up against the possible dangers to research participants if they are encouraged to divulge illegal behaviours. The maximum degree of safeguarding of research participants’ privacy is therefore required. Researchers should avoid being placed in situations where mandatory reporting of behaviours to authorities is required (for example in relation to the commissioning of a crime, or in relation to child abuse) In some cases there is provision for exemption from reporting requirements to be obtained for research purposes. Participant anonymity should be offered where possible. In cases where identifying information on research participants needs to be kept for research purposes (for example, longitudinal studies) it should be stored separately from collected data. Participants should be informed of confidentiality procedures and also the risks, however remote, that there are some circumstances where researchers may be required to report on data, for example if subpoenaed to do so in court. Researchers should not claim that they are willing to be martyrs or ‘will never reveal their sources’.

Informed consent

The patient/participant consent form needs to give clear details of the purpose of the study, the procedures to be carried out, the amount of time requested of the individual, and the possible dangers or side-effects (if a drug trial), but it is also important that the form is clear about the possible benefits for the individual. Quite a number of HIV research trials do not offer any specific benefit to the participant and it would be unethical in these cases to leave participants with the impression that this is so.
It may also be helpful to explain the concept of informed consent to potential research participants to help them in their decision-making.

**Provision of debriefing**

Some subjects may be distressed by issues raised as a result of their participation in some research projects; it is important for researchers to prepare for this possibility by providing counselling to help with debriefing should this be required. HRECs should play a role in determining the likelihood of such a provision being necessary given the nature of the research in question.

**Community involvement**

The Third National HIV/AIDS Strategy
http://www.health.gov.au/hfs/publ/hivstrat_4.htm speaks of the importance of involving people with HIV/AIDS and their advocates in policy decisions that are made about them. While it will not be likely that many HRECs around the country are able to include a person with HIV/AIDS or their advocate when considering HIV/AIDS-related research, attempts should be made to:

a) include physicians, health professionals or lay people with a good knowledge of HIV/AIDS issues on IECs that consider a large number of HIV research proposals; and

b) require researchers wishing to recruit HIV-positive people to their studies to consult the affected communities first before commencing their research. This may involve discussions with People Living with HIV/AIDS organisations or AIDS Councils about the nature of the research. Some AIDS Councils already have Research and Ethics Committees (not formal HRECs) to approve all research related to their members, and these committees will usually only approve research that has been approved by an HREC first.

In the light of NS 2.6, institutions might consider including health consumers as members of HRECs that deal with HIV/AIDS-related research.

Recruitment of HIV/AIDS research subjects may be difficult without the approval of these organisations for research to proceed. Issues such as the duration of the research (particularly when some participants may be ill), the use of appropriate, non-judgemental approaches and the language in written material (terminology such as ‘HIV victims’ or ‘sufferers’ will not be acceptable, for instance), best methods of recruitment, possible duplication of other research and the value of such research to the HIV/AIDS community will need to be discussed.

**Objectivity**

Positivist science places great store by the objectivity of researchers, which is normally taken to entail that researchers are disinterested, or at least identify and counter any personal commitments they may have to research outcomes. The notion of scientific objectivity has been extensively critiqued from both within the philosophy of science and from the perspective of other disciplines.

The emphasis on the partnership between governments, communities and researchers has been central to Australia’s successful HIV/AIDS strategies. In this context, emphasising a separation between the interests of researchers on the one hand and research participants on the other is counter-productive. The problem is particularly acute in social research, where much of the most successful Australian HIV/AIDS-related social research has been conducted on the basis of a reflexive relationship between researchers and the researched. That is, research priorities have been determined in relation to the individual and collective needs of the populations and communities most affected by HIV/AIDS,
research findings have come out of the experience of individuals and communities, and research results have been taken up at community level in responding to the impacts of HIV/AIDS, in turn creating new research needs in a cyclical process.

The ethical implication of these research paradigms is that role clarification should be valued, but disinterest and objectivity may hinder the research process more than they help it.

**Points to consider**

- Does the research proposal include adequate measures to protect confidentiality in research involving people with HIV/AIDS because of the risk of discrimination and stigmatisation resulting from errors made in this area?
- Has the committee considered the importance of involving people with HIV/AIDS, or their advocates, in research decisions made about them? This may involve suggesting further discussion with the communities concerned or support for HIV/AIDS clinical trials being vetted by a clinical trials advisory committee. Specific note should be made of the different constituent groups of people with HIV/AIDS, for example, women, gay men, heterosexual men, people who inject drugs, people with haemophilia, and of how issues about involvement in trials are likely to be different for each group.

**Suggested reading**


**CLINICAL TRIALS AND HIV/AIDS**

[See this Collection and the NS 12 and Commentary for a general discussion of clinical trials.]

The complex and rapidly evolving nature of HIV medicine has meant that people with HIV/AIDS have often relied on experimental or very newly approved drugs and therapeutic strategies to improve their lives and health. Therefore, while the longstanding requirement for proof of the safety and efficacy of new medicines remains, there is also an added and balancing imperative of timely access. This principle was at the heart of the 1991 Baume reforms of the Therapeutic Goods Administration. This Report also acknowledged that people with a potentially fatal or seriously disabling illness, for which no cure currently exists, have the right, if they wish, to take an informed risk in gaining access to new or experimental therapies.

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This has provided many opportunities and challenges for clinical research. For many people, particularly in the epidemic’s early years, clinical trials have been the only means of gaining access to therapy. This has been a matter of controversy, with some community advocates arguing that informed consent is not meaningful when a trial offers the only possibility of therapy for people facing potential death.

The establishment of compassionate or expanded access programs, by which manufacturers make new drugs available free of charge to some people, was, in part, a response to this concern. These schemes, now an established part of the HIV/AIDS scene, are normally used to bridge the gap between the approval of a new drug in the United States and its listing by the Pharmaceutical Benefits Scheme in Australia, usually a year or more later. However, some schemes have begun before United States approval has been given for a new drug. Priority for compassionate access is given to those in the advanced stages of disease with few other treatment options.

Some researchers have argued that these schemes expose people to new therapies of unproven, or insufficiently established, benefit and risk, do not usually provide means of collecting reliable data and may discourage people with HIV/AIDS from entering controlled clinical trials, upon which the development of effective and reliable therapy depends. However, community representatives argue that these schemes remove an element of compulsion under which people facing potential death have no effective therapeutic option other than joining clinical trials, and so are an important feature of the ethical conduct of research. They also argue that these schemes provide treatments for people who may not qualify for clinical trials and that compassionate access to new but important drugs appears to have averted death or disease progression in a number of people with few alternative treatment options.

The end-point parameters by which a trial measures the success or failure of an experimental treatment have also been considered controversial. Because HIV/AIDS takes so long to result in disease and death, and because the period of benefit of a particular therapy is likely to be finite, the practicality and ethics of conducting trials based on these usual end-points have been rigorously questioned. Throughout the world, trials based on surrogate marker end-points, such as viral load and CD4 counts, have tended to supplant clinical end-point studies. Because of the need for swift evaluation, and in recognition of the need to design trials that do not keep participants on a therapy for longer than the period of benefit, many studies of twelve months or less are now being conducted.

The National Statement now provides that research control groups should not be given a placebo where an effective treatment is currently available (NS 12.4(a)). When only one unproven antiretroviral agent was available for study, control group participants were ethically randomised to placebo. However, because therapy has advanced, it is generally unlikely that any antiretroviral study with only one agent would now be approved. In such a fast-moving field, debate over what constitutes an effective treatment is likely to continue.

Resolving these ethical dilemmas requires a close knowledge of the fast-moving field of HIV/AIDS medicine and the specific therapeutic needs of HIV-positive patients. Although HRECs are constituted according to international standards, their members are not selected for their knowledge of HIV/AIDS medicine. It is a matter of debate whether ethics committees are, alone, capable of fully resolving or identifying many of the ethical difficulties of this complex and specialised field. Whether they are able to adequately reflect the partnership approach on which the Australian HIV/AIDS response depends, and which requires the involvement of people with HIV/AIDS in all areas of policy that concern them, has also been questioned.

The Clinical Trials and Treatments Advisory Committee (CTTAC) of ANCAHRD (the Australian National Council on AIDS, Hepatitis C and Related Diseases) is required by its terms of reference to review and approve trial protocols proposed by the National Centre in HIV Epidemiology and Clinical Research and the Community HIV Research Network, and to appoint review subcommittees. CTTAC also oversees the current direction taken by HIV
clinical research, including the ethical issues surrounding new approaches to the treatment of HIV infection. This is recognition by the Government, under the National Strategy, of the need in this area for the judgment of independent people with knowledge of HIV/AIDS and of the value of the partnership approach to clinical issues.

In this respect, some redress for potential limitations of ethics committees in reviewing HIV/AIDS trials is achieved by prior review under the guidance of CTTAC. However, it should be noted that not all HIV/AIDS trials are approved by CTTAC, which only has responsibility for studies conducted by the National Centre for HIV Epidemiology and Clinical Research and the Community HIV Research Network. Any other HIV/AIDS trials would present at the first stage before an HREC under the CTX Scheme.

Debate about the role of ethics committees also arises within the context of multi-centre trials. Frequently, in order to provide the numbers for a valid trial, patients must be recruited through several hospitals and public clinics. Protocol approval is a complex process requiring expert evaluation of toxicology and other data. Delays and increased expense arise if each institution requires its own ethics committee to evaluate protocols separately (see also NS 3.1 and Commentary). There has been some progress towards sharing toxicology reports. Further difficulties arise with international trials, where a change required by one ethics committee must be negotiated with other institutions and stakeholders both in Australia and overseas.

(See this Collection page E111 for a general discussion of multi-centre trials.)

A proposal has been put forward for a single national ethics committee for HIV/AIDS clinical trials. It was hoped that this would avoid duplication of work, reduce costs and expedite the regulatory affairs process. Trials run by the Community HIV Research Network through general practice clinics are now able to use a single ethics committee, but proposals to include hospital-based trials in such a process have not been successful because individual hospitals are reluctant to devolve their legal responsibilities onto other bodies.

**VACCINE TRIALS AND HIV/AIDS**

**HIV vaccines**

Research into HIV vaccines raises additional issues with which HRECs should be familiar.

**Potential roles for vaccines**

Two potential uses of a vaccine in HIV/AIDS are envisaged. One is as a prophylactic vaccine to protect against primary infection with HIV and the second is the possible immunotherapeutic use of a vaccine to ameliorate the clinical course of HIV/AIDS as a complement, or alternative, to therapeutic drugs. The role of vaccines in prophylaxis has led to concerns that vaccine trials could not offer any immediate benefit to research participants, but only to society as a whole in the knowledge to be gained. As a result, it was argued that there is no ethical basis for clinical trials of any candidate vaccine that could cause any foreseeable adverse reaction.

These concerns may be justified in terms of vaccine trials related to vaccines being used in their prevention role, although vaccines as immunotherapy may require different standards and safeguards. This would be in line with the position that drugs for life-threatening conditions should have standards and safeguards for their use different from those required for non-life threatening conditions. This is a difficult and important issue that many HRECs will have to confront.

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Level of benefit

It is widely acknowledged that the early candidate vaccines for HIV are unlikely to demonstrate 100 per cent benefit for all people immunised. However, what constitutes an acceptable level of benefit? Other questions relate to the duration of the benefit. Is it persistent or transient over months, years or decades? Does the vaccine aggravate or ameliorate other infections that occur?

Participation in vaccine trials

The consent form will need to highlight the fact that participants in candidate vaccine trials may suffer active detriment and harm. HRECs should also consider the fact that testing of AIDS vaccines presents a type of risk rarely experienced by volunteers participating in other research studies, that is, social risk. The consequences of having HIV antibodies include widespread discrimination in health care, employment, housing and access to goods and services from groups such as health and life insurance companies, difficulties with entry to defence forces and foreign services and in international travel.48 Some researchers have proposed that volunteers be given certificates stating that any HIV antibodies present are due to immunisation rather than natural infection.49

Another major ethical problem for HIV preventive vaccine trials is posed by the actual recruitment process: balancing the need for exposure of research participants to HIV versus the ethical need to discourage people from such exposure. With a preventive vaccine trial, the fastest result will be achieved if all volunteers engage in unsafe behaviour so that any limitation in infection given by the vaccine can be measured. Nevertheless, most researchers acknowledge that all volunteers who receive candidate preventive vaccines need to be counselled about how to avoid becoming infected with HIV.

However, the net result of encouraging people to reduce their risk of HIV infection, which may lower the rate of new infections, will be to increase the amount of time and (or) the number of research participants needed to determine whether a vaccine is effective. Therefore, the process will be prolonged, to the possible detriment of early widespread introduction of an effective HIV preventive vaccine. Similarly, it may be essential to require that individuals in vaccine trials who are found to have acquired HIV infection be immediately offered antiviral therapy, which usually dramatically reduces virus levels and may prevent disease progression if intervention is sufficiently early. If, as widely expected, vaccines cannot achieve protection against infection, however, treatment with antivirals will compromise the ability of the trial to measure the efficacy of the vaccine in preventing disease.

Points to consider

- If the study is a clinical trial, does the research proposal conform to NHMRC requirements for minimum standards of participant care?
- Have women been excluded from HIV clinical trials on the basis of their reproductive potential?
- Ethics committees who are asked to consider an application to stage a HIV vaccine trial, whether of a preventive or therapeutic kind, will need to consider very carefully the likely implications for participants if they are to become infected with the virus and the necessity for swift treatment access if this was to happen. Much care must be taken in ensuring that potential participants are fully aware of the risks

48 The presence of HIV antibodies precludes entrance, even as a tourist, to many countries.
49 C.O. Tacket & R. Edelman, ‘Ethical issues involving volunteers in AIDS vaccine trials’, Journal of Infectious Diseases, vol. 161(2), 1990, p.356. A number of Australian insurance companies have refused to provide insurance to individuals identifying themselves as gay, even when such individuals tested negative for HIV and stated that they were in a long-term relationship.
and benefits of the trial before giving their consent to participate. It seems likely that it will be difficult for a clinical trial of an HIV vaccine to meet the assurances of the Helsinki Declaration that research participants will not be harmed and that there is a possibility of benefit to future people with HIV/AIDS.

**Suggested reading**


HUMAN PARTICIPANTS, JUSTIFICATION OF RESEARCH INVOLVING

A number of different arguments have been presented to justify research involving human participants, including research that presents some risk of harm to those participants. These include the value of knowledge (per se) and the value of the future benefits expected to flow from research, such as better health care, greater ability to frame policies for the benefit of the community, more efficient delivery of services and more effective educational practices. It is generally accepted, however, that research involving human participants requires justification because such research necessarily entails some disruption, even if innocuous, to a person's normal course of activities.50 It is the task of an HREC to assess whether specific projects justify the proposed level of disruption, risk of harm and intrusiveness, keeping in mind the NHMRC requirement to give priority to the avoidance of harm to research participants.

In assessing whether involvement of participants in specific research projects is justified, ethics committees need to consider whether there are any special features of the research methodology, the participant population or the research topic that merit special consideration. Different research methodologies and areas involve different emphases with regard to risks, potential future benefits and specific ethical considerations.

HRECs should assess whether there are good reasons for approving the research, for seeking further justification from the researcher for conducting the research in the manner proposed, for recommending modifications and justifying those recommendations, or for recommending that the research not be approved. HRECs also play an educative role by drawing the researchers' attention to potential ethical problems and suggesting alternative practices that aim to avoid such problems, thereby contributing to a climate of ethical research practice. (See NS 2.1–2.48 and Commentary page C17 and below for a detailed account of the role of HRECs.)

Suggested reading


Medical Research Council of Canada (MRC), Natural Science and Engineering Research Council of Canada (NSERC) and the Social Sciences and Humanities Research Council of Canada (SSHRC), Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, Ottawa; MRC., NSERC & SSHRC, 1998.


50 Dodds, S., Albury, R., & Thomson, C., Ethical Research and Ethics Committee Review of Social and Behavioural Research Proposals, Canberra, Department of Human Services and Health, 1995.
HUMAN RESEARCH ETHICS COMMITTEES

[NS 2.1–2.48 and Commentary]

HISTORICAL, SOCIOLOGICAL AND ETHICAL BACKGROUND

More than 25 years ago, the NHMRC issued a Statement that resulted in the establishment of a national system of ethics committees. The main task of these committees was to assess research projects involving human participants. Since 1973, it has been a condition of NHMRC funding that such research projects be assessed by a properly constituted ethics committee. Over the years, the processes and procedures of these committees have been gradually refined and their responsibilities extended. Their numbers have increased to more than 200 and they now carry a substantial burden of responsibility for reviewing all new research projects. This responsibility includes the initial assessment of research proposals, and monitoring the conduct of approved projects. Some ethics committees also provide guidance on clinical issues and policy within the health care environment, but this is not a role envisaged in the National Statement.

Most Australian researchers have developed professionally in an environment where the ethical aspects of research involving human participants have been open to the scrutiny of an ethics committee. While researchers may sometimes experience difficulties satisfying the demands of an ethics committee and may, at times, question the intrusion of such a committee, few would any longer deny the need for independent scrutiny of the effect of research practice on participants.

However, there have been vigorous debates over the years in which the work of ethics committees has been subjected to both criticism and praise. There have also been debates about substantive ethical issues in research practice. Questions have been raised about the morality of research involving minors and adults unable to make rational decisions, about cross-cultural issues and about problems associated with particular types of research. These discussions have helped refine the procedures and practices of ethics committees. However, the various debates and criticisms have also distracted attention from the positive contributions of these committees.

The extent to which the style of deliberation developed by ethics committees is a sophisticated and innovative adaptation of established practices that is particularly appropriate for dealing with contemporary moral and social problems has not been widely recognised. Indeed, the functions of these committees are not easy to define. An analogy with expert professional committees does not adequately capture the specificity of what ethics committees do, as well as their remarkable ability to respond to new and diverse circumstances.51

One of the features of Western societies in recent years has been a growing recognition of the value of there being variety and diversity and of the need to foster different cultural forms and theoretical viewpoints. One result of this process has been a shift away from the traditional searches for an irrefutable foundation for truth and a single, universally valid category of the ‘good’. Today, there is not one ‘good’ but an infinity of goods, and not one method of ethics, but a multiplicity of frameworks within which ethical analysis and debate can occur.52


Within this contemporary context, the types of situations or events recognised as having moral content are much broader than they were in the past and, therefore, ethical discussion cannot be devoted primarily to the identification of ‘universal’ norms for action. In addition, the research process now appears to consist of a complex set of value-laden practices embedded in the social and cultural structures of an evolving society. This means that ethical principles formerly considered universal should now be understood as conditions of possibility. That is, they should be considered relative to a diversity of social and cultural contexts, subject to the personal interests and values of particular individuals and to the need for responsiveness to specific circumstances and changing local contexts.

Given this diversity in values and culture, it is not surprising that societal means for resolving differences should also have become more varied. Perhaps as a result of this, the composition of ethics committees worldwide has been broadened in many ways. The community now demands some say in what is considered acceptable in research practice. It is no longer appropriate for individual researchers to make these assessments independently. However, the role of researchers has not been dismissed. On the contrary, this, too, has been broadened. It is generally recognised that, as a result of their experience, researchers may be particularly aware of some of the ethical dilemmas and potential problems relevant to their particular field of research practice.

The issues that ethics committees deal with are extremely complex. A research project is more than a set of protocols with some standard ethical criteria attached. Rather, it is a complex intervention in a network of relationships, each of which has a distinctive structure and raises specific ethical issues of its own. Even an apparently routine research proposal may embrace a remarkable array of moral issues. In order to develop appropriate ways of dealing with these issues, ethics committees need to establish procedures for scrutinising principles, norms and values without sacrificing the specificity of particular situations. However, these procedures also need to be subject to ongoing moral discussion and development and, therefore, remain in flux.

An analogy with legal processes may be useful. Legal institutions are required to balance a number of competing principles, such as autonomy and a concern for uniformity. They must also recognise the impossibility, in multi-cultural and multi-centred societies, of producing substantive normative standards that are universally valid. Ethics committees confront similar challenges. In addition, like legal tribunals, these committees, by subjecting relevant activities to close scrutiny, help communities develop greater self-understanding, as well as general rules for regulating disputes. As with legal processes, ethics committees promote the capacity to resolve disputes by means of rational argument, structured discussion and clear communication.

Again, as in the legal situation, the setting within which these reflections take place should not be completely arbitrary. Accordingly, ethics committees require a structure and members should be chosen for specific competencies, for example, as medical practitioners or as social or behavioural scientists. In addition, the role of the committee is subject to certain

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57 Ibid., pp.104–111.
58 Ibid., pp.177–186.
assumptions, such as the essential validity of the research process, and to certain principles, such as those referred to in the National Statement.

This structured context makes it possible for relevant local issues to be identified and discussed. This also means that members engage in dialogues that cut across their personal points of view, although the latter are not completely eliminated. In this way, the microethics of research relationships can be closely scrutinised, problems can be anticipated and solutions negotiated.

While the ethics committee system is sophisticated and rigorous and has contributed significantly to the understanding of ethical issues involved in research practice, these committees, as already noted, also face significant challenges. This has been documented in several recent reports. These challenges include a perceived lack of ability to assess or respond to specific types of research, such as that involving innovative clinical practice, and to issues of concern to women, Indigenous Australians, gay men and women and other community groups. An increasing focus on legal issues and the threat of litigation has also been noted. In addition, researchers often feel alienated from the review process. There has also been wide criticism of some of the procedures adopted by ethics committees, especially with respect to multi-centre trials, drug trials, monitoring of the research process and the protection of privacy. Problems may also result from the wide variability in ethics committee decisions, from processes that are often cumbersome and onerous to researchers and from the perception that a great deal of time is often wasted by individual committees considering issues that have already been exhaustively addressed elsewhere.

However, it should also be pointed out that the expanding national grid of ethics committees provides no formal means of contact between committees and no means by which one committee can gain access to, and review, the decisions of others. Therefore, each committee, whether in a large metropolitan hospital or a small town, is working in relative isolation.

Nevertheless, despite these difficulties ethics committees have undoubtedly contributed to reducing harm to research participants, as well as to a growing recognition of the implications of research practice for participants’ lives at many levels within each phase of the research process. It is this aspect of ethics review that may, in the end, be the most significant. That is, the underscoring of a need for research to be conducted in a way that is fair and ethical and subject to public scrutiny and critical reflection. The existence of these committees creates a culture in which ethical research becomes an ideal shared by most, if not all, of those involved in the process.

THE 1996 IEC REPORT

The 1996 Commonwealth Department of Health and Family Services Report of the Review of the Role and Functioning of Institutional Ethics Committees states an ethics committee ‘must be capable of functioning independently. The ethics committee should be considered a part of, but independent within, the institution, performing an advisory function for the institution.’


It further states the following:

- While an ethics committee has the power to withhold approval from a research project, and to advise the institution to discontinue that project, it is essential that all matters dealt with by HRECs should be considered in a cooperative and constructive manner. This should always be the intention of the committee, the institution and all other parties to the process.

- There is a requirement for balance and diversity within a committee’s membership, as well as a need for effective recruitment and appointment of members with preferred attributes and qualities.

- All committee members, and researchers, should be provided with adequate training and education in research ethics, as well as in the role and functioning of Human Research Ethics Committees.

- HRECs should make provision for monitoring of research in progress, which may include: random inspections of research sites, data and signed consent forms; interviewing research participants; on-site monitoring of the research process; monitoring of study results by an independent person; or other quality control mechanisms. The main consideration in deciding what form of monitoring is appropriate is the risk to participants in the research project.

- A reporting system for the management of complaints should be easily accessible, provide for anonymity, provide for a prompt and efficient response, allow for immediate access to the highest administrative authority of the institution, and promote the effective resolution of problems. People nominated to receive complaints should respond urgently when there is any suggestion of harm to research participants, researchers or any other person. Research participants, researchers or any other person involved in the research process may forward complaints about an HREC.

- Allegations of serious misconduct by researchers may require the establishment of an investigation panel. Complainants, and the persons complained about, must be protected from any form of harassment while the investigation is carried out.

- An appeal against a decision can be made and should be referred to an independent mediator.

- If funding has been provided for a research project that is subsequently rejected, the institution will need to determine its obligations to the funding body.

THE PLACE OF HREC REVIEW IN ETHICAL RESEARCH

The ethical features of research involving human participants begin with the researcher’s decision to conduct research in one area rather than another, continue throughout the research process and extend beyond the researcher’s direct involvement to the publication of findings and the use of those findings by commercial organisations, governments, institutions and other researchers. The HREC approval process is only one stage in the ethics of research. Therefore, it should not be assumed that HREC approval ensures that a research project is ethically acceptable in all aspects. Nevertheless, the ethics committee process is an important and independent check on the ethics of research practice.

According to the National Statement, research that warrants HREC review is that which has potential for infringing the requirements of respect for persons, beneficence and

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justice (NS Preamble pp.7–8). In assessing research proposals against these criteria, each HREC member brings their own ethical outlook and set of values to the deliberative process. While this is appropriate, it is also important that members agree to some shared decision-making procedures, particularly in relation to the resolution of conflicting views about specific issues.

**MEMBERSHIP**

**Qualities and attributes of members**

An institution may consider that there are particular qualities and attributes most appropriate in HREC members, although these are not a requirement of the National Statement. It is suggested that committee members should possess the following attributes:

- **an ability to communicate well**, which includes a capacity to listen to, and appreciate, the views of others and to formulate and express a considered opinion. This is essential for all members of the committee. So, too, is a willingness to enter into a process in which differences and conflicting points of view can be explored and resolved.

- **an interest in ethics** and a capacity to understand the issues, although lack of formal training in ethics should not be a reason for exclusion from a committee. In situations where specific training in ethics is considered institutions may agree to provide appropriate sponsorship. (See below under Education and Training.)

- **sufficient time** to attend meetings and to read research proposals and other relevant documents. The amount of time required should not be underestimated and prospective members should be made aware of this.

**Minimum requirements for membership**

The appointment of members to HRECs involves certain minimum requirements. Beyond this, institutions retain the authority to use their own judgment. The following is an outline of the minimum requirements, along with suggestions as to how these might be applied (NS 2.6–2.12).

The NHMRC requires that HRECs be made up of at least seven members. The rationale for this minimum, and for the various categories of membership, is based on a need for representation of a diversity of views. Committee membership should also be gender-balanced and include a relative proportion of institutional and non-institutional members. As additional members are appointed over time, the institution should ensure that the membership continues to reflect this diversity and balance (NS 2.9).

**Lay members**

There should be at least two members who are lay people, one man and one woman. That is, these members should not have any affiliation with the institution and should be independent of, and not currently involved in, medical, scientific or legal work. Members in this category will hold a non-institutional viewpoint and will focus specifically on the welfare of research participants. Such members are presumed to have no bias in relation to the research enterprise or the institution, bringing a perspective to the review of research proposals that is external to both the organisation and the research professions. Ideally, lay members will come from the local community, or from a community from which research participants may be drawn, such as a particular ethnic or Aboriginal population.
Care should be taken in the recruitment, appointment and induction of lay members. Without appropriate selection and adequate preparation, these people may feel overawed and unable to contribute to decision-making in committee meetings. This has been identified in the literature as a potential problem.\(^{62}\) For this reason there is a worldwide trend toward greater community representation on ethics committees.\(^{63}\) For example, the London College of Physicians' Guidelines on the Practice of Ethics Committees in Medical Research Involving Human Subjects states explicitly that lay members should be ‘persons of responsibility and standing who will not be overawed by medical members.’\(^{64}\) These Guidelines also state that ‘individuals who are acquiescent and may be thought likely to give automatic approval are...not suitable members.’\(^{65}\)

It is therefore appropriate to seek out community members who are sufficiently confident to put a point of view, who are not easily overawed, and who can withstand pressure, or perceived pressure, to approve research proposals against their better judgment. The Report of the Review of the Role and Functioning of Institutional Ethics Committees http://www.nhmrc.gov.au/publications/synopses/e34syn.htm describes appropriate ‘lay’ members as:

...respected by the community, articulate, curious, and able to advance an argument. The qualities important in lay members include the ability to represent the community (with current or recent community involvement) and to mirror community standards.\(^{66}\)

In addition, where an institution is located within a particular community which is the subject of research, or where a great deal of research reviewed concerns a particular ethnic or Aboriginal population, the institution may select lay members from amongst those populations especially...where the research...is principally carried out amongst those groups.\(^{67}\) The use of advocates (see NS 2.25) is another means to this end.

**Persons with knowledge of, and current experience in, areas of research regularly considered by the committee**

Ethics committees should be adequately informed about all relevant aspects of research protocols, including scientific and methodological requirements. Therefore, there should be at least one member of the committee with sufficient skill and knowledge to identify the important issues that arise in all categories of research likely to be submitted to that committee, as well as instances where external expert advice should be sought. For example, an experienced medical researcher, qualified to practice medicine in Australia, is necessary on a committee that frequently considers research protocols involving physically invasive procedures or medical interventions. A researcher with experience of qualitative research methods should be appointed if the committee often assesses qualitative research proposals. Similarly, an educational psychologist may be needed on a committee dealing with a great deal of research into children’s development (NS 2.6(c), 2.7). As the Report of the Review of the Role and Functioning of Institutional Ethics Committees states ‘The essential attributes of this person are an ability to understand and comment on issues of scientific merit and a firm grounding in research methods.’\(^{68}\)

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\(^{65}\) Ibid.

\(^{66}\) Ibid.

\(^{67}\) Ibid.

\(^{68}\) Ibid, p.45.
Person with knowledge of, and current experience in, the professional care of people

The most appropriate kind of person to fulfil this function will, again, depend on the areas of research that are regularly considered by a particular committee. For example, this person may be a nurse, a social worker, a clinical psychologist or a medical practitioner (NS 2.6(d)). On a hospital HREC, the most appropriate person is likely to be a medical practitioner. On a university committee, the appropriate person may be a clinical psychologist or a social worker, depending on the nature of the research concerned.69 Whichever is the appropriate ‘caring profession’, the appointing institution should ensure, as the NS paragraph requires, that the member has both the formal qualifications to practice in Australia as well as practical experience.

Minister of religion

This category is not narrowly defined and could include ‘a person who performs a similar role within a community, such as an Aboriginal elder’ (NS 2.6(e)). Accordingly, it could be appropriate to appoint a Christian minister, a Jewish rabbi, an Islamic imam or some other individual from the relevant community who fulfils a similar role. An ethicist or moral philosopher is not regarded as an appropriate alternative to a minister of religion, although she or he may be a member of an HREC in some other capacity.70

Lawyer

A suitable committee member would be a lawyer interested in the ethics of research, familiar with the relevant law in medicine and other areas of research, or at least prepared to become familiar with these, and ‘aware of the limitations of the law in many aspects of medical research’.71 It should also be noted that this member ought not represent the interests of the institution. Where a legal opinion is required on an issue potentially affecting the institution, it is the institution’s lawyer, not the ethics committee legal member, from whom such an opinion should be sought. Finally, committees are advised not to take an overly legalistic stance in their deliberations.

Appointment of members

[NS 2.10–2.12 and Commentary]

Members with research expertise and professional care members

Many committees will be in a position to recruit members with research expertise and professional care members from within the staff of the institution or its affiliates. Although it has been argued that reviewers of research proposals should be external to the institution concerned, people from within the institution do possess several advantages. They are more familiar with common practices within that institution, are more readily available for informal consultation, are often in a better position to influence attitudes toward conducting ethical research and are well placed for a more formal educative role within the institution or region.72

However, where a staff member or affiliate of the institution is invited to join a committee, it should be made clear that they are invited as a person with knowledge of, and current experience in, relevant areas of research. They are not there to represent

69 Ibid p.45.
70 Ibid, p.45.
71 Ibid., p.7.
72 McNeill, op.cit., p.20.
other staff or a departmental perspective, but to advise on the welfare of research participants and on issues relating to the scientific merit of research.

In some institutions it may be difficult to locate people with the relevant expertise, for example, where the field is new or where the expertise is not available within the institution. In these situations, recruitment activities will need to extend beyond the institution.

Where suitable members are available from within the institution but are reluctant or unable to take time from their primary duties, the institution should formally allocate employee time to this role. In general, institutions should enable staff members to attend committee meetings and should take the contributions of staff members to HREC work into consideration when reviewing career advancement.

Lay members, ministers of religion and lawyers

Many institutions have recruited lay members through public notices or advertisements, inviting interested persons to apply and stating the personal/professional characteristics sought. Selection of successful applicants has been based on criteria previously established by the committee, similar to those discussed above. Ethics committees should avoid relying on recommendations of committee members to fill vacancies for lay members. The risk is that the person recommended will already have a relationship with the institution and lack the necessary independence.

Suitable appointments of a minister of religion will depend on the community that the institution serves or from which the majority of research participants are drawn. A suitable person will possess the characteristics described above and be familiar with the views of the relevant community. Candidates may be recruited by advertisement or by discussion with key people in the community. Ministers of religion, as with other committee members, may be affiliated with the institution, for example, as a chaplain. However, again, it should be made clear that they are invited to join the committee as knowledgeable members of relevant communities rather than as members of staff.

Lawyers may be recruited in a similar way to other members. In the past, lawyers acting for the institution in other matters have been invited to join ethics committees. Indeed, in some instances it has been regarded as part of the consultancy work for which they are paid. This is undesirable because it is likely to lead to conflicts between responsibilities to the institution and responsibilities to the committee and research participants. The lawyer should be able to advise the HREC on the legal implications for research participants, the researcher and the institution of the research being considered.

Induction and support of new members

It is important that new members are provided with adequate information about their role and all the necessary resources, administrative support and training required for them to function effectively. New members should be given a formal Notice of Appointment prior to attending their first meeting (NS 2.12.) They should also be provided with copies of the committee’s Terms of Reference, the National Statement, any previous reports on the committee’s activities, and any other relevant material about the committee’s processes, procedures and protocols. An up-to-date list of members’ names and contact information, including the administrative support person and other relevant personnel, should also be made available. This list might also describe each committee member’s role and area of expertise as a resource guide for other members.
While it may seem obvious, committee chairpersons and other established members should make a special effort to welcome new members and to provide any necessary assistance. This is especially important when a new member is from outside the institution. New committee members should also be encouraged to ask questions, request clarification of any matter not clear to them and to take part in the discussion.

Education and training

Education of committee members comes about in both informal and formal settings. The Report of the Review of the Role and Functioning of Institutional Ethics Committees [http://www.nhmrc.gov.au/publications/synopses/e34syn.htm] notes that a major step in the education of committee members is the provision of accurate and comprehensive information...followed by ongoing forums for communication and discussion' both between committees and with the Australian Health Ethics Committee.\(^73\) The IEC Report notes that a major step in the education of committee members is the provision of accurate and comprehensive information...followed by ongoing forums for communication and discussion' both between committees and with the Australian Health Ethics Committee. The Report also notes that there are 'a number of ethics courses which are offered by universities and ethics centres in Australia, some of which are directly aimed at [HREC] members.' Appropriate courses deal with both generic and specific issues in the ethics of research practice. The Report recommends that 'Institutions should make available sufficient (ongoing) funding to enable its [HREC] members to avail themselves of opportunities for relevant in-service training and development.'\(^74\)

The experience of institutions that have supported ethics committee members in attending such educational courses is that these members, and others within the institution, have benefited. Committee members can then share their newly gained knowledge and understanding with the rest of the committee, as well as make a valuable contribution to any educational activities that the committee might conduct within their institution. Relevant in-service training and development might also be offered to the committee’s administrative support person and to researchers within the institution.

An ethics committee might also consider convening more formal courses, conferences, seminars or forums, in which all relevant parties could be encouraged to participate. While it is not the HREC’s direct responsibility to educate student researchers, this is such an important issue that HRECs should consider working closely with those who are responsible for instructing students in the ethical aspects of their research projects.

Consideration might also be given to inviting researchers, and others, to attend committee meetings as observers. In order to protect the confidentiality of research proposals and committee proceedings, consent of the parties involved should be sought or, as with clinical case descriptions, potentially identifying information should be

\(^73\) Report of the Review of the Role and Functioning of Institutional Ethics Committees, op.cit., p.49.
\(^74\) Ibid., p.50.
\(^75\) Ibid, p.50.
omitted. (See above in this Collection for a more detailed discussion of confidentiality in relation to research protocols and ethics committee proceedings.)

**Reimbursement and payment of ethics committee members**

If committee members are employees of the institution, or a related institution, then reasonable out-of-pocket expenses should be covered by the employer. However, other members, and especially members from outside the institution, are not usually recompensed for these expenses. While there is no NHMRC ruling on this matter, it is reasonable to expect that expenses such as travel, parking and additional child care be reimbursed. 76 Traditionally, members of HRECs have provided their services on a voluntary basis. However, some institutions offer ‘sitting’ fees. Such payments may be justified by the considerable time taken up by committee work, especially for members who are not otherwise paid for their time. However, the appropriateness of payments to members of HRECs is an issue to be determined by individual institutions.

The IEC Report cautions that ‘Where a sitting fee is paid care should be taken to ensure that this does not result in an apparent or actual conflict of interest for the member(s) concerned.’ It would not be appropriate, for example, for payment to members to be related in any way to funds received from any person or organisation with a financial interest in the approval of research projects reviewed by that committee. 77

**Reporting to the institution**

Each HREC should report regularly (at least annually) to the administering body of its institution. Reports should supply information on committee membership and the committee’s work. This includes the numbers and types of proposals approved on first application, proposals approved after preliminary review and modification by researcher(s), and proposals rejected. The report should also include a description of any monitoring of research in progress, any complaints received, and any ethical issues that may have an impact on research participants, the institution, or its staff. The report should also outline any action taken against any researcher who has failed to comply with the committee’s decisions and recommendations. Where approval has been withdrawn from a research project a description of that research, and reasons for withdrawal of approval, should be included.

**Reporting to the public**

In order to engender confidence in the processes of review and to be open to public accountability, HRECs could produce an annual report or contribute to the annual research report of their institution. 78 Another potential outlet is the circulation of information through the Internet.

**Responsibility within, and relationship to, the institution**

An ethics committee must be understood within its context, that is, as part of an institution or organisation. An HREC has responsibilities to that organisation, as well as relationships with other members and, in some situations, other committees, departments and groups within the organisation. Obviously, an HREC also has a direct relationship with researchers who submit research proposals for review.

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76 Ibid., pp.47–48.
77 Ibid.
78 Ibid, p.55.
The nature of the relationship between ethics committees and other bodies and authorities within the administering institution, as well as the committee's authority and jurisdiction, should be clearly specified. The HREC makes recommendations to the institution and, therefore, the ethical conduct of research projects and of researchers is ultimately the responsibility of the institution involved. This means that organisations are responsible for ensuring that activities under their jurisdiction meet the standards required by the NHMRC.

Therefore, HRECs act on behalf of their institutions in maintaining appropriate standards for research conducted within that institution. In most organisations this is, strictly speaking, an advisory role. However, in practice, the executive of an institution would only act contrary to this advice for good reason. Institutions should therefore ensure that HRECs have sufficient independence to fulfil their required functions. This includes the recognition that committees may initiate the review of issues or policies related to the conduct of research for which they are responsible.

SUBCOMMITTEES AND OTHER HUMAN RESEARCH ETHICS COMMITTEES WITHIN THE INSTITUTION

The manner in which a committee functions in order to fulfil its responsibilities may vary. For example, some committees with a high workload might delegate certain tasks to subcommittees. In other situations it may be more appropriate to form more than one HREC, or use advisory committees. This may be appropriate in large organisations, such as some universities and hospitals, where the volume of research proposals reviewed is extremely high and proposals originate from many different disciplines.

Appropriate task-focused subcommittees might include:
- scientific review subcommittees;
- committees for conducting expedited review of low-risk research;
- discipline-based subcommittees for review of undergraduate, honours and masters-by-course-work research projects;
- other special-purpose subcommittees, for example research involving Indigenous Australians; and
- committees that consider issues of general policy about the conduct of research and the assessment of research proposals.

It is recommended that there be some common membership between the HREC and any subcommittees, with the chair of the subcommittee drawn from the main committee. Such a system allows an HREC to recruit members from a range of disciplines, thereby providing the necessary range of expertise.

However, whatever the particular arrangements may be, it should be made clear which committee is responsible for advising the institution. Ethics committees responsible for approving studies must be properly constituted. Therefore, where subcommittees,

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79 While most committees may function in an advisory capacity, some may have been given an executory power, such as the power to authorise research to proceed.

80 Where an institution chooses not to follow the recommendation or advice of its HREC it would be prudent to record the reasons for this decision as it may have legal implications and consequences.

81 As the 1996 Commonwealth Department of Health and Family Services Report of the Review of the Role and Functioning of Institutional Ethics Committees states, ‘The committee must be capable of functioning independently. The ethics committee should be considered a part of, but independent within, the institution, performing an advisory function for the institution.’ Commonwealth Department of Health and Family Services, Report of the Review of the Role and Functioning of Institutional Ethics Committees, Canberra: Commonwealth of Australia, March 1996, p.44.
advisory groups or departmental committees assist the HREC responsible, these groups should be constituted in conformity with the National Statement. For simplicity, it is recommended that any committee responsible for advising an institution on approval of research proposals be identified as an HREC. All other groups, subcommittees and departmental committees function by recommendation to an HREC. While these groups, subcommittees and departmental committees may have professional responsibilities and duties of care to offer responsible and reliable advice to an HREC, as already noted, they should not be responsible for advising the institution directly as they do not have the capacity of a properly constituted HREC.

**WORKLOADS**

For those institutions that review very few research proposals, secretarial and administrative costs could be reduced by amalgamation with another HREC. Such amalgamation might involve another ethics committee within the same institution, or a committee attached to another organisation. The IEC Report [http://www.nhmrc.gov.au/publications/synopses/e34syn.htm](http://www.nhmrc.gov.au/publications/synopses/e34syn.htm) suggests that where committees meet infrequently, or review few proposals, concerns arise about the ‘time spent serving on committees’, as well as about maintaining the ‘breadth and depth of experience needed by committee members to maintain an adequate level of review.’ The Report therefore invites committees with small workloads, such as those reviewing fewer than 50 research proposals a year, to ‘consider the possibility of amalgamation’ with another committee.\(^{82}\)

However, the Report also acknowledges that there may be good reason for maintaining a committee even though the number of research projects reviewed is small. This would be appropriate if the research reviewed was of such a specialised nature that the necessary expertise would be difficult to replicate on a committee dealing with a wider range of proposals. An example of such a specialised committee might be an HREC in a Red Cross Blood Bank.\(^{83}\)

Conversely, where there is a great deal of research to review it may well be appropriate for an additional HREC to be formed or for subcommittees to be created, all supported by a single administrative office. Obviously, if this latter course were to be followed, these administrative services would need to be adequately resourced.

**NETWORK SUPPORT**

Networks are developing in a number of States to assist HRECs. The initiative for this development is being generated by the HRECs themselves. As an example, in New South Wales a person has been appointed to coordinate and support the ethics committee in the public health system in that State, and there are strong universities networks in both New South Wales and Victoria. In Queensland, some ethics review is being conducted within the regional health authority structure.

**FREQUENCY OF MEETINGS**

Most Australian HRECs meet monthly. A schedule of regular meetings, including deadlines for protocol submission, should be drawn up, taking into account the expected numbers of research proposals to be reviewed, patterns of peak demand (which are often related to the timing of grant application results) and the number of applications that the committee can review at a meeting.

\(^{82}\) Ibid, Recommendation 19, pp.52–53.

\(^{83}\) Ibid.
Effective publication of a timetable within the institution(s) or organisation(s) is important.

A submission deadline should allow time for initial administrative consideration of research protocols prior to drafting and distribution of the agenda and other relevant documentation. This provides an opportunity for researchers to be advised of, and rectify, any obvious omissions. It also allows for any processes of preliminary review that a committee may have decided upon. These might include distribution of applications to particular reviewers and distribution, where required, to reviewers external to the committee for independent review of scientific or other issues.

It is preferable to have a consistent closing date, as well as a clearly defined policy about whether late applications will be accepted and, if so, in what circumstances. Acceptance of late applications can place undue pressure on the committee to the point where it is unable to follow proper processes.

POLICIES IN RELATION TO FREQUENTLY REVIEWED ETHICAL ISSUES

Policies in relation to frequently reviewed ethical issues may assist committees to reach effective decisions in a time-efficient manner. For example, some committees have found it useful to formulate policies about:

- requirements for participant information (See the Commentary on NS 1.7 for a general discussion of this issue, and on NS 12.1–12.13 for specific information in relation to clinical trials);
- research involving deception of participants (See the Commentary on NS 17.1–17.2 for a general discussion of this issue, and the Research Law Collection, ‘Deception, research involving’ (page L21) for an account of the legal aspects);
- legitimate omission of a written consent document (See the Commentary on NS 14.1–14.13 in relation to epidemiological research; this Collection (page E129) in relation to qualitative research; and the Research Law Collection (page L13) for a general discussion of the legal aspects of informed consent);
- recruitment of participants;
- use of audio and videotaping (see the Research Law Collection for a general discussion of the legal aspects of privacy of information (page L43) and confidentiality (page L7);
- oral history and confidentiality; and
- research into criminal activity (see the Research Law Collection (page L37) where the legal aspects of this issue are discussed).

Developing such policies would be a continuing process as new issues arise. However, this does not mean that HRECs should consider themselves bound by precedents. Each new application should be assessed as unique. In addition, draft policies could be circulated within the research community and among other ethics committees, thereby encouraging critical reflection and comments on a wider scale and promoting the sharing of expertise between ethics committees.
MEETING AGENDA

A typical meeting agenda would include the following items:

- apologies;
- minutes of last meeting;
- matters arising from the minutes;
- subcommittee reports, for example, reports from scientific, discipline-based or expedited review subcommittees;
- ratification of expedited review or other subcommittee decisions;
- applications pending;
- new applications;
- applications for renewal of approval;
- variations to approved protocols;
- regular review of the progress of research projects already approved;
- any other business, including notifications of significant adverse events and complaints; and
- details of the next meeting.

The time taken to discuss individual research proposals will vary according to the quality of applications, the types of research involved, the nature of the ethical issues raised, the adequacy with which the researchers have dealt with ethical and scientific issues and the extent of pre-meeting responses from members.

APPLICATION FORMAT FOR RESEARCH PROTOCOLS

Consideration of research proposals will be helped by the use of a standard written application form that provides all the information required by the HREC. In general, applications should normally include at least the following:

- the title of the project;
- the names, qualifications and positions of all researchers;
- a summary of the project in plain language;
- a general indication of the type of research proposed, including, for example, whether it will involve qualitative and/or quantitative methodologies, or whether it is a drug trial;
- a full protocol, including, where appropriate, a clear statement of the rationale and background of the research, the questions to be asked, the methods to be employed and techniques of data analysis to be applied;
- a description of the kinds of participants to be recruited, including details of inclusion and exclusion criteria, how participants are to be recruited and by whom;
- details of any invasive, uncomfortable or potentially distressing procedures to be employed and the strategies in place for minimising harm to participants;
- where appropriate, information about any interruptions to, or interference with, the normal care of research participants;
- where appropriate, contingencies for dealing with any emergencies that may arise;
- information about any drugs, therapies or other procedures, including questionnaires or focus group discussions, to be employed as part of the research...
process, in sufficient detail to allow full assessment of possible implications and effects;

- a participant information statement in plain language, providing information about the aims of the project, what will be expected of participants, any risks to which they may be exposed, data storage, confidentiality, indemnities, right to withdraw and procedures for obtaining further information or lodging complaints (responsibility for completion should be assigned to a specific member of the research team);

- a copy of the consent form;

- information about proposed payments to participants and a financial statement by researchers sufficient to allow assessment of whether any conflicts of interest are likely to arise;

- a declaration by the researcher of any other conflicts of interest;

- an account of procedures to be adopted for data storage indicating where, in what form and for how long, personal information will be stored and who will have access to it;

- information about indemnities to be provided for research participants, where relevant;

- other information required in relation to the local requirements of the institution within which the research is to be conducted;

- a review of the ethical issues arising in relation to the consent process or any other aspect of the proposed research and the steps that will be taken to deal with these;

- relevant permissions and undertakings by researchers and appropriate others;

- any other necessary information arising out of the particular nature of the proposed research, as discussed elsewhere in this Handbook; and

- any necessary information about legislation and NHMRC documentation concerning information privacy.

The completed form should be accompanied by all necessary documentation, such as supporting scientific information, information from regulatory agencies, correspondence with other HRECs, questionnaires and proposed advertisements or public notices. The committee should specify the number of copies of the proposal, and supporting documentation, to be submitted by the researchers. On receipt of the application each research proposal should be assigned a unique project identification number in order to facilitate future correspondence and to allow accurate record keeping (NS 2.30).

APPLICATIONS, PRELIMINARY REVIEW OF

Some committees may choose to carry out a preliminary review to assess the scientific merits of a proposal and to identify important ethical issues. In some situations, a specially constituted subcommittee undertakes such review; in others, it is carried out by primary reviewers designated for each project. If the latter approach is adopted, regard should be given to the distribution of work between committee members and to members’ areas of expertise. In addition, some committees pair lay and other members from outside the institution with an institutional member.

Following the preliminary review process, the chief researcher would normally be advised by the HREC of the main issues identified and to seek comments or further information, as required. Such advice might include suggested ways in which the research protocol could be amended in order to render it acceptable. A preliminary review process therefore expedites discussion and decision-making and enables a committee to focus on difficult or unresolved issues.
A decision may be made either during the preliminary review process, or subsequently, to invite the researchers to a meeting of the full HREC to discuss the proposal. A small number of committees require all researchers presenting proposals to attend an interview, while others restrict such interviews to proposals involving contentious ethical issues or invasive or potentially risky procedures. Interviews provide opportunities for detailed assessment of scientific and ethical questions, for provision of information about the conduct of the proposed project, for assessing the capacity of the researchers to fulfil their responsibilities and for negotiating possible amendments to research proposals.

Approvals might also contain explanations of the reasoning behind a particular decision, non-binding recommendations suggesting ways in which the proposal might be improved, or other relevant comments. For example, researchers may be reminded of accepted institutional practices, such as the retention of research data for a certain time period. The committee may also wish to explain to researchers that approval of the proposal does not create a precedent for future research, the particular protocol having been approved as a unique project.

**Deliberation, ethical, in the review of research proposals**

HREC members should consider the following issues when assessing research proposals based on the requirements of the National Statement.

**Justification of human participation in the research**

- What are the risks to potential research participants (NS 1.3, 1.6, 1.14)?
- Is the proposed level of disruption to participants’ normal activities justified (NS 1.2)?  
- Is the research question worth asking? Is it likely to lead to new information or new understanding about a significant topic? Is it likely to provide useful confirmation of earlier research? Peer review assessments of the scientific merits of the proposal, or the significance of the project, are often useful guides.
- Does the design of the project increase the likelihood that the study will succeed in providing an answer to the research question? Is the methodology appropriate to the topic? Does the design reduce unnecessary risks of harm to participants (NS 1.13, 1.14)?
- Are the likely benefits of the research project sufficient to justify the disruption, or even risks, to which participants will be exposed? Are the proposed techniques the least invasive ones necessary to carry out the project? Access to expert knowledge about the research topic, the research population and the methodology may assist the committee in assessing the risks associated with particular projects. Members of HRECs should remember that risks include not only tangible physical risks, but also risk of psychological or social harm. The more harm likely to befall a participant, the less acceptable the research will be (NS Preamble page 8 and 1.6; 1.17).

**The researcher**

- Does the researcher have the skills and the institutional, or other, support required to conduct the research project without undue risk of harm to participants? What qualifications does the researcher have to conduct this specific research, involving this research population, and using this methodology? What supervisory or support mechanisms exist to help the researcher in the conduct of the project (NS 1.15)?

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• Does the institution through which the research is to be conducted have adequate resources to respond to problems that may arise in the course of the project (NS 1.15)?

The research participants

Information, risks and consent

• What will potential participants know in advance about the research topic? Have potential participants prior contact with the researcher while the project was being designed? What information will these people be given before they decide whether or not to participate (NS 1.7, 1.8, 1.10)?

• How will the project affect participants? How do potential participants find out that they are being approached? What does the project involve for participants while it is being conducted? For example, how long will it take? Will it involve pain? Is it likely to be distressing? What effect, if any, will the completed research have on participants' lives (NS 1.5, 1.7)?

• Have the possible risks been considered from the perspective of potential participants (NS 1.4, 1.6, 1.14)?

• Can potential participants decide whether or not, and when, they will participate? Can they control who has access to information about them? Will they have the opportunity to decide how much or how little of the project they will participate in? Will they be advised that they can withdraw from the project at any time? Will there be any negative effects if they do withdraw and are there any conditions on their withdrawal (NS 1.7–1.12)? (See the Research Law Collection, page L13, for an account of the legal aspects of consent and the provision of information in research practice.)

Privacy and control over information

• Personal information, and the distribution of that information, is as much an ethical concern as the type of physical involvement of individuals in research. Similarly, intrusions into participants' private affairs can significantly affect the acceptability of research (NS Preamble p.9, 1.2, 1.19, 1.20, 18.1–18.5).85 (See the Research Law Collection, page L43 for an account of the legal aspects of privacy of information.) How is the privacy of participants likely to be affected by the research? To what extent can participants retain control over personal information? Does the method of recruitment respect the privacy of potential participants?

Research involving collectivities

• Does the proposal involve participants who are members of a particular group to the extent that additional sensitivity to the special interests of that group is appropriate? How does the proposal respond to the concerns of this group (NS 1.19, 8.1–8.2, Commentary)?

Research involving people in dependent relationships, or whose capacity to make informed decisions is limited

• The dependency of a research participant on the researcher, or on the institution where the research is being conducted, is of particular concern in recruiting project participants and ensuring minimal disadvantage in the event of withdrawal from

85 Berglund, op.cit., p.83.
the project (NS 1.10, 7.1–7.3). Does the proposed research involve participants who are in dependent relationships or whose ability to refuse to participate is limited for any reason? If so, what justifies involving that particular population in the research project? What steps will be taken by the researcher to protect the interests of those participants? Are these steps adequate?

**Inducements**

- Are participants to receive any payment or reward for taking part in the project? If so, does this constitute an inducement to participate? Alternatively, does payment constitute due recognition for the contribution of participants to the research project? Money can act as an inducement to participate, influencing the decision on whether or not to take part. As a general guide, reward for participation should be smaller recompense than would induce a decision to participate for that ‘reward’. There is a risk that payments to researchers may influence their recruitment of participants or treatments of results (see also NS 1.10, 12.6). Are researchers to receive any payment or reward for conducting the research? If so, will this influence their recruitment of participants or their treatment of results? (NS 1.10).  

Once HREC members have considered the above points they will be in a position to evaluate the proposal. Having assessed the merits of the research proposal, the committee is then able to recommend approval, conditional approval or rejection of the proposal.

**APPROVAL OF RESEARCH**

HRECs should assess whether there are good reasons for approving the research, for seeking further justification from the researcher for conducting the research in the manner proposed, for recommending modifications and justifying those recommendations, or for recommending that the research not be approved.  

Approval is granted when the HREC is satisfied that it is appropriate that the research has a sound scientific design, that the risks and burdens to participants are adequately balanced by the benefits of the research and that the rights and welfare of participants will be protected if the research is conducted as proposed. A written statement of approval signed by the chairperson of the committee, or their nominee, should be issued to the researcher/s, clearly indicating any conditions of approval and the duration for which approval is given.

It is also important that all documents, in their first form, that will be seen by potential participants are approved by an HREC, including plain language statements, consent forms, questionnaires, recruitment advertisements and letters of invitation (NS 2.24).

**Conditional approval**

Conditional approval may be granted where the committee considers that commencement of the study would be justified if certain conditions were met. Typically, such conditions involve changes to information statements or consent forms, clarification of recruitment procedures, clarification of follow-up strategies, or details regarding data storage. Review of an application may be deferred if substantial additional information is required before further consideration of the project is possible.

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86 For further discussion of payment for participation in research see Dodds, et al., op.cit., pp.60–61.

87 HRECs also play an educative role by drawing the researchers’ attention to potential ethical problems and suggesting alternative practices which aim to avoid such problems, thereby contributing to a climate of ethical research practice.
When deciding to grant conditional approval, an HREC needs to specify precisely how it will be satisfied that the conditions have been fulfilled, for example by delegating that determination to the chairperson or a subcommittee. The usual condition is that the research cannot begin until the conditions have been fulfilled in the manner specified.

Nevertheless, HRECs may also decide to establish procedures to be followed should a consensual decision not be reached. It should be noted that decisions taken by a simple majority do not amount to a ‘general agreement’ and for this reason they should be avoided. Therefore, the size of a required majority, such as two-thirds, should be decided in advance for those occasions when general agreement is not attainable. Even so, where particular members of a committee have strong objections to granting approval for a specific proposal, their views should be respected and every attempt made to find a mutually acceptable resolution.

A committee decision may involve requesting particular amendments to a research protocol, requesting that a particular condition be met prior to full approval being granted, requesting changes to a participant information statement, or requiring an interim safety or efficacy analysis after a specified time. Ethics committees may also defer or reject applications. Review of an application may be deferred if substantial additional information is required before further consideration of the project is possible. In these situations, it may be helpful to refer responses from the researchers to specific members of the committee who can then provide a report and recommendations at the next meeting.

**MINUTES AND RECORDING DECISIONS**

HRECs are required to establish working procedures for the preparation of minutes (NS 2.13). Minutes of meetings should be taken by a person competent to do so. It is not appropriate for minutes to be taken by a member of a committee who is also participating in the decision-making process.

The recording of decisions is often assisted if the chairperson suggests appropriate formulations of decisions taken. Points of contention can then be recognised and resolved immediately.

Minutes of meetings should be produced as soon as practicable following the relevant meeting and checked by the chairperson as a true and correct record of the proceedings. It is then usual to circulate the minutes to all members of the committee.

Minutes should contain a sufficient account of discussion of each protocol to show that all relevant ethical issues were identified and discussed. In general, to encourage free and open discussion, and to emphasise the character of HREC deliberations, particular views of individual members should not normally be attributed by name in the minutes. Exceptions to this may arise in rare situations where a member feels the need to record his or her objection to a decision taken by the committee. The record of proceedings should include reference to views provided by absent members. Decisions need to record any conditions or amendments required. The fact that a member of a committee with an interest in the proposal under consideration leaves the meeting while that proposal is discussed should be recorded in the minutes.

**Reasons for decisions**

HRECs need to provide justification for decisions taken. This means that:

- the committee is obliged to consider the reasons given by researchers for conducting their research in the way proposed;
- members of the committee should be prepared to justify their assessment of specific projects and be able to articulate the reasons for their concerns; and
because the committee ‘must record decisions in writing and should include reasons for rejection’ (NS 2.14), it is clearly a matter of common and appropriate practice for ethics committees to advise researchers of the reasons for any requests for amendments to research protocols. (See also in this Collection a more detailed discussion of HREC decision-making processes and outcomes (above), notification of assessment results (see ‘Notification of decisions’ below) and amendments to research proposals (page E88.)

In summary, justification requires the provision of reasons that adequately support a course of action, or a decision. These reasons should be relevant to the decision, of sufficient weight and must not be overridden by other relevant considerations.

**Notification of decisions**

HRECs may wish to establish a timeframe for notification that meets their particular needs, but they should notify researchers of the committee’s decision as soon as practicable following the meeting at which their research proposal has been reviewed. If the proposal is approved, the letter should state all conditions of approval. If any amendments are required before approval, letters should state those amendments clearly, together with the reasons why they are required. If conditions need to be satisfied before approval, the researcher should be asked to provide the committee with evidence of compliance before the project begins. Letters should contain all essential details to meet the needs of funding agencies.

If a proposal is not approved, full reasons should be given.

There are occasions when a written account does not fully convey the reasons for a committee’s concerns or conditions and a prior telephone discussion with the researcher can often prevent a lack of understanding. An HREC may also wish to discuss difficult issues with a researcher at a later meeting of the committee. Although this can be a time-consuming process, it can also promote understanding between committees and researchers.

It should be noted that an unconditional letter of approval from an HREC is required before a clinical trial commences. Where the HREC has approved a clinical trial subject to minor amendments, it may authorise the chair, with or without advice from the subcommittee, to certify that those amendments have been made and issue the letter of approval. The chair should report to the full committee at its next meeting. This would overcome the time delay involved in having to wait for final approval at the next scheduled meeting.

HRECs are required to retain a copy of each research protocol and application for approval on file, including any information sheets, consent forms or relevant correspondence, in the form in which they are approved (NS 2.32). It can be useful to date-stamp and formally record approval of the documentation on the final approved copy.

**EXPEDITED REVIEW**

[NS 2.27–2.29 and Commentary]

**Types of research suitable for expedited review**

If an HREC wishes to use a simplified or expedited review process it needs to determine the class, or classes, of research to which expedited review might apply. The committee should also determine how many members are to be involved in each case, the extent to which tasks may be delegated to specific subcommittees, and the relationship between
the chairperson of the main committee and chairpersons of any subcommittees, as well as the scope of the latter’s authority. The committee should also decide on the manner in which decisions are to be reported to, and ratified by, the main committee.

Although circumstances may vary, examples of situations in which expedited review might be permitted include:

- social science questionnaires on non-controversial, non-personal issues;
- observational studies in public situations which focus on non-sensitive issues;
- studies of existing de-identified data, documents, records, pathological or diagnostic specimens;
- studies that do not involve an intervention that could result in significant harm to participants;
- collection of certain biological specimens, including hair, nail clippings or saliva;
- certain projects involving discarded tissue;
- applications for approval of amendments to previously approved research protocols; and
- studies that are substantially similar to another study already approved.

Note, however, that any of the above circumstances could, in some situations, become sensitive issues. The use of discarded body tissue by researchers, for example, is a sensitive issue within many Aboriginal groups and any research proposal including the use of such material would not be appropriate for expedited review. Social, cultural, or religious issues related to any of the above examples might suggest the need for review by the full HREC.

Having established those categories of research that can be considered for expedited review, the committee may then delegate the identification of appropriate proposals to one of its members, such as the chairperson. Alternatively, an HREC may delegate the selection of appropriate research for expedited review to an executive secretary, or a subcommittee, such as a student research subcommittee or a discipline-based subcommittee.

Having made this initial determination, the application can then be forwarded to a review team for assessment. Individual committees may decide how many members should be involved in this stage of the process and who they should be. In general, it is prudent to provide that all applications be considered by at least two committee members, one of whom has sufficient expertise to assess the scientific aspects of the proposal and one a ‘layperson’ or other non-institutional member. Alternatively, the reviewers could be a subcommittee consisting of a limited number of HREC members, a student research subcommittee or a discipline-based subcommittee. The two latter may include only one member from the HREC, who normally acts as chairperson.

Reviewers may seek further information or request clarification of specific issues from researchers before making their recommendations to the full HREC. Where any reviewer believes that any aspect of the application should be considered by the full HREC, this view should be respected. All other HREC members should have access to at least a summary of the proposal and should be able to examine the full application if they wish to do so. In some situations the chairperson, acting on the advice of reviewers from within the committee, might approve commencement of a project involving low risk to participants, subject to ratification at the next meeting of the full committee.

In general, applications considered for expedited review should provide the same information as normal applications and should use the same application form. While it could be open to researchers to request expedited review, that determination remains within the committee’s control.
Amendments to research protocols

The agreement of an HREC should be obtained before variations to approved protocols can be introduced. Where such variations do not affect the substance of the original proposal, and where no major new ethical issues are raised, an expedited review process is appropriate. Typically, a request for amendment should be submitted by the researchers and should include a brief summary of the original project, an account of the nature of the proposed changes, an explanation of why these changes are considered necessary, and an assessment of any ethical issues arising from them. This request could be dealt with in a similar manner as for expedited review, relying on appropriate HREC members. These members may then recommend to the chairperson of the committee that the amendment be accepted, that conditions or changes be required, or that the matter be referred for further discussion to the full HREC. A report should be provided to the full committee at the next meeting.

Urgent review for safety reasons

If a protocol amendment is required for safety reasons, that is, in order to protect the welfare of participants in a trial, then urgent review is necessary. HRECs should have a procedure in place to enable them to meet for such an urgent review.

Suggested reading


HUMAN TISSUE, RESEARCH INVOLVING

[NS 15.1–15.9 and Commentary]

Biomedical research using human tissue samples has played a significant role in advancing medical scientific knowledge and contributing to our understanding of the causes and management of a wide range of diseases. Clearly, medical science and the community as a whole have benefited from these efforts. However, in recent years, a number of factors have led to attention being focused on ethical questions arising from procedures employed for collecting human tissue as research material. These include the rapid increase in medical research activity in recent years and the growing number of commercial applications for its outcomes.

At the same time, the rise of a consumer movement has eroded the dominance of medical paternalism and empowered patients to request more information, and, in the research context, to require information about methods and outcomes of proposed research projects. Also relevant to defining what is ethical in this arena is an increased cultural diversity within Australia and a re-emergence of mainstream interest in spirituality, characterised by holistic understandings of the human body as integrated with mind and spirit. These social and cultural perspectives of the body conflict with scientific approaches, which are more mechanistic or view the body as a resource.89

On this basis, consideration of the ethical implications of using human tissue samples for research must include the rights and interests of individuals who provide the tissue, within the context of their own, and society’s, concepts of human dignity and physical, spiritual and cultural integrity. In this way, relationships between researchers and tissue donors, and other conditions under which tissue may be collected and used, can be properly defined, ensuring that advances in medical scientific knowledge are not achieved at the expense of ethical principles.90

FACTORS FOR CONSIDERATION

Institutions need to consider a number of factors when developing policies on using human tissue for research purposes.

These factors will impact differently on the consideration of relevant ethical issues. These issues include: avoiding or limiting injury to the body of the donor, either actually or symbolically; the preservation of privacy and confidentiality for donors and their families; and obtaining consent for the removal of tissue from donors or from authorised third parties.

Factors include:

- the original reason for which the tissue is collected—that is, whether it is donated for the purpose of research or removed as part of a medical procedure performed for a therapeutic purpose. This is an important issue for organisations and for their HRECs to examine, as it has legal implications. For further discussion on intent and ethical acceptability, see ‘Avoiding and limiting injury’ below. For discussion on legal issues, see the Research Law Collection, ‘Human tissue, research involving’, page L35.

90 Note that this section does not deal with the distinctive issues associated with research involving the use of tissue removed at autopsy.
• the timing of tissue collection in relation to the research—that is, whether the
tissue to be used has been collected previously, as in the case of stored samples,
or whether it is to be collected prospectively;
• the nature and amount of tissue, for example, whether it is regenerative or non-
regenerative or whether it is a blood sample or organ biopsy;
• the research use to which the tissue will be put—that is, whether this will be
epidemiological, non-identifying use, or identifying use, given that the results of
such research may have consequences for the donor or the donor's family. Policies
need to address how tissue could be used in genetic research and what additional
procedures need to be in place to protect the interests of and ensure the consent
of those affected. Further reference should be made to Commentary on NS 16.9
and 16.10.

Policies also need to provide for the possibility that information of clinical
importance to the health of the donor may be discovered. This possibility is a
further ground for seeking consent (see NS 15.7) but also requires a procedure for
recording and disclosing that information.

• potential commercial applications for research outcomes and whether the donor, or
an authorised third party, understands and approves of the research and its
objectives (see next section for further discussion).

Institutional policies also need to deal with issues of religious and cultural sensitivity to
the collection, storage and use of particular human tissue samples.

Sub-paragraph 15.1(c) refers to the professional removal of tissue as an expression of
respect for persons. Institutional policies about the collection of human tissue need to
establish that this can be done only by those with suitable training and experience.

Sub-paragraph 15.1(f) refers to the need for accountability in care and usage of tissue
samples as an expression of respect for persons. Institutional policies need to be
sufficiently transparent and public so that accountability can take place.

COMMERCIAL DEVELOPMENT OF TISSUE SAMPLES AND CONSENT

Potential tissue donors/research participants should be provided with all information
about the possible uses and outcomes of the research during the consent process. If
there is a possibility of commercialisation, and the person has been informed of this, they
can make an informed choice about whether to be involved. Most donors choose to
donate for altruistic or non-commercial reasons. However, an HREC should also ensure
that the potential for monetary gain arising out of the commercial development of tissue
samples is not used as an inducement to recruit research participants. Further reference
can be made to this Collection on ‘Conflicts of interest’, page E25.

HRECs need to be aware of the legal implications that might arise from these issues.
There is some debate about whether individual patients have rights, in property or
otherwise, over their removed tissue. On the basis of commonsense, if not of law, it is
envisaged that a donor would have more claim to rights in relation to tissue specifically
taken for research than in relation to tissues removed in the course of therapeutic
procedures. Further reference could be made on this issue to the Research Law
Collection, ‘Human tissue, research involving’, page L35.

This information should be presented in a manner suitable for the individual whose
consent is being sought. Researchers should take account of contextual circumstances
and cultural sensitivities, especially in relation to certain tissue or human products or
certain types or applications of research. Potential donors should be given the
opportunity to ask questions about the research use of their tissue.
In view of the complexity of the task of obtaining consent for the use of tissue in research, HRECs may consider requiring researchers to arrange that appropriately trained professionals be engaged to undertake this.

**AVOIDING AND LIMITING INJURY**

A basic ethical requirement in using human tissue for research purposes is that injury to donors be avoided or limited. In its report on *Human Tissue: Ethical and Legal Issues*[^1], the Nuffield Council on Bioethics explores this requirement, reasoning that respect for other human beings, and according them dignity, entails maintaining the integrity of the body so that the body, or its parts, are not injured. That is, neither the body nor its parts should be destroyed, damaged or degraded for the purposes of collecting tissue.

However, the Report also observes at the outset that such a requirement is ‘complex’ and ‘that in certain circumstances, injury can be avoided, or limited, only by inflicting injury’.[^2] The Council therefore concludes that it is ethically acceptable to collect tissue in a way that would otherwise be interpreted as injurious, where the use of that tissue directly, or indirectly, contributes to therapeutic activity. The therapeutic context and the intent of those removing tissue therefore become defining factors in determining the ethical acceptability of different sources of tissue for use in research.

Surplus surgical tissue is tissue removed during a surgical procedure that is not required for transplantation or histological examination and would normally be discarded. For example, bone and cartilage are removed during most joint replacement operations, skin is removed during plastic surgery procedures and thoracic and abdominal surgeons remove whole, or parts, of various viscera. In the majority of situations there will be no question that removal of tissue during a surgical procedure occurs with a direct therapeutic intent in relation to the patient concerned, and therefore, provided confidentiality and consent requirements are met (see below), research use of the tissue is ethically acceptable.

However, as the Nuffield Report points out, ‘there may…be examples of action in therapeutic contexts by health care professionals which [are] not clearly and unambiguously guided by a therapeutic intention’.[^3] Therefore, HRECs should be assured of the therapeutic context and intent of personnel involved in tissue collection for proposed research purposes.

Removal of tissue from donors specifically for the purpose of a research project should also be carefully considered. It should be noted that uniform legislative provisions in each State and Territory of Australia only allow for consensual donation by adults of regenerative tissue for transplantation to another living person, or for therapeutic, medical or scientific purposes.[^4] Consensual removal of non-regenerative tissue from adult persons is impliedly restricted to the purpose of transplantation to another living person. Separate provisions deal with donations of tissue from children.[^5]

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[^2]: Ibid., p.40
[^3]: Ibid.
[^4]: See Transplantation and Anatomy Act 1979 (Qld) div. 2 & 3; Human Tissue Act 1983 (NSW) div. 2 & 3; Human Tissue Act 1982 (Vic) Div 2 & 3; Human Tissue Transplant Act 1979 (NT), Div 2 & 3; Transplantation and Anatomy Act 1978 (ACT) div. 2 & 3; Transplantation and Anatomy Act 1983 (SA) div. 2 & 3; Human Tissue and Transplant Act 1982 (WA) div. 2 & 3; Human Tissue Act 1985 (Tas) div. 2 & 3. Note that ‘regenerative tissue’ is defined as tissue that, after injury or removal, is replaced in the body of a living person by natural processes.
[^5]: Ibid.
In certain circumstances, even without a direct therapeutic intention for removal of regenerative tissue in relation to a particular donor, a research project’s more general, or indirect, contribution to therapeutic activity may justify action that might otherwise be considered injurious, that is, removing tissue from the body of a living person. In terms of considering whether a research project meets this criterion, it is worth noting the Nuffield Council’s observation that:

…the findings of research cannot be known in advance. It is therefore not feasible to set tight limits on the types of scientific research that may lead to deeper understanding. Since such research could be a stepping-stone to therapeutic advances, it should be viewed as ethically acceptable.96

CONSENT

The legal and ethical reasons for requiring that consent for medical treatment be obtained from patients are well established.97

Uniform legislation in each Australian State and Territory also reflects this in relation to the donation of non-regenerative or regenerative tissue for transplantation and the donation of regenerative tissue for medical or scientific purposes.98 By prohibiting trade in human tissue, this also reinforces the ethical position that supply of human tissue from living donors for transplantation, medical or scientific purposes should be an expression of altruism by means of a consensual gift.99

There has been considerable debate amongst ethicists and members of the legal and scientific communities as to what constitutes valid consent in different circumstances. However, the requirement for consent to be informed and genuine is generally accepted. The National Statement requires that consent should:

- be voluntary; and
- be specific to the purpose for which the tissue is to be used; and
- follow the provision of full information about the project, including advice as to whether, after completion of the research for which consent is given, tissue samples are to be stored (NS 15.5).

Therefore, consideration should be given to requiring that those responsible for obtaining consent:

- attempt to ensure that consent is as genuine as possible by communicating clearly, according to the individual capabilities of potential donors or authorised third parties to understand procedures and risks;
- take account of contextual circumstances and cultural sensitivities, especially in relation to certain tissue or human products or certain types or applications of research.

96 Human Tissue: Legal and Ethical Issues, op.cit., p.43.
97 See the Research Law Collection. This section also deals with capacity to consent and special considerations applying to adults and children who are incompetent to consent. See also Breen, et al., op cit, ch. 3 for a more general account of consent.
98 See legislation cited at n. 106 above above.
For tissue collected within the context of medical treatment, consent procedures usually relate to diagnostic tests and routine archiving, with any surplus tissue being discarded. If researchers wish to make other use of the stored or surplus tissue, in order for consent to be informed or genuine the patient must have been told of the possibility of either type of tissue being used in future research, and also have been given the opportunity to object to this, or even to opt for disposal of all tissue.

**STORAGE OF TISSUE AND CONSENT**

If a participant's tissue is to be stored after the completion of a research project, they should be informed of this beforehand. Participants should also be told if the purpose of storing their tissue is for use in future research. If the participant expresses a wish that their tissue not be employed in further research purposes, or for specific types of research, their decision should be respected.

Where a tissue sample is not to be used for further research, researchers should honour the wishes of the participant (if any were expressed at the time of consent) with regard to the disposal of the sample. Some participants or collectivities will have sensitivities in this area.

In considering the issue of consent, HRECs need also to examine the nature of the new research. Where it is proposed that human tissue samples previously collected and stored for research be used for a research purpose different from that of the previously approved research, consent for the use of the tissue samples in the new research should generally be obtained.

HRECs should also note that the specificity of consent will be a relevant consideration if it is considering whether to approve research without consent (see NS 15.8).

This position in relation to consent should be viewed against a background of debate about whether individual patients have rights, in property or otherwise, over their removed tissue. There is no clear statutory or case law position on this issue. However, the issues were examined in the United States in the much-publicised case of Moore v Regents of the University of California, in which a patient sued his physicians and a biotechnology company for using his biopsied tissue without his consent and transforming it into a patented commercial cell line, without him sharing in the financial benefits. The court found for the defendants, reasoning that to give the patient a property right to his tissue would 'destroy the economic incentive to conduct important medical research'. (See the Research Law Collection for a detailed discussion of the legal aspects of the use of human tissue in research, page L35.)

Following Moore's Case, the Nuffield Council on Bioethics gave further consideration to the issues involved and ultimately proposed in its Report that tissue removed from patients in the course of treatment should be considered abandoned. However, the Council also proposed that the possibility that the tissue may be stored, used in the treatment of others, or used in medical education and research should be indicated in general terms in standard consent procedures for medical and surgical interventions where tissue is to be removed for diagnosis or treatment.

This recommendation was subsequently tested against the views of surgical in-patients by a team of medical practitioners and medical students who conducted questionnaire-based research on 384 postoperative adult surgical patients. The research found strong
support among patients for the use of tissues in medical education, research and science. Few patients (39: 10 per cent) believed that they retained ownership of tissue removed at surgery. Most believed that the tissue belonged to the hospital (103: 27 per cent), to nobody (103: 27 per cent) or to the laboratory (77: 20 per cent). Most patients had not been given any information about the possible uses of their tissue after removal. The authors were of the view that the main conclusions of the Nuffield Report were endorsed by their findings and that the recommendation about patient information and consent procedures should be implemented at the earliest opportunity.\(^\text{103}\)

However, another commentator has questioned the assumption of abandonment of patient tissue and asserts that ‘there are many situations in which patients would not be indifferent to the use of the samples they provide during their diagnosis and treatment’. \(^\text{104}\) This same commentator gives the example of patients who ‘would consider the property to be theirs if they suspected that it had been removed from them inappropriately and they wished to obtain a further histological opinion in contemplation of litigation.’ \(^\text{105}\)

This material emphasises the importance of researchers proposing and implementing appropriate consent procedures that take account of the context of tissue removal, and the particular circumstances of the donors and the research project.

**WAIVER OF CONSENT**

\[\text{NS 15.8}\]

**The nature of any existing consent relating to the collection and storage of the sample**

This applies particularly to stored material that has previously been used in research. HRECs need to consult relevant consent documents and decide whether the original consent given by the donor is in the spirit of the new research.

Some organisation or researchers seek ‘blanket consent’ from research participants for the use of their tissue in future research. This is done as a way of dealing with the uncertainty of future research needs and of avoiding the inconvenience of obtaining renewed consent. Depending on the case-by-case circumstances, an HREC may find that this is acceptable. For example, it may be adequate to seek consent ‘for the purposes of breast cancer research’. This informs the participant about the use of their tissue and gives the researchers some room to move with regard to future research on the tissue. However, wherever the research is of a different nature to the original, consented to, research, and the other provisions of these paragraphs on research with human tissue have been taken into account, an HREC should not allow the requirement for consent to be waived.

**The justification presented for seeking waiver of consent, including the extent to which it is impossible or difficult or intrusive to obtain specific consent**

In some situations it will be impossible, or extremely difficult, for researchers to obtain the consent of the original donors for the use of stored tissue samples. Tissue from an archaeological site is an obvious example. This provision would also apply where the samples may have been stored for a long time and the donors are untraceable or have died, or it may be excessively difficult for other reasons to trace the donors. Where such

\(^{103}\) Ibid, p.66.


\(^{105}\) Ibid
a situation arises, an HREC may approve the use of these samples, provided they are used in a de-identified form. Where it is technically impossible to de-identify the stored tissue sample, the committee may approve its use in a potentially identifiable form. However, in this case, protection of the codes becomes important. The committee will need to decide whether the code that links the information and material to the identifiers should be held by the researchers or by a third party.

In some situations, an HREC may believe that the procedures required to obtain consent are likely to cause unnecessary anxiety for those whose consent would be sought. This may be applicable in situations where tissue samples are accessed by authorised persons and identifiable data removed before the researcher gets access to the data. To require consent in this case would violate the privacy of research participants.

The proposed arrangements to protect privacy, including the extent to which it is possible to de-identify the sample

If an HREC waives the requirement for consent it should particularly ensure that the researchers have adequate experience and resources to maintain privacy. If possible, the tissue should be used in de-identified form. See also NS 15.9.

The extent to which the proposed research poses a risk to the privacy or wellbeing of the individual

The proposed research might be a risk to the privacy of the participants whose tissue is to be used. Accordingly, both the nature of the research and the risks it poses and the protective measures need to be considered.

Whether the research proposal is an extension of, or closely related to, a previously approved research project

It is important that that consent to research with human tissues be explicit and unambiguous in its scope. The principle that is reflected is respect for persons, which is better upheld by specific consent provisions rather than by loose and ambiguous expressions that can be used to attempt to justify further research without fresh consent.

The possibility of commercial exploitation or derivatives of the sample

HRECs should be more cautious about waiving consent where there is a possibility that the tissue sample may have use in commercial activities. The considerations mentioned above in relation to NS 15.5(c) on this issue remain relevant here.

Relevant statutory provisions
These may include the Human Tissue Acts referred to earlier in this section, or other Commonwealth or State/Territory legislation. Further reference should be made to the Research Law Collection, ‘Human tissue, research involving’, page L35.

PRIVACY AND CONFIDENTIALITY

Research participants need to be protected from breaches of privacy and the confidentiality of information derived from investigation of their tissue.

The challenge for medical institutions and researchers is to provide adequate security, that is, rules of conduct and physical systems that reasonably protect the relevant information. An HREC should be assured that researchers have access to appropriate
facilities, equipment and qualified staff to ensure the integrity of stored information and tissue samples.

HRECs need to consult the Privacy Act 1988 (Cth) and guidelines issued under that Act, as well as State/Territory legislation regulating the privacy of personal information.

In addition to consulting relevant legislation, an HREC should develop arrangements for protecting privacy and confidentiality in accord with relevant standards such as Standards Australia Personal Privacy Protection in Health Care Information Systems (AS4400-1995).

Within the context of genetic or other research investigating medical conditions that may have been previously undiagnosed, if information is made available for the research project beyond strictly defined parameters, it is possible that living donors may suffer social or economic disadvantage, such as through social stigmatisation, loss of employment or denial of insurance. Donors may also react adversely to being informed of research results such as the likelihood of late onset symptoms of a genetic disorder (see NS 16.15 and Commentary for further discussion of this issue).

These considerations will be more, or less, relevant depending on whether the tissue used is:

- identified—meaning that it can be readily linked to a particular individual, usually because it is named or has other identifiers such as date of birth or an address that allow the particular individual to be identified. In particularly small sets of data, even information such as a postcode may be an identifier.

- potentially identifiable (coded, re-identifiable)—where the material has had its identifiers removed and replaced by a code. In such cases it is possible to use the code to re-identify the person to whom the data relate so that the process of de-identification is reversible. This may have practical difficulties for tissue blocks stored by pathology laboratories, which cannot have identifiers removed as these are often an integral part of the tissue specimen. However, it may be possible to use part of the stored sample in coded or de-identified form for research, while retaining part in identified form for the primary purpose for which it has been stored.

- de-identified (not re-identifiable, anonymous)—where identifiers have been removed permanently or the tissue has never been identified. 'De-identified' has the same meaning as 'anonymous', 'not identifiable' and 'not re-identifiable'.

Researchers need to find an appropriate balance between maximising the protection of confidentiality by maintaining tissue anonymity and decreasing the usefulness of the sample as a source of other information that could enhance the research, such as sex, age, race, medical history or lifestyle.

A lack of identifiers also makes it impossible for researchers to directly offer potential benefits of the study to donors or their families. This may be a particularly relevant issue in situations where researchers detect indicators of a medical condition where early intervention might be beneficial. If this is judged likely to occur, the HREC may require procedures to allow participants to be identified to facilitate appropriate follow-up. In this case, the researcher should also show due consideration in the research protocol of a plan to manage the disclosure of such information to participants, including access to medical advice or counselling.

The legal and ethical basis for requirements of confidentiality in research involving humans is dealt with in detail in the Research Law Collection. A comprehensive overview of confidentiality requirements within the Australian medical context is also available in various texts.\(^\text{107}\)

The American and British pathology societies claim in their *Consensus Statement of Recommended Policies for Uses of Human Tissue in Research Education and Quality Control* that ‘there is no controversy among health care workers and researchers regarding the privacy rights of patients and the obligation to safeguard confidentiality. There is also no disagreement with the fact that confidential information has been and will continue to be at risk for inappropriate disclosure.’\(^\text{108}\)

The challenge for medical institutions and researchers becomes one of providing adequate security, that is, rules of conduct and physical systems that reasonably protect the relevant information. And, in this regard, the Consensus Statement also observes that ‘the number of individuals and institutions with legitimate access to medical records is large and information technology has placed more and more components of medical records in electronic form, adding new dimensions to the need for security of information to be taken in providing adequate security.’\(^\text{109}\) In the context of research, these considerations apply to information that may become part of the donor’s medical record during the processing of specimens for research purposes and the derivation and storage of information during research processes.

In addition to a requirement for ‘professional confidentiality to be observed’, the National Statement directs that identification of human tissue samples used in research ‘must be limited to the minimum necessary to achieve the stated objectives of the study’ and ‘[I]f the study may produce information relevant to the health and wellbeing of the person from which it was derived, the HREC may require procedures to allow participants to be identified to facilitate appropriate follow-up’ (NS 15.9). Where relevant, this may involve providing counselling and other support services.

**Suggested reading**


\(^\text{109}\) Ibid, p.9.


Royal College of Pathologists, Consensus Statement of Recommended Policies for Uses of Human Tissue in Research Education and Quality Control, London: Royal College of Pathologists, 1999. Endorsed by American and British Pathology Societies.
The National Statement is intended to apply to all research involving human participants, and not simply to medical or health research. While the ethical issues involved in some social science research fit well within the emphases of this Handbook, other research—for example, research into political oppression, or research uncovering scandals of importance to public policy—do not fit as readily into the National Statement’s principles. Generally, an HREC would consider the potential value of the research in furthering knowledge, in uncovering information and in social significance and weigh that against the potential risks and harms of the research.

In the case of humanities and social science research projects, where there is normally no risk of physical harm from the conduct of the research, HRECs should ensure that the primacy of protection of research participants is not overridden by the social value or contribution to knowledge that comes from having the research conducted and the findings published.

Suggested reading
INTELLECTUAL OR MENTAL IMPAIRMENT, RESEARCH INVOLVING

[NS 5.1–5.4 and Commentary]

DECISION-MAKING CAPACITY

The decision-making capacity is both a legal and an ethical concept that addresses a person's capacity to act on their own behalf. In a research context, this refers to the ability of potential research participants to make an informed choice about whether or not to participate in a particular project. This includes the ability to comprehend relevant information, to understand the consequences of a particular choice in relation to that information and to make a choice. It is essential that HREC members understand that while decision-making capacity may be limited for many individuals, there are a variety of ways in which decision-making occurs, and this should be taken into account when assessing relevant research proposals.

People in this situation may experience fluctuating levels of decision-making ability, which may, in turn, be a result of the course of a mental illness, or a response to treatment or medication, or a response to changes in general physical health. Others may possess limited decision-making capacity that still enables them to indicate consent or refusal. There are also people in this group who lack the ability to make decisions requiring a significant degree of reflection.

NS 5.2 does not provide relevant criteria for assessing the level of decision-making capacity of potential research participants who have an intellectual or mental impairment, so an HREC should closely scrutinise criteria proposed by researchers.

CONSENT

The capacity to choose to participate in a research project does not require a capacity for making every type of decision. It simply requires the potential participant to be sufficiently capable of choosing whether or not to take part in a specific project. Therefore, consent to research should be obtained from an intellectually impaired person where such 'sufficient' decision-making ability exists and, where impairment is temporary or recurrent, consent should be sought at a time when the person is capable of making a choice (NS 5.2(a))

Consent must be both informed and voluntary. HRECs should be fully satisfied that no element of coercion is involved in obtaining consent. The committee will need to be aware of the constraints of the setting in which the person will be approached, as well as the role of the individual making that approach. Such constraints can have a negative influence on a potential research participant's ability to comprehend relevant information and to feel free to make her or his own choice. Ethics committees should consider whether people in this situation are in need of independent advocacy services (NS 2.25).
IMPAIRED CAPACITY FOR COMMUNICATION, RESEARCH INVOLVING PEOPLE WITH

According to NS 6.7, research involving people with an impaired capacity for communication includes situations ‘where the impairment is an acute state requiring dependence on medical care’, as well as situations that are non-acute. People in both types of situations may need to use specialised methods of communication in order to convey their wishes about consent, or otherwise, to taking part in a research project. If a person is unable to communicate their wishes in any way at all then the relevant statutory authority will need to act on their behalf.

INTERNATIONAL RESEARCH

The principle of justice (NS 1.5) must be applied when considering a research proposal. The benefits of research should be made available to the participants that bear the burden of that research. Without this principle, participants could be exploited for the purposes of the research while its benefits go wholly elsewhere—for example, back to first-world patients who can afford to pay the high price of the treatment.

This principle is intended to prevent researchers from recruiting participants who could benefit from already existing treatment that they were not getting. This exploitation might occur either with third-world populations, or with research subjects in first-world countries who are unable to pay for existing treatment available to those better off. Thus, the application of the principle prevents researchers, in testing an unproven treatment, from recruiting their research subjects solely on the basis that they do not have access to the best existing treatment for the disease for which the new treatment is being tested. This is ethically unacceptable because it may involve exploitation in the selection of research subjects. Participation in research should not deprive subjects of the optimal available standard of health care.

The issue raised by this principle is that not all subjects are equal: some will have access to better health care than others. This can be argued to be irrelevant to research, but has been argued to be relevant where the same research is conducted in populations so radically different that one will have access to health care far superior than the other, especially after the research. However, the issue for research, especially with drugs, is that, because involvement in the research provides access to superior treatment than is otherwise available, when participants leave the research, they will suffer differently. Those with access to treatment equivalent to that in the research will not experience discrimination: those that do not, will. The issue is ethically one of both justice and consent. Is it fair to subjects that they be included in a research project that will offer superior treatment than is otherwise available, but only for the duration of the research, after which they will return to a lower standard? Alternatively, is it essential that the risks involved in how their health care will change when the research ceases must be included in a disclosure to all potential subjects?

PLACEBO USE IN DEVELOPING COUNTRIES

Some sponsors of clinical trials in third-world countries have argued that the use of a placebo is acceptable if treatment of established efficacy exists but, for economic reasons, is not readily available in that third-world country. Most, if not all, commentary on this proposal from an ethical perspective has rejected the argument. Australian HRECs have the responsibility for examining research proposals undertaken overseas by researchers under the aegis of an Australian institution. In doing so, an HREC should apply the same considerations in relation to placebo use as it would apply to a trial undertaken locally (NS 1.21 and 12).

Suggested reading

JUSTICE

[NS 1.5–1.6 and Commentary]

Justice involves both the idea of treating people as moral equals and the idea of treating people differently where relevant differences between them justify such differential treatment. For example, justice requires treating people as equals before the law. However, the law may justly discriminate between people, for example, by holding those who lack the capacity to be fully responsible for their actions less culpable, or by protecting those who are less able to protect themselves.

The importance of distributive justice in relation to the recruitment of research participants is also emphasised in the recent Canadian Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans:
http://www.nserc.ca/programs/ethics/english/policy.htm

Historically, concern for justice in research involving human subjects has focused on whether research subjects were treated fairly: were they overburdened relative to the direct benefits they received from their participation in research?

Contemporary concerns with justice in research have broadened: are the overall benefits and burdens of research distributed fairly, and have disadvantaged individuals and groups received a fair share of the benefits of research?

The above two concerns form the basis of the principle of distributive justice: members of society should neither bear an unfair share of the direct burdens of participating in research, nor should they be unfairly excluded from the potential benefits of research participation.

The concerns raised by the principle reflect broader obligations to respect human dignity and diversity. They should, therefore, receive the formal attention of researchers, Canadian REBs (Research Ethics Boards), research institutions and sponsors.110

SELECTION AND RECRUITMENT OF RESEARCH PARTICIPANTS

Concern for potential participants' privacy and self-determination, for a fair distribution of research benefits and burdens, and for the appropriateness of participant selection methods form the basis for HREC assessment of proposed selection and recruitment procedures. Justice requires avoidance of over-recruitment of particular participant populations and assessment of the fairness of asking participants to bear research burdens.

This applies both to the populations identified for participant recruitment and the means by which potential participants are approached. If public hospital or clinic records, or registers of service consumers, are to be the source for identifying potential participants, then some members of the community are more likely to be approached than others. In addition, researcher access to these kinds of records would expose some people to invasion of privacy before they make a decision about whether or not to take part in the study. In general, researchers should not be given access to contact information by institutions or organisations unless the individual concerned has already agreed to disclose that information to the researcher.111


111 Some support groups have registries of people willing to be approached for research purposes, with the person who is to be approached for recruitment having already agreed to make their details available to researchers.
Although some disadvantaged groups have been unfairly over-researched in the past, it is also possible for disadvantaged groups to be under-researched. Some groups, such as pregnant women, children and those who are suffering from multiple illnesses have, historically, been excluded from participation in drug research. (See also ‘Women, inclusion in research’, page E165, in this Collection.) As a result, there is limited information available about the safety and efficacy of drug use in relation to these groups.

In addition, HRECs need to review the proposed methods of recruitment, as well as the contents of any proposed recruitment advertisements. Recruitment methods should ensure that the purpose of the approach to potential participants is absolutely clear, and that the approach is not misleading in any way, for example, suggesting or implying that participants will benefit directly from taking part in the study when this is not the case. Privacy and confidentiality should also be respected when researchers are devising methods of recruitment. As noted above, it is not acceptable to obtain contact details of potential participants from a third party and then to approach these people when the latter have not given prior consent. (See a more detailed discussion of these issues in relation to research with women, page E165, and gay men and lesbians, page E43, in this Collection.)

The term ‘benefit’, as opposed to ‘harm’, refers to that which positively affects the interests or welfare of an individual or group. Although the potential benefits of any favourable research outcome include increased knowledge, improved policies or enhanced service provisions, the focus of this principle is on the benefits and burdens of research as experienced by participants in that research.

**BALANCING JUSTICE AND RESPECT FOR PERSONS**

Concern for the wellbeing of certain groups of people in the future must not lead to negation of the rights of current research participants. Protection of research participants from harm is the major justification for HREC assessment of the risks and benefits of research proposals. 112

It has been argued that this emphasis on protection against harm is overly protective as it may negate a person’s right to participate in ‘risky’ research if they so desire. HRECs should attempt to balance these conflicting views by complementing the emphasis on risk minimisation with a similar emphasis on consent in those situations where potential participants may be willing to take greater risks without sharing in the benefits of the research, for instance in early phase trials of vaccines or other drugs. HRECs need to evaluate whether, even if there is informed consent, this is ethically acceptable and this degree of risk is suitably balanced by benefits and to whom they will accrue. HRECs need to consider whether to allow adults capable of independent decision-making to assess risks on their own terms.

MONITORING RESEARCH

[NS 2.33–2.38, 12.8(d) and Commentary]

MONITORING RESEARCH IN PROGRESS

HRECs should ensure that mechanisms for monitoring research and managing adverse events are in place and that the committee receives regular reports. As noted earlier, ethics committees will be asked to report on monitoring procedures, and any problems encountered, in their annual compliance report to the NHMRC (see NS 2.48).

At a minimum, researchers are required to forward an annual report to the HREC about the progress of their research and compliance with any conditions of approval (NS 2.35). This report should include a statement on whether anything adverse has occurred in the course of the research, especially any serious or unexpected adverse effect on participants (NS 2.37). It is always possible that a potential harm was not anticipated at the planning and approval stage of a project and a researcher's report may alert the committee to a concern about the welfare of research participants.

However, HRECs may also decide to require more frequent reports from researchers, more detail on some aspect of the research process, more information about other activities conducted in the research centre, or more information about any adverse events occurring in associated research programs undertaken by collaborators or associates at other centres. For example, a researcher may become aware of an adverse event in some other centre in relation to a multi-centre drug trial. An HREC should require the provision of such information, and researchers are responsible for ensuring that objective monitoring procedures are established and that they report adverse events regardless of the site at which they occur.

An ethics committee may adopt any mechanism for monitoring that it considers appropriate, including random inspections of research sites, data and signed consent forms, or the interviewing of research participants (with the prior consent of both research participants and researchers) (NS 2.36). Where on-site monitoring has occurred, researchers have often responded with a greater respect for the review process.113 Such activities also provide committee members with an opportunity to become better informed about the way in which research is conducted within their institution.

Ethics committees may also use existing mechanisms within their institution or organisation to ensure that research is properly monitored (NS 2.33). For example, quality control mechanisms could be modified to alert an HREC to problems arising as a research project progresses. Alternatively, it may be appropriate to institute specific on-site monitoring of the research process with regard to a particular study.

HRECs should closely scrutinise any proposed monitoring arrangements made by the sponsoring company concerning research proposals for evaluating pharmaceutical products. Does this ensure adequate protection for research participants? The committee may require additional or alternative safeguards, including monitoring of study results by independent persons. For example, in clinical trials of new pharmaceutical agents, independent review committees will usually be necessary for adequate monitoring of results for both safety and efficacy. Or a committee may consider that the manner in which a substance is administered to research participants requires close on-site supervision by an independent nurse or medical practitioner. Similarly, a study may be so sensitive that the committee feels the consent process, or a survey involving open-ended questions, requires on-site monitoring.

When an HREC decides that active monitoring of a research project is necessary, committee members will need to consider who is most appropriate to carry this out. This might be members of the committee. In this situation, it is advisable to choose one committee member with expertise in the particular area of research, and a ‘lay’, or community, member. An alternative would be to employ a salaried officer, or an independent person, with the necessary expertise.\textsuperscript{114}

With regard to multi-centre research, HRECs might consider consultation with other committees and institutions involved in a particular trial in order to ensure adequate and consistent monitoring (see NS 3.2–3.8, and see the following section of this Collection for a detailed discussion of multi-centre trials.)

**MANAGEMENT OF ADVERSE EVENTS**

This is an issue of paramount importance for HRECs in view of their primary responsibility to protect research participants from harm. This matter is discussed at length in relation to clinical trials, which is clearly an area of research practice where participants may encounter serious harm. It is suggested that the reader refer to this detailed account of the management of adverse events—see NS sub-paragraph 12.8(d) and relevant Commentary.

\textsuperscript{114} Ibid.
MULTI-CENTRE RESEARCH

[NS 3.1–3.8 and Commentary]

Multi-centre research includes research conducted at two or more administratively and/or geographically separate institutions either by the same, or different, researchers. Many types of research may be involved, including clinical trials of drugs or devices, epidemiological studies, health services research and psychological or social science studies. Multi-centre studies may be local, national or international. The research project may be conducted jointly by researchers affiliated with different institutions or by a researcher who changes affiliation from one institution to another (see NS 3.1–3.5).

As readers of this volume will be aware, at present there is a great deal of unnecessary duplication in the review of multi-centre research proposals. As a solution to this problem, the National Statement recommends collaboration among all participating HRECs in order to ‘accelerate timely consideration and avoid unnecessary duplication’ of review of such proposals (NS 3.4(d)).

SCIENTIFIC AND ETHICAL REVIEW

Scientific review processes should be arranged so as to minimise unnecessary duplication, avoid unnecessary delay, and maintain protocol consistency between centres. Where possible, therefore, participating HRECs should share scientific and technical assessments and aim at reaching agreement on necessary protocol changes. Ethical review processes should enable HRECs to effectively discharge their ethical obligations and legal duties, prevent unnecessary delay and harmonise decisions between participating ethics committees.

Nevertheless, local variation in certain HREC requirements is often appropriate. For example, plain-English information statements and consent forms are normally customised for each participating centre with regard to institutional letterhead, names and contact phone numbers of researchers, complaint procedures, and so on. Therefore, individual HRECs may recommend any changes that they consider appropriate, provided the integrity of the research is not compromised. However, where inconsistencies between decisions create serious logistic difficulties, or compromise the scientific integrity of a study, participating committees should collectively review their decisions and attempt to harmonise these. Many of the difficulties associated with multi-centre studies may be avoided by informal discussion and negotiation between researcher and HRECs early in the planning phase.

HUMAN RESEARCH ETHICS COMMITTEE JURISDICTION

HREC jurisdiction is determined by whether or not the institution or organisation owes a duty of care to the proposed research participants. Multi-centre studies normally require approval by the ethics committee at each participating institution. In some circumstances, however, an institution may agree to accept or endorse the recommendations of an HREC at another institution without giving the research proposal detailed consideration. This normally occurs when the organisations involved have a pre-existing formal or informal affiliation, such as multi-campus institutions, universities and their affiliated teaching hospitals, regional hospital groupings, and so on.
Ethical consideration of community research\textsuperscript{115} is usually conducted by a single HREC at an institution with which the principal researcher is affiliated. Monitoring of approved research is normally the responsibility of the HREC that gave the approval.

The following is an account of a suggested protocol for collaboration between HRECs when reviewing multi-centre research proposals, based on NHMRC recommendations (NS 3.1–3.8) However, it should be emphasised that the following is a suggestion only and that ethics committees may choose to negotiate other arrangements.

**A MODEL FOR CONDUCTING MULTI-CENTRE RESEARCH**

The decision about whether it is necessary for an HREC to consider any proposal will need to be based on the following grounds:

- the existence of some involvement in the proposal by one or more researchers from its institution;
- the nature of the institution; and
- the extent to which it has responsibility for prospective participants.

If a researcher from the institution to which the HREC belongs is involved in the proposal, consideration of the proposal is often required irrespective of whether it will be undertaken within the institution itself, elsewhere in Australia or overseas (see NS 1.21). However, if there will be no involvement by any researcher who is a member or affiliate of the institution, the requirement for HREC consideration should be decided on the basis of the relationship of the institution to the proposed participants in the research.

This relationship will itself be substantially influenced by the nature of the institution and the nature of the research. If, for example, the institution to which the HREC is attached is a hospital and the participants will include patients for whose welfare the institution is responsible, HREC consideration of the proposal is essential. On the other hand, if the proposed participants are adult students of a university who are to be administered a questionnaire by researchers based outside that university, consideration of the proposal by the HREC may not be required. This will depend on the nature and object of the research. For instance, if the object is to compare the educational experiences of students in different universities, HREC review would be justified. If the object was to research aspects of the lifestyle of Australian students, there would be less justification for HREC review. (In the latter situation, it may well be that the researchers would contact personnel and/or the HREC of that university. This could be for the purpose of informing the university of the study, as a courtesy, and/or or facilitating some assistance in contacting students. This could be called a matter of etiquette rather than ethics).

**Choosing a coordinating researcher, institution and ethics committee\textsuperscript{116}**

Multi-centre studies may be researcher-initiated or they may be initiated by a sponsor, such as a pharmaceutical manufacturer, a research institution or a government body. Once those involved in planning a multi-centre study have identified the participating\textsuperscript{117} researchers and institutions, they should nominate a coordinating researcher and institution by mutual agreement.

\textsuperscript{115} Community research: studies where participants are recruited outside an institutional or organisational setting. The distinguishing criterion between institutional and community research is whether any institution owes a legal duty of care to the participants.

\textsuperscript{116} Coordinating researcher /centre/HREC: all multi-centre research studies conducted within Australia should have a designated coordinating researcher responsible for overseeing the administration of the study. The institution at which the coordinating researcher is located, or with which he or she is affiliated, is the coordinating centre and the ethics committee at that centre is the coordinating HREC.

\textsuperscript{117} Participating researchers/centres/HRECs: all researchers and their associated institutions and HRECs involved in the conduct of the study.
**MULTI-CENTRE FLOWCHART**

1. Planners nominate **coordinating researcher**
2. Prepare and distribute application to **participating researchers**
3. **Common submission deadline** → Application submitted to all **participating HRECs**
4. **Scientific assessment deadline** → Scientific assessments submitted to **coordinating** HREC and distributed to all **participating** HRECs
5. **Ethics assessment deadline** → **Participating** HRECs send recommendations to **coordinating** HREC
6. **Harmonisation**
7. **Notification**
Early in the planning process the coordinating researcher should contact the chair or secretary of the HREC at their institution requesting agreement to act as coordinating committee for the study. The coordinating researcher should also advise of the need to arrange a scientific assessment that can be shared with participating committees.

If the study is an international one, the sponsor or initiating researcher(s) may appoint a national coordinating researcher responsible for coordinating the involvement of participating centres within Australia. However, it should be noted that in some circumstances United States Food and Drug Administration (FDA) requirements might not permit this.

**Role of the coordinating researcher**

The coordinating researcher should liaise with the participating researchers and sponsor in relation to organising the study and seeking ethical approval. Where appropriate, the coordinating researcher should arrange a meeting of participating researchers to discuss issues such as protocol details, ethical concerns, independent monitoring arrangements, record-keeping, intellectual property and publication policies, funding, and insurance and indemnity arrangements. If they are not already available, the coordinating researcher should prepare and distribute a detailed protocol, a model plain-English information statement and a consent form to participating researchers. The coordinating researcher should also consult participating researchers to set a common submission deadline, taking account of the meeting schedules of participating HRECs. All researchers should undertake to submit applications to their local ethics committee by that date.

**Application procedures: submission of ethics application**

The application form used by the coordinating HREC should be submitted to all participating committees. The coordinating researcher should send the completed application form to the coordinating HREC. A list of the names and contact details of all participating researchers and ethics committees should also be provided.

The coordinating researcher should send an electronic copy of the application, including the protocol, model plain-English information statement, consent form, and list of participating researchers and institutions to each participating researcher. Participating researchers should then add information specific to their centre, and may modify the information statement and consent form according to local preferences, before submission to the local HREC. The completed application form, together with the list of participating researchers and ethics committees, should be submitted to the local HREC by the common submission deadline. The coordinating researcher should make it clear to participating researchers that late applications will delay the approval process for all centres.

**Shared scientific assessment: role of the coordinating committee**

It is the responsibility of the coordinating HREC to arrange an independent scientific, technical and/or safety assessment and to make this available to all participating committees. On receipt of a multi-centre application, the coordinating committee should decide on a mechanism for obtaining a shared scientific assessment. This should normally be done after consultation with participating HRECs.

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118 Common submission deadline: the date by which all participating researchers are to submit ethics applications, including the study protocol, plain-English information statement, consent form and list of other participating researchers and centres to their local ethics committee.

119 Shared scientific assessment: Scientific, technical and/or safety assessments solicited by the coordinating HREC and distributed to participating committees. The coordinating committee normally chooses assessors after consultation with participating HRECs.
Assessors may be nominated from within the coordinating institution, from amongst participating institutions, or from elsewhere. Many HRECs have established scientific subcommittees with the appropriate expertise to provide such assessments. In some situations, a regional, statewide or national expert group may be available to conduct assessments. In other situations an ad hoc assessment panel may be considered more appropriate. The coordinating HREC should set a date by which assessments are due. The scientific assessment deadline should normally occur within four weeks of the common submission deadline. On receipt of the assessments the coordinating committee should send copies to each participating HREC.

The coordinating HREC should check whether any participating committees intend to obtain additional independent scientific assessments. If so, the committees concerned should send copies of these assessments to the coordinating HREC for distribution by the scientific assessment deadline. The coordinating committee should consult with participating committees in setting an ethics assessment deadline, taking account of various meeting schedules. The ethics assessment deadline should normally occur within four weeks of the scientific assessment deadline.

**Ethics assessment: role of participating committees**

Participating committees should complete their evaluation of the scientific assessments and ethical issues by the ethics assessment deadline, provided the application was received by the common submission deadline. They should also agree to advise the coordinating committee of their recommendations by the ethics assessment deadline. If, for valid reasons, a participating committee cannot meet these deadlines then the coordinating committee should be informed.

**Harmonisation**

The coordinating HREC is responsible for collating and distributing the recommendations of participating committees. This should normally occur within two working days of the ethics assessment deadline. Participating HRECs should attempt to reach a consensus on any changes to be made to the study protocol.

If necessary, the coordinating committee may arrange a teleconference between representatives of participating committees in order to resolve differences of opinion on substantive issues. Normally, such meetings should be arranged within 10 days of the ethics assessment deadline. If substantive differences of opinion cannot be satisfactorily resolved then participating HRECs may decide to seek additional expert advice.

Once agreement has been reached on the study protocol, it is not appropriate for participating HRECs to require further changes. Notification to researchers of agreed protocol changes and local committee decisions about the plain-English information statements and consent forms should normally occur within two weeks of the ethics assessment deadline.

**Protocol amendments**

Amendments to the study protocol made as a result of new information, such as adverse reactions or unanticipated logistic difficulties, should be approved by all participating HRECs. If amendments are substantive, the coordinating committee should communicate directly with participating HRECs and collate their responses.

**Additional centres**

If there is a request to add further centres to a multi-centre study after the proposal has been fully evaluated and approved, the coordinating committee should consult with all participating HRECs about deciding on this. Once an approved multi-centre study has
begun, it is not generally appropriate for HRECs at ‘additional’ centres to require further changes to the protocol. However, these HRECs may recommend locally appropriate changes to the plain-English information statement and consent form, provided these do not jeopardise the scientific integrity of the study.

**Rejection of a multi-centre research proposal**

If a particular HREC rejects a multi-centre research proposal that has been approved elsewhere, the reasons for rejection should be conveyed to the coordinating committee and distributed to other participating committees.

**Resources**

Coordinating HRECs may require additional resources in order to carry out the above role effectively.
NEONATAL INTENSIVE CARE RESEARCH

The extreme vulnerability to harm of infants means that all but the most minimal intrusion is likely to be contrary to the child’s best interests (See NS 6.4–6.5). And, as discussed in ‘Children and young people, research involving’ above, the National Statement does not permit research to be carried out that is contrary to a child’s best interests. An HREC will need to assess whether additional handling of low birth weight infants for the purposes of research is justifiable, as well as the collection of any blood samples additional to those necessary for diagnostic purposes.
PHARMACEUTICAL INDUSTRY, PHYSICIANS AND

Prescription pharmaceuticals include commodities that are unique in our society in the sense that a consumer is legally prevented from accessing them without the intervention of two professionals: a medical practitioner to write a prescription and a pharmacist to dispense the drug. This complex system has evolved primarily because the condition being treated by the product is one that requires expertise in diagnosis and monitoring treatment. It has been seen by some as designed to protect the public against exploitation, to ensure that potentially dangerous items are not sold inappropriately and to reassure people that the person making recommendations about their treatment has no financial conflict of interest. It should also be noted that pharmaceuticals sold over-the-counter, as well as ‘alternative’ medications, might also be subject to research requiring HREC review.

It is obvious that new drugs will need to be tested on humans before they can be widely used in the community. It is also obvious that some drugs will be potentially valuable and that the pharmaceutical company will have strong incentives to market the drug as quickly as possible. Most countries have sophisticated regulatory systems that must be traversed before the drug can be legally marketed. Regulation is largely concerned with the balance between safety and efficacy, but regulatory systems are also becoming increasingly involved in assessment of cost-effectiveness. In Australia there are two main levels of regulation with respect to drug trials: the Clinical Trial Exemption Scheme (CTX) and the Clinical Trial Notification Scheme (CTN). These are discussed in detail in this Collection under ‘Clinical trials’ page E11. Briefly, under the CTX Scheme a trial undergoes primary assessment by the regulatory agency, while under the CTN Scheme ethics committees are responsible for assessing and approving a clinical trial.

The following are the main concerns for an HREC in reviewing research involving potentially commercial pharmaceuticals.

- Clinical trials for commercial products need to be shown to have scientific merit, and not to be functioning primarily as commercial promotions or to familiarise medical practitioners with a particular drug and thereby encourage its use.
- Costs to institutions may be considerable and demands on clinicians, nursing staff and others may potentially detract from patient care.
- Clinicians who also adopt the role of researchers may face conflicts between their duties to their patients, their interests in research and possible personal benefits.
- Participant privacy may be infringed as drug companies may require access to patient records in order to verify data or to ensure the proper conduct of a trial.

It is generally recommended that researchers should not derive any direct personal or financial benefits from the conduct of a pharmaceutical industry sponsored clinical trial, although reasonable costs incurred by such participation may be covered. More subtle conflicts arise when there are less tangible benefits flowing to the clinician from participation, such as the donation of equipment to research laboratories, payment for research personnel to participate in conferences, or even the provision of infrastructure, such as renovation of laboratory space. It is widely agreed that as far as possible, all payments or benefits should be publicly declared and open to scrutiny by HRECs. (See this Collection for a general discussion of conflicts of interest in research practice, page E25.)

To ensure proper conduct of the clinical trial, drug companies may require access to participants’ medical records. Prospective participants in a clinical trial should be advised of the possibility of this and the primary researcher should assume responsibility for supervising such access.
The main purpose of research involving pharmaceuticals should be the provision of new information for the benefit of the whole community. This generally requires the publication of results, negative as well as positive, preferably by the researchers. On occasions, drug companies stipulate that publication cannot be undertaken without their permission. This raises the possibility of serious limitations to the dissemination of knowledge and should be strongly discouraged by HRECs.
PRISONERS, RESEARCH INVOLVING

HRECs may receive proposals for research involving prisoners. While prisoners appear to be particularly suitable as research participants (they have time to participate in long-term studies and research may offer a relief from tedium and a chance to earn a small income), HRECs should be conscious of the difficulties of prisoners giving voluntary consent.\footnote{Council for International Organisations of Medical Science, ‘International ethical guidelines for biomedical research involving human subjects’, 1993, in Manual for Research Ethics Committees, Kings College London, v.(23)1.}

In particular, prisoners should not be put under pressure to participate. They should not be offered inducements or be led to believe that they will receive specific rewards, such as early parole, in return for their participation.
PRIVACY

See Research Law Collection, page L45.
PSYCHIATRIC RESEARCH

INTRODUCTION

Historically, psychiatric treatment and research involving people with psychiatric conditions has sometimes served as a ‘legitimating’ vehicle for extreme assaults on human life and dignity, as in the former Soviet Union and Nazi Germany. However, even in more ‘normal’ times, and under non-totalitarian regimes, psychiatric research involving people suffering from mental illness can still be perverted and, rather than fulfilling its promise of improved understanding of mental illness and its treatment, can result in serious harm to research participants. The following discussion focuses on five areas: respect for persons, risks, informed consent, confidentiality and privacy, and conflicts of interest.

RESPECT FOR PERSONS

Respect for a person’s dignity, rights and welfare is always paramount over the requirements of the research process and the potential benefits of the research itself.

This is perhaps even more critical for research in psychiatric settings, in view of centuries of exploitation of, and discrimination against, mentally ill people. Medicine generally, and psychiatry in particular, have mixed track records with people in this situation, sometimes serving as beneficent advocates and sometimes abusing their authority and contributing to the stigmatisation of their patients. Researchers, therefore, need to act with particular sensitivity when carrying out research with people suffering from any psychiatric disorder, especially where the person’s ability to make rational decisions is reduced.

BALANCING RISKS AND BENEFITS

People suffering from psychiatric illness may be experiencing extreme levels of distress, disturbances of thinking or feeling, or other distortions of their inner world. They therefore constitute a potentially highly vulnerable group, especially with regard to psychological harms. The involvement of such vulnerable people in a research project may provoke changes in their thinking and feeling that may lead to a significant worsening of their mental state. They may suffer adverse reactions such as anxiety, depression, confusion, guilt, shame, reduced self-esteem, a feeling of being stigmatised, or an exacerbation of their underlying illness. Although responses may be transient, the risks to the participant’s emotional health must be carefully considered. Certain research methods may also revive extremely distressing unresolved issues, for example inquiring about a person’s current sexual history may conjure up disturbing feelings associated with past sexual abuse.

Apart from past abusive sexual experiences and other forms of physical or emotional childhood abuse, there are other potentially sensitive areas, such as a possible forensic history or an adult experience of loss, abuse or trauma. When participation in the proposed research project will focus or touch on one or more of these potentially sensitive themes, the research proposal should include extra specific strategies for monitoring and providing therapy or treatment for any episodes of distress triggered by participation. Ethics committees should also assess whether or not people with known vulnerability to such distress should even be approached as potential research participants.
INFORMED CONSENT

Two issues need special consideration in relation to psychiatric research involving people suffering from mental illness. Firstly, possible inability of the potential research participant to make rational and considered decisions and, secondly, the protection of people subject to legislated involuntary treatment. Inherent in both these situations is the risk of real or perceived coercion. These issues are discussed in the sub-sections following.

Information given to potential psychiatric research participants suffering from mental illness (or to their carers, guardians or proxy respondents) should include a full account of procedures, risks and benefits, and should be presented in a way that they can understand. Consent or refusal must be given voluntarily and the researcher should attempt to remove any sources of pressure that may jeopardise the voluntariness of consent.

HRECs need to note the inherent difficulty in achieving this if the researcher is also the person’s treating psychiatrist, upon whom they depend for ongoing care. This almost inevitably constitutes ‘undue pressure’ and it is highly questionable whether real freedom to consent or refuse to participate in a research study is possible under these circumstances. Ethics committees will need to consider, in each instance, whether or not an independent advocate, acting exclusively in the potential research participants’ best interests, should be appointed to manage the recruitment process.

Other possible difficulties include potential participants not being given sufficient time to consider the information provided before being required to make a decision, as well as not being given adequate information to enable them to make an informed decision. Any attempt to justify the provision of limited information on the assumption that people suffering from psychiatric illness would not be able to understand a detailed account, or that they would be upset by such information, is not ethically acceptable. Indeed, extra effort should be made to ensure that the necessary information is communicated as clearly and comprehensively as possible.

Finally, ethics committees need to be aware that obtaining, and giving, informed consent or refusal should be an ongoing process rather than a one-point-in-time exercise. Ethics committees should ensure that a research proposal contains clearly defined strategies for achieving this.

Rational decision-making and mental incompetence

Most people receiving psychiatric treatment are quite capable of giving informed consent or refusal. However, an important subset is not. Thus we are faced with a dilemma: on the one hand, we have serious and disabling disorders about which both society and researchers hope to gain new knowledge; on the other, patients may be the least able to consent. Disorders such as psychotic depression, schizophrenia, postnatal depression, delirium or dementia can cause temporary or permanent inability to make rational decisions. This mental incompetence of its very nature presents a major ethical challenge in terms of whether these people should be involved in research studies.

A further complicating factor is that an inability to make rational decisions is not usually total. A person in this situation may be capable of making rational decisions in some areas but not others. A person may be hallucinating, or extremely distressed by panic attacks, or have a degree of memory impairment but still be capable of consenting or refusing to participate in research.

On the other hand, certain delusional states may indicate that a person is not able to make a rational decision about participation in research. For example, a person suffering
from psychotic depression may be in danger of incorporating the research experience into their delusional belief. A person's competence or judgment may be temporarily impaired following a severe trauma, for example, assault, rape or a motor vehicle accident. People in this situation may be very distressed by a request to participate in a research project, or they may be vulnerable and 'excessively' willing to comply. Again, the ethical requirement for competence-based informed consent conflicts with the need for greater understanding of post-traumatic psychiatric disorders and the possibility that research conducted close to the time of the trauma may be extremely informative.

**Real or perceived coercion**

A person suffering from mental illness may feel intensely vulnerable and may become highly dependent on, or idealise, the treating professional. This can occur in psychodynamic psychotherapies, where intense emotions towards the therapist that develop in the patient are interpreted as part of the therapeutic process, but are by no means restricted to that setting. Consenting to take part in a research project may well be motivated by a person's wish to please—or not to displease—their medical practitioner, nurse, psychologist or other mental health carer.

When people are treated as involuntary patients, further ethical challenges arise. Typically, mental health law takes pains to protect the rights of people in this situation, who may perceive themselves as having little or no choice when asked to participate in a research project. Researchers are obliged to make explicit to involuntary patients that they are free to consent or refuse and that their decision will in no way affect their continuing treatment. These patients are extremely vulnerable to the coercive pressures, and ethics committees should carefully assess whether the support of an independent advocate is necessary when such people are approached with a request to take part in a research project.

**CONFIDENTIALITY AND PRIVACY**

The privacy of research participants must be respected and the confidentiality of their personal information safeguarded. (See the Research Law Collection for a discussion of the relevant legal aspects of confidentiality of information, page L7.) HRECs should note that these requirements are especially critical in that information about people involved in psychiatric research is of a particularly sensitive and highly personal nature.

Other issues requiring special mention are as follows:

- Obtaining sensitive information about the research participant’s family or significant others may be a feature of the study design. For example, this may require seeking information about whether or not the participant has a family history of mental illness, about the type of family environment in which the person was reared, or about the quality of their marital relationship. Principles of safeguarding confidentiality apply to collecting these data as well, and even more so, since family members may not have given informed consent for such information to be obtained or shared with researchers.

- Identification of research participants in published reports or in conference presentation, may be more likely in research with this group of people. The researcher investigator should therefore use ‘composite’ illustrations or, if it is absolutely necessary to resort to individual illustration (as is often the case), should carefully disguise the clinical material.

- In exceptional circumstances, information about a research participant subject emerges that has forensic implications or indicates a risk to the safety of others. Researchers may in this case be legally and/or ethically obligated to breach
confidentiality in line with the Tarasoff judgment (in which it was argued that a clear risk to an identified person justifies the breach). For example, a woman suffering from severe postnatal depression may divulge infanticidal thoughts. As mentioned in the section on risks above, the researcher may need to consult with family and/or professional caregivers if evidence emerges that a participant's mental state, health and safety are at risk and their insight is limited or absent. If the researcher cannot obtain the participant's consent when they believe it is necessary to secure family or professional assistance, a duty of care may override respect for the research participant's right to privacy.

CONFICTS OF INTEREST

Funding bodies that support research, scientific journals that publish the results and subjects who participate in biomedical research expect that researchers will strive for objectivity in the conduct of all aspects of the research process. They expect this to apply to many researchers in this field who may face a range of potential conflicts of interest situations. (See this Collection for a general discussion of conflicts of interest in the context of research practice, page E25.) Committees should require researchers to declare all conflicts of interest and should take appropriate steps when such a situation is found to exist.

Points to consider

- Is it essential to involve mentally ill people in the research project being assessed?
- Have all ethical requirements for free and informed consent or refusal on the part of potential research participants been met?
- Has the researcher selected research assistants who possess adequate skills and sensitivity for this role? If not, is there a plan to incorporate appropriate training into the research program?
- Has the ethics committee ensured that there is a satisfactory process requiring researchers to report adverse events suffered by research participants as quickly as possible? Does the research design provide for the implementation of remedial strategies in the event of adverse reactions?
- Does the research design allow for the immediate withdrawal from the project of any participant who suffers a significant and (or) severe emotional reaction, such as suicidal thoughts? Does the design also contain strategies for providing people in this situation with adequate care, support and treatment? Does the design ensure that people with a known history of these problems will not be recruited for the study and thereby knowingly exposed to increased suffering? Does the design contain a clear account of what would constitute ‘undue comfort or distress’?
- Does the researcher face any potential conflicts of interest situation(s) in relation to the research proposal under review?

Suggested reading

QUALITATIVE RESEARCH

While there is a range of views on qualitative methodologies and the application of specific methods. The following is a more detailed discussion of the issues raised elsewhere in this Collection about ethics and qualitative methodologies in the statement of research questions. It should also be noted that most social science disciplines, through their professional associations and bodies, have published relevant ethical guidelines. HRECs should refer to these where appropriate.

Qualitative methods are used in many different disciplines. While there is a clear distinction between qualitative and quantitative approaches, many research protocols combine features of both and it is important to recognise that the two approaches share much in common. However, while quantitative approaches are best suited to answering certain kinds of questions, qualitative approaches are best suited to answering others. As noted in the NHMRC document referred to above, qualitative methods are especially appropriate for investigations in the following areas.

- the influence of economic, political, social and cultural processes on health, illness and disease;
- understanding the experiences of individuals and communities in relation to health, illness and disease;
- understanding interactions between individuals, and within social settings, in relation to health care and health care decision making;
- eliciting contextual data in explaining the results of quantitative studies;
- eliciting contextual data in order to improve the methodological validity of survey instruments; and
- elaborating on causal hypotheses emerging from clinical and epidemiological studies.

Types of methodological approaches, and specific methods, include in-depth, open-ended interviews with groups or individuals, where participants are encouraged to tell their own stories; direct observation of behaviours and interactions; written and documentary information; and participatory methods, including photo novellas, diaries, art and drawing, and other creative ways of relating experience and knowledge.

- Qualitative approaches are designed to best reflect an individual's experiences in the context of their everyday life. Therefore, most qualitative research is much less formally structured than quantitative approaches, though no less rigorous. What is important to note is that qualitative approaches have a different logic to quantitative approaches to research.
- Qualitative designs do not always begin with specific, testable hypotheses precisely because these methods are particularly suited to exploring health issues at the initial stages where problems are not well understood.
- All qualitative designs should have an initial set of research questions that can be better defined as the research progresses.
- Sampling procedures are designed to yield a rich set of data on smaller samples than in most quantitative studies. The logic of qualitative sampling rests not so much on generalisability, nor on representativeness, but on notions of 'saturation'; that is, the point at which no new insights are likely to be obtained. Therefore, sample size is not so much a criterion for judging the rigor of a sampling strategy, but, rather, for judging the extent to which issues of saturation have been explicitly thought through.
There are many different approaches to the analysis of qualitative data and these are often based on different epistemological (theory of knowledge) assumptions. A research proposal should be judged on the extent to which the techniques of analysis have been made explicit and the extent to which the data might be exposed to different, or alternative, interpretations.

**Ethical Issues in Qualitative Research**

All research proposals, both qualitative and quantitative, should make provision for obtaining informed consent from potential research participants as required by the NHMRC (NS 1.7–1.12). However, in some qualitative studies it may be more appropriate to gain consent verbally rather than in writing. This is relevant where the participant may feel particularly vulnerable, as in research related to sexual issues or illegal or stigmatised activities. Here, written consent is likely to result in significant harm to the participant in that they are potentially identifiable. In addition, in participant observation studies it is virtually impossible to obtain consent from all observed individuals. Examples of such studies are ethnographic studies of particular settings; observing ‘sun-smart’ behaviours at a school or on a beach; ‘social mapping’ of the use of urban spaces; observations of eating and smoking patterns amongst social groups; and participant observation of self-help groups or national conventions such as Alcoholics Anonymous or Narcotics Anonymous. Indeed, obtaining consent would interfere with the strength of the ‘naturalist’ approach of ethnography. Seeking consent from participants in these situations may lead to behavioural changes that would invalidate the research, while public observation that neither identifies a person nor intrudes into their daily activities may well be ethically justifiable. Nevertheless, it is essential that the research proposal provide a clear account of exactly how verbal consent will be obtained and recorded, as well as provide adequate ethical justification for such a decision. A research proposal should also provide adequate justification for a decision not to seek consent at all from project participants.

In considering a request to waive consent in relation to the above types of studies, HRECs should refer to the NHMRC requirements:

> It is ethically acceptable to conduct certain types of research without obtaining consent from participants in some circumstances, for example, the use of de-identified data in epidemiological research, observational research in public places, or the use of anonymous surveys (NS 1.11).

This is reinforced by the Council for International Organizations of Medical Sciences http://www.who.int/ina-ngo/ngo/ngo011.htm in *International Ethical Guidelines for Biomedical Research Involving Human Subjects*:

> When the research design involves no more than minimal risk…and it is not practicable to obtain informed consent from each subject…the ethical review committees may waive some or all of the elements of informed consent.123

In summary, an HREC should expect any research protocol to clearly state the logic for obtaining consent. If consent is to be verbal rather than written, or if there is a request to waive consent, this needs to be clearly argued for and justified in the research proposal.

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As noted above, small sample size does not constitute adequate justification for rejection of a qualitative research proposal. Principles for establishing sample sizes in qualitative research should be clearly stated in the research proposal, which should set out the logic and methods for sampling in language that is easily understood. It is also common for qualitative studies not to specify an exact sample size at the commencement of the research project. This is because the principle of ‘saturation’ guides sampling. Also, in general, sampling strategies are not random but purposive.

Many qualitative researchers argue that one of the strengths of this approach, compared to the more intrusive quantitative approaches employed in much health and biomedical research, is that the relationship between the researcher and the research participant is more equitable. While this may be true in many situations, status and power differentials can still exist.

For example, good qualitative research requires the establishment of rapport between the researcher and the participant, and this can mean that the participant takes the researcher into their confidence, thereby establishing a social relationship. This can be particularly problematic when the researcher leaves the ‘field’. This can also be problematic in small communities where the researcher is part of the community, or setting, being researched. Here, the researcher has access to private information about ‘actors’ in this social setting, and this can have a complex effect on the former’s social relations when the ‘research cap’ is off. In particular, problems can occur when ‘peers’ take the role of researchers, thereby obtaining access to information about their friends that they would not normally be aware of.

Therefore, power relationships between researcher and participant in qualitative research, although often more equitable than in quantitative studies, are not always free of complications that may result in increased vulnerability for participants. It is therefore important that the ways in which these power issues will be dealt with are fully described in the research proposal.

In some respects qualitative research, perhaps more than surveys, poses the risk of generating unanticipated consequences precisely because of the ‘reflexive’ process. Here, research participants explore their feelings and experiences, and this can raise painful issues and open old emotional wounds. Interviews can also trigger feelings for the researcher. It is not uncommon for interviews to become confessions for the participant. And while participants are often thankful for the opportunity to discuss these experiences, psychological harm such as embarrassment, worry and loss of self-esteem can occur.

Adequate support for both researchers and participants should be available as needed. This might include debriefing for the interviewer and counselling for the participant, particularly in studies investigating sensitive areas such as physical or psychological trauma or abuse, death, dying and grief. These support strategies should also be available to both parties at the point of disengagement and termination of the research relationship.

Maintaining confidentiality can, at times, be difficult when carrying out qualitative research precisely because of the nature of the way in which data are collected. Whereas a questionnaire filled out anonymously is an assurance of confidentiality, a face-to-face, in-depth interview is explicitly based on building a relationship between researcher and participant, if only for the duration of that interview. Even when identifying information is not collected, the interview is not anonymous. Researchers must also be aware that they cannot promise participants absolute confidentiality. For example, if legally required to testify in court researchers must do so and mandatory reporting of information that has
been revealed by a participant may be required. In addition, the law does not necessarily protect ‘field notes’ and researchers need to be particularly careful about what they record and how this information is stored. While these issues have been widely discussed in the relevant literature and at professional gatherings, confidentiality in qualitative research remains problematic.

Because qualitative studies typically consider smaller samples and focus on local communities or groups, publishing results can be especially problematic if the findings are negative, or the results might further stigmatise or marginalise participant groups. In these situations, consideration should be given to the way research results will be reported and to what extent the participant group should influence decisions about the dissemination of results.

**Points to consider**

- Are HREC members familiar with the general principles of qualitative research and how these may differ from the principles on which quantitative studies are based?
- Even though qualitative research proposals commonly do not include sets of specific hypotheses to be tested, they should include a set of clearly set out research questions or research objectives. Have these been included in the research proposal under review?
- In general, informed consent should be obtained in writing. However, there are legitimate instances when consent is not possible, or when it may need to be verbal rather than written. Research proposals should state clearly how consent will be obtained and, where a waiver is requested or verbal consent only is to be obtained, a clear rationale and reasons justifying such a course of action should be provided. Have these criteria regarding consent been met?
- HREC members should recognise that while, in general, qualitative research is non-threatening and non-intrusive, it can still result in harm for the research participant. Power relationships between researcher and research participant should be acknowledged, along with the possibility of unanticipated consequences. Does the research proposal provide a clear account of how these unanticipated consequences will be dealt with if they do eventuate? Does the research proposal provide a clear account of appropriate strategies for supporting both the participant and the researcher when the research relationship ends?
- Ethics committees should be aware that ethical guidelines for qualitative research have been developed and published by a number of social science professional bodies. Do HREC members refer to these when conducting assessments of multidisciplinary research proposals, for example, sociological, anthropological and public health proposals?
- Are HREC members aware of the areas of difficulty in relation to ethical assessment of qualitative research proposals?
- Given the diversity and complexity of the range of qualitative methods, it is unlikely that any one member of an HREC will have the expertise to assess the range of methodological approaches likely to arise. Are ethics committee members aware that it is appropriate to consult experts on qualitative aspects of research proposals as needed?

**Suggested reading**


RADIATION, RESEARCH INVOLVING

USE OF RADIOACTIVE MATERIALS

Radioactivity and radiation are natural phenomena to which all humans are continuously exposed. This includes traces of radioactive material in the earth's crust, radioactive gases in the air that we breathe, natural radioactive potassium in the body from food and drink and cosmic rays from space. This is often referred to as 'background radiation'.

Diagnostic medical procedures are the most likely source of additional radiation exposure. Radiation may be delivered by X-rays passing through the body during diagnostic radiological procedures. Alternatively, internal exposure may occur during 'nuclear medicine' procedures, which use injected or ingested radioactive materials, that is, radiopharmaceuticals, to measure or image metabolic processes.

At one extreme, very high levels of radiation dose have clearly defined adverse effects. At the other extreme, higher 'background' radiation levels in certain geographical sites, or relatively small increases above background levels of exposures to radiation, have no proven adverse effects and may possibly even be beneficial. This presents some difficulties for Human Research Ethics Committees (HRECs) in evaluating the relative risks and benefits of research protocols using radioactive materials or X-rays. Nevertheless, prudent practice dictates the use of conservative radiation risk estimates, which assume that the negative effects from radiation may increase in a 'straight line' with the increase in the level of radiation dose from the very lowest to highest levels, with no assumed threshold below which there is no adverse effect at all. This assumption is known as the 'linear no-threshold hypothesis'.

The international radiation protection community has, over many years, developed and applied the ALARA principle in developing guidelines that balance the benefits of radiation exposures against possible risks. This principle states that human exposures to radiation should be ‘As Low As Reasonably Achievable, with economic and social considerations taken into account’.124

Within the context of medical and research exposures, this is usually taken to mean that each individual should receive no more radiation than is necessary to obtain reliable information and that no more research participants should be irradiated than is necessary to answer a particular scientific question. It is also taken to mean that special steps should be taken to minimise radiation exposures to people with elevated risk of adverse effects from radiation based on pregnancy or youth.

MEASUREMENT AND REGULATION OF RADIATION EXPOSURE

For each research protocol that includes exposure of research participants to radiation, the dose of radiation exposure should be calculated by an appropriate institutional or external radiation physicist/radiation safety officer.

Radiation dose should be expressed in the following SI unit: 1 milliSievert (mSv) effective dose. This unit takes into account the type, intensity and duration of radiation, the amount and type of body tissues irradiated and the different radiation sensitivity of the irradiated tissues. The average natural background dose rate in Australia is 2 mSv/year. Medical exposures contribute about another 0.5–0.7 mSv/year. The current recommended

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The likelihood of adverse effects associated with diagnostic medical radiation exposures is generally considered to be low, but any possible effects may not present until many years after the radiation exposure. The two adverse effects most commonly associated with radiation exposure are an increase in the incidence rates of certain cancers and genetic damage.

The risk of cancer at low radiation doses (less than 50 mSv) is not proven, but by extrapolation to low doses of those risks obtained from analysis of research participants exposed to high doses, a maximum lifetime risk of cancer can be estimated at 1/18,000 per 1 mSv effective dose (compared with a 25 per cent lifetime natural risk of death from cancer). Evidence for cancer induction by moderate doses of radiation is strongest for children and progressively weaker with advancing age at the time of exposure.

The risk of adverse effects can be reduced by choosing research participants for irradiation who are over the age of 50 or beyond childbearing age, where this would not compromise the scientific value of the study. Because of the greater radiation sensitivity of children, participants under 18 years of age should usually be excluded from research with irradiation unless the condition or process being studied is peculiar to people under

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126 Ibid.
127 Ibid.
128 Ibid.
the age of 18. In this situation, particular care is needed to ensure that the lowest radiation exposure needed to obtain the necessary results is used.

The human embryo is especially susceptible to damage from exposure to radiation, particularly between seven and 17 weeks of pregnancy. Therefore, pregnant, or even possibly pregnant, women should be excluded from protocols involving radiation exposure.

Research involving radiation could also pose risks to laboratory personnel, nursing staff, and, occasionally, relatives of research participants. This should be avoided by ensuring that all irradiations are supervised by individuals with appropriate radiation training and State radiation worker licensing.

Researchers should ensure that potential radiation risks during research are minimised and that participants receive only the amount of radiation necessary to obtain the desired information. Research protocols should be reviewed by experts with appropriate qualifications and training and, as already noted, the number of participants included in the study should not be significantly greater than that required to answer the scientific question.

C O N S E N T

Researchers should ensure that potential research participants are clearly informed whenever participation in research studies involves exposure to radiation. Participants must be given sufficient information if they are to make a meaningful decision as to whether or not to participate. One problem with communicating associated risks of radiation to potential research participants is that the risks from small radiation doses are not totally proven or quantifiable, although estimated upper limits of risk are available by extrapolation from higher doses. A further problem is that mathematical expression of these risks may be difficult for most potential participants to comprehend.

Several ways of explaining the potential risks associated with exposure to radiation have been suggested, although none are totally satisfactory. One method involves comparing the proposed ‘research effective dose’ with the ‘natural background effective’ dose received each year, or with ‘occupational effective dose’ limits. Another method involves comparing the maximum estimated risk of death from the proposed radiation dose with that of more familiar activities such as air travel or cigarette smoking. The uncertainties surrounding these risk estimates should be made clear to potential participants.

It may be appropriate to express the assessment of risk in more than one way, in order to maximise the informed nature of consent. However, it is not recommended that research radiation exposure be compared to exposure from chest X-rays. While this comparison has the advantage of familiarity and acceptability, it suffers from the disadvantage that the actual exposure to radiation from a chest X-ray may vary tenfold. Researchers should ensure that potential research participants have access to expert advice to answer questions they may have about proposed radiation exposure.

Points to consider

• What effective dose of radiation will the participant receive during the proposed study, and what effective dose of radiation have they received in other research studies over the previous five years? Does this comply with NHMRC requirements? Have the requirements of all relevant State and Territory legislation and the NHMRC Recommendations for Limiting Exposure to Ionising Radiation (1995) been met?
• Have pregnant women and unnecessarily young participants been excluded?
• Is the participant a healthy volunteer, or is she or he a patient with a medical condition that may benefit from diagnostic or therapeutic consequences of the radiation exposure?
• Have statutory notification and approval requirements for ‘healthy volunteer’ radiation exposures been satisfied?
• Does the scientific merit of the study justify the possible risks of radiation exposure?
• Does the consent form explain the likely radiation risks in terms that are both accurate and likely to be understood by participants?

**Suggested reading**


RESEARCH - ANALYSIS OF DATA

ANALYSIS AND INTERPRETATION OF DATA

Although research involving human participants is justified on the basis of the value of potential benefits, those benefits may be foregone and risks to the community, or future people suffering from the relevant illness, increased if the analysis and interpretation of results is inadequate. It is often not recognised that significant ethical issues may arise in relation to the analysis and interpretation of data.\(^\text{129}\)

BIAS IN QUANTITATIVE EMPIRICAL RESEARCH

Much empirical research involves comparison of two or more groups and the determination of differences between these groups with regard to a single factor of interest. The results of a study undergo statistical analysis based on the assumption that the groups are representative of the defined population and that the measurements taken on the sample were true reflections on what the researcher was actually trying to measure. In reality, however, a number of biases can complicate the analysis and interpretation of data.

Bias may be defined as any factor that tends to produce results or conclusions that differ systematically from the truth.\(^\text{130}\) This includes errors in analytical methodology and errors of interpretation. Research is open to bias from many sources, including errors in statistical analysis.\(^\text{131}\) Most errors related to statistical analysis relate to failure to use appropriate statistical methods. For example:

- failure to distinguish between independent and dependent observations;
- failure to adjust for confounding variables; or
- failure to appreciate the assumptions of normality and equality of variance underlying parametric significance tests.\(^\text{132}\)

Therefore, HRECs should be satisfied that the researcher has the skills and resources necessary for appropriate data analysis.

Over-interpretation of data, or misinterpretation of statistical significance, is also a problem in research. This is particularly the case where a data set is ‘dredged’ (retrospective sub-group analysis) for any significant relationships without reference to the purpose for which the study was set up, or where researchers perform interim analyses of results before sufficient numbers of participants have been enrolled. In these situations, some relationships may appear statistically significant, whereas in fact they occur purely by chance.\(^\text{133}\)


BIAS IN QUALITATIVE RESEARCH

Qualitative research methods and analysis have also been criticised on the basis of their perceived ‘intrinsic’ biases. Critics of qualitative research have claimed that it is too subjective, too value-laden, not replicable or generalisable, frequently invalid, and that it produces trivial conclusions. Many of these criticisms, however, can be answered by the fact that they arise from a positivist tradition and so reflect fundamental differences in theoretical approaches to research.134

As with quantitative research, much of the potential for bias can be minimised through rigorous study design and the employment of various techniques. These include recognition by researchers that observers are also research instruments; ‘disciplined subjectivity’;135 explicit incorporation of the subjective aspects of interaction between researcher and participant into the study design; and ‘triangulation’, whereby information obtained is considered tentative until corroboration by information collected by other means.136 HRECs, therefore, should be satisfied that the research project is designed to allow for appropriate analysis of the information obtained.

RESEARCH - COMMUNICATION OF RESULTS

Researchers have an obligation to communicate both the results of their research and the meaning of those results, in a clear, concise and sensitive manner. This may be particularly important where results are open to various interpretations, where research involves a complex appreciation of risk or uncertainty, and where the research yields an average or group result, for example, drug trials or epidemiological studies, that may have limited significance for the individual participant.\(^{137}\)

One option for researchers would be to use electronic means of communication to provide participants, consumer groups and other scientists with relatively cheap and rapid access to research results published in professional journals.\(^{138}\)

It is important to note that research does not occur in a social or political vacuum. Political pressure, the researchers’ desire to publish study findings and the interest of participants and the wider community in research results may all lead to premature release of such results. This may be particularly damaging if research findings gain political potency and are acted upon before peer review has taken place, ultimately harming the research process and, possibly, individuals.\(^{139}\) Generally, researchers should make their results, their interpretation of these results and the assumptions or value judgments underlying this interpretation, available to relevant individuals, groups and the wider community, as appropriate.\(^{140}\)

Individual participants should be notified of research results as soon as these have been identified, or after publication. Following publication is probably preferable, as the results will then have been subjected to some degree of peer review. Participants can then be advised of any errors in, or criticisms of, the presentation and interpretation of research results. However, one objection to this approach is that results are made available to the wider community before project participants are aware of them, including any specific significance they might have for particular individuals. In some situations, presenting participants with a summary\(^{141}\) of the work may be appropriate, particularly where, for whatever reason, the work is not published in a peer reviewed journal.

PARTICIPANTS’ RIGHTS

Do participants have the right to review and comment on research results before they are published? This may be the case in some types of social science research where the study has involved organisations and/or individuals within those organisations.\(^{142}\) It must be recognised, however, that there may be potential for conflict over the way research results are presented and interpreted.

One objection to a requirement to notify participants of research results is that they may be misunderstood and participants may fail to appreciate either the significance of the

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\(^{140}\) A. Herxheimer, ‘Clinical trials—two neglected ethics issues’, *Journal of Medical Ethics*, vol. 19, 1993, pp.211–218.


results for themselves, or the limitations of any generalisations they might make from the research findings. It may be helpful to participants to publish a version of the research report in non-technical language with a clear explanation of the significance of the conclusions. Also, when individual results are communicated to participants, the information should be presented and explained clearly and the opportunity given for questions to be asked, and answered, appropriately.

In biomedical research, it may be most appropriate that results are returned to the participant via their general practitioner, thereby providing the participant with a familiar setting in which to discuss these results. Any necessary follow-up could also be organised by the general practitioner. Where such an approach is adopted, it will be vitally important that the researchers provide appropriate information to the general practitioner involved. In addition, the cost of such a consultation should generally be included in the research funding and not borne by the participant.

In other areas of research, including social science or epidemiological studies, research results may be communicated through organisations that have the confidence of the participants, such as support groups or community services.143

COMMERCIAL-IN-CONFIDENCE

In some types of research, researchers and HRECs may need to consider the extent to which limitations on disclosure can be justified for reasons of the commercial-in-confidence nature of the information.

143 Higginson & Chu, op.cit.
RESEARCH DESIGN AND PURPOSE

As the United States National Institutes of Health http://www.unmc.edu/irb/guidelines/ Institutional Review Board Guidebook makes clear:

…if a research study is so methodologically flawed that little or no reliable information will result, it is unethical to put subjects at risk, or even to inconvenience them through participation in such a study. One question that every IRB [Institutional Review Board] member asks is 'To what degree is it our responsibility to review the underlying science of the proposed research?' Clearly if it is not good science, it is not ethical.144

CHOICE OF RESEARCH METHOD: QUALITATIVE AND QUANTITATIVE TECHNIQUES

There are many types of research design and no single ideal research methodology. While the features of one methodology may compensate for the limitations of another, each methodology has associated ethical concerns.145 In addition, the strategies used to achieve methodological rigour will vary depending upon the type of research and the potential risks to participants.

One way of classifying research design is to divide it into quantitative and qualitative methodologies. Quantitative methodologies place great emphasis upon the generalisability of the study from the experimental group to the wider community. This requires the extensive use of measurement and statistical techniques. The most prominent quantitative methodology is the randomised control trial (RCT). In qualitative methodologies, the goal is to gain insight into specific aspects of the study group, or the results of an intervention.

Qualitative research methodology is used to study the economic, socio-political or cultural factors that influence the topic being investigated; the manner in which communities and individuals interpret the topic; interactions between participants in social institutions; and the context of research and specific policies. In humanities research, qualitative methods are used to develop greater understanding of language, literature, historical events, and so on. The goals of social science research are broader and more diffuse than biomedical research: to understand social relations, to evaluate public policy, and to explain the nature of cultural change.

The different epistemological perspectives (or theories of knowledge) within social science have produced different approaches to social science research in terms of both data collection and methods of analysis. While these are sometimes characterised as the differences between quantitative and qualitative research, the lines are not clear-cut. Many important questions require research designs that use a number of methods, ranging from secondary analysis of data that have already been collected for another purpose, such as examination of public documents and media, to lengthy in-depth interviews with a few individuals. This information can then be analysed, or interpreted, in many ways. In addition, some projects may challenge established epistemological frameworks because the former incorporates the perspectives and experiences of people who were previously ignored or devalued in Western social science.

Social science encompasses a humanities tradition of research based on systematic reading and interpretation that sometimes seems to border on speculation, as well as a

scientific tradition of research with a strong emphasis on observation and collection of information, but which also includes a level of interpretation. These two approaches tend to emphasise different techniques and report findings in different ways. Allan Kellehear summarises the differences between the two by outlining the rationales for hypothetico-deductive research design, in the scientific tradition, and ethnographic-inductive research design, in the humanities tradition.

**Hypothetico-deductive rationale for research**
- read first (literature review);
- develop an idea (theoretical framework);
- go out (methods);
- test it (results);
- see if you were right in the first place (discussion).

This approach is more related to the scientific tradition of research. Projects frequently involve controlled experimentation, carefully constructed questionnaires, detailed content analysis of documents, or recorded conversations. If enough data is appropriately collected, they can be analysed using statistical methods. When done well, various research studies build on one another, that is, it is possible to replicate or falsify them, and the results are generalisable, at least within the population from which the research sample was drawn. Deductive research projects are particularly useful for what is sometimes called ‘theory testing’ within a discipline.

**The ethnographic-inductive rationale for research**
- read first (literature review);
- gain experience, participate, listen, record (ethnographic description);
- describe the theoretical implications of what you saw/heard (discussion);
- explain where you were and how you went about your task of understanding (background to the study).

The humanities tradition of research shapes the ethnographic-inductive approach. Projects frequently involve participant observation, semi-structured interviews, focus groups or thematic analysis of documents or conversations. Data collected in this way are usually not in a form that is statistically analysable. Sampling strategies are frequently purposive rather than random, therefore findings are less generalisable. The results of various similar studies can be compared but seldom build on the findings of past studies. Inductive research projects are particularly useful for ‘theory building’ since the findings often point to ‘puzzles’ or unexplained phenomena.

Qualitative methods may include in-depth, open-ended interviews with groups or individuals; direct observation of peoples’ activities, behaviours and interactions; or gathering written data from records, publications or questionnaires. Qualitative research places less emphasis upon the generalisability of results, and often does not involve the use of statistics. Many authorities now recommend that much research should involve both qualitative and quantitative methodologies in order to provide a well-rounded understanding of the research topic from a number of perspectives.

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147 Ibid., p.20.
148 Ibid., p.23.
Biomedical research has traditionally emphasised the value of quantitative techniques. This may result in a degree of bias when biomedical researchers on HRECs are assessing research proposals that employ qualitative methodologies. It is important that qualitative studies be fairly considered by ethics committees as these projects have different, but equally important, approaches to research questions, methodology, outcome measurement and interpretation of results.

One difficulty that HRECs may face in determining when and why a researcher using qualitative techniques should seek ethics committee approval is that research questions frequently grow out of social and professional interactions. In addition, the information that forms the research findings is not neatly separable from other information gathered by the researcher.

...I mean, consider somebody who devotes their life to studying the Liberal Party, who has growing connections, over time, with people, some of which are fairly personal, some of which are rather impersonal. At what point can we say she is engaged in a project, at what point does she apply to the HREC? This is really very tricky indeed. And while it would be nice to have a clear definition, it is exceedingly difficult.\footnote{R. Albury, S. Dodds, C. Thomson with L. Secomb, Ethical Research: Issues for Institutional Ethics Committees, Wollongong: University of Wollongong, 1996, p.33.}

That is, when does preliminary ‘exploration’ become formal research? One practical answer that should guide HRECs is that such activities become formal research projects when they reach the point of involving the administration of questionnaires. While some researchers might believe that a ‘simple’ questionnaire is ‘harmless’ and should not require HREC approval, questionnaires that explore sensitive issues can trigger significant stress reactions in participants. It is therefore the role of the HREC to assess such research proposals.

Qualitative research projects, like quantitative projects, must demonstrate a reliable and rigorous approach to study design, data collection and data interpretation. Guidelines for qualitative research may be useful for HREC members who are unfamiliar with qualitative techniques.\footnote{Ethical Aspects of Qualitative Methods in Health Research, op.cit.}

**OBSERVATIONAL AND EXPERIMENTAL STUDIES**

A different way of classifying research is to divide it into ‘observational’ and ‘experimental’ studies. In observational studies, participants are merely observed and compared. In experimental studies, the researcher carries out an intervention involving participants and then observes the effects of that intervention. Either category may include both quantitative and qualitative methodologies.

**Observational studies**

Observational studies are typified by retrospective epidemiological research. (See Commentary on NS 14.1–14.13 for a detailed account of epidemiological research.) While this kind of research rarely poses a direct risk of harm to participants, there are still important ethical issues to be considered. The major issues associated with descriptive studies are privacy, confidentiality and the effects of research findings on individuals and communities. The use of health and other records to establish trends and patterns may risk infringement of privacy and violation of confidentiality. The publication of observational research findings may be prejudicial to some collectivities within the community and so may affect the wellbeing of collectivity members (NS 8.1–8.2).
Issues of privacy are particularly important in epidemiological research where researchers may examine details of hospital records, census information or records owned by other health agencies. This is an undeniable threat to peoples’ privacy, although if records are de-identified it may not constitute a threat to confidentiality. It has been argued that such information should not be available to researchers without the participants’ express permission, but this has been vigorously opposed by researchers who believe that this restriction would severely limit epidemiological research. Federal and State law, as well as health department policies, concerning the privacy of health and other records place limits on who may access such records for research purposes. Conditions are also placed on the use of that information.152 (See Research Law Collection for a discussion of the legal aspects of privacy of information page L43 in relation to research practice.) When HRECs are evaluating this type of research proposal, they should examine whether the potential benefits of the research justify the breaches of privacy. Community consultation may be an important part of this process.

Experimental studies

Experimental studies are sometimes divided into ‘therapeutic’ and ‘non-therapeutic’ research, or into ‘clinical’ research (research combined with clinical care) and ‘non-clinical’ research.153 In therapeutic research, the intervention is intended to be of direct benefit to the participant, as well as to provide further information about the generalisable efficacy of the procedure or treatment. For example, a person with a rare disease may be given a new drug in the hope that it will offer them direct benefits.

In non-therapeutic research, the intervention associated with the research is not intended to be of direct benefit to the participant but has the more limited goal of increasing human knowledge that may benefit certain members of the community at some future time. However, the distinction between therapeutic and non-therapeutic research is controversial, largely because of the difficulty of assessing the primary aims of research and the range of potential benefits to participants.154

HOW CAN HRECS ASSESS RESEARCH DESIGN?

HRECs may not be well qualified to assess all questions of methodology and research design. There are three ways in which this issue can be addressed.

- A committee may simply accept the scientific merit of the study methodology and design where rigorous methodological review has already been carried out by government or other independent funding agencies.155
- A committee may have the relevant expertise available within the committee membership.
- A committee might seek external expert opinion, either on an ad hoc basis, or by setting up a methodology/research design subcommittee that assesses all research proposals before these are reviewed by the main committee.

In assessing research design, HRECs should be aware of the potential for statistical and interpretative bias. (See this Collection for a detailed discussion of bias in the analysis and

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152 Ibid., ch. 18.
interpretation of research results page E139. For a detailed account of the role and function of HRECs, see NS Commentary 2.1–2.48 and this Collection page E67.

**Points to consider**

- Will the research design produce data that have a reasonable chance of answering the research question?
- In the case of experimental studies, is there genuine uncertainty about alternative treatments?
- Are the researchers competent to conduct the study, given the research question, methodology and the participant population?
- Is the study statistically valid? Do the researchers have the necessary statistical expertise, or, if not, have they obtained the assistance of a statistician?
- If there is a control group, are these people receiving the best available proven therapy? If the study includes a placebo control, is this justifiable? Is there an available therapy of proven benefit?
- Does the study involve review of personal records? If so, are researchers required to obtain consent prior to accessing these records? Are there adequate strategies in place to protect participants from risks of invasion of privacy and breaches of confidentiality?
- If the study is a clinical trial, how and when will the results be monitored? By whom? How will decisions be made about whether or not stopping or altering a trial is necessary? On what basis will these decisions be made?
- Does the proposed methodology expose participants to unacceptable risks of harm?
RESEARCH QUESTION, STATEMENT OF

Research involving human participants generally involves some degree of invasion of privacy, inconvenience, or risk of harm for those participants. Even where they have made informed decisions to take part in a project, the study may still be unethical if it lacks a well-considered research question and imposes risks of harm, inconvenience and intrusion upon participants without adequate justification. It is generally accepted that, whatever the potential benefits of research, there is no justification for treating people solely as a means to an end. And this is consistent with the National Statement, which, as discussed in Section 1, requires that the protection of the welfare and rights of research participants take precedence over possible future benefits to the community (NS Preamble, p.1). As Peter Singer notes:

We value knowledge, but we do not value it so highly that we are prepared to support the acquisition of knowledge at the cost of violating other ethical principles that we consider important.\(^\text{156}\)

This concern is even more pronounced if a particular research proposal presents a poorly constructed research problem. In addition, according to the National Statement, ‘scientific inadequacies also have ethical implications. Projects without scientific merit are wasteful of resources and needlessly subject participants to risk.’ (NS 1.13) It is therefore essential that HRECs determine that the question/s addressed by a particular project actually merit investigation.

WHAT ARE THE CRITERIA FOR AN ACCEPTABLE RESEARCH QUESTION?

Every research proposal must demonstrate that the research is justifiable in terms of its potential contribution to knowledge and is based on a thorough study of current literature as well as prior observation, approved previous studies, and where relevant, laboratory and animal studies. (NS 1.13)

Researchers’ accounts of the significance of research problems should be expressed in language that is easily understood by intelligent, non-specialist members of HRECs. As stated in a 1990 report of The Royal College of Physicians of London http://www.rcplondon.ac.uk/

...(a)lthough some research is complex and specialised, we believe that it should always be possible for an investigator to display the relevance of his research in terms which can be understood by a Research Ethics Committee, particularly if the Committee makes use of its power to co-opt additional members.\(^\text{157}\)

HRECs should consider whether a research proposal contains a clear and useful hypothesis or specific objectives, and whether there is sufficient uncertainty about relevant outcomes or efficacy to justify further research.\(^\text{158}\) While there are some situations in which it is justifiable for multiple studies to address the same issue, such as the accrual of sufficient data to reach a meaningful conclusion or the assessment of the reproducibility of results in other settings, research is frequently repeated unnecessarily.\(^\text{159}\) Therefore, research proposals that re-examine previously answered

\(^{156}\) P.Singer, ‘Ethics and the limits of scientific freedom’, The Monist, vol. 7
\(^{158}\) Ibid.
questions, that fail to take proper account of the results of existing research, and that lack scientific validity or are poorly constructed, are generally unethical, particularly if they are intrusive or involve risk of harm to participants.

In addition, where research is commercially funded, for example, by a pharmaceutical company, the question may arise as to whether the aim of the research is to provide new and valuable information, or whether the project is primarily a marketing exercise. The latter may include ‘familiarising’ physicians with the use of a new drug under the guise of scientific research. Therefore, it is essential that research applications are supported by a systematic and thorough literature review, or some other evidence of the importance of the specific research project.

THE CONTEXT OF THE RESEARCH QUESTION

The relevance of the research enterprise to participants' needs and community concerns has been the subject of recent debate. As noted in the Introduction to the Manual, the assumption that researchers are the best judges of community concerns and needs is no longer accepted. According to Dodds, et al.:

In the formulation of the problem researchers are likely to benefit from discussion with selected members of the population from which research participants will be drawn. Potential participants and community advocates have insider knowledge of their communities and can point to sources of information that an outsider might discount or overlook. Indeed such formal conversations are likely to shape the topic in a way that increases its usefulness as a contribution to the local community and to the wider society. At the very least, for evaluation research, such conversations would offer the researcher a second perspective on the goals and outcomes that are being evaluated. These discussions are likely to increase the authenticity of the research project. Many argue that researchers and sponsors of research have an obligation to ensure that research carried out in the community reflects the experiences and concerns of the community. Researchers and sponsors should also consider communicating with representatives of the relevant communities before finalisation of the research question.

An example of guidelines requiring such community consultation can be found in the NHMRC Guidelines on Ethical Matters in Aboriginal and Torres Strait Islander Health Research (Interim). These Guidelines require HRECs to ensure researcher consultation with the Indigenous community that will, if in agreement, be taking part in the proposed research project. Such consultation should include community controlled services and agencies, as well as State, Territory or Federal agencies.

It is now generally accepted that the Australian public, as ‘owners’ of publicly funded research, should have some influence in setting research agendas. It is also generally accepted that the perspectives of target participant populations, the general public and consumer advocates may contribute important insights into issues and possible outcomes, thereby improving the quality of research. Increasingly, these wider perspectives are being included in setting research agendas, in methodological debate, in specific

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161 Dodds, et al., op.cit., p.6.

162 NHMRC, Guidelines on Ethical Matters in Aboriginal and Torres Strait Islander Health Research (Interim), Canberra, Commonwealth of Australia, 1991.

project formulation\textsuperscript{164} and in interpreting research findings.\textsuperscript{165} While the value and practicalities of incorporating these perspectives may vary according to the research topic being investigated, it is important that researchers and HRECs address the issues surrounding community participation, including appropriate community representation and recognition of such consultation.

\textbf{HOW ARE RESEARCH QUESTIONS ASSESSED?}

Although research proposals supported by major competitive funding bodies, for example, the NHMRC and the Australian Research Council, will be subject to an assessment of the significance of the research question by that funding body, HRECs also need to review the significance of the research question. Where research is not supported by external funding, HREC assessment may be the only review of the research proposal’s scientific merit and design prior to publication. In its initial assessment of the merit of the research question, an ethics committee is largely dependent upon the relevant information offered by the researcher. Given the nature of HRECs and the wide range of research topics reviewed, the process of review depends very much on the integrity of researchers. Therefore, an environment of trust and mutual respect between ethics committees and researchers is essential (NS 1.1, 1.13). For example, ethics committees may be dependent upon the researcher’s review of the literature in order to determine whether the same, or similar, research has previously been carried out.

However, HRECs can ensure competent assessment of the merit of research questions by:

- using expert skills of existing committee members;
- co-opting experts to assist the committee as needed;
- requiring that research proposals be supported by a rigorous and systematic review of the literature and, where relevant, by prior laboratory and animal experiments;
- inviting researchers to attend committee meetings in order to describe the proposed research project and to answer relevant questions; and
- instituting independent ‘scientific review committees’.

RESPECT FOR PERSONS

[NS 1.2, 1.4 and Commentary Preamble]

Respect for persons has a number of aspects. The central concern is respect for individual as well as individual decision-making. These ideas are related to a range of ethical concerns, including recognition of, and respect for, the inherent value of persons, recognition of the value of self-determination to the wellbeing, happiness and moral development of individuals, and respect, within a liberal democracy, for individual freedom, including freedom of choice.

If a pluralist account of human preferences and human good is adopted, respect for personal choice and promotion of the conditions required for exercise of that choice become central issues in the ethics of research practice. Therefore, considerable emphasis is placed on the general requirement of consent to participation in research. However, there is also a cultural aspect to respect for persons. Individuals are also members of groups of one sort or another and realise their values, in part, through their interactions with other members of those groups. Respect for persons, then, includes respect for the groups with which members identify themselves.\textsuperscript{166} The National Statement endorses this view.

However, while respect for persons emphasises self-determination, autonomy and individual choice, it should not be taken to exclude respect for those whose capacities for self-determination and the exercise of personal choice are compromised or absent. A person in this situation should still be treated with the respect due to persons as described above. This may involve protecting or promoting their remaining capacity for autonomy, respecting prior expressions of self-determination, and protecting the person against exploitation, discomfort and harm.

Furthermore, NS 1.4 ranks the ethical importance of respect for the personal dignity and wellbeing of participants above the value of research in terms of the benefits to be gained from advances in knowledge. This means that a research proposal should be designed in a way that demonstrates sufficient regard for the interests, rights, welfare, dignity and choices of research participants.

RISK

The Royal College of Physicians of London attempts to define risk objectively. It defines ‘less than minimal risk’ as ‘…the level of risk accepted in everyday life. Examples might be the measurement of height or weight, the collection of a urine sample or the giving of a venous sample by an adult.’ The College uses the term ‘minimal risk’ to cover situations: ‘…where the level of psychological or physical distress is negligible though there may be a small chance of a reaction which is itself trivial, for example, a mild headache or feeling of lethargy’; or where: ‘…there is a very remote chance of serious injury or death, comparable to the risk of flying as a passenger on a scheduled aircraft.’

However, it may be difficult to define risks in purely objective terms. Purely objective accounts of harm do not allow for the subjective nature of appraisals of risks and benefits. Different people experience harms and interpret risks in very different ways. Incidents that may be shrugged off by one person may be considered devastating by another.

The term ‘benefit’, as opposed to ‘risk’, refers to any favourable outcome from research and may be expressed as an advantage to the individual participant or as a potential benefit to certain members of society at some future time. The major potential benefits of research lie in increased knowledge, improved service provision, greater understanding and improved policies. Assessment of the overall potential benefit of research frequently incorporates the combined probabilities and magnitudes of several potential benefits.

The ethical difficulty with analysing risks and benefits in relation to research practice is that the risks are not often borne by the people for whom the possible benefits will accrue. Given this, potential benefits are unlikely to outweigh the risks for individual research participants. The overall danger is, therefore, that concern for the wellbeing of certain groups of people in the future may lead to negation of the rights of current research participants. Again, protection of research participants from harm is the major justification for HREC assessment of the risks and benefits of research proposals.

Nevertheless, it has also been argued that this emphasis on protection against harm is overly protective as it negates a person’s right to participate in risky research if they so desire. For example, according to Daugherty, et al.,

It is interesting to note that this paternalistic system developed and became established in clinical trials as the rest of society and other health care institutions increasingly recognised the importance of autonomy and the right of patients to decide what is in their own best interests. …With the development of the acquired immunodeficiency syndrome (AIDS) epidemic, activists have demanded modifications in the research and regulatory process, thereby challenging the Nuremberg paradigm. …Activists claimed that persons who have life-threatening illnesses do not need protection from the potential harms of research trials. They argued that the role of the federal government and of such regulatory bodies as the FDA should be to maximise patient opportunity and choice to participate in clinical research rather than to maximise patient safety.

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HRECs could attempt to balance these conflicting views by complementing the emphasis on risk minimisation with a similar emphasis on consent in situations where potential participants may be willing to take greater risks and where, in the presence of informed consent, this is reasonable. Ethics committees should enable adults capable of independent decision-making to assess risks on their own terms. However, where participants (for example, children) are unable to make an independent decision, HRECs should be particularly diligent in protecting participants from harm.

For example, an individual may wish to risk his or her welfare by agreeing to participate in an interesting and risky experiment with only remote chances of increasing knowledge (that is, for the future benefit of others), and which would not in the eye of a disinterested observer be a justified risk. Preventing such an individual from making this choice (provided that the individual has been provided with sufficient information as to the consequences of their actions) is to not respect their autonomy and therefore compromise the ethical principle of respect for persons.
SCHOOLS, RESEARCH IN

Some research proposals may involve schoolchildren as participants. This raises a number of ethical issues. First, lines of communication are often more complex here than is usual with research involving other groups. These projects may involve the child in the classroom, the child’s parents, the class teacher, the school principal, the Department of Education and the researcher. An HREC should be particularly careful to ensure that the requirements of the National Statement (paragraphs 1.7–1.12, 4.2) with regard to informed consent are not compromised by circumstances such as these.

School personnel cannot give consent on behalf of students, teachers or parents, nor can they disclose information for research purposes about these groups, without the prior knowledge and consent of the person concerned. In addition, where a research proposal includes sensitive questions, an HREC will need to decide whether these are acceptable given the level of invasion of privacy involved. If sensitive questions are approved, the committee will need to be assured that the qualifications and experience of the researchers are such that the project would be carried out with minimal risk to participants. The committee should also be satisfied that appropriate risk management strategies are included in the protocol of any project where there is a risk of participants becoming distressed as a result of such sensitive questions.

In addition, if the research proposal involves a comparison of disabled and non-disabled children, or more able children with less able children, an HREC should consider any potential for embarrassment, discrimination, invasion of privacy or any other harm to any of these children. Similar considerations apply when researchers propose to take advantage of other ‘captured populations’, such as children attending a kindergarten, preschool, sporting or recreational facility.

Suggested reading


STUDENTS, RESEARCH INVOLVING

The use of course credits as compensation for students taking part in research projects is controversial. If the basis for such participation is educational benefit, it is desirable that other options be made available, such as short papers, book reports and other research-based activities. If participation does involve educational activity, students might be able to forgo certain study components to compensate them for time spent participating in research.\textsuperscript{171}

Sometimes, it is argued that some experience of being a research participant may be relevant education for students likely to be responsible, as researchers, for undertaking research on others at a later stage of their careers. This is not a universally agreed position and involves relying upon a different kind of benefit to participants than that usually involved in weighing risks and benefits of research.

TERMINALLY ILL PEOPLE, RESEARCH INVOLVING

[NR 6.6]

Palliative care is concerned with the care of individuals with advanced and terminal illness. It focuses on the maintenance of function, comfort and the treatment of symptoms rather than disease. Such care also extends to family members and continues into the bereavement period. Nursing care occupies a central role in supporting people in this last stage of illness and a great deal of research in this area has been initiated by this particular professional group.

Some members of HRECs have felt that it is unacceptable to involve terminally ill people in research. Nevertheless, experience in academic units providing palliative care suggests that consent for participation in studies is usually given gladly by these people, hoping that even in the last phase of life they may make some contribution. In other situations, people who are terminally ill may be highly vulnerable to unrealistic expectations of direct and immediate benefits from taking part in a particular research project. It is essential that researchers do not encourage potential participants to develop such expectations, nor should they use such expectations to justify a higher risk than that involved in the individual's current treatment (NR 6.6).

Another important issue is that the intimate relationship of caring professionals with dependent, aged and vulnerable patients may make it difficult for individuals to make an independent decision about whether to participate in a study. This close relationship may lead staff to protect their patients too closely against what they consider an unnecessary intrusion.

In addition, competence to make considered decisions might be affected by both disease and medications. Or families may withhold knowledge of the presence of a disease such as cancer, as well as discussion about prognosis, from the person concerned. This would mean that providing information adequate for consent to participate in a research project might be compromised.

Many research participants are unable to complete a necessary study period with regard to biomedical research because of deterioration or change in circumstances. For example, a study population sufficiently large to provide a valid comparison of interventions has often proven impossible to achieve within a given time. Randomised control trials are difficult to complete. Studies are often qualitative and descriptive, as in 'quality of life' projects, and may focus on the needs of carers as much as on the person with terminal illness. Published studies have rarely satisfied the strict criteria of evidence-based medicine. This may or may not be viewed as a problem, depending on the professional allegiance of the person making such an assessment.

UNCONSCIOUS PEOPLE, RESEARCH INVOLVING

[NS 6.8–6.9]

As an unconscious person has no apparent capacity for cognition or communication, they are clearly unable to take part in the consent process in any way at all. Therefore, consent or refusal for participation in research will, again, need to be given by an authorised person or the relevant statutory authority.
WOMEN, CLINICAL TRIALS INVOLVING EXCLUSION OF WOMEN OF CHILD-BEARING AGE FROM CLINICAL TRIALS

Women of child-bearing age have often been under-represented in clinical trials because of concerns about risks to the fetus in utero. As a result, adequate information about drug metabolism in female subjects may not be available, with the possible consequence that recommendations about factors such as dosage may be imperfect. Potential value from use of a drug in pregnant patients who might be expected to benefit from it may not be realisable because of lack of trial information. In deciding upon the issue of incorporation of women of child-bearing age in a clinical trial, an HREC should consider any information available on teratogenic or fetotoxic effects of the drug in animal studies. HRECs should also examine the likely benefits accruing from use of the drug in patients in this group and not necessarily decide on their exclusion.

HIV/AIDS clinical trials and women

The bases for inclusion of women in clinical trials have been considered controversial since they were first conceptualised. This has been particularly noted in the HIV/AIDS sector. The inclusion of women in clinical trials for HIV/AIDS is a responsibility of researchers that requires careful consideration. This is especially so given that the results of clinical trials gathering data on the effects of a drug on men are then used as the basis for the licensing of that drug for both men and women. The generalisability of these results should have been called into question. The exclusion of women from clinical trials, either by design or simply by not facilitating access, has resulted in the following concerns.

Difficulties in the recruitment and retention of women

Problems in recruiting and retaining women as research participants are often caused by the incorrect assumption that HIV-positive women have a similar community, and similar demographics, to the majority of HIV-positive men. HIV-positive women are fewer in number and are usually isolated geographically from each other. Confidentiality is a major issue in the lives of all HIV-positive people, but this is especially so for women, who must often take into account a lack of knowledge in their community, the wellbeing of their children, and the stigmatisation of women with HIV. Women are sensitive to being seen entering a clinical site known to specialise in STDs or HIV.

These problems can be resolved by such simple measures as conducting the trial from more sites over a wider geographical area and (or) locating, and recommending, ‘understanding’ general practitioners based in the relevant community. In addition, providing gender-specific psychosocial support to women participants during, and after, clinical trials may make participation in these projects more acceptable to women.

Collection of gender-specific data

It is the responsibility of researchers to systematically collect gender-specific data as part of every clinical trial in order to identify any clinically important differences between men and women that may, or may not, exist. Regardless of whether or not they are proven to exist, it is still a biologically plausible possibility that they do and that the effects of both the body on the drug, and the drug on the body, may be significantly different between men and women.
**Women’s reproductive capacity**

Women involved in clinical trials should be viewed as women first, rather than as potential mothers, just as men are seen as men and not just potential fathers. If a woman states that she is not at high risk of becoming pregnant during a trial, regardless of her sexuality, she should be given access to that trial without having to use a specific drug method of birth control, especially in light of limited data on drug interactions, or to be abstinent. Conversely, if a woman is entered into a trial to study the effects of a drug on her fetus and/or vertical transmission, it is equally pertinent that the effects of the trial drug on reproductive capacity should be looked at. Women should not normally be denied access to trials on the basis of reproductive potential when no knowledge yet exists about the trial study factor’s effect on reproductive potential. When the trial may be of benefit to these women, either presently or because of long-term knowledge gained, there are stronger grounds for their inclusion.

**See also:**

WOMEN, RESEARCH INVOLVING

WOMEN, INCLUSION IN RESEARCH

The standard ethical concern here is the problem of women being excluded from research populations. As a result, there is a lack of information about the extent to which the results of such studies apply to these excluded women. What is less often considered is what happens to women when they are included in research studies. The most pressing problems in women's health often involve women from marginal or vulnerable social groups. When these women are included in research, a different set of ethical considerations need to be considered so that the research process itself does not increase their disadvantages. These two separate ethical considerations will be discussed below.

WOMEN, EXCLUSION FROM RESEARCH

Because of the potentially harmful effect of research interventions on the fetus, pregnant women, or women of childbearing potential, have been excluded from, or have been under-represented, in studies that include women who are not in this category. Women who are breast-feeding have also been excluded from research projects in situations where an intervention poses a potential risk to the infant. Additional concerns focus on protecting women's reproductive capacity in research involving hormonal changes. There may also be concerns about fear of liability by research sponsors should harm accrue to the fetus or to the woman. When the aim of these exclusions is to protect the fetus, ethical principles about the safety of fetuses are relevant.174 The problem addressed here concerns the categories of women who are excluded or under-represented.

The effect of excluding women from research populations is to cast doubt on the extent to which research results apply to these women. While it may be possible, in some situations, to extrapolate study results to women who are not part of the study population, there may be doubt about the extent to which this is scientifically justifiable. For example, studies may define the most effective dosages for a particular drug under investigation. However, it may not be clear what the correct dosages are for women as they are not represented in the study. Such exclusion is of particular importance if the disease or disorder disproportionately affects women, or when access to a new, experimental treatment for a life-threatening or serious disease is only available to people enrolled in a research study.

Women should not be excluded from study populations simply on the basis of gender or reproductive stage. Study designs should include appropriate representation of women in all study populations unless a clear rationale can be provided for exclusion or under-representation. Only where the potential risk to woman or fetus cannot be justified should women be excluded. An alternative course of action might be to study these women separately, in a way that minimises the risk. However, it is not always clear who is to make the judgment that the risk to woman or fetus is unacceptable. HRECs should consider the possible participation of the women concerned, or representative community groups, in this decision-making process.

WOMEN, INCLUSION OF VULNERABLE WOMEN

Australia is unusual in having a National Women’s Health Policy, devised after extensive consultation with women and with government, professional and community organisations.175 The issues raised here are consistent with this Policy, which emphasises

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the need for consultation with relevant community groups about research priorities and about the design and conduct of the research.

While women of childbearing potential are subject to specific risks, especially with respect to medical or pharmaceutical interventions, there are also ethical problems with regard to other groups of women. While women involved in a study may not be exposed to significant additional physical risk, the process of participating in research may have other adverse effects. This problem is particularly acute in situations where women are vulnerable; living under difficult circumstances; or when any additional risk, however small, may prove harmful. Young women may be vulnerable because they are homeless; during childbirth women may be vulnerable to the combined effect of physical and social change; and in midlife, or older age, women may be vulnerable because of a combination of physical, social and cultural factors.176

Unfortunately, but not surprisingly, research issues identified as particularly important for women’s health commonly involve vulnerable groups, including women exposed to violence and occupational health risks and women enduring the exacting demands of their role as carers. These problems are aggravated by the negative stereotyping to which all women are subjected, as well as by low socioeconomic status. Such difficulties are further compounded in relation to Aboriginal women or women from non-English-speaking backgrounds.177

However, despite these problems, women belonging to vulnerable groups should not automatically be excluded from research. When assessing research proposals involving vulnerable groups of women, HRECs should consider the way in which these women will be required to participate in the research. Study designs should use methods of data collection that minimise intrusion into the women’s lives.178 The informed consent process then becomes the means of addressing any remaining, unavoidable intrusion(s). Where appropriate, methods of data collection can be designed to allow women the opportunity to nominate and discuss their major, relevant health concerns.179

Lastly, given the lack of information about the health of women in general, and vulnerable groups of women in particular, there is a need for researchers to review the way in which they disseminate research findings. Dissemination of results in the peer-reviewed literature adds to the stock of scientific knowledge but has little direct impact on vulnerable communities who act as research participants.

**Canadian guidelines**

The Canadian Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans [http://www.nserc.ca/programs/ethics/english/policy.htm](http://www.nserc.ca/programs/ethics/english/policy.htm), in discussing the recruitment of women for participation in research, explicitly addresses the question of unjust exclusion: ‘Article 5.2 Women shall not automatically be excluded from research solely on the basis of sex or reproductive capacity.’180

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176 National Women’s Health Policy: Advancing Women’s Health in Australia, op.cit.


178 Wyn et al., op.cit.

Article 5.2 imposes obligations of equitable treatment of potential participants on both ethics committees and researchers, pointing out that while some research is properly focused on particular populations that include few women, or none at all, the latter should be represented in most studies.

Article 5.2 is also clear about automatic exclusion from research on the basis of sex or reproductive capacity, rejecting such an approach as a discriminating and unethical use of inclusion or exclusion criteria.181

Both of the above documents are consistent with the National Statement (paragraph 1.5(c). HRECs need to assess the relative harms and benefits of research for these groups of potential participants rather than automatically excluding them. The issue here is the justification for exclusion and inclusion of participant groups who might benefit in the future from such participation, or from research findings that will thereby reflect the range of people affected by the condition being investigated.

**Points to consider**

- Have women been excluded from the study population simply on the basis of gender or reproductive stage? If so, is there a clear rationale for exclusion or under-representation in terms of the potential harm to women and (or) fetuses?
- Have women or representative community groups, and not just researchers, participated in the assessment of the degree of risk that may be involved for women and (or) fetuses and whether this is acceptable?
- Does the research proposal involve vulnerable women? If so, have these vulnerabilities been taken into account?
- Have research methods been adapted to minimise intrusion into research participants’ lives?
- Does the informed consent process address unavoidable intrusion(s)?
- Will the research findings be disseminated to research participants and relevant community groups?

**Suggested reading**


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181 Ibid
A Research Law Collection
EXPLANATORY NOTE

This is a collection of opinions on recurrent legal issues relevant to research involving humans. It is not an exhaustive collection and suggestions for additional topics are welcome. The opinions have been written by some of the contributors, who are listed at the front of this Handbook, and the views they express are not all necessarily shared by NHMRC. Nonetheless, they provide an informative range of opinion on important legal matters relevant to research involving humans.

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CHILDREN AND YOUNG PEOPLE, RESEARCH INVOLVING

CONSENT TO A CHILD’S PARTICIPATION IN RESEARCH

[NS 4.2]

Who is a child? In most jurisdictions, under age of majority legislation the age of majority is 18. Beyond that age, people can make their own medical decisions in the same ways as any other adult. In New South Wales and South Australia, the age for making medical decisions is 14 and 16 respectively: a person who gives medical or dental treatment to a person under the age of 16 is protected from liability if a parent or guardian has consented; a practitioner who performs medical or dental treatment on a person 14 years or older with the consent of that person is similarly protected from liability. In South Australia, a person 16 years of age or older may make decisions about his or her own medical treatment as validly and effectively as an adult.

CONSENT BY CHILDREN UNDER THE AGE OF MAJORITY BUT WITH SUFFICIENT COMPETENCE TO DECIDE

[NS 4.2(a)]

Even before a child reaches the age at which he or she could consent under the relevant legislation, the child may be lawfully competent to consent to at least some procedures. This depends on whether the child is a ‘mature minor’ under the Gillick test, approved by the High Court of Australia in 1992 in Marion’s case. This means that the person has ‘achieved a sufficient understanding and intelligence to enable him or her to understand fully what is proposed.’

See also, Consent to Medical Treatment and Palliative Care Act 1995 (SA), s. 12: http://www.parliament.sa.gov.au/legislation/5_legislation.shtm treatment may be provided to a child if the parent or guardian consents or, if the child consents and (a) the medical practitioner is of the opinion that the child is capable of understanding the nature, consequences and risks of the treatment and that the treatment is in the best interests of the child’s health and wellbeing, and (b) that opinion is supported by the written opinion of another medical practitioner who has examined the child.

In deciding whether a child is competent to consent, it is not clear precisely what amounts to sufficient ‘understanding and intelligence’, that is, the threshold a child must reach before he or she can consent to his or her own treatment. It will be a question of fact to be determined in each case, depending on the age and level of maturity of the child and the nature of the procedure. A child who is ‘Gillick-competent’ is legally competent to give an effective consent to a medical procedure by him or herself. Additional consent is not legally required from a person with parental responsibility. The National Statement does recommend that consent from a parent or guardian should be obtained in addition to the child’s consent ‘in all but exceptional circumstances’ (NS 4.2(b)). That is a wise precaution rather than a strict legal requirement. Parental consent does protect the researcher if there is a later dispute about whether the child was really ‘Gillick-competent’.

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1 Minors (Property and Contracts) Act 1970 (NSW), s.49.
2 Consent to Medical Treatment and Palliative Care Act 1995 (SA), s. 6.
3 Gillick v West Norfolk AHA (1986), AC 112 (HL).
4 Secretary, Department of Health and Community Services v JWB and SMB (Marion’s case) (1992), 175 CLR 218.
5 Marion’s case, sup. at p. 237.
YOUNGER CHILDREN

[NS 4.2(c)]

If a child is under the age of 18 (or 14 or 16 under the legislation in New South Wales and South Australia, respectively), a parent generally has authority to consent to that child’s participation in research (a parent here means a person with ‘parental responsibility’). However, children should only be permitted to participate in research where their participation is indispensable to that research. (NS 4.1(b)) A parent may only consent if the proposed research is not contrary to the child’s best interests (NS 4.3). A child’s refusal to participate in research must always be respected. (NS 4.4)

CONSENT OF ANY ORGANISATION OR PERSON REQUIRED BY LAW

[NS 4.2(c)]

There are some procedures that the High Court of Australia has ruled as being so serious that neither a child nor a parent could give a valid consent to it. These are procedures which involve invasive, irreversible and major surgery; a significant risk of making the wrong decision either as to a young person’s present or future capacity to consent or about what are the best interests of a young person who cannot consent; or where the consequences of making a wrong decision are particularly grave. Such procedures have been held to include sterilisation and gender re-assignment; in future, the category of cases may be extended. The only way that such serious procedures can be carried out is where a court has stated that, in the particular circumstances, it would be lawful for them to be done, and a parent may then consent to the procedure.

RESEARCH CANNOT BE CARRIED OUT THAT IS NOT IN A CHILD’S BEST INTERESTS

[NS 4.3]

Parental authority is limited to consenting to procedures that are in a child’s best interests. For this reason, parents could not lawfully consent to a child’s hand being amputated so that the child is a more pitiable beggar, an example given by the High Court in the same case. Best interests means best medical interests. If there is a doubt about a child’s welfare, any person may apply to a court for an order authorising treatment or other measures to protect the child. It seems that proposed research need not actually benefit the child but rather that it should not harm the child.

CHILD’S REFUSAL TO PARTICIPATE

[NS 4.4]

Under the Family Law Act 1975 (Cth), people with ‘parental responsibility’ have legal authority to consent to legal procedures for the child and the child has no legal right to countermand the parent’s consent.

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6 Family Law Act 1975 (Cth), s. 61B.
7 Marion’s case, sup at pp. 237-8.
8 Ibid., p. 240.
CLINICAL TRIALS

HRECs have statutory obligations under the *Therapeutic Goods Act 1989* and the Therapeutic Goods Regulations. These are described in Appendix 2 of this Handbook.
COMPLAINTS

HEALTH COMPLAINTS LEGISLATION

All jurisdictions have legislation establishing formal complaint mechanisms for patients to complain about health services. The relevant legislation and complaint bodies include the following (however, there is additional legislation in some jurisdictions for certain types of complaints):

- Health and Community Services Complaints Commission;
- Health Care Complaints Act 1993 (ACT), Health Complaints Unit; http://www.act.gov.au
- Health Services (Conciliation and Review) Act 1987 (Vic.); http://www.vic.gov.au/subindex.cfm?link_ID=15, Health Services Commissioner; and
CONFIDENTIALITY

There are numerous provisions in the National Statement that require HRECs to ensure that adequate safeguards exist to protect the confidentiality of information obtained during a research project.

MEANING OF CONFIDENTIAL INFORMATION

The essential characteristic of information that is confidential is that the information is inaccessible to the public. It does not matter that the information is simple, novel or of little objective value, as long as it is more than trivial. Further, the form of the information is irrelevant: the protection is attracted to words, written documents, designs, diagrams, photographs or even genetic structures.

SITUATIONS WHERE A DUTY OF CONFIDENTIALITY ARISES

A duty to maintain confidentiality arises in all relationships between health professionals and their clients, although there are some exceptions when confidential information may be lawfully disclosed to other people. The use of information in research is not automatically such an exception.

Note also that a duty to maintain confidentiality and not to disclose information can fall on people who gain confidential information after its initial disclosure. If HREC members were to obtain information about particular participants, for example, they would have a similar duty to keep it confidential, as does the researcher who first obtained the information. This applies whether the researcher is authorised to tell someone else about a particular participant or is in breach of the duty to maintain confidentiality. In both cases, third parties have an obligation to maintain confidentiality as soon as they are aware of the confidential nature of the information.

The obligation to maintain confidentiality continues as long as the information remains confidential. Whether publication of the information terminates its confidential character is a matter of fact in each case.

CIRCUMSTANCES WHERE CONFIDENTIAL INFORMATION MAY BE LAWFULLY DISCLOSED

Confidential information may be lawfully disclosed in certain circumstances:

- where the person concerned consents (the consent would need to be given by a competent person, voluntarily and based on adequate information);
- where it is mandated or permitted by statute or court order. An example of the former is mandatory reporting of notifiable diseases and suspected child abuse. An example of a court order is a subpoena requiring production of data gathered in research. A judge could, however, exercise judicial discretion in deciding whether it should be admitted in evidence. Often it will be excluded as it is not the best evidence of the facts in issue; and
- where it is in the public interest. This is a limited and ill-defined common law principle based on the broad notion that a private obligation of confidence gives way to the obligation which ‘lies on every member of the society to discover every design which may be formed contrary to the laws of society, to destroy the public welfare’. Disclosure of criminal activity or other civil wrong, even if it involves

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disclosing information that is confidential, may sometimes be justified on this ground. However, that disclosure must be in the public interest. For example, if the public interest is not advanced by the disclosure, it may not be permissible to breach confidentiality.

The notion of the public interest is not reducible to a set of hard and fast rules. Nevertheless, it is not met simply because information is to be used in research. Disclosure of matters that are ‘medically dangerous’ to the public may be justified even if the information was originally received in confidence. As with crimes, this will only be the case where disclosure is in the public interest. For example, in one case, disclosure of confidential information about the risks of a drug that had been withdrawn from the market was held not to be justified because there was no longer any danger to the public that that disclosure could prevent.10

Where there is conduct that is neither criminal nor medically dangerous, but which misleads the public, disclosure may be justified. However, it is not sufficient to rely on some idea of the public’s right to know. There must be a threat to the public interest that could be avoided or alleviated by disclosure, such as avoiding an epidemic of an infectious disease. Prospective benefits from research are not enough.

OBTAINING CONFIDENTIAL INFORMATION FROM THIRD PARTIES

HRECs and researchers are usually well aware that confidential information about participants cannot be disclosed without consent or other lawful justification. It is sometimes less well understood that other people from whom researchers seek information may also be subject to a duty of confidentiality and that release of information for research purposes may be a breach of that obligation. This will often be the case, for example, where information is sought by a researcher from an institution such as a school or a hospital. The names, addresses, ages and other information about pupils and their families held by a school, or of patients in a hospital, are usually subject to a duty of confidentiality, that is, the information was given to the school or hospital for limited purposes and these commonly do not include research. To release that information to a researcher for another purpose will breach that obligation.

As indicated above, where the circumstances are such that researchers ought to know that such release will breach confidence, they become subject to the same duty. If information is released, it should be subject to an express promise of confidence from the researcher. Confidentiality is thus usually as relevant to participant recruitment as it is to participant consent and publication of results of research.

Researchers planning to recruit participants from the clientele of an institution such as a school, hospital, club or association need to recognise that the information in the pupil or patient registers or membership records of such institutions is confidential. The clients and members are the ones to whom the obligation of confidence is owed and it is their consent, and not that of the institution or club, that is necessary to release that information. One means of communicating with potential participants without breaching the confidentiality owed to them is to request the institution to distribute the researcher’s invitation to participate in the research project to members of that institution. Potential participants are then free to contact the researcher directly.

It is important to recall that it is not only personal identifying information that can be the subject of the duty of confidentiality. That duty can attach to any information obtained for the purpose of, in the course of, or as the result of, the conduct of research. This is of particular relevance to the publication of research results. The detailed content of a final

10 Schering Chemicals Ltd v Falkman (1981), 2 All ER 321.
The purpose for which the confidential information is obtained needs to be carefully considered and clearly expressed, especially when the information could be used for further research consequent upon that for which the information was initially gathered. Unless this possibility of secondary use is made clear, such further use could be restrained.

Where information is collected in the course of research, disclosure of that information for other purposes will be, prima facie, a breach of the duty of confidentiality. The usual exceptions of consent and compulsion of law will be available. However, the more difficult and unclear question will be the other circumstances in which disclosure of that information is justified because it is in the public interest.

Consistent with the policy supporting statutory obligations to disclose information about risks to public health, it could be argued that disclosure in order to prevent some other social harm, or harm to an identifiable group, should be similarly justified. The predictability of that harm and its tangible nature will be important and will clearly need to be of greater weight than some general idea of the public right to know, which, as noted above, would not of itself justify disclosure. Going public with confidential information gathered for research purposes in order to draw attention to some social injustice would not fall within any recognised exception to the duty, no matter how compelling the need to remedy that injustice may appear.

INFORMATION OBTAINED FROM PUBLIC AUTHORITIES

Public authorities collecting confidential information often have statutory obligations of confidentiality that prevent confidential information being disclosed to other people, such as researchers. Relevant Federal and State statutes include the following.

Commonwealth statutes

Relevant Commonwealth Acts include the following:

- The Archives Act 1983 (Cth) protects confidential records from public access even when other records in the Archives become available to the public.
- The Australian Institute of Health Act 1987 (Cth) protects information in the records of the Institute now called the Australian Institute of Health and Welfare.
- The Census and Statistics Act 1905 (Cth) prevents staff disclosing census results but permits the Minister to determine that certain information be disclosed (s.13).
- The Epidemiology Studies (Confidentiality) Act 1981 (Cth) allows controls to be imposed on a wide range of research activities, including those that would fall within conventional definitions of social and behavioural research. It applies when Commonwealth regulations declare Commonwealth epidemiological studies to be prescribed studies to which the Act applies. One example is the Vietnam Veterans Study.
- The Health Insurance Act 1973 enables personal information gained in the course of quality assurance activities to be withheld from public disclosure and from production in legal proceedings.
- The National Health Act 1953 applies to specific types of research regarding the operation of departmentally funded institutions. There are statutory prohibitions of
disclosure of personal information in reports. Examples include nursing home standards (ss. 45DA and 45DC) and certain inquiries regarding professional conduct (s. 134A). The Act also contains provisions directing compliance with guidelines issued by the Privacy Commissioner under the Privacy Act (ss. 135AA and 135AB). The guidelines will address storage, use, disclosure and some linkages of personal information. They will not be applicable to information that identifies providers or referrers of services in respect of which claims for payment are made by persons, or database information maintained for identifying persons eligible to be paid benefits under specified programs (s. 35AA(2)).

**State statutes on gathering information for public purposes**

State statutes and guidelines on gathering information for public purposes and the confidentiality exemption provisions include:

- **Freedom of Information Act 1989** (NSW) Schedule 1 cl. 13(a); [http://138.25.65.50/databases.html#nsw](http://138.25.65.50/databases.html#nsw)
- **Guidelines for Release/Access to Health Records**, Health Department of Western Australia, 1986;
- **Health Act 1937** (Qld) s. 100(1); [http://www.legislation.qld.gov.au/](http://www.legislation.qld.gov.au/)
- **Health Administration Act 1982** (NSW) s. 22; [http://138.25.65.50/databases.html#nsw](http://138.25.65.50/databases.html#nsw)
- **Medical Practice Act 1992** (NSW) s. 190; [http://138.25.65.50/databases.html#nsw](http://138.25.65.50/databases.html#nsw)

It should be noted that the freedom of information legislation applies to patients in public hospitals in all jurisdictions except ACT, where the legislation enables private patients to gain access to their medical records. In other jurisdictions, patients who are treated in a private hospital or by a private practitioner have no legal right to see their records although the hospital, or practitioner, may choose to disclose them on the
patient's request. Also, it is possible that the patient may obtain access to the records by applying for a court order that they be revealed (a court order is within the discretion of the court but can be enforced), or by the patient complaining to a health complaints body that he or she was unreasonably denied access to the records (this might lead to an agreement by the hospital, or practitioner, that the records, or some of them, should be shown to the patient).
CONSENT

LEGAL REQUIREMENTS CONCERNING CONSENT

It is a legal requirement that medical procedures must not be undertaken without the consent of those involved, or without other lawful justification, such as an emergency. Under the law of battery, sometimes called trespass, any physical contact with a person, however slight, without his or her consent, or other lawful justification, may give rise to a legal claim for compensation. Each individual who initiates, directs or engages in research that involves touching a person is responsible, under the law of battery, for ascertaining that the person has consented to the procedure.

INFORMATION REQUIRED FOR CONSENT TO BE EFFECTIVE

[NS 1.7]

A person’s consent is legally effective if that person is informed in broad terms of the nature of the intended procedure and then gives consent. The procedure is then not a battery even if the person does not fully understand what is involved unless there has been misrepresentation or fraud, which may vitiate the consent. Although medical practitioners also have an obligation to provide additional information about a proposed procedure before the participant agrees to it, such as information about potential risks and side effects (see below), failure to provide that information does not make the consent ineffective.

One example of a guide to this decision appears in the NHMRC’s General Guidelines for Medical Practitioners on Providing Information to Patients. This guide was written for clinical and not research contexts.

COMPETENCE TO GIVE CONSENT

[NS 1.7]

A person is competent in law if he or she is:

- an adult or a ‘mature minor’ within the Gillick test (see ‘Children’ above); and
- able to understand what the procedure involves and to consent to it.

There is little Australian law on the determination of competence. However, some recent English cases and law reform statements give some guidance. In Re C, the Court noted three stages in the decision-making process: first, comprehending and retaining treatment information; secondly, believing it; and thirdly, weighing it in the balance to arrive at a choice. The Law Commission of England and Wales proposed a similar approach. The Commission suggested that a person lacks capacity, that is, is incompetent, if he or she is:

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11 Rogers v Whitaker (1992), 175 CLR 479 (HCA); Chatterton v Gerson (1981), 1 QB 432.
12 Ibid at pp. 489–90.
14 Re C (adult: refusal of medical treatment) (1994) 1 WLR 290; (1994), 1 All ER 819.
15 Law Commission of England and Wales, Consultation Paper No 129, Mentally Incapacitated Adults and Decision Making, para. 2.20.
unable to understand or retain the information relevant to the decision, including
information about the reasonably foreseeable consequences of deciding one way
or another or failing to make the decision; or
unable to make a decision based on that information.16

FREE AND VOLUNTARY CHOICE

[NS 18–1.9]

A free and voluntary choice denotes that there was no coercion or fraud in obtaining
consent. The Nuremberg Code17 http://ohsr.od.nih.gov/nuremberg.php3 requires that a
research participant be able to exercise ‘free power of choice, without the intervention of
any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of
constraint or coercion.’18 And: ‘If information is withheld in bad faith, the consent will be
vitiates by fraud.’19 Note, however, that in Australian law, consent will be invalidated
only where a person is not provided with information about the nature and purposes of
what is purposed.20

Examples of fraud or deceit invalidating consent are rare. Consent will be ineffective
where it has been obtained as a result of some actual or threatened physical violence or
deliberate and fraudulent withholding of information.21 Where a person initially refused a
procedure but later, after being questioned by a physician while affected by pre-
operative medication, reluctantly agreed, the consent was held not to have been legally
effective.22 Beyond these clear examples, legal principle gives way to ethical conduct.
While law may render consent ineffective when it is extracted under pressure or fear,
ethical assessment will question the reliability of consent affected by lesser influences.

Some other legal contexts offer possible sources of relevant principle. In contract law,
the incompetence of a person to contract will only have consequences where that
incompetence is known to the other party to the contract. Law offers a remedy where
advantage has knowingly been taken of the less competent party. The remedy is usually
release from the contract, but can include compensation for loss that has resulted from
performing contractual duties. It is said that developments in contract law in Australia
have shown an increasing reliance on principles permitting release from contractual
obligations where insistence upon performance by one party would, in the light of their
knowledge of all the circumstances, be unconscionable.23

The essence of these developments lies in the recognition that relief should be available
to a person in order to prevent loss from the performance of a contract where that
person is, to the knowledge of the other contracting party, in a disadvantageous position,
or suffering from a disability of which the other party takes advantage.24 The relationship
between researchers and research participants can be likened to one of contract,
although the participant’s freedom to withdraw would be an unusual term. This
relationship often involves very similar imbalances of knowledge and ability to those that

16 Ibid., para. 2.24.
17 ‘Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10’,
18 Ibid., para. 1.
19 Chatterton v Gerson (1981), sup. at p. 443.
20 Rogers v Whitaker (1992), sup. at p. 489.
22 Beausoleil v Sisters of Charity (1964), 53 DLR 2d 65.
23 Carter J. & Stewart W., ‘Commerce and conscience: the High Court’s developing view of contract’,
23 WALR 49.
have been the basis for release from contractual obligations. A researcher's sensitivity to those imbalances, and to the need to act so that advantage is not taken of those less able, particularly for the purpose of recruitment as research participants, would reflect these emerging legal principles.

In some particular relationships, one party is in such a position to influence the other that the exercise of undue influence is presumed. Therefore, for a contract between such parties to be legally effective, the dominant party must prove that that influence was not exercised. These can be fiduciary relationships, such as those between guardian and ward, but can also arise in specific situations of dependence. Although the High Court of Australia has held that the relationship between medical practitioner and patient is not a fiduciary one, it was acknowledged that medical practitioners may have certain fiduciary obligations towards their patients, such as a duty not to benefit unfairly from the 'unequal' relationship between them.

Where the relationship between a researcher and participant involves the possibility of such a degree of influence being exercised by the researcher, similar considerations about the exercise of undue influence could lead to doubt as to whether the participant's consent was voluntary. The principles in contract law permit relief from an otherwise binding commitment, thereby protecting the less powerful party from harm resulting from the undue exercise of influence by the other. It is possible that the circumstances of some researcher and participant relationships involve a degree of influence that not only induces participants to enrol in a project, but also to remain when they would otherwise prefer to withdraw from the study. Where continued enjoyment of essential benefits or services is understood by recipients to be dependent on continued participation in a research project, participants may choose not to withdraw even though they find continued involvement is burdensome, stressful or otherwise harmful. In the light of these principles, it could be argued that participation procured as the result of such influence is not voluntary.

INFORMATION

Information about 'risks, inconveniences and discomforts of research'
[N§ 1.7(a)]

Although a valid consent can be obtained if a participant understands in broad terms what is proposed in a research procedure, researchers also have a legal duty to take reasonable care in providing other information to participants so they can make an informed choice about whether to take part. This includes information about potential risks and side effects. A person who is not given sufficient information of this type and agrees to a procedure to which he or she would not have agreed if adequately informed, may be able to sue in negligence if he or she suffers injury or loss as a result of the procedure, even if there is no negligence in its actual performance.

The general test for the information that must be given before a procedure is carried out was described by the High Court of Australia in Rogers v. Whitaker. The court said that it is part of a medical practitioner’s duty of care to inform a patient of a ‘material’ risk inherent in any proposed treatment. A risk is material if ‘…in the circumstances of the particular case, a reasonable person in the patient’s position, if warned of the risk, would be likely to attach significance to it or if the medical practitioner is or should reasonably be aware that the particular patient, if warned of the risk, would be likely to attach significance to it.’

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25 A fiduciary relationship is one in which one party is bound to exercise rights and powers in good faith for the benefit of another; for example, as between trustee and beneficiary.
26 Breen v Williams (1996), 186 CLR 71 (HCA) at 83.
28 Ibid at p. 490.
In determining what is a ‘material’ risk for the purpose of the test in *Rogers v Whitaker*, a court would almost certainly require a higher standard of disclosure for research than that needed for therapeutic procedures. The reason is that a reasonable person would be more likely to attach significance to risks if the procedure is not being undertaken for that person’s own benefit, but, rather, to benefit someone else. This is borne out by the decision of a Canadian provincial court in an action brought by a participant who was injured while taking part in a research project to test a new anaesthetic. Finding for the plaintiff, the court said that the duty to disclose risks was ‘at least as great as, if not greater than’ the duty where therapy was being considered. The court continued:

> There can be no exceptions to the ordinary requirements of disclosure in the case of research as there may well be in ordinary medical practice. The researcher does not have to balance the probable effect of lack of treatment against the risk involved in the treatment itself. The example of risks being properly hidden from a patient when it is important that he (sic) should not worry can have no application in the field of research. The subject of medical experimentation is entitled to a full and frank disclosure of all the facts, probabilities and opinions which a reasonable man (sic) might be expected to consider before giving his (sic) consent.29

This statement rejects absolutely any reliance in experimental procedures on what the High Court in *Rogers v Whitaker* 30 referred to as ‘therapeutic privilege’, that is, the medical practitioner’s limited discretion to withhold information in the patient’s interests.

However, these judicial statements do not provide a simple answer to the practical question: what must be disclosed? Some guidance is given by the NHMRC’s General Guidelines for Practitioners on Providing Information to Patients.31

More specific advice about information disclosure in the research context is given by the United States Federal Regulations made pursuant to the National Research Service Award Act 1974.32 This legislation was intended to apply to all types of research involving humans, whether medical or otherwise. Although not binding in Australian law, it offers a useful guide to information disclosure that would, in all likelihood, fulfil the less specific Australian standards.

The United States Federal Regulations state that information given to a prospective research participant should be in language understandable by the participant. There is an absolute prohibition on ‘any exculpatory language through which the subject is made to waive or appear to waive any of the subject’s legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.’33

The Regulations list the following as those matters to be disclosed to participants:

- a statement that the study involves research, an explanation of the purposes of the research, the expected duration of the participant’s involvement, a description of the procedures to be followed and identification of any procedures that are experimental;
- a description of any reasonably foreseeable risks or discomforts to the participant;

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30 *Rogers v Whitaker*, sup. at p. 486.
• a description of any benefits to the participant, or to others, which may reasonably be expected from the research;
• a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant;
• a statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained;
• for research involving more than minimal risk: an explanation as to whether any compensation and any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
• an explanation of whom to contact for answers to pertinent questions about the research and the research participant’s rights, and who to contact in the event of a research related injury to the participant; and
• a statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and that the participant may discontinue involvement at any time without penalty or loss of benefits to which the participant is otherwise entitled.

When it is appropriate, additional matters are to be disclosed. These are:
• a statement that the particular treatment or procedure may involve risks to the participant, or to the embryo or fetus if the participant is or may become pregnant, which are currently unforeseeable;
• anticipated circumstances under which the participant’s involvement may be terminated by the researcher without regard to the participant's consent;
• any additional costs to the participant that may result from involvement in the research;
• the consequences of a participant’s decision to withdraw from the research and the procedures for orderly termination of involvement by the participant;
• provision of a statement to the participant advising that they will be notified of any significant new findings which develop during the course of the research and which may relate to the participant’s willingness to continue their involvement in the project; and
• the approximate number of participants involved in the study.

Insofar as this type of information is legally required to be given, this is on the basis that an ordinary person in the position of a potential participant in a research project would be likely to attach significance to it: the test in Rogers v Whitaker (above).

There are also other matters that HRECs may consider should be included in the information provided to participants in relation to particular research projects. For example:
• the means of protecting confidentiality and intellectual property;
• whether insurance protection will be provided; and
• if there is a possibility of confessions of illegal activity or reportable conduct, whether researchers may be mandated to disclose this to the relevant authorities.

Again, these matters should be discussed if an ordinary person would be likely to attach significance to them.
Comprehension

The Nuremberg Code http://ohsr.od.nih.gov/nuremberg.php3 makes express reference to the need for comprehension of disclosed information.34 Somewhat less specific reference appears in the National Statement, while the United States Federal Regulations require only that the information be disclosed in language ‘understandable’ to the participant.35 The law is probably similar, requiring that information must be disclosed in an appropriate manner and form, rather than that it must be understood. The High Court of Australia, for example, said in Rogers v. Whitaker that no special medical skill is involved in disclosing information, but: ‘Rather, the skill is in communicating the relevant information to the patient in terms which are reasonably adequate for the purpose, having regard to the patient’s apprehended capacity to understand that information’.36

The law’s preference for standards that depend on an objective test is understandable. It is much easier to establish whether information was disclosed than whether it was understood. Also, in negligence, the focus is upon the medical practitioner’s duty to take care, rather than the patient’s level of understanding.

Consent for the collection of information

There are specific legislative provisions that require consent to be obtained before personal information is collected. The Privacy Act 1988 (Cth)37 requires federal agencies collecting personal information about people to obtain consent before the information is collected, stored, used or disclosed. Information Privacy Principles 10 and 11 in the Act deal respectively with use of collected personal information for a purpose other than that for which it was collected and disclosure of such information. In both principles the consent of the person to whom the information relates is sufficient to authorise disclosure, though there are circumstances in which information may be used or disclosed even without consent, for example, to protect third parties.

The Privacy Act does not define the requirements for consent, the standard of information to be provided before consent is sought, or the criteria for determining competence. These are left to the common law.

See also:

‘Intellectual or mental impairment, consent and’ in this resource, page L39

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36 Rogers v Whitaker, op cit., at p.490.
37 Privacy Act 1988 (Cth), s. 14 and the National Statement (Appendix 2) set out 11 Information Privacy Principles.
COPYRIGHT

Copyright is essentially a right to prevent the copying, or more precisely the unauthorised reproduction, of certain subject matter. Copyright protection arises under the Copyright Act 1968 (Cth). The duration of the exclusive rights varies with the subject matter. For example, copyright for literary and artistic works usually lasts for the life of the author plus 50 years from the year of the author's death. Copyright for films, broadcasts and sound recordings lasts for 50 years from their making.

The subject matter protected by copyright includes original works of literature, art, music, drama, films, records and television and radio broadcasts. Protection is automatic in that the subject matter is protected from the time it is first reduced to some tangible form, for example, first written down or taped. Because copyright protection is automatic, it follows that there is no copyright registration system in Australia.

The requirement of 'originality' does not mean that the subject matter has to be 'novel' or 'inventive' in the sense that those concepts are used in patent law. Originality requires that the particular subject matter must actually have originated from the person claiming the copyright and not have been copied from elsewhere; and that that person must have used some skill and labour in the making of the subject matter.

Copyright protection extends beyond the making of unauthorised reproductions to activities such as importing and selling copyright subject matter. Copyright does not protect the ideas contained in subject matter but only the form in which particular ideas are expressed. So, for example, the idea of making a film about the life of Oscar Wilde was not protectable but the particular form the film took was protectable. Copyright does not protect against the independent creation of subject matter because in that case no copying is involved.

IF THERE IS A LEGALLY PROTECTED INTELLECTUAL PROPERTY INTEREST, WHO OWNS IT OR HAS AUTHORITY TO USE IT?

The general rule on ownership is that the creator of the intellectual property is the first owner of it. The major exception is the case of employees. Where an employee acting in the course of his or her employment creates intellectual property, it belongs to the employer. There is, therefore, no need for an assignment in that situation, although employees are sometimes requested to sign assignments to put the issue beyond doubt. In other cases, ownership of intellectual property can be transferred by assignment from one person to another. Usually, the transfer is made in return for payment of money, or other consideration, by the subsequent owner to the current owner, but that is not essential for the assignment to be effective.

The right to exploit intellectual property without a transfer of ownership can be granted by way of a licence and the licensee then has lawful authority to exploit the intellectual property. The licensor remains the owner of the intellectual property right. Without permission, the exploitation would be an infringement of the intellectual property right of the owner. Usually a licence is granted expressly, and is in writing. In some circumstances a licence will be implied.

AGREEMENT BETWEEN ANY RELEVANT PARTIES ABOUT THE USE THAT MAY BE MADE OF INTELLECTUAL PROPERTY

Even if there is a legally protected intellectual property interest and the researcher does not own or have authority to use it, it may be possible to vary the situation by agreement. For example, information and data gathered during the course of a research project may be protected as confidential information, but that may be modified by
agreement between the relevant parties. The research participants may negotiate a right of first access to the results of the research; the dissemination of the results could be limited to particular persons or entities, but otherwise kept confidential; the identities of the research participants (which would otherwise be considered confidential) could be disclosed.
DECEPTION, RESEARCH INVOLVING

The use of covert methods of gaining information in the course of research is controversial and complex and the variety of covert methods makes any single application of principles difficult. The use of such covert methods is perhaps of greatest legal significance in relation to participant agreement to enrol in a research project; however, in the context of confidentiality, some comment is necessary. The important point is that the covertness of the method is unlikely to be regarded as preventing the duty of confidentiality from arising. It is probable that researchers who conceal the fact that they are researchers when they gain information from potential participants still owe those participants the same obligation to respect their confidence as they would have had if their researcher status had been disclosed.
DISCRIMINATION

NS 1.5 addresses the issue of discrimination in the recruitment of participants for research. The issue emerges in a more specific context of clinical trials at NS 12.2(d)(ii), which requires that such trials have an appropriate method of recruitment.

HRECs should consider whether the method of recruitment for any research, and particularly a clinical trial, is:

- discriminatory;
- unethical according to the National Statement. For example, where people are selected or excluded on the grounds of race, age, sex, disability or religious or spiritual beliefs, except where the exclusion or inclusion of particular groups is necessitated by the research; or
- unlawful because it contravenes relevant legislation.

This section deals with unlawful discrimination.

IDENTIFYING UNLAWFUL DISCRIMINATION

In identifying unlawful discrimination, HRECs might consider the following questions:

Is there direct or indirect discrimination?

Direct discrimination. In most Australian jurisdictions, direct discrimination occurs when a person is treated less favourably than another person on the basis of an attribute that they possess that the other person does not. The attribute must fall within the list of grounds set out in the legislation (see below). A classic example in the research context is the exclusion of participants from a clinical trial because of the colour of their skin.

In addition to attributes actually possessed, the legislation also prohibits discrimination based on attributes or characteristics that are thought to relate generally to people possessing the primary attribute. For instance, direct discrimination would occur if women were excluded from a clinical trial because they are thought to be less reliable participants because of their child care responsibilities.

Indirect discrimination. Indirect discrimination refers to policies and practices that, though not obviously discriminatory, nevertheless consistently result in a disadvantage for a certain group. The group must be definable by a relevant ground under the legislation (see section below).

An example that might be relevant for HRECs is the requirement of written consent for participation in research. While this does not directly discriminate, it may indirectly discriminate on the grounds of race if, because of past disadvantage, certain racial groups are less likely to be able to read and sign a consent form. Alternatively, some racial groups may have a cultural discomfort with written forms. In such a situation, the HREC could avoid discrimination by suggesting that the researcher should offer an opportunity for audiotaped consents, or another more appropriate form of consent.

The requirement for written consent forms might also indirectly discriminate against people with sight impairments (see below).

There are provisions prohibiting indirect discrimination in all jurisdictions in Australia, except the Northern Territory, and the definition of indirect discrimination is reasonably consistent. One exception is the Sex Discrimination Act 1984(Cth), which at s. 7B incorporates a test of reasonableness. This means that, if the condition, requirement or practice is reasonable in the circumstances, it is not unlawful under the Act even if it has an indirect discriminatory effect (see below).
Is the discrimination on a ground identified in the legislation?

Grounds of unlawful discrimination at federal level are as follows:

- disability: Disability Discrimination Act 1992 (Cth), s. 7B;
- race, including discrimination on the grounds of race, colour, national or ethnic origin, immigration, or that of a relative or associate and offensive behaviour based on racial hatred: Racial Discrimination Act 1975 (Cth); and
- sex, including discrimination on the grounds of sex, sexual harassment, marital status, pregnancy, potential pregnancy and family responsibilities in employment: Sex Discrimination Act 1984 (Cth).

Further grounds are listed in the Human Rights and Equal Opportunity Commission Act 1986 (Cth), which provides for complaints about discrimination on the grounds of religion, political opinion, age, medical record, criminal record or impairment; mental, intellectual or psychiatric disability; sexual preference; and trade union activity. These grounds can be the subject of a complaint and investigation by the Human Rights and Equal Opportunity Commission, but there are no remedies under the act for the complainant.

Grounds of unlawful discrimination for State and Territories include the following (note that this is not a complete list; there are other grounds):

- age (all states except Tas.);
- breastfeeding (Qld, NT);
- homosexuality (NSW, SA, NT, ACT);
- lawful sexual activity (Vic.);
- political belief or activity (Vic., WA, Qld, ACT, NT);
- religious belief or activity (Vic., WA, Qld, ACT, NT);
- trade union activity (Vic., Qld, ACT, NT);
- transexuality (NSW, SA, NT, ACT); and
- vilification: on grounds of race, transgender status, homosexuality and HIV/AIDS infected status in NSW; on grounds of race or religion in Qld; and on grounds of race in the ACT.

Does the discrimination fall within an area covered by the legislation?

The primary areas in which discrimination is prohibited are employment, education and the provision of goods and services and facilities. Research in educational institutions that involves humans could breach anti-discrimination legislation. However, because of the way the legislation is framed, it is more likely that unlawful discrimination might arise in the context of access to goods, services and facilities. For instance, where a clinical trial is taking place in a hospital, and access to the trial represents access to a health service, it could be argued that denial of access on a discriminatory ground is prohibited. Note that all equal opportunity statutes in Australia contain provisions making discrimination unlawful in the supply of, or access to, goods and services.

Is this one of the circumstances in which discrimination is legal because it is covered by an exception, or is reasonable in the circumstances?

All of the anti-discrimination statutes contain some general exceptions, as well as exceptions specifically related to provision of goods and services. For example, it is not unlawful discrimination to provide services only to one sex if they can only be provided
to one sex, or to provide services to men and women in a different manner. And it is lawful not to provide special facilities for an impaired person if it is unreasonable in the circumstances.

Each of the anti-discrimination statutes, except for the Racial Discrimination Act, includes a provision enabling a person to obtain a temporary exemption from the operation of an Act.

The National Statement envisages that potentially discriminatory research may be undertaken if discrimination is ‘necessitated by the research’. It is not clear whether this accords with the test of ‘reasonableness’ that would justify discrimination. HRECs should determine both what is necessary and what is reasonable and, if there is doubt, advise researchers to seek an exemption under the legislation.

EXAMPLES OF DISCRIMINATION ISSUES FACING HRECS

Discrimination on the grounds of sex in access to a clinical trial

In Alyschia Dibble (Estate of the late) v. St. Vincent’s Hospital Sydney Ltd. a complaint of sex discrimination was lodged against the hospital in relation to the provision of goods, services and facilities. The complainant, a woman who was HIV positive, had been denied admission to a clinical drug trial being conducted at the hospital. The reason given for the denial was that there was a risk of pregnancy as she was still capable of menstruating. The complainant claimed that there was no risk of her becoming pregnant because she had not engaged in sexual activity with men for many years, and that, even so, she offered to have a tubal ligation.

The complainant died before the matter was properly heard and the President of the Human Rights and Equal Opportunity Commission (HREOC) determined that the proceedings had abated on her death. On appeal at first instance the decision of the HREOC was upheld, but subsequently the Full Federal Court overturned the decision and said the matter could proceed. It is still awaiting hearing. The primary question for the court will be whether the discrimination was reasonable in the circumstances.

Researchers wishing to exclude women based on certain risk factors may be able to argue that the exclusion is reasonable because:

- recruitment of women as research subjects is difficult. This does not justify excluding women. On the contrary, it raises the question of whether positive efforts should be made to recruit women;
- women increase the difficulty of obtaining clean data because of hormone changes associated with the menstrual cycle. However, as Darvall states, focusing on men reduces the generalisability of the data and is scientifically untenable. Also, if women are excluded from trials, practitioners may be reluctant to use the ultimate product if its safety has not been tested, for example, for women, fertile women and pregnant women. If women do use the product, far more may suffer adverse effects than if women were included in the trial;
- legal liability may arise for fetal injury if women of childbearing age are included. Women should not be lightly excluded because of childbearing capacity. In

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38 Alyschia Dibble (Estate of the late) v. St. Vincent’s Hospital Sydney Ltd (1905), EOC 92–702.
39 Stephenson v HREOC (1996), EOC 92-833.
40 Grounds for excluding women are mentioned by Leanna Darvall in ‘Autonomy and protectionism: striking a balance in human subject research policy and regulation’, 1993, 11(2) Law in Context 82 at 89.
v Mount Isa Mines 42 (women excluded from jobs in the lead industry), Lockhart J said that 'The presence of intention, motive or purpose, relating to health does not necessarily detract from the conclusion that there is discrimination on the ground of sex'.43 Furthermore, excluding women of childbearing capacity is not necessary or reasonable where the woman has indicated that she is not sexually active, or that she has no intention of becoming pregnant. Darvall quotes Carol Levine who argues that women, if adequately informed, should be permitted to decide for themselves whether to participate. However, it may be justifiable to exclude women who are fertile and sexually active if there is a known high risk to future children and no known or minimal benefit to women. Darvall justifies this exclusion on the basis that no form of contraception is 100 per cent reliable and fetal injury may occur at a time when a woman does not realise that she is pregnant.44 It is, of course, possible that a man's gametes may give rise to a pregnancy while the man is undergoing a research trial that has harmful effects on male gametes. If so, the ground of sex is not a reasonable basis in all circumstances for treating men and women differently. In the American case of International Union UAW v. Johnson Controls Inc fertile men, but not fertile women, were given a choice as to whether they wished to risk their reproductive health for a particular job. Only women with childbearing capacity were excluded from lead-exposed jobs. The court held that decisions about the welfare of future children must be left to the parents who conceive, bear, support and raise them rather than the employers who hire those parents. However, a major factor influencing the court was that the basis of discrimination was not fertility, but female fertility.

43 Ibid., at pp. 79, 739.
The same principles concerning the need for consent and the provision of information, where possible, apply to these patients as well as to those referred to in relation to ‘Research involving persons with an intellectual or mental impairment’ (NS 5.1–5.4) and ‘Research involving persons highly dependent on medical care’, (NS 6.1–6.10).

Emergency care research

An emergency requiring immediate measures to save a patient’s life, or to prevent serious damage to the patient’s physical or mental health, is an exception to the usual requirement that medical procedures may not be undertaken without consent. However, the emergency only justifies those measures that are necessary to avert the immediate harm. Also, it is questionable whether a medical practitioner is entitled to rely on the emergency doctrine if the patient has earlier specifically refused the procedure in the event that he or she should later become incompetent. The reason for this is that one basis for the emergency doctrine is implied consent, and consent cannot be implied if the person has made contrary wishes known.

There is no legal principle of general application that would permit a patient being enrolled in research arising from an emergency unless the procedures were in the patient’s best interests and undertaken to avert an immediate risk to the patient’s life or health.
ETHICS AND LAW

The National Statement (Preamble, p. 4) focuses primarily on ethical principles, but also refers to the need for research projects to conform to relevant legal requirements and for HRECs to be satisfied that the research that they approve is lawful.

HRECs should familiarise themselves with the central legal issues of consent, confidentiality and privacy. It is also the responsibility of HREC members to keep up to date with relevant State and Commonwealth legislation, regulations and guidelines. These are constantly changing. Also, HRECs should take care in directly applying legal principles relating to medical treatment to medical research. For treatment, the law may allow greater intervention in a person’s best interests, even in the absence of full information and consent. For research, the law will require fuller information to be given and then a formal consent, usually in writing, by the person asked to take part in the research or someone else who has lawful authority to consent on the person’s behalf. (This generally means a parent if the person is under 18; or, if the person is over 18, an agent or guardian appointed under legislation, in jurisdictions that have such legislation.)

It is obviously not possible to address every situation that may arise and, in any event, the law is often not clear. Principles drawn from legislation, such as that relating to privacy, are relatively precise but there is little relevant legislation. There have been very few court cases about research involving human participants either in Australia or elsewhere, and it is often difficult to predict the application of principles drawn from common law. If there is any doubt about the lawfulness of any proposed conduct related to research or its approval, committee members should seek legal advice external to the committee.

The work of HRECs is essentially a values-based deliberative process aimed at achieving consensual decision-making. The legal requirements should be viewed within this context. In cases of doubt, specialist legal opinion, or more than one opinion, external to the committee, may need to be obtained.
The Freedom of Information Act 1982 (Cth) allows people to gain access to information about themselves held by Commonwealth agencies, but exempts various documents from access. Documents specifically protected from access under the Act include the following.

- Documents produced in the course of research that contain information relating to research, the disclosure of which prior to the completion of the research would be likely to unreasonably expose the researcher, or his or her agency, to disadvantage. This exemption applies only to research conducted by an officer of any agency specified in a schedule to the Act. The only agency there specified is The Australian National University (s. 43A).

- Documents the disclosure of which would involve unreasonable disclosure of personal information about a person other than the person requesting it, or which would found an action for breach of confidence (ss. 41 and 45).

More general exemptions apply to documents where their disclosure would disclose opinion, advice, recommendation, deliberation or consultation that has been obtained or taken place as part of the deliberative processes of the agency, where that disclosure would be contrary to the public interest. The responsible minister is given the power to certify that disclosure of such documents is, in any particular instance, contrary to the public interest. Wide as this category potentially is, its application to research is limited by excluding reports that concern the results of studies, surveys or tests and opinions on those results written by scientific or technical experts, whether employed by the agency or not (s. 36).

Section 40 provides exemption for documents whose disclosure would, or could be expected to, prejudice either the effectiveness of procedures or methods for the conduct of tests, examinations or audits by an agency, or the attainment of the objects of those tests, examinations or audits. The section adds the same exemption for documents that would adversely affect personnel management, proper and efficient conduct of operations or the conduct of industrial relations. Even where documents fall into these categories, they cannot be treated as exempt if their disclosure is, on balance, in the public interest.

Most Australian states and territories have enacted similar legislation. HRECs may need to consult local statutes to clarify exemptions.

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HUMAN RESEARCH ETHICS COMMITTEES

LEGAL RESPONSIBILITIES OF HRECS AND INSTITUTIONS

Individual committee members have legal, as well as ethical, responsibilities in relation to the protection of the interests of research participants, and can, in principle, be sued, for example, by an injured participant or an aggrieved researcher. To date, this has not occurred in Australia, although there have been cases overseas.47

To protect committee members, and especially those who may not otherwise be protected, such as 'lay' members, institutions are required to indemnify all members of their HRECs and to accept legal responsibility for decisions taken. The National Statement requires institutions to provide HREC members with legal protection covering any liabilities that ‘may arise in the course of bona fide conduct of their duties’ (NS 2.12).48 Where an ethics committee is shared between one or more institutions, the latter are required to jointly accept legal responsibility (NS 2.3, 2.12). (For an account of indemnity and compensation concerning research participants in clinical trials, see NS Commentary 12.7.)

RESPONSIBILITIES OF MEMBERS

There is an important decision of the Supreme Court of New South Wales49 in relation to the responsibilities of members of boards. That case decided that once a group has elected a member to serve on a statutory board that member becomes subject to the overriding and predominant duty to serve the interests of the board in preference to serving the interests of the group that elected the member. This decision establishes that a member of an HREC serves the interests of the HREC, specifically, under NS 2.5, to protect the welfare and rights of the participants.

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48 It is important to note that such indemnity does not protect committee members with regard to legal action arising from negligence or any other action that is contrary to the law.

49 Bennetts v Board of Fire Commissioners of NSW (1967), 87 WN (NSW) 307.
HUMAN TISSUE, RESEARCH INVOLVING

LEGAL ASPECTS IN THE USE OF HUMAN TISSUE SAMPLES

Removal of tissue from donors specifically for the purpose of a research project needs careful consideration. Uniform legislative provisions in each State and Territory of Australia allow adults to donate, with consent, regenerative tissue for transplantation to another living person, or for therapeutic, medical or scientific purposes. The donation of non-regenerative tissue from adults, with consent, is impliedly restricted to the purpose of transplantation to another living person. Separate provisions deal with donations of tissue from children.

In the case of tissue donation, consent procedures should be in line with the Human Tissue Acts in each State and Territory. These Acts prescribe the procedures to be followed, including the person whose consent must be obtained, that is, either the donor, a parent (if the donor is a child), or the senior available next-of-kin (if the donor is deceased and has not indicated an intention before death to donate tissue). The Acts also include provisions about the use of tissue obtained during an autopsy for research purposes. However, the Acts do not cover the use of tissue that has been taken or stored during clinical treatment.

CONSENT TO USE TISSUE

Tissue for research may come from living donors or from cadavers. It may be specifically donated for research purposes or it may be stored after being obtained for a therapeutic procedure. The consent procedure will depend on which of these categories is relevant.

The use of tissue taken for therapeutic procedures is problematic, in particular in relation to the consent that is required. People do not own, or have property in, their tissue and when the tissue is removed, they do not have a property interest in it that legally requires that their consent must be obtained before it is used in research. There is no case specifically on this point in Australia but the legal principle that would probably be applied is illustrated by the American case Moore v Regents of the University of California. In Moore’s case, a patient sought compensation for the unauthorised use of cells removed from his body. The cells were developed by researchers into a cell line and used to produce biological agents. A patent was obtained by the researchers for the cell line and the methods for producing the biological agents. One issue was the ownership of the cells removed from the patient’s body and of the resulting patent. The majority of the court held that patients do not own their cells after their removal. They held, further, that patients have no rights to share in the proceeds of a patent in such cases. This is because the owner of a patent is the inventor, or that person’s employer, who is the person

50 See Transplantation and Anatomy Act 1979 (Qld) div. 2 & 3; Human Tissue Act 1983 (NSW) div. 2 & 3; Human Tissue Act 1982 (Vic) div 2 & 3; Human Tissue Transplant Act 1979 (NT), Div 2 & 3; Transplantation and Anatomy Act 1978 (ACT) div. 2 & 3; Transplantation and Anatomy Act 1983 (SA) div. 2 & 3; Human Tissue and Transplant Act 1982 (WA) div. 2 & 3; Human Tissue Act 1985 (Tas) div. 2 & 3. Note that ‘regenerative tissue’ is defined as tissue that, after injury or removal, is replaced in the body of a living person by natural processes.

51 Ibid. See also Children and Young People, research involving, pp L1-2.

52 see footnote 2 above.

responsible for the inventive effort. It is important to note that, even if the court had found that the patient owned the cells, the patient would still not have been entitled to share in the proceeds of a patent because the patient has contributed nothing to the inventive effort.

What this means for researchers is that they can probably lawfully use stored tissue for research purposes with the consent of the institution that is holding it and need not seek the specific consent of the person whose tissue it is. However, in view of the National Statement’s emphasis on ‘respect for persons’ (NS 15.1), it is preferable to seek consent even for the use of stored tissue in research.
ILLEGAL CONDUCT, RESEARCH INVOLVING

KNOWLEDGE OF ILLEGAL CONDUCT

In the course of their study, researchers may obtain information about a child at risk from child abuse or other type of criminal activity. HRECs should ensure that researchers have considered the possibility of this occurring in the research protocol and have plans in place to address such situations.

An HREC should be satisfied that the researcher is aware of any State or Territory legislation/regulations about the reporting of such information. For example, under section 316 of the Crimes Act 1900 (NSW), it is an offence for a person who knows or believes that a serious offence has been committed to fail, without reasonable excuse, to bring information to the attention of the police force or other appropriate authority.

ILLEGAL CONDUCT

Where a researcher is planning to gather information from participants that is likely to include facts about illegal conduct, it would be good practice for the HREC to obtain legal advice. If the illegal conduct is a felony (a serious offence involving people or property), the researcher may also commit an offence if he or she becomes aware of the facts constituting the felony and does not report it to the police.54 The duty of confidentiality is overridden by the public duty to disclose facts about felonies. There is no similar offence of concealing or failing to report less serious offences (misdemeanours) but liability is possible for other offences, such as conspiracy, being an accessory and attempting to conceal a crime, although proof of more active conduct would generally be necessary and not mere knowledge of what had happened. The legal advice should include whether appropriate warnings should be given to research participants and whether any disclosure duties will arise. This includes not only disclosure of criminal activity to police but also other types of notifiable activity, such as child abuse, to the appropriate authorities. See also ‘Confidentiality’, page L7.

INTELLECTUAL OR MENTAL IMPAIRMENT, CONSENT AND

CONSENT FOR INCOMPETENT ADULTS

The fact that a person has an intellectual or mental impairment does not of itself mean that the person is not competent to consent to a medical procedure. In fact, such people are presumed to be competent until the contrary is shown.55

If, after the person's competence has been considered or assessed in relation to the proposed procedure, the person is assessed as not being competent, consent must be sought from someone who has lawful authority to consent on his or her behalf. In Victoria, for example, this may be an agent appointed by the person while competent, under the Medical Treatment Act 1988.56 Alternatively, in jurisdictions that have guardianship legislation it may be a guardian appointed by a guardianship board, or tribunal, or by a court.

Members of HRECs in New South Wales need to be aware that, under recent amendments to the Guardianship Act 1987, the New South Wales Guardianship Board must give consent for clinical trials involving persons suffering from an intellectual disability.57 One of the pre-requisites for the Board’s consent is that an HREC has first given consent to the research. It follows that, in New South Wales, HRECs are no longer the ultimate decision-makers in respect of clinical trials that propose to involve intellectually disabled people.

A guardian acting on behalf of a person unable to make an informed decision should find out as much as possible about the person’s values, preferences and wishes. This may involve discussions with family and close friends, or the person’s medical practitioner and other health carers, provided that the latter are independent of the research team. Methods of direct communication appropriate to the needs of the person concerned should be employed and this may require the involvement of health carers with the necessary skills.

Research must not be contrary to the person’s best interests

A proxy decision-maker, such as an agent or guardian, is limited to making decisions in the represented person’s best interests. The decision-maker does not have the full autonomy of a competent adult making medical decisions that affect only him or herself, where the person may choose or refuse any procedure even if that is not to the person’s advantage.

The refusal of a person with an intellectual or mental impairment must be respected

A person who is competent despite an intellectual or mental impairment is legally entitled to refuse a medical procedure and it will be a battery to treat the person in the light of that refusal unless there is some other lawful justification for the treatment. The refusal cannot be overridden by consent from an agent or guardian.

If the person is incompetent but refuses the procedure, that refusal is not legally effective and consent can be given by a proxy decision-maker such as an agent or guardian. However, that person’s authority to consent is limited to consenting to procedures that are in the best interests of the represented person.

55 Marion’s case, sup. at p. 239.
56 Medical Treatment Act 1988 (Vic), s. 5A b
57 Guardianship Act 1987 (NSW), s. 45AA.
In relation to research, the National Statement gives ethical weight to any refusal by a person with intellectual or mental impairment (NS 5.4).
INTELLECTUAL PROPERTY

[NS 19]

Intellectual property rights are the legal rights that may be asserted in respect of the produce of the human intellect. To be accorded legal protection, the ‘produce’ must be more than an idea. It must fall within the types of interests that are protected by law in Australia. The main intellectual property interests that may be encountered by HRECs are patents, copyright and confidential information. It is an offence for a researcher to infringe these rights by doing an act without the permission of the owner which the owner has the exclusive right to do, for example: manufacturing and selling an article the subject of a patent; making an article in accordance with a registered design; making copies of a literary or artistic work; using a trade mark; or using or disclosing a trade secret. The importance of this for HRECs is that both the researcher and the institution in which this occurs may be exposed to legal liability.

The remedies for infringement of intellectual property rights include:

- an injunction (a command of the court requiring a person to refrain from further engagement in the infringing activity);
- delivery up of infringing articles to the owner of the intellectual property right for destruction of those articles;
- damages to compensate the owner of the intellectual property right for the loss he or she has sustained as a result of the infringement; and
- as an alternative to damages, an account of profits, requiring the infringer to give up the profits made as a result of the infringing activity to the owner of the intellectual property right.

Issues of this kind may arise in a number of situations involving HRECs. Research proposals presented for review by HRECs will often contain information that is confidential as to the design, content and scope of the proposal. A member of an HREC is bound by an obligation of confidence not to disclose such information, without the authority of the authors of the proposal, to a person not a member of the HREC and may be liable for an action for breach of confidence for an unauthorised disclosure. If the unauthorised disclosure included making a copy of the document containing the research proposal, there would also be a breach of copyright in the literary work constituting the document.

Information and data gathered during the conduct of research would not normally be considered confidential (although the identity of the human participants from whom the information and data were derived might well be the subject of an obligation of confidence). The primary objective of the exercise would be to increase knowledge by the dissemination of the information and data. In some cases, however, the entity funding the project might require a delay in publication in order to secure intellectual property rights that might otherwise be invalidated by premature publication. In such cases, premature publication would constitute a breach of confidence, provided that the requirement for confidentiality was made clear, either expressly by agreement between the funder and the researchers, or impliedly from all of the circumstances. In other cases, there might be a condition attached to the project (for example, by the funder or the human participants) that the information and data obtained be disclosed only to particular persons or entities. In such a case, disclosure to other persons would constitute a breach of confidence.

The examples discussed in the previous paragraph raise a point of general importance: intellectual property rights (as with other rights), including the use that can be made of information, can be modified by agreement. It is essential that, as far as possible, all
relevant intellectual property issues are identified and dealt with before a research project commences. While such issues are not primarily the responsibility of HRECs, it is likely that they will impinge on the deliberations of HRECs from time to time.

The following questions may assist HRECs in recognising legal issues.

**Does a research protocol involve a legally protected intellectual property interest?**

**Patents.** A patent granted under the *Patents Act 1990* (Cth) confers a monopoly on the owner to exploit the invention for a maximum of 20 years (for a ‘standard’ patent) or a maximum of six years (for a ‘petty’ patent). Patents are granted for inventions which cover the whole field of technology, as opposed to fine art. Thus, methods and processes of manufacture, articles of manufacture and devices for manufacturing such articles can all be inventions. There are two main groups of subject matter that are generally not considered as patentable inventions: those things that are protectable by copyright law (see below), and those things that are no more than ideas, schemes or formulae and that have no practical, physical dimension in which they can be commercially exploited. In addition, there is one specific exclusion, namely that human beings and biological processes for their generation are not patentable inventions. Biological substances such as genetic sequences have, however, been patented.

An invention must necessarily involve a degree of inventiveness. Essentially, to be patentable, an invention must be novel, that is, not have been described previously or used previously; and involve an inventive step, that is, not be obvious as judged against what was previously generally known in the relevant technological field. Thus, an invention may be novel but so obvious that it is not considered worthy of the grant of a patent.

See also ‘Copyright’, page L19.
PRIVACY

PRIVACY ASPECTS OF A RESEARCH PROJECT

[NS 18.1–18.5]

Australian common law does not recognise any general right of privacy in the sense that the expression is commonly used, that is, the right to prevent unconsented intrusion by photographic or sound technology into private conduct, correspondence and conversations. Instead, the Privacy Act 1988 (Cth) sets out the 11 Information Privacy Principles (IPPs), reproduced in the National Statement at Appendix 2. In any particular situation, the statutory language of the Act and the IPPs will be important, but the sense of the IPPs can be adequately gained by reading the plain-English version attached to the Act.

PERSONAL INFORMATION

[NS 18.1–18.5]

Conduct will only infringe IPPs if that conduct involves personal information that relates to an individual. Personal information means information, or an opinion, that can be part of a database, whether true or not and whether recorded in a material form or not, about an individual whose identity is apparent, or can reasonably be ascertained from the information or opinion.

CONSENT TO THE COLLECTION, USE AND DISCLOSURE OF PERSONAL INFORMATION

IPPs 10 and 11 permit some use or disclosure of personal information where any one of the five exceptions defined in those Principles applies. The first exception is consent by the person who is the subject of the information, to its use or disclosure. If this consent is obtained, there is no unauthorised disclosure of personal information under the Act.

WHEN CONSENT MAY BE WAIVED

Note that the Privacy Act and the IPPs contain no general exemption for research. The principal means for dispensing with the need for consent is the procedure in the Guidelines under Section 95 of the Privacy Act 1988 (Cth). http://www.nhmrc.gov.au/publications/synopses/e26syn.htm. The effect of Section 95 is that disclosure or use of information that would otherwise be unlawful, would, if made in accordance with the Guidelines, now be lawful. There is, however, an overriding requirement. It is a condition of approval of the Guidelines that the federal Privacy Commissioner be satisfied that the public interest in the promotion of research of the kind to which the Guidelines relate outweighs to a substantial degree the public interest in maintaining adherence to the IPPs.

SECTION 95 GUIDELINES

The Guidelines apply to medical research approved by an HREC in which access is sought to information held by Commonwealth government agencies. The Privacy Act defines ‘medical research’ as ‘including epidemiology’, extending the usual meaning of medical research to include epidemiology. It follows that most social and behavioural
researchers cannot rely on the Privacy Guidelines as a means of gaining access to information held by Commonwealth agencies where, but for those Guidelines, that access might involve breach of an IPP.

Where access to information held by Commonwealth agencies under the Section 95 Guidelines is sought, the Guidelines set out procedures to be followed by HRECs. In essence, the Guidelines provide that use or disclosure of information for the purpose of medical research will be lawful if an HREC has determined that the public interest in the research outweighs to a substantial degree the public interest in privacy. The Privacy Guidelines provide a list of 21 factors to which the HREC must have regard in reaching that final determination as well as a detailed guide for researchers as to what they need to submit to an HREC.

The Privacy Act does not state who is to make the decision about whether the access to personal information that is sought might involve an agency in breach of an IPP. However, it seems likely that it will be made by the agency in question, given that it is the agency, and not the researcher, who is at risk of infringing the Act. Section 72 of the Privacy Act permits the federal Privacy Commissioner to make a determination that the public interest in an agency carrying out a certain act or engaging in a practice that may breach an IPP, outweighs to a substantial degree the public interest in adhering to that IPP. In other words, the federal Privacy Commissioner does have power, subject to this overriding balance of public interests, to authorise an agency to use or release personal information for purposes other than those for which it was collected.

However, in relation to research other than medical research, only an agency can apply for such a determination. People whom the federal Privacy Commissioner considers to have a real and substantial interest in the application can receive notice of an intended determination and can participate in a conference prior to that determination becoming final.

Suggested reading


Guidelines under section 95a are under development.


Privacy Act 1988 (Cth) http://scaleplus.law.gov.au

Relevant State legislation
RESEARCH, REGULATION OF

A number of authors include coverage of legal aspects of the Australian system of research ethics review before the issue of the National Statement on Ethical Conduct in Research Involving Humans. Nevertheless, they present helpful outlines of the regulatory framework.

See:


Bennett B, Medical Law, LBC, 1997, Ch 6.


The following contains a detailed summary of the current system and a discussion of relevant legal issues, Laws of Australia, Volume 20.12, Medical Technology, ch. 2.
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Appendix 2
Human Research Ethics Committees and the Therapeutic Goods Legislation
HUMAN RESEARCH ETHICS COMMITTEES AND THE THERAPEUTIC GOODS LEGISLATION

THE TGA IS A DIVISION OF THE COMMONWEALTH DEPARTMENT OF HEALTH AND AGED CARE

June 2001
These guidelines

The aim of this document is to outline to Human Research Ethics Committees (HRECs) the role and responsibilities required of them under the Therapeutic Goods legislation. It describes the role of HRECs in relation to the supply of unapproved therapeutic goods in connection with the operation of the Clinical Trial Notification Scheme, the Clinical Trial Exemption Scheme, the Special Access Scheme, and in the approval of Authorised Prescribers. Each of these mechanisms for supply of unapproved therapeutic goods is discussed briefly within the document. Members of HRECs wishing to obtain an in-depth understanding of the regulation and supply of unapproved therapeutic goods via these mechanisms should consult the following TGA publications:

- Access to Unapproved Therapeutic Goods – the Special Access Scheme
- Access to Unapproved Therapeutic Goods - Clinical Trials in Australia
- Access to Unapproved Therapeutic Goods - Authorised Prescribers
- Access to Unapproved Therapeutic Goods – Personal Importation

The TGA has also developed a publication Access to Unapproved Therapeutic Goods in Australia that is a consolidation of all the documents in the series.

Abbreviations and Acronyms

- AHEC: Australian Health Ethics Committee
- ARTG: Australian Register of Therapeutic Goods
- CPMP: Committee for Medicinal Products
- CTN: Clinical Trial Notification (Scheme)
- CTX: Clinical Trial Exemption (Scheme)
- DSEB: Drug Safety and Evaluation Branch, TGA
- HREC: Human Research Ethics Committee
- NHMRC: National Health and Medical Research Council
- ICH: International Conference on Harmonisation on Technical Requirements for Registration of Pharmaceuticals for Human Use
- Good Clinical Practice: ICH Guideline for Good Clinical Practice (document CPMP/ICH/135/95)
- the National Statement: National Statement on Ethical Conduct in Research Involving Humans
- SAS: Special Access Scheme
- the Act: Therapeutic Goods Act 1989
- TGA: Therapeutic Goods Administration
- the Regulations: Therapeutic Goods Regulations 1989

Acknowledgments

The contribution of the Australian Health Ethics Committee to the development of this guideline is greatly appreciated.
1. INTRODUCTION

The Therapeutic Goods Act, 1989 establishes a uniform, national system of regulatory controls to ensure the quality, safety, efficacy and timely availability of therapeutic goods for human use. Responsibility for the regulatory controls lies with the Therapeutic Goods Administration (TGA) as the national regulatory authority for therapeutic goods.

The TGA controls the supply of therapeutic goods through three main processes:

• the pre-market evaluation and approval of products intended for supply in Australia;
• the licensing of manufacturers; and
• post market surveillance.

Under the Act, therapeutic goods for human use that are imported, manufactured in Australia, supplied by a corporation, supplied interstate or to the Commonwealth, or exported must be included in the Australian Register of Therapeutic Goods (ARTG) unless specifically exempted.

Items which are exempt from entry on the ARTG are set out in Schedule 5 (Regulation 12(1)), Schedule 5A (Regulation 12(1A)) and Regulation 12A. These exemptions allow individuals to gain limited access to unapproved therapeutic goods through the following mechanisms:

• the Special Access Scheme (categories A and B);
• clinical trials (CTN and CTX schemes);
• authorised prescribers; and
• importation for personal use.

The figure below provides a graphic representation of these mechanisms and the sections of the Act and Regulations relevant to their operation.

* Section 19(1)(a) allows supply for Category A and Category B patients but, in practice, Category A cases are dealt with under section 28 and regulation 12A.
Human Research Ethics Committees play an important role in the regulation of the supply of unapproved goods under the Act in connection with the operation of clinical trials (both the CTN and CTX Schemes), the Special Access Scheme and approval of Authorised Prescribers.

The full text of relevant sections of the legislation can be found in Appendix 1.

The full legislation can be found at the following website:


It is important to appreciate that unapproved therapeutic goods have undergone little or no evaluation of quality, safety or efficacy by the Therapeutic Goods Administration. Accordingly, use of all such goods carries with it some risks that have not been defined in the Australian context. As such, use of these products is considered to be experimental and should be guided by the principles and practices as outlined in the National Statement on Ethical Conduct in Research Involving Humans. It is in relation to this issue, that HRECs are relied upon because of their developed expertise in assessing risks and precautions in research involving humans.
2. CLINICAL TRIALS

Clinical trials of unapproved therapeutic goods can be conducted in Australia under either the Clinical Trial Notification (CTN) Scheme or the Clinical Trial Exemption (CTX) Scheme. These two schemes, described below, have quite separate legislative bases.

Notification under the CTN scheme or application under the CTX scheme is required for:

- any medicine or device not entered on the ARTG, including any new formulation of an existing product or any new route of administration, or
- the use of a registered medicine or device beyond the conditions of its marketing approval, including new indications extending the use of the product to a new population group and the extension of doses or duration of treatments outside the approved range.

The choice of which scheme (CTN or CTX) to follow lies firstly with the sponsor and then with the HREC. Studies in which medicines and medical devices that are already included on the ARTG and are used within their approved indications and doses do not need to be subject to CTN or CTX requirements. However where they constitute research they will still need to be approved by an HREC.

Clinical Trial Notification (CTN) Scheme

Legal Basis

The legal basis for the CTN scheme is found in the general powers of Section 18, then Regulation 12 then Schedule 5A Item 3 (including Regulation 12AD).

Section 18 permits the regulations to exempt goods from the Act. Regulation 12 states that goods specified in Schedule 5A are exempt provided that conditions set out in that schedule are met. Schedule 5A item 3 exempts goods used in experimentation in humans provided that certain conditions are met. These conditions are:

- the sponsor notifies the TGA using the approved CTN form and paying the appropriate fee
- the trial must be approved by the sponsor of the goods and the sponsor of the trial (if not the sponsor of the goods) having regard for the advice of the HREC which reviewed the protocol and is assuming responsibility for the monitoring of the trial.
- the terms of approval of the sponsor or the body or organisation conducting the trial for the sponsor must be no less restrictive than terms advised by the HREC.
- the TGA must not:
  > have become aware that to start or continue the trial is not in the public interest
  > have directed that the trial not start or be stopped.
- The sponsor has not received advice from the HREC that is inconsistent with continuation of the trial.
- The conditions set out in regulation 12AD must be complied with.
  > Regulation 12AD sets out that use of therapeutic goods must be in accordance with Good Clinical Practice, the protocol approved by the HREC and the National Statement.
  > Regulation 12AD also requires that the trial must cease if the ethics committee inform the principal investigator that the use is inconsistent with the protocol they have approved or any other condition to which approval for use was given.
Procedure for CTN

Under the CTN scheme, all material relating to the proposed trial, including the trial protocol is submitted directly to the HREC by the researcher at the request of the sponsor. The TGA does not review any data relating to the clinical trial and the HREC is responsible to ensure that there is an assessment of the scientific validity of the trial design and the safety and efficacy of the medicine or device as well as the ethical acceptability of the trial process.

The TGA ‘Notification of Intent to Conduct a Clinical Trial’ form (the CTN Form) is submitted by the investigator on behalf of the sponsor to the HREC and to the Approving Authority. Once the sponsor, the principal investigator, the Chairman of the HREC and the person responsible from the institution or site where the trial will be conducted (called the Approving Authority) have signed the CTN Form, it is submitted by the sponsor of the trial to the TGA along with the appropriate notification fee.

The Therapeutic Goods Regulations require that the notification be in a form approved by the Secretary of the Department of Health and Aged Care. Sponsors must use the current CTN form (located at Appendix 2). Use of old (out-of-date) CTN forms will invalidate the notification.

Clinical Trial Exemption (CTX) Scheme

Legal Basis

The legal basis for the CTX is found in sections 19(1)(b) and the following subsections 19(1A), 19(2)(b), 19(3), (4) and (4A), then regulations 12AA to 12AD.

Under subsection 19(1)(b) of the Act, the TGA may give approval for the import, export, or supply in Australia of goods used solely for experimental purposes in humans and which are not included in the ARTG. This provision enables access by sponsors, including medical practitioners to use otherwise unapproved drugs in clinical trials conducted under the CTX Scheme.

Subsection 19(1A) allows TGA to set conditions on the approval of a CTX application. These conditions are set out in the regulations (see below).

Subsection 19(2)(b) requires that the CTX application must be in writing, contain the information required by the TGA and the application must be accompanied by the appropriate fee. Subsection 19(3) allows for fees to be charged.

Subsection 19(4) provides that the CTX application must be evaluated and notice given of the approval within 28 days of the decision being made and if refused reasons for the decision must be given.

Subsection 19(4A) provides for conditions to be specified in the regulations which may relate to the preconditions on the use of the goods, principles to be followed in the use of the goods, the monitoring of the use and results of the use of the goods and the circumstances in which use of the goods must cease.

Regulations 12AA to 12AD set out the conditions which may be applied to be CTX trial.

Regulation 12AA provides that the TGA may require the following information to be provided:

- the names of members of the HREC that approved the proposed clinical trial and is assuming responsibility for monitoring the conduct of the trial
- the name of, and contact details for, the principal investigator for each trial
- the name of the person which will be in charge of the trial site or each site if more than one
- information about whether or not any conditions specified by the HREC have been met.
Regulation 12AB requires the sponsor and the principal investigator to provide written assurances to the TGA before the trial commences:

- that the trial will be conducted according to GCP
- that any requests for information about the conduct of the trial will be complied with.
- that they will allow a TGA auditor (authorised person) to do the things mentioned in regulation 12AC.

Regulation 12AC outlines the powers of a TGA auditor in relation to a trial site.

Regulation 12AD sets out that use of therapeutic goods approved under CTX must be in accordance with Good Clinical Practice, the protocol approved by the HREC and the National Statement. It also requires that the trial must cease if the ethics committee inform the principal investigator that the use is inconsistent with the protocol they have approved or any other condition to which approval for use was given.

**Procedure for CTX**

A sponsor cannot commence a CTX trial until:

- written advice has been received from the TGA regarding the CTX application; and
- approval for the conduct of the trial has been obtained from an ethics committee and the institution at which the trial will be conducted.

An application for a CTX trial must be in the form required by TGA.

The CTX application comprises summary information about the product, including the overseas status of the drug, proposed guidelines for the use of the product in the trial (called the Proposed Usage Guidelines), a pharmaceutical data sheet, and a summary of the preclinical data and a clinical summary.

It is important to note that the TGA does not receive, evaluate or comment directly on the trial protocol. The primary responsibility of the TGA is to review the safety of the product. The TGA decides whether or not to object to the proposed usage guidelines for the product. If an objection is raised with the sponsor, the trial cannot proceed until the objection has been overcome. If the TGA has no objection, the researcher submits the data package to the relevant HREC.

Even if no objection is raised, the TGA usually provides comments on the accuracy or interpretation of the summary information supplied by the sponsor.

The HREC in each host institution/organisation is responsible for approving the proposed trial protocol after reviewing the summary information received from the sponsor and the investigator and any additional comments from the TGA. The HREC is also able to request any additional information they believe is necessary to undertake review of the proposed research.

There are therefore two CTX forms (Parts) that must be submitted by the sponsor to the TGA:

- Part 1 constitutes the formal CTX application. This form is completed by the sponsor of the trial and submitted directly to TGA with data for evaluation.
- Part 2 is used to notify the commencement of each new trial conducted under the CTX as well as new sites in ongoing CTX trials.

This form is submitted by the investigator on behalf of the sponsor to the HREC and to the Approving Authority. Once the HREC and the Approving Authority approvals have been received by the principal investigator, the trial can commence on the condition that the sponsor of the trial submits the Part 2 form to the TGA within 28 days of commencing to supply the goods.

The sponsor may conduct additional clinical trials without further assessment by the TGA, provided such use falls within the original approved Proposed Usage Guidelines. However, HREC approval of each protocol and approval from the institution/organisation for the conduct of each trial are still required. A notification (using the Part 2 form) for each subsequent trial must be made to TGA.
The Therapeutic Goods Regulations require that the notification be in a form approved by the Secretary of the Department of Health and Aged Care. Sponsors must use the current CTX Part 2 form (located at Appendix 3); otherwise the notification will be invalid.

**HREC Responsibilities in relation to the Regulation of Clinical Trials**

This section should be read in conjunction with the *National Statement on Ethical Conduct in Research Involving Humans, 1999* (the National Statement).

The difference between CTN and CTX is the level of involvement of the TGA in reviewing data about the therapeutic good involved in the trial before the trial begins.

In CTN trials the TGA does not review any data before the trial begins. The responsibility for this review lies with the HREC and the principal investigator. The HREC and the institution are responsible for establishing what information should be provided in support of an application and how that application will be handled by the committee.

In CTX trials the TGA reviews summary data about the therapeutic good (medicine or medical device). The TGA then provides comment to the HREC about the product. The TGA also stipulates the minimum data which must be provided to the HREC. This data includes summary information about the product, the overseas regulatory status of the product and the Proposed Usage Guidelines for the product. The HREC and the institution may require additional information to be provided in support of an application.

HRECs are responsible for reviewing clinical trial protocols for both CTX and CTN. The responsibility for the conduct of the trial rests with the principal investigator and the sponsor. The HREC provides advice to the sponsor and the institution on the trial before it begins and during the course of the trial.

Approval for the trial to be conducted at the site rests with the institution or body where the trial is to be conducted (called the Approving Authority).

Clinical trials, both CTN and CTX must be conducted according to the protocol which the HREC has approved, Good Clinical Practice (GCP) and the National Statement. Should the HREC become aware that the trial is not being conducted according to these standards, the HREC should inform the principal investigator that the use is inconsistent with the approved protocol or any other condition to which approval for use was given (National Statement paragraph 2.44).

The HREC should also advise the Sponsor, the Approving Authority and the TGA of their concerns. This may lead to investigation and withdrawal of the approval of the trial by the sponsor, the Approving Authority or the TGA.

Having approved a trial protocol, under both CTN and CTX, the HREC is assuming responsibility for monitoring the conduct of the trial. In signing the CTN and the CTX form they are agreeing to this responsibility.

HRECs also need to be aware of relevant State and Territory laws pertaining to the supply of therapeutic goods or to issues relating to medical practice which may be relevant to a clinical trial proposal.

The National Statement outlines requirements and obligations of HRECs when they consider and reach decisions regarding clinical trials. While the whole document is relevant the following sections are particularly important for clinical trials with therapeutic goods:

- general guidance in Section 2;
- guidance specifically in relation to clinical trials and trial protocols in Section 12;
- obligations relevant to monitoring of clinical trials for both HRECs and their institutions in guidelines 2.33 - 2.38 and 12.9;
- obligations of the HREC in relation to suspension or discontinuation of research in guidelines 2.44.
TGA recommendations to HRECs reviewing a trial proposal

Each proposed protocol and related informed consent form should be reviewed in conjunction with data provided by the sponsor to support the proposal. If the HREC does not understand any part of the proposal or wishes to see more information it should, consistent with guideline 2.8 of the National Statement, ask for the necessary information and defer the proposal until it is satisfied that the interests of trial participants have been safeguarded.

When assessing the appropriateness of the protocol for clinical trials involving the use of unregistered medicines, the HREC should consider the mechanisms proposed, if any, for continued access to treatment with the unregistered medicinal products by patients for whom treatment has been found to be effective and where long term therapy would be appropriate following completion of the trial. The HREC should consider the advisability of having a post study supply component in the research protocol.

The process of the CTX scheme is intended to provide sufficient guidance for HRECs to proceed without needing to seek further information. However, at no time should an HREC be constrained from asking for further information or seeking advice, especially in order to secure participant safety and welfare.

In relation to proposals to conduct a trial under the CTN Scheme, the HREC will need to determine whether the clinical trial would be best considered under the CTN or CTX scheme, or does not meet the requirements of either scheme. In some institutions, a proposal for a clinical trial may be reviewed by a research or drug subcommittee before the HREC. An HREC may wish to consult additional expertise from sources outside its institution. The HREC may determine that it does not wish to review the proposed trial under the CTN scheme and recommend its review under the CTX scheme.

It is not possible for the TGA to give directions on when a CTN or CTX should be used. The decision will be influenced by many factors including the size of the institution, the experience of the investigator, the experience and expertise of the HREC and related committees and the nature of the therapeutic good involved. Should the HREC be unsure of the decision advice from another more experienced HREC or the TGA could be sought.

If the HREC is of the opinion that it is appropriate for the trial to proceed and approves the protocol, the proposal is usually considered by the institution/organisation that makes the final decision on whether the trial may proceed. If approval to conduct the trial is given, the sponsor submits the relevant clinical trial notification form to the TGA. The chairperson of the HREC should sign the form.

No HREC should give ethical endorsement to any trial about which it has reservations. Any reservations the HREC may have should be resolved with the investigator or sponsor before the form is signed or conditions should be specified to ensure ongoing compliance should this be required.

In signing a notification form and approving a clinical trial protocol, the HREC accepts responsibility for monitoring the progress and conduct of the trial. This is a significant ongoing role for the HREC and one that the Therapeutic Goods Regulations impose solely on the HREC. The TGA is not required to undertake routine monitoring of clinical trials.
TGA recommendations for monitoring clinical trials

The National Statement sets out obligations relevant to monitoring for both HRECs and their institutions (guidelines 2.33 - 2.38 and 12.9). The HREC and its institution may adopt such review mechanisms as are appropriate, including the appointment of a monitor, independent of both the researcher and the sponsor. The TGA recommends that HRECs have clearly defined mechanisms that require researchers to advise them of:

- any serious unexpected adverse events that occur during the trial, including those that have occurred at other sites involved in the study [see below].
- new information from other published or unpublished studies which may have an impact on the continued ethical acceptability of the trial, or which may indicate the need for amendments to the trial protocol; and
- deviations from, or changes to, the protocol that either eliminate immediate hazards to trial participants, significantly affect the conduct of the trial, or increase risks to participants.

It is also recommended by TGA that any such information be accompanied by comment from the researchers on what implications, if any, they believe the new information has for the trial.

Serious adverse events are those noxious and unintended responses to the drug that:

- result in death;
- require in-patient hospitalisation or prolongation of existing hospitalisation;
- result in persistent or significant disability/incapacity;
- result in birth defects;
- are life threatening.

An event should be considered unexpected if the nature, severity or frequency of that event is not documented in the current Australian Product Information if the product is approved for marketing, or in the most current Investigator’s Brochure if the product is unapproved.

It should be noted that the TGA does not receive overseas reports of individual adverse reactions. The TGA requires sponsors to report all individual reports of adverse reactions, which occur in Australia. Good Clinical Practice requires sponsors of trials to inform investigators at all participating sites of individual reports at all sites worldwide. HRECs should develop procedures to ensure they are able to handle such reports appropriately.

The TGA does require that sponsors report any significant safety concerns or actions taken as a result of the analysis of adverse reaction reports within Australia and overseas, including action by overseas regulatory agencies. The TGA will ensure that any such advice has been reported to the Australian investigators and the HREC.

The HREC, as well as the researcher, must consider a serious adverse or unexpected event in the context of information on the drug as well as the underlying disease. For example, a fatal or serious outcome may be identical to, or resemble, the primary efficacy endpoint of the study. Such an event would be considered disease-related. Some assessment of whether the event is drug-related should be undertaken and appropriate measures taken to protect patient safety. Reports of serious and/or unexpected events occurring at other institutions participating in the study are also of value to the HREC. Such reports may signal events not yet seen at their institution, for example, by virtue of the fact that enrolment numbers are lower than elsewhere. Review of the details of these events along with an assessment of causality and the actions taken in other institutions will help guide the HREC in taking appropriate steps to protect patient well being.
Guidelines 2.44, 2.45 and 12.10 of the National Statement outline the circumstances when research should be discontinued. TGA recommends that if an HREC has concerns about the conduct of a clinical trial they should seek advice firstly from the investigator and sponsor. If the researcher has not allayed their concerns despite adequate time to do so, then they should consider withdrawing ethical approval. The HREC should advise the researcher, the relevant institution/s and the TGA of any decision to withdraw approval.

An HREC may discuss any concerns they have with any aspect of a clinical trial with the TGA. TGA has the authority to conduct an audit of a clinical trial where necessary on safety grounds and to investigate non-compliance with the trial protocol or accepted standards for the conduct of a trial.

TGA Administrative Requirements - implications for HRECs

In relation to clinical trials conducted under the CTN and CTX Schemes, sponsors are required to notify the trials to TGA by sending a completed clinical trial notification form (CTN form (Appendix 2) or CTX Part 2 form (Appendix 3)) to the TGA. The forms include separate sections for details of the HREC. They require the chairperson of the HREC to certify that the HREC has approved the clinical trial protocol and has assumed responsibility for monitoring the conduct of the trial, having regard to the advice provided by the National Statement. Also, the HREC is required to certify it has notified its existence to AHEC. An ethics committee which has not notified its existence to AHEC is not recognised as an ethics committee under the Act. In such a case, the conditions under which an exemption from Part 3 of the Act is created to allow lawful supply of the unapproved good will not have been met, the therapeutic goods cannot be supplied and, therefore, the trial cannot commence.

The TGA also recommends that the HREC inform the TGA if it withdraws its approval of a clinical trial, including reasons for the withdrawal.
3. THE SPECIAL ACCESS SCHEME

Legislation

The Special Access Scheme (SAS) refers to arrangements which provide for the import and/or supply of an unapproved therapeutic good on a single patient, case by case basis under Sections 18 and 19(1)(a) of the Act. These arrangements are:

- supply to a patient and notification to the TGA (as delegate of the Secretary) by a medical practitioner that the patient is in category A, under section 18 of the Act.

Category A patients are defined in regulation 12A(5) as persons who are seriously ill with a condition from which death is reasonably likely to occur within a matter of months, or from which premature death is reasonably likely to occur in the absence of early treatment.

A medical practitioner who forms the view that his/her patient meets that definition can, having obtained the informed consent of the patient or the patient's legal representative and completed the relevant notification form, import and/or supply the unapproved therapeutic good to that patient without approval from the TGA.

- approval from the TGA to supply an unapproved therapeutic good to a single patient is given under section 19(1)(a) of the Act.

- approval from an ‘external delegate’ (external to TGA) to supply an unapproved therapeutic good to a single patient is given under section 19(1)(a) of the Act.

A person, who is not employed by the TGA or the Commonwealth Department of Health and Aged Care, may be given a delegation under Section 57(3) of the Act to approve the supply of unapproved therapeutic goods by another practitioner. These external delegates are provided with a set of treatment protocols for those therapeutic goods that can be approved. Medical practitioners within an institution may make an application to the external delegate at that institution for approval to supply unapproved therapeutic goods.

When issuing an authority to supply an unapproved therapeutic good, the TGA will specify to whom authority is given and for which particular drugs and their indication.

HREC Responsibilities in relation to Supply of Unapproved Therapeutic Goods under Section 19(1)(a) of the Act (Special Access Scheme/External Delegates)

HREC responsibilities in relation to the Special Access Scheme are primarily concerned with the granting of approvals under section 19(1)(a) of the Act by ‘external delegates’. In accordance with Regulation 47A(6)(b), all applications approved by an external delegate must be approved by an HREC. In practice, external delegations are rare and thus, HRECs will not be asked to deliberate on such issues as a matter of routine.

TGA recommendations to the HREC

Before agreeing to an approval by an external delegate, the HREC should be provided with the following information:

- the product for which approval is sought;
- whether that unapproved product is included on the list of products which can be approved by the external delegate;
- details about the product to be prescribed, including an assessment of the efficacy and safety of the product;
• the medical condition (also known as the ‘indication’) for which approval is being sought;
• an assessment of the seriousness of the condition being treated;
• the intended mode of use/treatment regimen and whether this conforms to the treatment protocol;
• the clinical justification for use of the unapproved product, including the nature and availability of alternative treatments.

The HREC could also consider their knowledge of the practitioner requesting the supply from previous research activities of the practitioner that have been considered or monitored by the HREC.

In deciding whether to agree to approval by the external delegate, the HREC should be aware that the external delegate should be guided by the same considerations as would apply within TGA for granting of approvals under Section 19(1)(a) of the Act. These considerations are outlined in detail in Section 5 (pages 19-20) of this document.

Although not specifically required under the Act, an HREC may also be asked to comment on the appropriateness of an informed consent form used in conjunction with the use of an unapproved good. One of the conditions TGA imposes on approvals to supply an unapproved therapeutic good is that the patient gives their informed consent. The issue of informed consent in relation to the supply of unapproved products is discussed in Section 6 (page 23) of this document as well as in the National Statement.
4. AUTHORISED PRESCRIBERS

Legislation

Under subsections 19(5-9) of the Act and Regulation 12B, the TGA is able to grant a medical practitioner authority to prescribe a specified unapproved therapeutic good or class of unapproved therapeutic goods to specified recipients or classes of recipients (identified by their medical condition). An Authorised Prescriber can then prescribe that product for that condition (also known as the ‘indication’) and no approval from the TGA is required for each individual patient. The legislation requires:

- An Authorised Prescriber to be a medical practitioner;
- A medical practitioner to obtain endorsement from an appropriate HREC; or
- Where a medical practitioner does not have access to an HREC and this can be demonstrated to TGA, the medical practitioner may obtain endorsement from a specialist college having an established expertise relevant to the use of the medicines concerned.

Under regulation 12B(4) medical devices may only be approved for medical practitioners practising in hospitals. Approval must be obtained from the HREC at the institution at which the practitioner practices. Approval will not be given to medical practitioners to use medical devices outside the hospital setting. Thus, endorsement of the prescriber by the HREC is critical to the Section 19(5) approval process by TGA.

TGA recommendations to HRECs endorsing medical practitioners for the purposes of authorisation under Section 19(5) of the Act

The following information is presented as a guide for an HREC when considering a request from a medical practitioner for endorsement as an Authorised Prescriber. The HREC needs to assess not only the safety of the product in relation to its proposed use, but also the suitability of the medical practitioner. The HREC should consider:

- the indication for which the product will be prescribed;
- whether the practitioner is seeking to treat a condition in his/her area of specialty or training and expertise. In general, endorsement should be given only when the practitioner has training and expertise appropriate for the proposed use of the product. The consideration could include knowledge that the HREC may have from the practitioner’s research activities that have been considered by the HREC and such other information as the HREC requests the practitioner to provide;
- details about the product to be prescribed, including an assessment of the efficacy and safety of the product. This should take into account the regulatory status of the product in overseas countries with regulatory standards comparable to those in Australia (ie, USA, UK, The Netherlands, Canada and Sweden), or if not approved in any of these countries, whether the product has been the subject of clinical trials either in Australia or these overseas countries. In addition, it is important to consider whether the product has been officially withdrawn from the Australian market or refused registration because of safety concerns;
- for medicines, the route of administration and dosage form;
- the clinical justification for the use of the product. This should include an appraisal of the nature of alternative treatments (ie marketed products) available for the indication and the circumstances under which the unregistered product could be used in preference to marketed products; and
- information to be given to the patient about the product; and
- the informed consent form.
Guidance on how HRECs should use this information, particularly in relation to how to balance the seriousness of the condition being treated against the level of evidence provided in support of the efficacy and safety of the product, is provided in Section 5 (pages 19-20). The HREC may also wish to seek advice from a Scientific or Research Subcommittee or a Drug and Therapeutics Subcommittee, if available, when considering the above issues.

The HREC should also ascertain that the unregistered product is not intended for use in a clinical trial. Approval as an Authorised Prescriber is not appropriate in this circumstance. Clinical trials being conducted in Australia require notification under the CTN scheme or approval under the CTX scheme.

The HREC may consider it appropriate to impose conditions on the endorsement. The nature of any conditions imposed will be a matter for the HREC to decide. Examples of possible conditions are:

- a requirement for the Authorised Prescriber to provide regular reports to the HREC outlining the number of patients for whom the unregistered product has been prescribed; and
- requirements for reporting any suspected adverse reactions.

**What happens when a section 19(5) authorisation is revoked by the TGA?**

The HREC may also receive requests for endorsement from medical practitioners who have had their Authorisation revoked by the TGA as a result of a registered product having become available for the specified indication. When a product either containing the same active ingredient or in the same therapeutic class as the unregistered product is evaluated and registered for treatment of the specified indication, the TGA will revoke existing 19(5) authorisations for unregistered products.

If the Authorised Prescriber wishes to continue to use the unapproved product, he/she is required to submit a new application to TGA for Authorisation under section 19(5). The applicant is required by TGA to provide:

- sufficient clinical justification as to why the registered product is not suitable for use in the patient group; and
- a new letter of endorsement from an HREC for continued use of the unapproved product. The HREC’s letter of endorsement should state that endorsement has been given with the full knowledge that an evaluated and approved treatment has become available.

This course of action is imposed in part because it is the TGA’s responsibility to encourage at all times the availability of approved (fully evaluated) products. To do otherwise would remove the incentive for a sponsor to seek registration of the unapproved product or for other sponsors to seek registration of alternative products for treatment of the indication.

**Review of an endorsement**

The TGA recommends that an HREC review its endorsement of the Authorised Prescriber if it becomes aware of:

- inappropriate use of the product by the Authorised Prescriber;
- a concern about the safety of the product;
- failure of the Authorised Prescriber to comply with conditions imposed by the HREC; or
- failure of the Authorised Prescriber to comply with State/Territory legislation.

An HREC may become aware of such circumstances as a result of complaints from patients, or from medical or nursing staff at the institution concerned. If, as a result of its reconsideration, the HREC is satisfied that the welfare and/or rights of patients are not or will not be protected, the TGA recommends the HREC advise its institution and the TGA of its concerns.
The TGA has the authority to inquire about the use of unregistered therapeutic goods and, where necessary, release information about inappropriate use of therapeutic goods to relevant State and Territory authorities.

The HREC should advise the TGA whenever it withdraws an endorsement. Withdrawal of endorsement by the HREC will result in the TGA revoking the Authorisation. The TGA recommends that when an HREC withdraws its endorsement, the HREC should be satisfied that there are appropriate arrangements in place for alternative treatment of patients.

**TGA Administrative requirements - implications for HRECs**

The TGA requires, as part of a medical practitioner's application to become an Authorised Prescriber, a letter of endorsement from the HREC. It is recommended that the letter include:

- a clear statement that endorsement is being given for the purpose of the medical practitioner becoming an authorised prescriber under Section 19(5) of the Act;
- the name of the medical practitioner being endorsed;
- the drug and indication for which endorsement has been given;
- the site(s) at which use is covered by the endorsement;
- any conditions the HREC has imposed on the endorsement; and
- the signature of the chairman of the HREC over his/her official title.

An example of a letter of endorsement is given at Appendix 4.
5. THE CRITERIA USED BY DELEGATES IN DECIDING WHETHER TO APPROVE SUPPLY OF UNAPPROVED THERAPEUTIC GOODS

(The following is provided for the information of HRECs.)

Applications for approval to supply unapproved products need to address criteria relating to the patient, the product and the prescriber. Applicants can also provide any other information they consider important. In considering whether to grant approval, the delegate will generally consider the quality and extent of the information provided and balance the position in relation to each of the criteria. Applications should address each criterion set out below and supply the information requested. In reaching a decision, the delegate will have regard to each of the criteria and approval is unlikely to be granted if each of the criteria have not been met.

Approval is given on a patient by patient basis to reflect the needs of different patients. The major criteria for determining whether approval should be given relate to the patient, the product and the prescriber.

**Criterion 1 - The patient**

The application should contain adequate clinical justification for the use of the product, including an appraisal of the seriousness of the patient’s condition being treated. When making an application, the practitioner will need to supply the following information:

<table>
<thead>
<tr>
<th>Patient details</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Initials</td>
<td>Date of birth (or age)</td>
</tr>
<tr>
<td>Sex</td>
<td>Patient ID or unit record number</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>If applying for an extension of use under SAS - previous approval number, if available</td>
</tr>
</tbody>
</table>

**Clinical justification**

This should include an appraisal of the seriousness of the patient’s condition and details of past treatment. If other registered treatments are available, the applicant will need to justify the use of the unregistered product in preference to those treatments. This should include an appraisal of the expected benefits from the use of the unapproved product.

**Criterion 2 - The product**

The application should indicate how the product is to be used and include an appraisal of the efficacy and safety of the proposed use of the product. The application should include:

<table>
<thead>
<tr>
<th>Product details</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>For unapproved medicines</td>
<td>Active ingredient</td>
</tr>
<tr>
<td></td>
<td>Trade name</td>
</tr>
<tr>
<td></td>
<td>Company/supplier (sponsor)</td>
</tr>
<tr>
<td></td>
<td>Dose form</td>
</tr>
</tbody>
</table>

| Administration and monitoring regime | For unapproved medical devices |  |
|--------------------------------------|-------------------------------|
| Name of device | Company/sponsor |
| Dosage | Route of administration |
| Duration of treatment |  |
Details of the techniques to determine both the efficacy of the treatment and the occurrence and severity of any adverse reaction. This could be provided in terms of clinical, biochemical, haematological and/or immunological monitoring. Monitoring should occur throughout treatment and in some cases it may be appropriate for monitoring to continue for a period thereafter. In the event that a practitioner requests an extension of use under SAS, outcomes of monitoring, including measures of patient response and safety parameters, are required.

**Efficacy/safety data**

Efficacy and safety data sufficient to support the proposed use of the product. A copy of any reference articles from which the data have been obtained should be included. Such references can range from evidence from published randomised controlled trials through evidence from published non-randomised trials and case reports, to consensus opinion. The level of evidence required will depend on the seriousness of the condition (see how to balance the criteria).

**Criterion 3 - The prescriber**

The application should be received from a doctor with qualifications and/or expertise appropriate to the condition being treated and the proposed use of the product. The application should contain:

- **Prescriber details**
  - Name
  - Postal address
  - Qualifications
  - Hospital and hospital department, if applicable
  - Phone number
  - Fax number, if available

**How to balance the criteria**

The following is a guide only. It does not cover all possibilities but may give the delegate and others a general guide as to how the complex issues impacting a decision may be balanced.

There is a hierarchy of evidence of efficacy and safety of the product, a hierarchy of evidence that affects the patient’s condition and a hierarchy of qualifications relating to the requesting doctor. There is thus a complex interaction of these hierarchies which will affect the decision to be made.

The product hierarchy effectively differentiates between:

- products which are not approved in Australia but approved in countries with a regulatory standard comparable to that in Australia (i.e., USA, UK, Sweden, Canada, The Netherlands);
- products which are not approved in Australia but approved in countries other than those with regulatory standards comparable to that in Australia;
- products which are currently under evaluation within TGA;
- products that are not approved anywhere and are still undergoing clinical trials.

These products can be further classified according to the types of evidence available. This can range from:

- evidence from published randomised controlled trials [highest level of evidence]
- evidence from published non-randomised trials
- individual case reports
- consensus opinion of specialist colleges and societies [lowest level of evidence]

The efficacy and safety data submitted in support of the application should be weighed against the seriousness of the condition. As a general rule, the less serious the clinical need, the higher the degree of evidence needed to support the use of the product. For example, a product that has been approved in a country with a regulatory system comparable to our own (USA, UK, Sweden, The Netherlands and...
Canada) is likely to be approved for supply under the SAS for any condition for which it has been approved in those countries. On the other hand, if the only evidence available is that from published case reports, it is unlikely that use of the product would be approved for anything but the most serious (almost life-threatening) of conditions. In this case, the prescriber will also have to demonstrate that other conventional therapies are unsuitable or unlikely to control the condition (clinical justification).

With respect to the clinical justification for the use of the unapproved product, the extent to which the application should address the use of available approved therapies will depend on the seriousness of the patient's condition and the amount of information that is known about the product. As a general rule, the less serious the clinical need, the greater the requirement to demonstrate those available therapies are clinically unacceptable.

In circumstances where the product has been previously withdrawn from, or refused entry to, the Australian market because of safety concerns, it will be expected that all conventional therapy has been tried and failed, or has been accompanied by unacceptable adverse reactions. The clinical justification should address the risk/benefit balance of using the proposed therapy.

The delegate may be aware of information of which the applicant is not based on general knowledge or previous applications eg overseas status of a product. The delegate is responsible for undertaking a limited search for information but the process time of an application will be improved if the applicant supplies all relevant information about the patient and the product to be used in the initial application.

In the event that another product is evaluated by TGA and approved for treatment of an indication, the level of evidence required in support of an application to use an unapproved product instead of the new product for that indication is high. This is particularly so for products with the same active ingredient or with active ingredients in the same therapeutic class.

Medical devices that are only a variation of a previous model or duplicate of the intended performance of an already approved medical device would require a very high level of evidence for approval of an application.

The clinical justification should include discussion as to why the newly approved product is not acceptable for the treatment of the individual patient and this should be based on medical reasons and not on grounds of cost or convenience. This requirement is imposed in part because it is the TGA's responsibility to encourage at all times the availability of approved (fully evaluated) products. To do otherwise would remove the incentive for a sponsor to seek registration of the unapproved product or for other sponsors to seek registration of alternative products for treatment of the indication. If a medical practitioner has an interest in the continued, long-term supply of a particular product, he/she should strongly encourage the sponsor to seek registration of that product in Australia.
6. INFORMED CONSENT IN RELATION TO THE USE OF UNAPPROVED PRODUCTS

Unapproved therapeutic goods have undergone little or no evaluation of quality, safety or efficacy by the Therapeutic Goods Administration. Accordingly, use of all such goods carries with it some risks that have not been defined in the Australian context. As such, use of these products is considered to be experimental and should be guided by the principles and practices outlined in the National Statement. The National Statement contains detailed guidance in relation to informed consent.

Specifically in relation to the supply of unapproved therapeutic goods, TGA recommends that HRECs consider whether the consent forms and/or patient information conveys the following information adequately:

- the product is not approved (ie registered or listed) in Australia;
- any risks and side effects that are known;
- the possibility of unknown risks and late side effects; and
- any alternative treatments using approved products which are available.

If the HREC is considering an application to supply unapproved products derived from any biological tissue including human blood or plasma, it needs to be aware that the TGA can give no guarantee as to the quality, safety or efficacy of these products, particularly as regards any prion or viral inactivation.

In this instance it is suggested that the HREC require the practitioner to use a consent form with wording identical, or as close as possible, to that used in the form titled ‘Consent to Treatment and Indemnity for Use of Products Derived from Human Blood or Plasma’ which is located at Appendix 5.
APPENDIX 1. EXCERPTS FROM THE LEGISLATION
The Therapeutic Goods Act

18 Exempt Goods

(1) The regulations may, subject to such conditions (if any) as are specified in the regulations, exempt:
   (a) all therapeutic goods, except those included in a class of goods prescribed for the purposes of this paragraph, or
   (b) specified therapeutic goods; or
   (c) a specified class of therapeutic goods; from the operation of this Part (except section 31A and sections 31C to 31F).

(2) An exemption in terms of paragraph (1)(a) has effect only in relation to such classes of persons as are prescribed for the purposes of this subsection.

(3) Where the regulations revoke an exemption, the revocation takes effect on the day, not being earlier than 28 days after the day on which the regulations are made, specified in the regulations.

19 Exemptions for Special and Experimental Uses

(1) The Secretary may, by notice in writing, grant an approval to a person for the importation into, or the exportation from Australia or the supply in Australia of specified therapeutic goods that are not registered goods, listed goods or exempt goods:
   (a) for use in the treatment of another person: or
   (b) for use solely for experimental purposes in humans;
   and such an approval may be given subject to conditions as are specified in the notice of approval.

(1A) An approval for the purpose mentioned in paragraph (1)(b) is subject to conditions (if any) specified in the regulations. Those conditions (if any) are in addition to any conditions imposed on the approval under subsection (1).

(2) An application for an approval must be made to the Secretary and must:
   (a) in the case of an application for use of the kind referred to in paragraph (1)(a) - be accompanied by such information relating to the goods the subject of the application as is required by the Secretary; and
   (b) in the case of an application for use of the kind referred to in paragraph (1)(b):
      (i) be made in writing; and
      (ii) be accompanied by such information relating to the goods the subject of the application as is required by the Secretary; and
      (iii) be accompanied by the prescribed evaluation fee.

(3) Without limiting the conditions to which an approval under subsection (1) may be made subject, those conditions may include a condition relating to the charges that may be made for the therapeutic goods to which the approval relates.

(4) Where an application for an approval is made, the Secretary must, after having considered the application and, in the case of an application for the use of therapeutic goods for experimental purposes in humans, after having evaluated the information submitted with the application, notify the applicant of the decision on the application within 28 days of making the decision and, in the case of a decision not to grant the approval, of the reasons for the decision.
(4A) The use by a person for experimental purposes in humans of specified therapeutic goods that are the subject of an approval granted to someone else under paragraph (1)(b) is subject to the conditions (if any) specified in the regulations relating to one or more of the following:

(a) the preconditions on the use of the good for those purposes;
(b) the principles to be followed in the use of the goods for those purposes;
(c) the monitoring of the use, and the results of the use, of the good for those purposes;
(d) the circumstances in which the person must cease the use of the goods for those purposes.

(5) The Secretary may, in writing, authorise a specified medical practitioner to supply:

(a) specified therapeutic goods for use in the treatment of humans; or
(b) a specified class of such goods to the class or classes of recipients specified in the authority.

(5A) An authority may be given subject to conditions (if any) specified in the authority.

(5B) The Secretary may impose conditions (or further conditions) on an authority given to a person under subsection (5) by giving the person written notice of the conditions (or further conditions).

(6) An authority under subsection (5) may only be given:

(a) to a medical practitioner included in a class of medical practitioners prescribed by the regulations for the purposes of this paragraph; and
(aa) to a medical practitioner who has the approval of an ethics committee to supply the specified therapeutic goods or the specified class of such goods; and
(b) in relation to a class or classes of recipient prescribed by the regulations for the purposes of this paragraph.

Paragraph (AA) does not apply in the exceptional circumstances (if any) prescribed by the regulations for the purposes of this subsection.

(7) The regulations may prescribe the circumstances in which therapeutic goods may be supplied under an authority under subsection (5).

(8) The giving of an authority under subsection (5) does not render the Commonwealth or Secretary or a delegate of the Secretary liable to a person in respect of loss, damage or injury of any kind suffered by a person as a result of, or arising out of, the use of therapeutic goods by that person or another person.

(9) In this section, “medical practitioner” means a person who is registered, in a State or internal Territory, as a medical practitioner.

20 Offences relating to importation, exportation, manufacture and supply of therapeutic goods

(1) A person is guilty of an offence if:

(a) The person intentionally:
   (i) imports into Australia therapeutic goods for use in humans; or
   (ii) exports from Australia therapeutic goods for use in humans; or
   (iii) manufactures in Australia therapeutic goods for use in humans; or
   (iv) supplies in Australia therapeutic goods for use in humans; and
(b) none of the following subparagraphs applies in relation to the goods:
   (i) the goods are registered goods or listed goods in relation to the person;
   (ii) the goods are exempt goods;
   (iii) the goods are subject to an approval or authority under section 19;
   (iv) the goods are subject of an approval under section 19A.

(1AA) An offence against subsection (1) is punishable on conviction by a fine not more than 240 penalty units.

(1A) It is a defence to a prosecution under subsection (1) if the defendant proves that the defendant was not the sponsor of the goods at the time of the importation, export, manufacture or supply, as the case may be.

(2) - (3) [Relates to registered or listed goods]

22 General Offences relating to this Part

(1) - (5) [Relates to registered or listed goods]

(6) A person must not intentionally or recklessly make a claim, by any means, that the person or another person can arrange the supply of therapeutic goods (not being exempt goods) that are not registered goods or listed goods.

(7) A person is guilty of an offence if:
   (a) the person intentionally does not act or omits to do an act; and
   (b) the person was reckless as to whether the act or omission would breach:
      (i) a condition of an exemption applicable under regulations made for the purposes of subsection 18(1); or
      (ii) a condition of an approval under section 19; or
      (iii) a condition applicable under regulations made for the purposes of subsection 19(4A); or
      (iv) a condition of an approval under section 19A.

(7AA) An offence against subsection (7) is punishable on conviction by a fine of not more than 60 penalty units.

(7A) A person who whom an authority under subsection 19(5) has been granted must not supply the therapeutic goods to which the authority relates except in accordance with:
   (a) the authority, and
   (aa) the conditions (if any) to which the authority is subject; and
   (b) the regulations made for the purpose of subsection 19(7).

Maximum penalty: 60 penalty units

(8) - [Relates to goods approved under 19A]
31A Secretary may require information etc. about exempt goods

**Exempt goods for use for experimental purposes in humans**

(1) If therapeutic goods are exempt under section 18(1) from the operation of this Part (except this section and sections 31C to 31F) to allow for their use for experimental purposes in humans, the Secretary may give the sponsor a written notice requiring the sponsor to give to the Secretary specified information or documents relating to one or more of the following:

(a) the supply of the goods;
(b) the handling of the goods;
(c) the monitoring of the supply of the goods;
(d) the results of the supply of the goods;
(e) any other matter prescribed by the regulations for the purpose of this paragraph in relation to medicines of that kind.

**Statement by medical practitioner about medicine**

(2) If a medicine is exempt under section 18(1) from the operation of this Part (except this section and sections 31C to 31F) because a medical practitioner has signed a statement in accordance with regulation 12A of the Therapeutic Goods Regulations 1990, the Secretary may give the medical practitioner a written notice requiring the medical practitioner to give to the Secretary specified information or documents relating to one or more of the following:

(a) the condition of the person to whom the medicine is to be given or is given;
(b) the supply of the medicine;
(c) the handling of the medicine;
(d) the monitoring of the supply of the medicine;
(e) the results of the supply of the medicine;
(f) any other matter prescribed by the regulations for the purpose of this paragraph in relation to medicines of that kind.

**Compliance period**

(3) A notice under subsection (1) or (2) must specify a reasonable period within which the person to whom the notice is given must comply with it. The period must be at least 14 days starting on the day on which the notice is given.

31B Secretary may require information relating to approvals and authorities under section 19

**Approval under subsection 19(1)**

(1) The Secretary may give to a person who is granted an approval under subsection 19(1) in relation to specified therapeutic goods a written notice requiring the person to give to the Secretary specified information or documents relating to one or more of the following:

(a) the supply of the goods;
(b) the handling of the goods;
(c) the monitoring of the supply of the goods;
(d) the results of the supply of the goods;
(e) any other matter prescribed by the regulations for the purpose of this paragraph in relation to medicines of that kind.
(2) The Secretary may give notice to a person using specified therapeutic goods that are the subject of an approval granted to someone else under paragraph 19(1)(b) a written notice requiring the person to give the Secretary specified information or documents relating to either or both of the following:

(a) the use of the goods;
(b) any other matter prescribed by the regulations for the purposes of this paragraph in relation to goods of that kind.

Authority under subsection 19(5)

(3) The Secretary may give to a person who is granted an authority under subsection 19(5) in relation to specified therapeutic goods, or a specified class of therapeutic goods, a written notice requiring the person to give to the Secretary specified information or documents relating to one or more of the following:

(a) the supply of the goods;
(b) the handling of the goods;
(c) the monitoring of the supply of the goods;
(d) the results of the supply of the goods;
(e) any other matter prescribed by the regulations for the purpose of this paragraph in relation to medicines of that kind.

Compliance period

(4) A notice under subsection (1), (2) or (3) must specify a reasonable period within which the person to whom the notice is given must comply with it. The period must be at least 14 days starting on the day on which the notice is given.

31C Requirements in relation to information or documents sought under section 31A or 31B

When information or documents must be given etc.

(1) A person to whom a notice is given under section 31A or 31B must give the Secretary:

(a) the information or documents specified in the notice within the period specified in the notice; and
(b) the information specified in the notice in the form (if any) specified in the notice.

Way in which information given

(2) A notice mentioned in subsection (1) may require information to be given in accordance with specified software requirements:

(a) on a specified kind of data processing device; or
(b) by way of a specified kind of electronic transmission.

Offence

(3) A person mentioned in subsection (1) is guilty of an offence if the person fails to comply with that subsection.

Note: The privilege against self-incrimination is not a reasonable excuse for the purposes of subsection (3). However, the information given and the fact that a document was given under this section (and other information, documents or things obtained because of giving the information or document) generally cannot be used in a prosecution (see section 31 F).
Penalty

(4) An offence against subsection (3) is punishable on conviction by a fine of not more than 60 penalty units.

31D False and misleading information

(1) A person to whom a notice is given under section 31A or 31B is guilty of an offence if:
   (a) the person gives information to the Secretary in compliance or purported compliance with subsection 31C(1); and
   (b) the person does so knowing that the information:
      (i) is false or misleading; and
      (ii) omits any matter or thing without which the information is misleading.

Maximum penalty: Imprisonment for 12 months

(2) Subsection (1) does not apply as a result of subparagraph (1)(b)(i) if the information is not false or misleading in a material particular.

Note: A defendant bears an evidential burden in relation to the matter in subsection (2)

(3) Subsection (1) does not apply as a result of subparagraph (1)(b)(ii) if the information did not omit any matter or thing without which the information is misleading in a material particular.

Note: A defendant bears an evidential burden in relation to the matter in subsection (3)

31E False or misleading documents

(1) A person is guilty of an offence if:
   (a) the person produces a document to the Secretary; and
   (b) the person does so knowing that the document is false or misleading; and
   (c) the document is produced in compliance or purported compliance with subsection 31C(1).

Maximum penalty: Imprisonment for 12 months

(2) Subsection (1) does not apply if the document is not false or misleading in a material particular.

Note: A defendant bears an evidential burden to the matter in subsection (2).

(3) Subsection (1) does not apply to a person who produces a document if the document is accompanied by a written statement signed by the person or in the case of a body corporate by a competent officer of the body corporate:
   (a) stating that the document is, to the knowledge of the first-mentioned person false or misleading in a material particular; and
   (b) setting out, or referring to, the material particular in which the document is, to the knowledge of the first-mentioned person, false or misleading.

Note: A defendant bears an evidential burden to the matter in subsection (3).
31F Self-incrimination

(1) A person is not excused from giving information or a document under section 31C on the ground that the giving of the information or document would tend to incriminate the person or expose the person to a penalty.

(2) However, in the case of an individual:
   (a) the information given, or
   (b) the giving of the information, or
   (c) any information, document or thing obtained as a direct or indirect consequence of giving the information or document, is not admissible in evidence in criminal proceedings against the individual (except proceedings under, or arising out of, section 31D or 31E).

57 Delegation

(1) Subject to subsections (2), (6) and (8), the Minister or the Secretary may, by signed instrument, declare to:
   (a) an officer of the Department, or
   (b) an officer of an authority of the Commonwealth that has functions in relation to therapeutic goods, or
   (ba) an APS employee in an Agency (within the meaning of the Public Service Act 1999) that has functions in relation to therapeutic goods, or
   (c) a person occupying or acting in an office, or holding an appointment, declared by the regulations to be an office or appointment the occupant or holder of which may be a delegate under this section;

all or any of his or her powers and functions under this Act.

(2) The powers of the Secretary under paragraph 19(1)(a) may be delegated under subsection (1) only to a person referred to in paragraph (1)(a) or (c) who is registered, or eligible for registration, in a State or internal Territory, as a medical or dental practitioner or as a pharmacist.

(3) Subject to the regulations, the Secretary may, in such circumstances as are prescribed, by signed instrument, delegate all or any of his or her powers under paragraph 19(1)(a) to a person who is registered, in a State or internal Territory, as medical or dental practitioner.

(4) A delegate under subsection (3) is, in the exercise of a delegated power, subject to the direction of:
   (a) the Secretary, or
   (b) an officer of the Department authorised in writing by the Secretary, or
   (c) a person referred to in paragraph (1)(c).

(5) Without limiting the generality of matters that may be dealt with by regulations made for the purposes of subsection (3), the regulations may make provision in relation to the following:
   (a) the persons who may be delegates;
   (b) the circumstances in which delegates may grant approvals for the purposes of paragraph 19(1)(a);
   (c) the conditions to which any approvals granted by delegates are to be subject;
   (d) requiring information to be given by delegates to the Secretary.
The powers of the Secretary under subsection 19(5) may be delegated only to a person referred to in paragraph (1)(a) or (c) who is registered or eligible for registration, in a State or internal Territory as a medical or dental practitioner.

(7) The regulations may prescribe the circumstances in which, and the requirements subject to which, delegates may grant authorities under subsection 19(5).

(8) [relates to 19A]

(9) [relates to 6AA and 23AA]

The Therapeutic Goods Regulations

12 Exempt goods

(1) [Relates to schedule 5]

(1A) For the purposes of subsection 18(1) of the Act, the therapeutic goods or classes of therapeutic goods specified in an item in column 2 or Schedule SA are exempt from the operation of Part 3 of the Act (except section 31A and 31C to 31F) subject to compliance with the relevant conditions specified in column 3 of that Schedule.

(1B) [Relates to anti-D immunoglobulin]

(3) If:
   (a) therapeutic goods that, in relation to a provision of Part 3 of the Act, are exempt goods cease to be exempt goods; and
   (b) the sponsor if the goods has applied for registration or listing of the goods before the goods until the application for registration or listing is determined.

the goods are taken to be exempt goods until the application for registration or listing is determined.

12A UNAPPROVED MEDICINES – EXEMPTION IN LIFE THREATENING CASES

(1) For the purposes of subsection 18(1) of the Act, all medicines, other than medicines of a class or kind listed in the 9th Schedule to the Poisons Standard, as in force from time to time, are exempted, subject to subregulation (2), from the operation of Part 3 of the Act (except section 31A and sections 31C to 31F).

(2) The exemption of a medicine is subject to the following conditions:
   (a) the medicine is to be given to a person who satisfies the following criteria:
      (i) the person is a Category A patient (as defined in subregulation (5)); and
      (ii) the person, or the guardian of the person, has given informed consent (as defined in subregulation (5)) to the goods being given to the person; and
      (iii) the medical practitioner by whom, or at whose direction, the therapeutic good is to be given to the person has signed a statement in relation to the person in the form approved by the Secretary for the purposes of this paragraph; and
   (b) the good is dispensed on the prescription of a medical practitioner who has prescribed the medicine in accordance with good medical practice:
(3) A person who signs a statement referred to in subparagraph (2)(a)(iii) must send a copy of the statement to the Secretary within 4 weeks of signing it.

Maximum Penalty: $1,000.

(4) This regulation does not affect the operation of regulation 12.

(5) In this regulation:

- **Category A patient** means a person who is seriously ill with a condition from which death is reasonably likely to occur within a matter of months, or from which premature death is reasonably likely to occur in the absence of early treatment.

- **informed consent**, in relation to treatment or proposed treatment, means consent freely given by a person on the basis of information concerning the potential risks and benefits of the treatment that was sufficient information to allow the person to make an informed decision whether to consent to treatment.

12AA Applications for special and experimental uses.

Without limiting the information that may be required by the Secretary under subsection 19(2) of the Act, that information may include, in relation to therapeutic goods that subject of an application under subsection 19(1) of the Act for the use described in paragraph 19(1)(b) of the Act:

(a) the names of the members of the ethics committee that has given approval for each proposed clinical trial of the goods and that will have responsibility for monitoring that conduct of each trial; and

(b) the name of, and the contact details for, the principal investigator for each trial; and

(c) the name of the person who will be in charge of the trial (or each trial site, if the trial is to be conducted at more than one site), unless that person is the principal investigator; and

(d) information about whether or not any conditions specified by the committee have been met.

12AB Goods imported, etc, for experimental uses

(1) For subsection 19(1A) of the Act, this regulation specifies conditions attaching to an approval for the importation, exportation or supply of therapeutic goods for use solely for experimental purposes in humans.

(2) Before any clinical trials proposed to be undertaken in relation to the goods are started, the National Manager, Therapeutic Goods Administration, must receive from the person to whom the approval is granted, and the principal investigator for each trial site:

(a) a written assurance that clinical trials will be conducted in accordance with the Guidelines for Good Clinical Practice (the Practice Guidelines), as in force from time to time, published jointly by the International Conference on Harmonisation on Technical Requirements for Registration of Pharmaceuticals for Human Use and the Committee for Medicinal Products; and

(b) a written undertaking:

(i) to comply with requests by an authorised person, whether made before or after the start of a trial, to give information about the conduct of the trial; and

(ii) allow an authorised person to do the things mentioned in regulation 12AC.
12AC  Powers of authorised persons in relation to goods imported, etc, for experimental uses

(1) An authorised person may, in relation to a clinical trial mentioned in regulation 12AB:
   (a) enter the site of the trial; and
   (b) search the site and any thing on the site; and
   (c) inspect, examine, take measurements of, or conduct tests on (including by the taking of samples), any thing on the site that relates to the trial; and
   (d) take photographs, make video recordings or make sketches of the site or any thing on the site; and
   (e) inspect any book, record or document on the site that relates to the trial; and
   (f) request the principal investigator to:
      (i) answer any questions put by the authorised person; and
      (ii) produce any book, record or document requested by the authorised person.

(2) An authorised person is not entitled to do a thing mentioned in subregulation (1) if:
   (a) the principal investigator or any other person present at the site concerned and in apparent control, requests the authorised person to produce his or her identity card for inspection; and

   (b) the authorised person fails to comply with the request.

   Note  For identity card; see section 52 of the Act.

(3) The principal investigator, or any other person present at the site and in apparent control, is entitled to observe a search conducted under paragraph (1)(b), but must not impede the search.

(4) Subregulation (3) does not prevent 2 or more areas of the site being searched at the same time.

12AD  Use of goods for experimental purposes – specified conditions

For subsection 19(4A) of the Act, the following conditions are specified:

   (a) the use of therapeutic goods in a clinical trial must be in accordance with the Practice Guidelines;

   (b) the use must be comply with a procedural protocol determined by the ethics committee that gave approval for the clinical trial of the goods and that has the function of monitoring the conduct of the trial at each trial site;

   (c) the use must be in accordance with the ethical standards set out in the National Statement on Ethical Conduct in Research Involving Humans, as in force from time to time, published by the National Health and Medical Research Council;

   (d) the use must cease if the ethics committee mentioned in paragraph (b) informs the principal investigator that the use is inconsistent with:
      (i) the protocol mentioned in paragraph (b); or
      (ii) any condition subject to which approval for the use was given.
12B Exemptions for special and experimental use

(1) For paragraph 19(6)(a) of the Act, in relation to therapeutic goods that are medicines, a medical practitioner is in the prescribed class of medical practitioners if he or she is engaged in clinical practice outside a hospital and

(a) has demonstrated that, in relation to the proposed supply, he or she does not have access to an ethics committee that could approve the supply; and

(b) has, from a specialist college having an established expertise relevant to use of the medicines concerned, endorsement to supply the medicines.

(2) The class of recipients prescribed for the purposes of paragraph 19(6)(b) of the Act is the class of recipients consisting of persons each of whom is suffering from a life-threatening, or otherwise serious, illness or condition.

(3) For the purposes of paragraph 19(7) of the Act, the prescribed circumstances in which a medicine, or a class of medicines, may be supplied in accordance with an authority under section 19(5) of the Act are that the supplier of the medicine or class of medicines complies with the treatment directions (if any) mentioned in the authority for the medicine or class of medicine.

(4) For the purposes of paragraph 19(7) of the Act, the prescribed circumstances in which a therapeutic device, or a class of therapeutic devices, may be supplied in accordance with an authority under section 19(5) of the Act are:

(a) that the medical practitioner whom the Secretary authorises under subsection 19(5):

(i) is a specialist in clinical practice at a hospital; and

(ii) is endorsed by the ethics committee of that hospital; and

(b) that the authority states the particular therapeutic intervention, or class of therapeutic intervention, for which the authorised person may supply the therapeutic device or class of therapeutic devices.

47A Delegations – powers under paragraph 19(1)(a) of the Act.

(1) In this regulation, delegation means a delegation, under subsection 57(3), of the Act, of powers of the Secretary under paragraph 19(1)(a) of the Act, that relates to specified therapeutic goods.

(2) A delegation may only be to a person who:

(a) is a medical practitioner registered in a State or Territory and employed by an institution that has an ethics committee; and

(b) subject to subregulation (3), is proposed by the medical superintendent or, if there is no medical superintendent, the person occupying a position comparable to that of medical superintendent, of the institution, as a person to be a delegate under subsection 57(3) of the Act.

(3) If:

(a) a person proposes another person under paragraph (2)(b) as a person to be a delegate; and

(b) that other person becomes a delegate;

the first-mentioned person must supervise each approval that the delegate grants under the delegation.
(4) A delegation must describe the person or class of persons to be treated with the therapeutic goods to which the delegation relates.

(5) A delegation may be made for the purpose of allowing the delegate to grant an approval in relation to:

(a) a particular item of therapeutic goods; or
(b) a particular class of therapeutic goods;
   for treating a specific illness or condition.

(6) A delegate may grant an approval under a delegation only if:

(a) A medical practitioner other than the delegate has stated in writing that the person to be treated with the item of therapeutic goods to which the approval relates has an illness or condition that requires treatment with the item; and

(b) An ethics committee has agreed to the granting of approval under paragraph 19(1)(a) of the Act for the use, in the circumstances in which the delegate grants the approval, of the item of therapeutic goods to which the delegation relates.

Schedule 5A excerpt

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<tr>
<th>Column 1</th>
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<tbody>
<tr>
<td>Item 3</td>
<td>Therapeutic goods</td>
<td>Conditions</td>
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<td>Therapeutic goods used solely for experimental purposes in humans</td>
<td>(a) before starting to use the goods, the sponsor must notify the Secretary:</td>
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<td>(i) in a form approved by the Secretary; and</td>
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<td>(ii) in accordance with the requirements (if any) determined by the Secretary for the form of notification;</td>
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<td>that the sponsor intends to sponsor a clinical trial using specified goods; and</td>
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<td>(b) the notification must be accompanied by the relevant notification fee referred to in item 14 or 14A of Schedule 9; and</td>
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<td>(c) the approval of the goods for this purpose must be given by the sponsor (if the sponsor is conducting the trial), or by the body or organisation conducting the trial for the sponsor, having regard to the advice of the ethics committee that has, or will assume, responsibility for monitoring the conduct of the trial; and</td>
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<td>(d) the terms of the approval by the sponsor, body or organisation referred to in paragraph (c) must be no less restrictive than the terms advised by the ethics committee;</td>
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</table>
Schedule 5A excerpt continued…

<table>
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<tr>
<td>(e)</td>
<td>and the Secretary must not, at any time:</td>
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<td>(i) have become aware that to conduct or continue the trial would be contrary to the public interest; and</td>
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<td>(ii) have directed that the trial not be conducted, or be stopped; and</td>
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<td>the sponsor (if the sponsor is conducting the trial), or the body or organisation conducting the trial for the sponsor, must not receive, or have received, advice from the ethics committee that is inconsistent with the continuation of the trial; and</td>
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<td>the conditions set out in regulation 12AD must be complied with, as if that regulation applied to a person using therapeutic goods under this item.</td>
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APPENDIX 2. NOTIFICATION OF INTENT TO SUPPLY UNAPPROVED THERAPEUTIC GOODS UNDER THE CLINICAL TRIAL NOTIFICATION (CTN) SCHEME

(CTN FORM)
CLINICAL TRIAL NOTIFICATION SCHEME

Notification of Intent to Supply Unapproved Therapeutic Goods under the Clinical Trial Notification (CTN) Scheme

Therapeutic Goods Act 1989

To be used for:

• initial notifications of clinical trials involving medicines and/or medical devices under the Clinical Trial Notification (CTN) Scheme; or
• notification of one or more additional sites for a Clinical Trial previously reported under the Clinical Trial Notification (CTN) Scheme

THIS IS THE FORM APPROVED BY THE SECRETARY OF THE DEPARTMENT OF HEALTH AND AGED CARE

On completion please send this form to the Therapeutic Goods Administration:

<table>
<thead>
<tr>
<th>Courier address</th>
<th>Postal address</th>
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<tr>
<td>The Business Manager</td>
<td>The Business Manager</td>
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<tr>
<td>Business Management Unit</td>
<td>Business Management Unit</td>
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<tr>
<td>Therapeutic Goods Administration</td>
<td>Therapeutic Goods Administration</td>
</tr>
<tr>
<td>136 Narrabundah Lane</td>
<td>PO Box 100</td>
</tr>
<tr>
<td>Symonston ACT 2609</td>
<td>Woden ACT 2606</td>
</tr>
<tr>
<td>Australia</td>
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Cheques should be made payable to “Therapeutic Goods Administration”
PLEASE READ THE FOLLOWING INSTRUCTIONS BEFORE COMPLETING THIS FORM

• Notification under the CTN scheme (or application under the Clinical Trial Exemption (CTX) scheme) is required for clinical investigational use of:
  • any medicine or device not entered in the Australian Register of Therapeutic Goods, including any new formulation of an existing product or any new route of administration; or
  • a marketed medicine or device beyond the conditions of its marketing approval, including new indications extending the use of the product to a new patient group and the extension of doses or duration of treatments outside the approved range.

• Before completing this form, all parties providing certification should read about their respective responsibilities in the clinical trial. These roles are outlined in the following documents:
  • Access to Unapproved Therapeutic Goods - Clinical Trials in Australia, TGA, 2000
  • The National Statement on Ethical Conduct in Research Involving Humans, NHMRC, 1999
  • Guidelines for the Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies, NHMRC, 1999

• Under the Therapeutic Goods Act 1989, the Therapeutic Goods Administration (TGA) has the authority to enquire into and/or audit clinical trials, where necessary, on safety grounds and to investigate non-compliance with either Good Clinical Practice guidelines or legislative requirements. In addition, information concerning the supply and use of unregistered therapeutic goods may be released to State and Territory regulatory authorities under section 61 of the Therapeutic Goods Act 1989. Completion of this notification form requires the sponsor of the trial, principal investigator, Human Research Ethics Committee and the approving authority to agree, in writing, to make all records available to TGA on request and to cooperate with TGA investigations. The sponsor of the trial is also required to acknowledge the potential for release of information about the use of unregistered therapeutic goods to State and Territory regulatory authorities.

• For the purpose of notifying a Clinical Trial of Medicines or Medical Devices, the “sponsor of the trial” is the company, organisation, institution, body or individual (enterprise) that initiates, organises and supports a clinical study of an investigational product on human subjects. As a result, the sponsor of the trial takes responsibility for the overall conduct of the trial. The “approving authority” is the body, organisation or institution that approves the conduct of the trial at the site. Thus, the Human Research Ethics Committee (HREC) can also be the Approving Authority for a particular trial site. The same person can sign on behalf of the HREC and the Approving Authority but they should indicate their position or capacity in relation to each. Also, the same person may sign on behalf of the sponsor of the trial and the Approving Authority. However, because of the potential for conflict of interest, the same person cannot sign on behalf of the sponsor of the trial and the HREC.

• Key points for sponsors of the trial to check before completing and submitting the CTN form to the Therapeutic Goods Administration (TGA) are:
  • You will need to have a TGA Enterprise ID in order for your notification fee to be accepted and receipted by the TGA Business Management Unit. If you have not conducted business with the TGA before, you will need to obtain an Enterprise ID. Enterprise Details Forms (1531(9602)) are available from the Experimental Drugs Section or the TGA Business Management Unit and can be submitted simultaneously with this notification.
  • You will need to obtain signatures from the relevant Human Research Ethics Committee, Approving Authority and Principal Investigator for each site at which the trial will be conducted.
  • Sites may be notified in any sequence. That is, all sites can be notified in the first instance; notified in groups; or notified singly. The fee for notification of a multi site trial is the same as that for a single site trial providing the sites involved in the multi site trial are declared simultaneously.
However, if sites are notified individually or added for an existing trial, an additional fee equivalent to the fee for a single site applies to each notification. Full details of the fee structure for the CTN scheme can be obtained from the Business Management Unit of TGA.

- Each new and/or additional trial site must be notified to the TGA prior to the trial commencing at that site.
- You must assign a protocol number to each new trial. Take care not to assign to a new trial a protocol number used previously. Also, check that the protocol number notified to the TGA matches the version of the protocol approved by the Human Research Ethics Committee. When notifying additional sites, quote the protocol number exactly.
- The TGA assigns a unique clinical trial number. The clinical trial number will appear on an acknowledgement letter from the TGA. Subsequent notifications to TGA of additional trial sites and other correspondence relating to the clinical trial post acknowledgement, such as reporting of adverse reactions, should include the protocol number and the clinical trial number as points of reference.
- A CTN notification is not effective until the correct fee has been paid.
SECTION 1. TO BE COMPLETED BY THE SPONSOR OF THE TRIAL

1.1 Notification Type
Complete this section for all notifications. Select one box only. If multiple sites are being notified, complete a 'Trial Site Details' page for each site:

- Initial notification of a single CTN site (new trial)
- Subsequent notification of a single additional CTN site
- Initial notification of multiple CTN sites (new trial)
- Subsequent notification of multiple additional CTN sites

1.2 Use of Restricted Goods
Complete this section for all notifications of medicines only.

Does this trial involve the use of any medicine as an abortifacient or for "post-coital" or "emergency" contraception in women, or the use of a progesterone antagonist or a vaccine against human chorionic gonadotrophin for any purpose?

- Yes
- No

1.3 Sponsor of the trial
Complete this section for all notifications. In cases where a trial is sponsored by an individual, that person's name may also be the enterprise business name. Business details can be provided to TGA via the Enterprise Details Form. If in doubt, contact the Experimental Drugs Section.

- Sponsor name (Enterprise Business Name)
- Enterprise ID Code (If known)

1.4 Trial details
 Protocol Number
(Complete for all notifications; if adding a site, Clinical Trial Number)
If adding a site, Clinical Trial Number (assigned by TGA; see acknowledgment letter for previously notified sites. Leave blank if unsure)
**Title of study**
Complete for all notifications. Maximum of 255 characters. Title should indicate the aim of the trial and give a broad description of the trial. Include, for example: phase, indication(s) being treated, main medicines and comparators, use of placebo-control, focus of the study, patient population and any other significant or novel aspects. "A Trial of X" is not adequate. Similar detail is required for device trials.

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**Trial Type**
Complete for initial notification only of trials involving the use of medicines; tick relevant box(es) or otherwise describe.

- Phase 1
- Phase 2
- Phase 3
- Phase 4
- Bioavailability/bioequivalence

Describe if necessary: ____________

**This trial**
Complete for initial notification only; tick only those boxes which are applicable. Note: For the purpose of this document, gene therapy includes related therapies that overlap with the traditional concept of gene therapy by virtue of the fact that they introduce DNA into somatic cells. For example, modifications to immunisation strategies in which DNA, rather than protein, is used to generate an immune response for the purposes of prevention or treatment of chronic viral infection or as part of cancer treatment, would be considered a related therapy.

- involves the use of a medicine
- is placebo controlled
- is also being conducted in other countries
- involves the use of a device
- is comparator controlled
- involves gene therapy

**Expected trial start date**
(Complete for initial notification) / / 

**Expected trial completion date**
(Complete for all notifications) / /
**Medicine details**

Complete for all notifications of clinical trials involving medicines. Do not use for clinical trials involving the use of devices only. List the therapeutically active components in formulations being used in the trial. All medicines being trialed should be listed, including comparators. The form has space for three medicines. For more than four, attach details of additional medicines in the same format.

For the **Active Name**, enter the active ingredient name using where possible, the Australian Approved Name (AAN). If no AAN, BAN or USAN has been assigned, a code name (see below) or chemical name must be given. For the **Code Name**, enter code name/s used currently or previously to identify the drug. For the **Dosage Form**, enter a primary descriptor for dosage form (eg. tablet, injection) and include a secondary descriptor (eg. sustained release, microsphere emulsion) where necessary, particularly if a new dosage form is the focus of the trial.

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<th>Active name</th>
<th>Trade name</th>
<th>Code name</th>
<th>Dosage form</th>
<th>Strength</th>
<th>Biological origin</th>
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Device details

Complete for all notifications of clinical trials involving devices. Do not use for clinical trials involving the use of medicines only. Provide: name (trade name(s), if applicable); description of the device; details of design, composition, specification, mode of action and application; and method of use.

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<th>Site expected start</th>
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<tr>
<td>Site</td>
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<tr>
<td>Site address</td>
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1.5 Trial site details

Complete for all notifications. Submit a Trial Site Details page for each site at which the trial will be conducted. Enter the name and location of the site (e.g., name and address of hospital, institution, clinic or practice). For large institutions, the address need not include specific department details unless essential to identify the location or unless the unit/department/practice operates as a separate entity within the campus. In some rare circumstances, it will be appropriate to notify a trial as a composite site trial. For example, a GP-based trial conducted by a general practice network may need to be notified as a composite site trial. The site details should indicate clearly that there are multiple sites involved and include the name, address and contact numbers for the principal investigator. A list of all practices (sites) involved should be submitted as an attachment. The ethics committee and approving authority for such a trial must have appropriate authority for all sites. A sponsor intending to notify a composite site for the first time should contact the Experimental Drugs Section if they have any questions regarding the use of composite sites.
1.6 Sponsor certification

Complete this section last for all notifications. In the Name field, print the name of the person signing the form on behalf of the company, organisation, institution, body or individual sponsoring the trial (Do not enter a company or organisation name here - the entity name appears in Section 1.5). In the Position field, state the person’s position within, or relationship to, the entity sponsoring the trial.

I, the undersigned, certify:

- all details contained in this form are true and accurate, and all required information and signatures have been included;
- the sponsor of the trial named in section 1.3 of this form is taking overall responsibility for the conduct of the trial;
- the sponsor of the trial has met or agrees to meet all Human Research Ethics Committee conditions of approval;
- the investigator(s) has/have training and experience relevant to the conduct of this trial;
- the participating institution has resources adequate for the proper conduct of the trial;
- the sponsor of the trial has received an undertaking from the investigator(s) to conduct the trial in accordance with the Guidelines for Good Clinical Practice as described in regulation 12AB(2)(a) of the Therapeutic Goods Regulations and the National Statement of Ethical Conduct in Research Involving Humans as described in regulation 12AD(c) of the Therapeutic Goods Regulations;
- the sponsor of the trial agrees to report all serious and unexpected adverse reactions to the Therapeutic Goods Administration;
- the sponsor of the trial agrees to conduct the trial in accordance with the Guidelines for Good Clinical Practice as described in regulation 12AB(2)(a) of the Therapeutic Goods Regulations and the National Statement of Ethical Conduct in Research Involving Humans as described in regulation 12AD(c) of the Therapeutic Goods Regulations;
- the sponsor of the trial agrees to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12MC and regulation 12AB of the Therapeutic Goods Regulations; and
- the sponsor of the trial accepts that information concerning the use of unregistered therapeutic goods may be released to State and Territory regulatory authorities.

Name (Print) __________________________ Position __________________________

Signature / / Phone __________________________

Fax __________________________
SECTION 2. TO BE COMPLETED BY THE PRINCIPAL INVESTIGATOR

The principal investigator is the person responsible for the conduct of the clinical trial at a trial site. In the case of a trial being conducted by a team of individuals at the site, the principal investigator is the responsible leader of the team.

Principal investigator certification

I, the undersigned:

• am the principal investigator at the site shown in section 1.5 of this form;
• agree to personally supervise the clinical trial at this site in accordance with the relevant current protocol(s) and will only make changes in a protocol after approval by the sponsor;
• have received and read the trial protocol and other relevant information;
• have met or agree to meet all Human Research Ethics Committee conditions of approval for this trial;
• acknowledge my obligations with respect to monitoring patient safety, record management and reporting requirements for adverse events;
• agree to ensure that all associates, colleagues and employees assisting in the conduct of the trial are informed of their obligations in meeting the above requirements;
• agree to promptly report to the Human Research Ethics Committee all unanticipated problems and will not make any changes to the trial without Human Research Ethics Committee and sponsor approval, except where necessary to eliminate apparent immediate hazards to subject safety;
• agree to conduct the clinical trial(s) in accordance with the Guidelines for Good Clinical Practice as described in regulation 12AB(2)(a) of the Therapeutic Goods Regulations and the National Statement of Ethical Conduct in Research Involving Humans as described in regulation 12AD(c) of the Therapeutic Goods Regulations;
• agree to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations;
• accept that information concerning the use of unregistered therapeutic goods may be released to State and Territory regulatory authorities.

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<th>Name (Print)</th>
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SECTION 3. TO BE COMPLETED BY THE HUMAN RESEARCH ETHICS COMMITTEE
RESPONSIBLE FOR MONITORING THE TRIAL

This section must be completed by a Human Research Ethics Committee (HREC) that satisfies the following definition of an ethics committee, as set out in the Therapeutic Goods Act 1989, otherwise the notification is invalid:

A committee constituted and operating in accordance with guidelines issued by the National Health and Medical Research Council as in force from time to time and which has notified its existence to the Australian Health Ethics Committee.

HREC certification should not be given until all conditions of approval of the protocol by that HREC have been met. Wherever possible, the certification should be completed by the Chair or Deputy Chair of the Human Research Ethics Committee. Guidelines for the approval of clinical trials by HRECs are located at Chapter 12. The National Statement on Ethical Conduct in Research Involving Humans, 1999 and in the TGA publication ‘HRECs and the Therapeutic Goods Legislation’.

For trials of gene therapy and related therapies, the proposal must be approved by all relevant bodies as per the NHMRC Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies.

HREC name

HREC address

Postcode

Protocol Number approved by HREC

Does the trial for which approval is being given involve the use of gene therapy or a related therapy?
(See NHMRC Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies)

Yes ☐
No ☐

If the trial involves gene therapy or a related therapy, has the Gene and Related Therapies Research Advisory Panel (GTRAP) agreed that the trial can be conducted under the CTN Scheme?

Yes ☐
No ☐
Human Research Ethics Committee Certification

I, the undersigned, certify:

- I am a member of the above named Human Research Ethics Committee;
- the above named Human Research Ethics Committee is a properly constituted ethics committee and operates in accordance with the guidelines issued by the National Health and Medical Research Council and has notified its existence to the Australian Health Ethics Committee;
- the above named Human Research Ethics Committee, having regard to the guidance provided by the National Statement on Ethical Conduct in Research Involving Humans and, where applicable, the Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies, has approved the clinical trial protocol identified above and has assumed responsibility for monitoring the conduct of the trial; and
- the above named Human Research Ethics Committee agrees to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations.

Name (Print) ____________________________

Signature ____________________________

Position ____________________________

Phone ____________________________

Fax ____________________________
SECTION 4. TO BE COMPLETED BY THE AUTHORITY APPROVING THE CONDUCT OF THE TRIAL

Complete for all notifications. In cases where the Human Research Ethics Committee or Approving Authority for more than one site is the same, it is still necessary to submit a Trial Site Details Page for each site. The bodies approving the conduct of the trial at each site need to be declared individually. This requirement also still applies in cases where, for example, an Area Health Service or Hospitals Group may encompass several different institutions.

The Approving Authority must appoint a person to be responsible for giving approval on its behalf. The terms of approval for the conduct of the trial must be consistent with the Human Research Ethics Committee’s (HREC) recommendations and these terms must be no less restrictive than the HREC advice.

Approving Authority name

HRREC address

Postcode

Approving Authority Certification

I, the undersigned

• am authorised to represent the body, organisation or institution at which the above mentioned clinical trial will be conducted and, having regard to the advice and approval of the trial protocol by the Human Research Ethics Committee responsible for monitoring the trial at this site, give approval for this trial to proceed;

• undertake that the use of the drug will comply with all relevant Commonwealth and State or Territory legislation; and

• undertake to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations.

Name (Print) Position

Signature Phone

Fax

52

2954 (0105)
APPENDIX 3. SUPPLY OF UNAPPROVED THERAPEUTIC GOODS UNDER THE CLINICAL TRIAL EXEMPTION (CTX) SCHEME

PART 2 NOTIFICATION OF THE CONDUCT OF A TRIAL UNDER A CTX APPROVAL
## CLINICAL TRIAL EXEMPTION SCHEME

**Supply of Unapproved Therapeutic Goods under the Clinical Trial Exemption (CTX) Scheme**

**Therapeutic Goods Act 1989**

**PART 2 NOTIFICATION OF THE CONDUCT OF A TRIAL UNDER THE CTX SCHEME**

To be used for CTX Scheme trials of medicines and medical devices

<table>
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<tr>
<th>For medicines</th>
<th>or</th>
<th>For medical devices</th>
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<tbody>
<tr>
<td>The Medical Advisor</td>
<td>Chief Clinical Advisor</td>
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<tr>
<td>Experimental Drugs Section</td>
<td>Conformity Assessment Branch</td>
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<tr>
<td>Drug Safety and Evaluation Branch</td>
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For Office Use Only – EDS/CAB

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<th>Date Notification received</th>
<th>CTX Number</th>
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PLEASE READ THE FOLLOWING INSTRUCTIONS BEFORE COMPLETING PART 2

- A sponsor cannot commence a CTX trial until:
  - written approval has been received from the TGA regarding the CTX application (Part 1); and
  - approval for the conduct of the trial has been obtained from an ethics committee and the institution at which the trial will be conducted.

There are two forms, each reflecting these separate processes (Parts), that must be submitted by the sponsor. Part 1 constitutes the formal CTX application. It must be completed by the sponsor and submitted to TGA with data for evaluation. Part 2 (this form) is used to notify the commencement of each new trial conducted under the CTX scheme as well as new sites in ongoing CTX trials. The notification, containing certifications of the sponsor, principal investigator, HREC and Approving Authority, is required under the TGA of the conduct of each specific trial and to demonstrate that all of the parties involved in the conduct of individual trials have complied with legislative and regulatory requirements and agree to release information to the TGA about the conduct of the trial in the event of an inquiry or audit of the trial by the TGA. There is no fee for notification of trials under the CTX scheme. Part 2 must be completed and submitted to TGA within 28 days of either the commencement of each new trial or the addition of a new site in an ongoing CTX trial.

- Under the *Therapeutic Goods Act 1989*, the Therapeutic Goods Administration (TGA) has the authority to inquire into and/or audit clinical trials, where necessary, on safety grounds and to investigate non-compliance with either Good Clinical Practice guidelines or legislative requirements. In addition, information concerning the supply and use of unregistered therapeutic goods may be released to State and Territory regulatory authorities under section 61 of the Therapeutic Goods Act 1989. Completion of this notification form requires the sponsor of the trial, principal investigator, Human Research Ethics Committee and the approving authority to agree, in writing, to make all records available to TGA on request and to cooperate with TGA investigations. The sponsor and principal investigator at each site are also required to acknowledge the potential for release of information about the supply and handling of unregistered therapeutic goods to State and Territory regulatory authorities.

- For the purpose of notifying a Clinical Trial of Medicines or Medical Devices, the “sponsor of the trial” is the company, organisation, institution, body or individual (enterprise) that initiates, organises and supports a clinical study of an investigational product on human subjects. As a result, the sponsor of the trial takes responsibility for the overall conduct of the trial. The “approving authority” is the body, organisation or institution that approves the conduct of the trial at the site. Thus, the Human Research Ethics Committee (HREC) can also be the Approving Authority for a particular trial site. The same person can sign on behalf of the HREC and the Approving Authority but they should indicate their position or capacity in relation to each. Also, the same person may sign on behalf of the sponsor of the trial and the Approving Authority. However, because of the potential for conflict of interest, the same person cannot sign on behalf of the sponsor of the trial and the HREC.

- Key points for sponsors of the trial to check before completing and submitting this notification to the Therapeutic Goods Administration (TGA) are:
  - You will need to obtain signatures from the relevant Human Research Ethics Committee, Approving Authority and Principal Investigator for each site at which the trial will be conducted.
  - Sites may be notified in any sequence. That is, all sites can be notified in the first instance; notified in groups; or notified singly. There is no fee associated with the notification of trials conducted under the CTX scheme.
  - You must assign a protocol number to each new trial. Take care not to assign to a new trial a protocol number used previously. Also, check that the protocol number notified to the TGA matches the version of the protocol approved by the Human Research Ethics Committee. When notifying additional sites, quote the protocol number exactly.
  - The TGA assigns a unique clinical trial number. The clinical trial number will appear on an acknowledgement letter from the TGA. Subsequent notifications to TGA of additional trial sites and other correspondence relating to the clinical trial post acknowledgement, such as reporting of adverse reactions, should include the protocol number and the clinical trial number as points of reference.
SECTION 1. TO BE COMPLETED BY THE SPONSOR OF THE TRIAL

1.1 Sponsor of the trial

Complete this section for all notifications. Use name stated in CTX application.

Sponsor name
(Enterprise Business Name)

Enterprise ID Code

1.2 Investigational drug/medical device

Use active name(medicines) or device name. Details must be consistent with those contained in CTX application (Part 1 form).

1.
2.
3.

CTX Number / / Complete for all notifications. Use the number assigned by TGA to the CTX application.

Relevant TGA file number(s) from previous correspondence

1.3 Notification Type

Complete this section for all notifications. Select one box only. If multiple sites are being notified, complete a ‘Trial Site Details’ page for each site.

Initial notification of a new CTX trial (single site) Subsequent notification of a single additional site

Initial notification of a new CTX trial (multiple sites) Subsequent notification of multiple additional sites

1.4 Trial details

Protocol Number 
(Trial start date / / )

(Complete for all notifications, maximum of 20 characters)

Expected completion date / /
Title of study

Title should indicate the aim of the trial and give a broad description of the trial. Include, for example: phase, indication(s) being treated, main medicines and comparators, use of placebo control, focus of the study, patient population and any other significant or novel aspects. "A Trial of X" is not adequate. Similar detail is required for device trials.

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<th>Title of study</th>
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Trial Type

Complete for trials involving the use of medicines only; tick relevant box(es) or otherwise describe.

- Phase 1
- Phase 2
- Phase 3
- Phase 4
- Bioavailability/bioequivalence

Describe if necessary

This trial

Complete for initial notification of new trial only; tick only those boxes which are applicable.

- Is placebo controlled
- Is a multicentre trial
- Is also being conducted in other countries
- Is comparator controlled

Comparators

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<td>Active name</td>
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<td>Trade name</td>
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<tr>
<td>Route of administration</td>
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<tr>
<td>Dosage form</td>
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<td>Strength</td>
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</table>

| 2            |
| Active name  |
| Trade name   |
| Route of administration |
| Dosage form  |
| Strength     |

| 3            |
| Active name  |
| Trade name   |
| Route of administration |
| Dosage form  |
| Strength     |
1.5 Trial site details

Complete for all notifications. Submit a Trial Site Details page for each site at which the trial will be conducted. Enter the name and location of the site (e.g. name and address of hospital, institution, clinic or practice). For large institutions, the address need not include specific department details unless essential to identify the location or unless the unit/body/practice operates as a separate entity within the campus. In some rare circumstances, it will be appropriate to notify a trial as a composite site trial. For example, a GP-based trial conducted by a general practice network may need to be notified as a composite site trial. The site details should indicate clearly that there are multiple sites involved and include the name, address and contact numbers for the principal investigator. A list of all practices/sites involved should be submitted as an attachment. The ethics committee and approving authority for such a trial must have appropriate authority for all sites operating. A sponsor intending to notify a composite site for the first time should contact the Experimental Drugs Section if they have any questions regarding the use of composite sites.

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<tr>
<th>Site</th>
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1.6 Sponsor certification

Complete this section last for all notifications. In the Name field, print the name of the person signing the form on behalf of the company, organisation, institution, body or individual sponsoring the trial. In the Position field, state the person’s position within, or relationship to, the entity sponsoring the trial.

I, the undersigned, certify:

- the TGA has approved the supply of the investigational product(s) listed in section 1.2 of this form;
- all details contained in this form are true and accurate and all required information and signatures have been included;
- the sponsor of the trial has met or agrees to meet all Human Research Ethics Committee conditions of approval;
- the sponsor of the trial named in section 1.1 of this form is taking overall responsibility for the conduct of the trial;
- the investigator(s) has/have training and experience relevant to the conduct of this trial;
- the participating institution has resources adequate for the proper conduct of the trial;
- the sponsor of the trial has received an undertaking from the investigator(s) to conduct the trial in accordance with the Guidelines for Good Clinical Practice as described in regulation 12AB(2)(a) of the Therapeutic Goods Regulations and the National Statement of Ethical Conduct in Research Involving Humans as described in regulation 12AD(c) of the Therapeutic Goods Regulations;
- the sponsor of the trial agrees to report all serious and/or unexpected adverse reactions to the Therapeutic Goods Administration;
- the sponsor of the trial agrees to conduct the trial in accordance with the Guidelines for Good Clinical Practice as described in regulation 12AB(2)(a) of the Therapeutic Goods Regulations and the National Statement of Ethical Conduct in Research Involving Humans as described in regulation 12AD(c) of the Therapeutic Goods Regulations;
- the sponsor of the trial agrees to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations; and
- the sponsor accepts that information concerning the use of unregistered therapeutic goods may be released to State and Territory regulatory authorities.

Name (Print)  
Position

Signature  
/ /  
Phone

Fax
SECTION 2. TO BE COMPLETED BY THE PRINCIPAL INVESTIGATOR

The principal investigator is the person responsible for the conduct of the clinical trial at a trial site. In the case of a trial being conducted by a team of individuals at the site, the principal investigator is the responsible leader of the team.

Principal investigator certification

I, the undersigned:

- am the principal investigator at the site shown in section 1.5 of this form;
- agree to personally supervise the clinical trial at this site in accordance with the relevant current protocol(s) and will only make changes in a protocol after approval by the sponsor;
- have received and read the trial protocol and other relevant information;
- have met or agree to meet all Human Research Ethics Committee conditions of approval for this trial;
- acknowledge my obligations with respect to monitoring patient safety, record management and reporting requirements for adverse events;
- agree to ensure that all associates, colleagues and employees assisting in the conduct of the trial are informed of their obligations in meeting the above requirements;
- agree to promptly report to the Human Research Ethics Committee all unanticipated problems and will not make any changes to the trial without Human Research Ethics Committee and sponsor approval, except where necessary to eliminate apparent immediate hazards to subject safety;
- agree to conduct the trial in accordance with the Guidelines for Good Clinical Practice as described in regulation 12AB(2)(a) of the Therapeutic Goods Regulations and the National Statement of Ethical Conduct in Research Involving Humans as described in regulation 12AD(c) of the Therapeutic Goods Regulations;
- agree to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations; and
- accept that information concerning the use of unregistered therapeutic goods may be released to State and Territory regulatory authorities.

Name (Print)  
Position  
Signature  
Phone  
Fax  

TGA text  7/3/02  10:30 am  Page 61
SECTION 3. TO BE COMPLETED BY THE HUMAN RESEARCH ETHICS COMMITTEE RESPONSIBLE FOR MONITORING THE TRIAL

This section must be completed by a Human Research Ethics Committee (HREC) that satisfies the following definition of an ethics committee, as set out in the Therapeutic Goods Act 1989, otherwise the notification is invalid:

A committee constituted and operating in accordance with guidelines issued by the National Health and Medical Research Council as in force from time to time and which has notified its existence to the Australian Health Ethics Committee.

HREC certification should not be given until all conditions of approval of the protocol by that HREC have been met. Wherever possible, the certification should be completed by the Chair or Deputy Chair of the Human Research Ethics Committee. Guidelines for the approval of clinical trials by HRECs are located at Chapter 12, The National Statement on Ethical Conduct in Research Involving Humans, 1999 and in the TGA publication 'HRECs and the Therapeutic Goods Legislation'.

For trials of gene therapy and related therapies, the proposal must be approved by all relevant bodies as per the NHMRC Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies.

<table>
<thead>
<tr>
<th>HREC Name</th>
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<tbody>
<tr>
<td>HREC address</td>
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<td>Postcode</td>
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Protocol Number approved by HREC

**Human Research Ethics Committee Certification**

I, the undersigned, certify:

- I am a member of the above named Human Research Ethics Committee;
- the above named Human Research Ethics Committee is a properly constituted ethics committee and operates in accordance with the guidelines issued by the National Health and Medical Research Council and has notified its existence to the Australian Health Ethics Committee;
- the above named Human Research Ethics Committee, having regard to the guidance provided by the National Statement on Ethical Conduct in Research Involving Humans and, where applicable, the Guidelines for Ethical Review of Research Proposals for Human Somatic Cell Gene Therapy and Related Therapies, has approved the clinical trial protocol identified above and has assumed responsibility for monitoring the conduct of the trial; and
- the above named Human Research Ethics Committee agrees to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations.

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<td>Position</td>
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Signature / /

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<th>Phone</th>
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Fax

2956 (0105)
SECTION 4. TO BE COMPLETED BY THE AUTHORITY APPROVING THE CONDUCT OF THE TRIAL

Complete for all notifications. In cases where the Human Research Ethics Committee or Approving Authority for more than one site is the same, it is still necessary to submit a Trial Site Details Page for each site. The bodies approving the conduct of the trial at each site need to be declared individually. This requirement also still applies in cases where, for example, an Area Health Service or Hospitals Group may encompass several different institutions.

The Approving Authority must appoint a person to be responsible for giving approval on its behalf. The terms of approval for the conduct of the trial must be consistent with the Human Research Ethics Committee’s (HREC) recommendations and these terms must be no less restrictive than the HREC advice.

Approving Authority name

Address

Postcode

Approving Authority Certification

I, the undersigned

• am authorised to represent the body, organisation or institution at which the above mentioned clinical trial will be conducted and, having regard to the advice and approval of the trial protocol by the Human Research Ethics Committee responsible for monitoring the trial at this site, give approval for this trial to proceed;

• undertake that the use of the drug will comply with all relevant Commonwealth and State or Territory legislation, and

• undertake to comply with requests by an authorised person, whether made before or after the start of a clinical trial, to give information about the conduct of the clinical trial and allow an authorised officer (regulation 47AA of the Therapeutic Goods Regulations) to do the things mentioned in regulation 12AC and regulation 12AB of the Therapeutic Goods Regulations.

Name (Print)  Position

Signature  Phone

//  Fax
APPENDIX 4. HREC LETTER OF ENDORSEMENT FOR AUTHORISED PRESCRIBERS
ETHICS COMMITTEE LETTERHEAD

[Dr’s name]
[Title (if applicable)]
[Dr’s address]

Dear Dr [ ],

Ethics committee endorsement for the purpose of becoming an Authorised Prescriber of an unapproved product under section 19(5) of the Therapeutic Goods Act

The [name] Human Research Ethics Committee hereby endorses you for the purpose of becoming an Authorised Prescriber under section 19(5) of the Therapeutic Goods Act.

This endorsement is restricted to the following circumstances:

Unapproved product: [drug/ device: trade and generic names if available]
Indication for use: [illness/condition/class of patient]
Site(s) covered by the endorsement: [hospital/rooms etc]
Conditions imposed by the HREC: [provision of usage reports to HREC]
[reporting of adverse events to HREC]

Please present a copy of this endorsement letter to the TGA as part of your application to become an Authorised Prescriber.

Yours sincerely

[ ]
Chair
[ ] Human Research Ethics Committee
Date / /
APPENDIX 5. CONSENT TO TREATMENT AND INDEMNITY FOR USE OF PRODUCTS DERIVED FROM HUMAN BLOOD OR PLASMA
SPECIAL ACCESS SCHEME

Consent to Treatment and Indemnity for Use of Products Derived from Biological Tissues including Human Blood or Plasma

I, ..........................................................................................................
(name of patient or parent/guardian)

understand that the Commonwealth can give no guarantee as to the quality, safety or efficacy of .............................................................................................................(name of product), particularly as regards any prion or viral inactivation procedures used in its manufacture. Accordingly, the Commonwealth can accept no liability for its safety, quality or efficacy.

I understand that this product is not registered for use in Australia but that use of the product may be approved under the provisions of the Special Access Scheme.

I confirm that the above statements have been explained to me and with this knowledge agree to administration of the product to me/my ward.

Patient's name: .................................................................

Signature of patient: ................................................................. Date: ............................................
(or parent/guardian)

Signature of witness: ................................................................. Date: ............................................

I have explained the above statements to the patient or the patient's parent/guardian.

Treating physician: .................................................................

Signature: ................................................................. Date: ............................................

Fax completed form together with request for SAS approval to:

The SAS Officer, TGA on 02 6232 8112

Human Ethics Committees and the Therapeutic Goods Legislation June 2001
Appendix 3
Australian Health Ethics Committee Information Sheets
The introduction of the CTN Scheme in 1991 deregulated the conduct of clinical trials in Australia by reducing the involvement of the Therapeutic Goods Administration (TGA). Under the CTN Scheme the TGA must be notified of clinical trials but it does not assess the science or safety of the trial. These responsibilities are devolved to the institution or organisation conducting the trial. The approval of an ethics committee is also required.

A review of the CTN Scheme in 1993 recommended some changes to the conditions which apply to trials conducted under the Scheme. As a result the Therapeutic Goods Regulations have been amended as shown below.

**Therapeutic Goods Regulations**

Schedule 5A (Therapeutic goods exempt from the operation of Part 3 of the Act subject to conditions), Item 3 as amended by Statutory Rules 1994, No 150, reads as follows:

“Therapeutic goods [ie drugs] used solely for experimental purposes in humans

a. before starting to use the goods, the sponsor must notify the Secretary [of the Commonwealth Department of Human Services and Health]:
   i. in a form approved by the Secretary; and
   ii. in accordance with the requirements (if any) determined by the Secretary for the form of notification;

that the sponsor intends to sponsor a clinical trial using specified goods; and

b. the notification must be accompanied by the relevant notification fee referred to in item 14 or 14A of Schedule 9; and

c. the approval of the goods for this purpose must be given by the sponsor (if the sponsor is conducting the trial), or by the body or organisation conducting the trial for the sponsor, having regard to the advice of the ethics committee that has, or will assume, responsibility for monitoring the conduct of the trial; and

d. the terms of the approval by the sponsor, body or organisation referred to in paragraph (c) must be no less restrictive than the terms advised by the ethics committee; and
e. the Secretary must not, at any time:
   i. have become aware that to conduct or continue the trial would be contrary to the public interest; and
   ii. have directed that the trial not be conducted, or be stopped; and
f. the sponsor (if the sponsor is conducting the trial), or the body or organisation conducting the trial for the sponsor, must not receive, or have received, advice from the ethics committee that is inconsistent with the continuation of the trial.”

**Bodies or organisations able to conduct trials**
The previous guidelines referred to trials being conducted in a “hospital or institution”. This was seen to limit the range of bodies which could conduct a trial. The revised regulations use the phrase “body or organisation”.

In addition, the wording makes it clear that “a sponsor” may conduct a trial without the involvement of any intermediary body. For example, if a health service body wishes to trial a drug for indications other than those for which it is marketed and the drug’s Australian supplier is not willing to be the sponsor, then the health service body can be both the sponsor and the body conducting the trial.

The “sponsor”, as defined by the Therapeutic Goods Act, 1989:
   a. exports, or arranges the export of, the goods from Australia; or
   b. imports, or arranges the importation of, the goods into Australia; or
   c. in Australia, manufactures the goods, or arranges for another person to manufacture the goods, for supply (whether in Australia or elsewhere); but does not include a person who:
   d. exports, imports or manufactures goods; or
   e. arranges the exportation, importation or manufacture of the goods; on behalf of another person who at the time of the exportation, importation, manufacture or arrangements, is a resident of, or is carrying on business in, Australia.

**Ethics approval**
The regulations now specify that approval for the conduct of the trial must be given by the body or organisation which is conducting the trial, rather than by the Chairperson of the Institutional Ethics Committee (IEC). This wording makes it clear that legal responsibility for the trial lies with the body or organisation conducting the trial. Ethics committee approval is still required and the approving ethics committee must be constituted and operating in accordance with guidelines issued by the National Health and Medical Research Council (NHMRC).

**Trials can be halted**
The regulation clarify the situation with regard to cessation of trials by stating that the approving ethics committee is responsible for monitoring progress of the trial and may recommend cessation of the trial. The sponsor or the body or organisation conducting the trial is obliged to act on such advice.

The Australian Health Ethics Committee is a principal committee of the National Health and Medical Research Council.

For further information, please contact the Australian Health Ethics Committee Secretariat, NHMRC, MDP 100, GPO Box 9848, CANBERRA ACT 2601

**Phone:** (02) 6289 9807  **Fax:** (02) 6289 9898  **Email:** ahec.nhmrc@nhmrc.gov.au
The Research Committee, a principal committee of the National Health and Medical Research Council (NHMRC) established the Gene Therapy Committee (GTC) in June 1993. This committee was renamed the Gene Therapy Research Advisory Panel (GTRAP) in 1997, and was recently renamed the Gene and related Therapies Research Advisory Panel (GTRAP). This Information Sheet is an update of Information Sheet 2, which should be discarded.

Part of GTRAP’s role is to assist HRECs to assess research protocols involving human somatic cell gene therapy and related issues, including xenotransplantation. HRECs give the final approval for research protocols and monitor gene therapy studies under their jurisdiction. The Australian Health Ethics Committee (AHEC) has advised HRECs not to approve studies involving gene and related therapy, including xenotransplantation, without GTRAP review.

At the date of this Information Sheet, the NHMRC was undertaking public consultation on whether or not xenotransplantation research should proceed in Australia and, if it does, what guidelines should be developed to direct such research. GTRAP will continue to advise HRECs on xenotransplantation research proposals until such time as these issues are resolved.

The Research Committee expanded the role of GTRAP for the 2003-2005 triennium to include an Expert Advisory Group to advise on human stem cell research within GTRAP’s brief.

Terms of Reference for GTRAP

Through the NHMRC Research Committee, GTRAP:

- provides advice to Council on scientific, medical and technical issues related to gene and related therapies, xenotransplantation and human stem cell research;

- provides scientific, medical and technical advice to HRECs, scientists and other interested parties during the formulation and ethical review of research in gene and related therapies and xenotransplantation. In relation to human stem cell research this would be limited to those cells that fall within the scope of the proposed Class 3 risk category outlined by the Therapeutic Goods Administration (TGA) in their Discussion Paper - The Regulation of Human Tissues and Emerging Biological Therapies*;

* GTRAP will only start to review stem cell work when the TGA adopts the above discussion paper as formal policy
functions as a source of information on gene and related therapies, xenotransplantation and human stem cell research to the public and other interested parties; and

maintains a register of research trials in which gene therapies or xenotransplantation have been used.

Membership of the Gene and Related Therapies Research Advisory Panel

To cover its broad brief, the composition of GTRAP includes:

- a core group of individuals with expertise in research, clinical medicine, the law and ethics; representatives from the TGA, the Gene Technology Technical Advisory Committee (GTTAC) and AHEC; and a lay person;
- a gene therapy specialty group;
- a xenotransplantation specialty group; and
- a human stem cell specialty group.

When dealing with gene therapy matters, the core and the gene therapy specialist group meet. A similar procedure is used in relation to xenotransplantation and human stem cell related issues.

Manner of carrying out its functions and committee procedures

GTRAP is established as a working committee of the Research Committee of the NHMRC, under Section 39 of the National Health and Medical Research Council Act 1992. As such, GTRAP is subject to the NHMRC’s endorsed Committee Procedures, including those relating to conflict of interest. GTRAP examines protocols for gene therapy and related technologies, including xenotransplantation, as submitted to HRECs and makes recommendations to HRECs as to whether these protocols are appropriate in terms of their scientific and medical content.

GTRAP meets face-to-face and conducts teleconferences to discuss protocols and issues when required. Regular contact is maintained by electronic means.

Approval process

Proposals for somatic cell gene therapy research and xenotransplantation undergo a process of review which involves an HREC, GTRAP, the TGA, an Institutional Biosafety Committee (IBC) and, when relevant, the Gene Technology Regulator.

All such proposals must be submitted to an HREC for initial ethical and scientific review. Researchers are advised to submit their proposals for human gene therapy in the form set out in the GTRAP document Guidelines for the Writing of Human Gene Therapy Proposals, a copy of which can be found at the GTRAP website. When it has completed its review, the HREC forwards the proposal to GTRAP, having identified any aspects of the proposal requiring specific comment.
• For xenotransplantation, pending the possible availability of Australian guidelines, GTRAP will continue to follow recommendations and guidelines from the USA’s Food and Drug Administration (FDA). For example, the FDA’s Centre for Biologics Evaluation and Research publication _PHS guideline on infectious disease issues in xenotransplantation_, which may be found at: [http://www.fda.gov/cber/gdlns/xenophys0101.pdf](http://www.fda.gov/cber/gdlns/xenophys0101.pdf).

• GTRAP assesses the proposal. As part of this process the investigator and sponsor may be asked to attend a GTRAP meeting, at which time the proposal is reviewed and specific issues raised. Following this meeting, a final or interim report is prepared by GTRAP and sent to the investigators and the relevant HREC. An interim report usually forms the basis for a teleconference between GTRAP, the investigators, the sponsor’s representative and a member of the HREC. At this teleconference outstanding issues are discussed. Additional meetings or teleconferences can be arranged as required and, before giving its final recommendations to the HREC, GTRAP may consult with other bodies concerned with monitoring the safety of innovative genetic manipulation techniques (OGTR) or the standards for product manufacture (TGA). A final report is then issued by GTRAP.

• GTRAP has recommended that, in general, gene therapy and xenotransplantation proposals follow the TGA’s Clinical Trial Exemption (CTX) scheme, unless GTRAP considers the Clinical Trials Notification (CTN) Scheme suitable. For example, CTN might be appropriate if the gene therapy vector has already been approved for a similar clinical use by a regulatory body such as the USA’s FDA.

• Proposals that fall under the jurisdiction of the Gene Technology Regulator must also be submitted to an IBC for initial assessment. When it has completed its assessment, the IBC forwards the proposal to the OGTR, having identified any aspects of the proposal requiring specific comment.

• The OGTR assesses the proposal and, before giving its recommendations to the IBC, may consult with GTRAP, or other bodies concerned with the safety of innovative genetic manipulation techniques.

• In the final step of the regulatory process, the HREC ensures that the proposal has been approved by all relevant bodies and decides whether or not the research may proceed.

• Although GTRAP works predominantly with HRECs, GTRAP’s expertise is always available to investigators, sponsors, and the public. In the case of investigators, it might be beneficial during the early pre-clinical phases for them to approach GTRAP to determine in advance what will be expected before the gene therapy product can be introduced into clinical trials.
Expedited Review & Expedited Risk Assessment by GTRAP

There are clinical studies which utilise genetic material and might not require a full formal review and approval by GTRAP since the risks of the procedure to patients and the community are no different from traditional drug-based therapies. For example, oligonucleotides that involve transient and non-integrating/altering genome events. See Information Sheet 7, Feb 2003, for more information on oligonucleotides and GTRAP review (http://www.health.gov.au/nhmrc/issues/committeehumansupport.htm). In these circumstances, GTRAP has developed a proforma for Expedited GTRAP Review. These requests will be considered out-of-session with a guaranteed response within 30 days.

In some cases, investigators, sponsors or HRECs may not be sure if their proposal requires GTRAP review, in which case GTRAP can provide informal advice (see contact details below). Alternatively, the lodging of the proforma for Expedited GTRAP Review will ensure that there is a written response from GTRAP within 30 days.

Following receipt of the proforma for Expedited GTRAP Review, GTRAP will determine if a full formal review is necessary, or the proposal is exempt from further review. Exemptions given will apply to all similar trials being conducted in Australia.

A Guide for the Writing of Gene Therapy Proposals


Current issues under discussion by GTRAP

Information about current issues under discussion by GTRAP can be found at the NHMRC website: http://www.nhmrc.gov.au/research/grap.htm.

Further information

For further information on GTRAP, or to request a copy of the above guide, please contact the GTRAP Secretariat:

Secretary, Gene and related Therapies Research Advisory Panel
NHMRC
MDP 109
GPO Box 9848
CANBERRA ACT 2601

Phone: (02) 6289 9860
Fax: (02) 6289 9836
Australian Health Ethics Committee

INFORMATION FOR HRECs: APRIL 1998

UNESCO Universal declaration on the human genome and human rights

Articles 22 and 23 of the UNESCO Universal declaration on the human genome and human rights read:

**Article 22** States should make every effort to promote the principles set out in this Declaration and should, by means of all appropriate measures, promote their implementation.

**Article 23** States should take appropriate measures to promote, through education, training and information dissemination, respect for the abovementioned principles and to foster their recognition and effective application. States should also encourage exchanges and networks among independent ethics committees, as they are established, to foster full collaboration.’

The Declaration was adopted, unanimously and by acclamation, at the 29th session of the General Conference of UNESCO on 11 November 1997. The Australian Government is strongly in agreement with the Declaration which is the result of more than four years work carried out by the UNESCO International Bioethics Committee – in particular within its Legal Commission – and is the final outcome of the meeting of the Committee of Governmental Experts held in July 1997.

Article 11 relates to the cloning of human beings. The Commonwealth Minister for Health and Family Services, the Hon Dr Michael Wooldridge, announced in January 1998 that the Australian Government would pursue ways of trying to ensure that the cloning of human beings does not take place in Australia. Dr Wooldridge has asked the Australian Health Ethics Committee to provide advice on the potential and need for further pronouncement or possible legislation regarding the cloning of human beings. This forms part of the current work program for this year and will be completed before the end of 1998.

The Australian Health Ethics Committee is a principal committee of the National Health and Medical Research Council.

For further information, please contact the Australian Health Ethics Committee Secretariat, NHMRC, MDP 100, GPO Box 9848, Canberra, ACT, 2601.

**Phone:** (02) 6289 9807  **Fax:** (02) 6289 9898  **Email:** ahec.nhmrc@nhmrc.gov.au
1. Background

Many institutions and organisations have adopted the practice of charging a fee to researchers or research sponsors for access to HREC review of research proposals. It appears, from submissions made to the AHEC, that these practices vary widely as to the amount of the fees, their conditions and their rationale. Some institutions regard the charging of such fees as inappropriate.

During public consultation for the National Statement on Ethical Conduct in Research Involving Humans, some submissions to the AHEC requested guidance on such policies.

In this response to requests, the AHEC recognises that the decision whether or not to adopt a policy of charging a fee for access to HREC review is, to an extent, an administrative decision. Some institutions and organisations regard fees as simply one means of defraying the costs of establishing and adequately resourcing an HREC, as required by the National Statement. A summary of what the National Statement requires appears in paragraph 4 below.

However, there are ethically relevant issues involved in a decision to adopt a policy of charging fees for access to HREC review. It is to these issues that this advice is directed.

2. Institutional Policies for Resourcing HRECs

Where an institution decides to rely on fees for access to consideration of research proposals by the institution’s HREC, it should develop and publish a comprehensive policy. That policy should address the rate or rates of fees; an explanation of how those rates were determined, eg by reference to the costs involved in the HREC process of consideration of all or different types of research proposals; by whom and in relation to which research proposals the fees are payable; in relation to which research proposals, if any, fees are not payable; the administrative arrangements for the payment of the fees and the use or uses to which the institution devotes the fee income.
3. Ethical Considerations
In reaching a decision to adopt such a policy, an institution or organisation needs to be satisfied that:

(a) the payment of any fee will not compromise the integrity of the process of ethical review of research proposals and the monitoring of approved research, for example, higher fees should not be charged for expedited review; and

(b) the imposition and administration of fees for access to HREC consideration will not impair or seem to impair the independence and autonomy of the HREC, for example, the collection, administration and use of the fees should be separate from administration of HREC activities; and

(c) implementation of a policy of charging fees for access to HREC consideration of research proposals will not have the effect of preventing the consideration of research proposals that would otherwise have been considered in the work of the HREC, for example, by charging high levels of fees for staff or student research.

Where an institution or organisation cannot be satisfied that all of these requirements will be met, the adoption of a policy to charge fees for access to HREC review of research proposals may result in that HREC ceasing to fulfil the requirements of the National Statement.

4. Establishing and Resourcing HRECs by Institutions and Organisations
Guideline 2.1 of the National Statement on Ethical Conduct in Research Involving Humans requires institutions and organisations in which research involving humans is undertaken to establish, adequately resource and maintain HRECs composed and functioning in accordance with the Statement.

The functions of HRECs set out in the National Statement include:

- protecting the welfare and rights of participants (2.5);
- being sufficiently informed about and addressing all relevant aspects of a research proposal (2.7, 2.8);
- preparing agendas, minutes, distributing papers to members, conducting meetings, promptly notifying decisions (2.13);
- recording details of decisions (2.30 – 2.32);
- monitoring all approved research (2.33 – 2.38);
- receiving and responding to complaints (2.39 – 2.43); and
- providing reports to NHMRC and the AHEC (2.46 – 2.48).

Guideline 2.2 of the National Statement requires institutions and organisations, when establishing an HREC, to set out its terms of reference including the scope of its responsibilities, relationship to non-affiliated researchers, accountability, mechanisms of reporting and remuneration, if any, to members. Guideline 2.3 of the National Statement provides that institutions or organisations (individually or jointly) must accept legal responsibility for decisions and advice received from the HREC and indemnify its members.

For further information, please contact the Australian Health Ethics Committee Secretariat, NHMRC, MDP 100, GPO Box 9848, Canberra, ACT, 2601.

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Australian Health Ethics Committee  
INFORMATION FOR HRECs: SEPTEMBER 2001  
Stem Cell Research

The Australian Health Ethics Committee has been approached by human research ethics committees (HRECs) seeking advice on how to review research protocols that involve stem cell research.

The following guidance is interim. Formal guidelines will be developed by AHEC in the context of its review of the 1996 NHMRC Ethical guidelines on assisted reproductive technology.

1. Research on stem cell lines derived from human embryos should be considered in the same way as any other research on human products (e.g., blood, tissue). All research proposals involving the use of stem cell lines derived from human embryos should be presented to an HREC for consideration.

2. The Ethical guidelines on assisted reproductive technology (1996) only permit destructive research on embryos under certain exceptional circumstances (section 6.4). If the stem cell lines have been derived through destructive research on embryos that meets the conditions laid down in these sections, then research on stem cell lines derived from human embryos is not explicitly prohibited.

3. In considering such research the HREC must consider whether the stem cell lines derived from human embryos have been derived in an appropriate manner (Ethical guidelines on assisted reproductive technology (1996) sections 6.4 and 11.1).

4. If derived in Australia, the research leading to the development of the stem cell lines must have occurred:
   • under the auspices of an HREC operating in accordance with the requirements of the National Statement on ethical conduct in research involving humans (1999) and the Ethical guidelines on assisted reproductive technology (1996); and
   • in compliance with prevailing Commonwealth and State or Territory legislation.

5. If the stem cell line derived from human embryos was imported to Australia, the HREC should endeavour to confirm that the cell line was developed in accordance with the:
   • Ethical guidelines on assisted reproductive technology (1996) (sections 6 and 11); and
   • National Statement on ethical conduct in research involving humans (1999) (paragraph 1.21).
Two necessary considerations are that the embryo from which the stem cell line was derived was excess to an IVF program and that the donors gave informed consent.

6. If there are doubts regarding the origin of a stem cell line, or the requirements of Australian standards can not be satisfied, then the HREC should not permit the research to proceed.

AHEC has commenced a review of the Ethical Guidelines on assisted reproductive technology and related publications. This review will include wide public consultation. Pending the outcome of that review, HRECs are to be guided by this Information Sheet.

Dr Kerry J. Breen
Chairperson
Australian Health Ethics Committee

For further information, please contact the Australian Health Ethics Committee Secretariat, NHMRC, MDP 100, GPO Box 9848, Canberra, ACT, 2601.

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Australian Health Ethics Committee
INFORMATION FOR HRECs: December 2005

The 2000 revision of the Declaration of Helsinki (the Declaration) generated controversy about Paragraphs 29 and 30, which pertain to clinical trials. In September 2001, the National Health and Medical Research Council (NHMRC) issued Information Sheet 6 for HRECs to resolve discrepancies between the 2000 revision of the Declaration and the National Statement on Ethical Conduct in Research Involving Humans (the National Statement).

Information Sheet 6B provides an update on this issue and replaces Information Sheet 6 as a source of guidance for HRECs.

The World Medical Association (WMA) responded to concerns expressed by several key bodies by further considering the Declaration at meetings between October 2001 and May 2004, and subsequently issued Notes of Clarification on both Paragraphs 29 and 30.

Paragraph 29
Paragraph 29 states:

“The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.”

After the revision, researchers and regulatory agencies, here and overseas, expressed concern that Paragraph 29 was very restrictive in prohibiting the use of a placebo whenever there exists current treatment. Paragraph 12.4 of the National Statement states that a placebo can sometimes be justified even where there exists current treatment.

In October 2002, the WMA General Assembly issued the following Note of Clarification on Paragraph 29 for inclusion in the Declaration:

“The WMA hereby reaffirms its position that extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of existing proven therapy. However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances:
- Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; or
- Where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive a placebo will not be subject to any additional risk of serious or irreversible harm.

All other provisions of the Declaration of Helsinki must be adhered to, especially the need for appropriate ethical and scientific review.”

AHEC considers that the WMA’s Note of Clarification on Paragraph 29 removes the inconsistency between the National Statement and the Declaration and now aligns closely with Paragraph 12.4 of the National Statement.

**Paragraph 30**

Paragraph 30 states:

“At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.”

Researchers, regulatory agencies and pharmaceutical manufacturers expressed concern that Paragraph 30 made unrealistic assumptions about factors such as the availability of treatment and infrastructure in third world countries and may also constitute irresistible inducement in such countries.

On 17 May 2004, the WMA issued a Note of Clarification on Paragraph 30 stating that:

“The WMA hereby reaffirms its position that it is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care. Post-trial access arrangements or other care must be described in the study protocol so the ethical review committee may consider such arrangements during its review.”

Noting that the National Statement itself does not contain post-trial treatment provisions, AHEC considers that the WMA’s Note of Clarification on Paragraph 30 is consistent with advice referred to in NHMRC’s Human Research Ethics Handbook. The Handbook advises (at E12, Protocol and Study Design), that HRECs should consider the mechanisms proposed for access to continued treatment where long term therapy would be appropriate following the completion of the trial.

AHEC advises that HRECs should continue to regard the NHMRC National Statement on Ethical Conduct in Research Involving Humans as the definitive guideline for the ethical review and conduct of research in Australia.

For further information, please contact the Australian Health Ethics Committee Secretariat, NHMRC, MDP 24, GPO Box 9848, Canberra, ACT, 2601.
Phone: (02) 6289 9575 Fax: (02) 6289 9580 Email: ahec.nhmrc@nhmrc.gov.au
The role of the Gene Therapy Research Advisory Panel (GTRAP), established under the NHMRC’s Research Committee, includes assisting HRECs to assess research proposals involving human somatic cell gene therapy and related issues, including xenotransplantation. Information on GTRAP’s functions and membership can be found in Information Sheet 2.

It has recently been brought to the attention of GTRAP that a number of studies pertaining to the therapeutic use of oligonucleotides have been approved by HRECs without consulting GTRAP.

Oligonucleotides are short molecules of DNA (or, sometimes RNA) that are usually less than 100 bases in length. They can be used for a variety of techniques in molecular biology (for example, the Polymerase Chain Reaction – PCR), and they can also have therapeutic uses in medicine. As an example, oligonucleotides are currently being used in an international trial to target cancer cells by blocking gene activity. These studies are unlikely to be problematic since they involve short acting oligonucleotides, which are not gene therapy products according to the United States’ Food and Drug Administration (FDA). However, the FDA does consider another class of oligonucleotides that are used to alter the DNA sequence to be gene therapy products. Oligonucleotides with an extended half life would also need to be reviewed more carefully.

Because of this potential confusion, GTRAP would prefer to sight each proposal for the therapeutic use of oligonucleotides which HRECs receive, to confirm that there is no safety concern.

To expedite the review of protocols which utilise oligonucleotides to block gene transcription, GTRAP will soon place on its web site, (http://www.health.gov.au/nhmrc/research/gtrap.htm), an abbreviated proforma which allows HRECs or investigators to provide sufficient information to GTRAP to enable a rapid risk assessment. In the case of oligonucleotides that have a very short half life, GTRAP will exempt these proposals from a full GTRAP submission, as detailed in the “Guidelines for the Writing of Human Gene Therapy Proposals”.

The exemption by GTRAP will apply to all centres involved in multi-centred studies which use the identical product and protocol.

For further information, please contact the Australian Health Ethics Committee Secretariat, NHMRC, MDP 100, GPO Box 9848, Canberra, ACT, 2601.

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INFORMATION FOR HRECs: NOVEMBER 2003

Research Involving Human Embryos Act 2002: Advice\(^1\) from the Australian Health Ethics Committee and the Licensing Committee of the NHMRC on the legislative requirements for obtaining proper consent for research on excess ART embryos

The Research Involving Human Embryos Act 2002 (RIHE Act) requires each licence to be subject to the condition that, before an excess ART embryo is used as authorised by the licence, each responsible person in relation to the excess ART embryo must have given proper consent to that use (Section 24). This interim document is intended to make licence applicants and HREC members aware of what constitutes proper consent in regard to this legislation\(^2\).

This advice is given to guide HRECs only in relation to consent to uses of embryos that have been declared, by the persons responsible, to be excess to their needs. The advice is not given for use in relation to consent to any other decisions about embryos or research in assisted reproductive technology.

Preamble

The RIHE Act (Section 8) defines proper consent, in relation to the use of an excess ART embryo, as consent obtained in accordance with the NHMRC Ethical Guidelines on Assisted Reproductive Technology 1996 (herein the Guidelines). The RIHE Act (Section 21) also determines that the NHMRC Licensing Committee must not issue a licence unless satisfied that the activity or project proposed in the application has been assessed and approved by a HREC that is constituted in accordance with, and acting in compliance with the NHMRC National Statement on Ethical Conduct in Research Involving Humans (1999) (herein the National Statement).

It is essential that applicants and HRECs have a thorough knowledge of these documents. It should be noted that provisions of the RIHE Act and any regulations made under it, take precedence over any guidelines issued by the NHMRC and its committees.

The decision to make their excess ART embryos available for research is a difficult one for many people. There are differences of opinion in our community regarding the moral status of the human embryo. It is important that licence applicants are sensitive in their approach to obtaining consent. It should also be noted that the relationship between people and embryos for which they are responsible can change over time.

The procedures outlined in this document must not be initiated until all persons responsible have agreed in writing that the embryos are excess. Consent for the specified research project must not be sought until embryos are declared to be excess.

\(^1\)This advice is based on the current NHMRC Ethical guidelines on assisted reproductive technology 1996 and legislation as at September 2003.

\(^2\)HRECs should follow this advice pending the completion of the revised reproductive technology guidelines.
Licence applicants report in writing that an HREC has assessed and approved the activity or project to which the licence relates so as to show compliance with the conditions specified in Section 24 of the RHIE Act. It is the responsibility of the HREC to ensure that the activity or project has been designed so that proper consent will have been obtained before an excess ART embryo is used. A HREC must also ensure that no member of the committee adjudicates on research in which that member has any conflict of interest (see National Statement 2.20).

In reviewing and approving the proposed process for obtaining proper consent, the following points should be taken into consideration.

**Principles of ethical conduct**

The National Statement clearly defines its primary purpose as the protection of the welfare and rights of participants in research. The values and principles that researchers are required to demonstrate and follow towards participants include integrity, respect for persons, beneficence and justice (see National Statement 1.1-1.21). The definition of participants in the National Statement includes those upon whom the research impacts. This translates into the need to obtain consent from persons responsible for the embryos, before any research activity is undertaken.

Proper consent means consent that is:
- informed;
- given by a person competent to do so;
- voluntary; and
- specific.

1. **Informed**

1.1 Persons responsible for the embryos should be provided with information, at their level of comprehension, about the purpose, methods and possible outcomes of research, including the likelihood and form of publication of research results (National Statement 1.7). This should be done as an oral explanation, supported by written information in plain language which is provided in sufficient time for it to be taken away, read and considered, prior to the giving of consent. This explanation should be given with sensitivity to the individual needs of the patient (Guidelines 3.1.2).

1.2 Where persons responsible are not fluent in English, it is recommended that an independent interpreter be used to convey information and answer questions. Written information must be translated into the language of the responsible persons (National Statement 2.26; Guidelines 3.1.2). Similarly, where persons responsible have other communication needs, appropriate facilities should be provided.

1.3 Informed decision-making is required for all persons responsible, including the spouses or partners of donors of gametes and embryos at the time of donation (Guidelines 3.2.5, 6.4). Licence applicants should be aware that in some cases, more than two adults will need to give consent for the use of any given embryo. These parties should be contacted at the time at which the future of the embryos is being decided and given the relevant information as outlined in this document.

1.4 The researcher is required to disclose to the HREC any financial interest in the research and the HREC must consider the extent to which disclosure of relevant financial aspects of research should be made to the persons responsible (National Statement 2.21). As persons responsible must be given all information which may be of significance (Guidelines 3.1), HRECs would normally decide to disclose all financial aspects to participants. For example, where researchers plan to request altruistic donation of embryos with the intention of gaining commercial profit, this must be made clear to the donors before consent is obtained.
1.5 Persons responsible should be provided with the name or position and contact details of the person nominated by the relevant HREC to receive complaints along with procedures for raising concerns or obtaining additional information on the research (National Statement 2.42).

1.6 Persons responsible must be informed that records may be viewed by NHMRC inspectors to meet the requirements of the RIHE Act.

2. Competence to make a choice

2.1 Persons responsible from whom consent is obtained must be competent to make a choice. Where a person responsible does not have the capacity to make a choice, the choice may be made by a person with lawful authority to decide for that participant. (National Statement 1.7).

2.2 Persons responsible are free to refuse to give consent to the use of an embryo without giving any explanation or justification for the refusal (National Statement 1.8).

2.3 Subject to prevailing state/territory legislation, where disputes arise between responsible persons about the use of an embryo, the embryo should be kept and not allowed to succumb until the dispute has been resolved and a decision taken about the embryo (Guidelines 3.2.8).

2.4 Should a person with responsibility to make decisions about an embryo die, the surviving person(s) responsible should make the relevant decisions about the use of the embryo, taking into consideration any advance directive from the deceased and subject to prevailing state/territory legislation.

2.5 Subject to prevailing state/territory legislation, should all responsible persons die, any advance directive from the deceased responsible persons should be considered. If there is no advance directive, or if an advance directive exists but has not been endorsed, or the advance directive cannot be complied with, the embryo should be allowed to succumb. (Guidelines 3.2.9).

3. Voluntary

3.1 Consent of persons responsible must be voluntary and not subject to any coercion, inducement or influence, such as financial or other rewards, that could impair its voluntary character. (National Statement 1.10)

3.2 In particular it is important that researchers be aware of the possibility of even unwitting coercion, for example where a doctor-patient relationship exists and the doctor is also the researcher (National Statement 7.1). For this reason, it is recommended that the person who approaches the persons responsible for the embryos to be used, be independent of their clinical care.

3.3 Any concealment of the purposes of a study from the persons responsible is not considered ethical and prevents informed and voluntary consent (National Statement 17.1).

4. Specific

4.1 Persons responsible should be provided with information about the intended use of the embryo. The consent form must specify the purpose for which that embryo or embryos may be used (Guidelines 3.2.5). Consent must be given for a specific purpose, for example, for destructive research (detail type of research and the rationale for the research). In the case of destructive embryo research, it must be made clear to the persons responsible for the embryo that the fate of individual embryos may not be able to be reported. The specific scope of the research and the consent sought must be made clear. For example, if stem cells were to be harvested from a given embryo, the persons responsible would be consulted about that use of the embryo, but, for the purpose of giving the proper consent required under the RIHE Act, would not need to be consulted about the subsequent use of those stem cells.
5. **Withdrawal of consent**

5.1 A person responsible must be free at any time to withdraw consent to further involvement in the research (*National Statement* 1.12). In the case of destructive embryo research, persons responsible for the embryo need to be aware that withdrawal is not possible after the embryo has been destroyed. In view of this, it is recommended that the consent of persons responsible to a use which will damage or destroy an embryo must not be acted upon until a suitable fixed period of time for re-consideration has been allowed, normally at least two weeks after their consent to such research. This ‘cooling-off’ period before consent becomes effective must be explained to the persons responsible when consent is obtained.

6. **Consent forms**

6.1 Consent should be given in writing (*Guidelines* 3.2.2).

6.2 The entire consent process, including forms and protocols, should be reviewed and approved by an HREC.

6.3 For clarity, terminology on the consent form should match definitions in the RIHE Act.

6.4 All of the documentation to be used in obtaining consent should be included in the application to the HREC (*National Statement* 2.24) as well as in the application for a licence to the NHMRC Licensing Committee.

For further information, please contact:

Australian Health Ethics Committee Secretariat  
NHMRC  
MDP 100  
GPO Box 9848  
Canberra ACT 2601

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Appendix 4
Australian Health Ethics Committee Bulletins
The HREC Bulletin is published by the Australian Health Ethics Committee (AHEC) as part of its support for Human Research Ethics Committees (HRECs). The primary purpose of the Bulletin is to inform HREC members of the work carried out by AHEC and to provide information about emerging issues. This Bulletin and previous issues are available online at http://www.nhmrc.gov.au/issues/committeehumansupport.htm.

Message from the Chair of AHEC

New Appointment to AHEC - Welcome Ms Bebe Loff

Following the resignation of Mr Robert Griew, Ms Bebe Loff was appointed to AHEC in November 2001 in the category of a person with understanding of health consumer issues. Ms Loff is a lawyer who currently holds a teaching position in the Department of Epidemiology and Preventive Medicine at Monash University in Melbourne. She has taught aspects of law and medicine in both the law and medical faculties for a number of years, including a postgraduate course entitled “Health, Ethics and Human Rights”.

Bebe was a temporary United Nations adviser assisting in the development of what became the UNAIDS guidance document entitled “Ethical considerations in HIV preventive vaccine research” (Geneva 2000). She is currently working on a project for the Department of Health and Ageing to devise ethical guidelines for preventive HIV vaccine trials conducted by Australian researchers. She has been a participant in the Global Forum on Bioethics in Research. During the late 1980s to early 90s Bebe was the Manager of the Policy and Legislation Review Unit of what was then the Health Department, Victoria, responsible for the legislative programs of Ministers of Health. She has been a member of numerous community-based organisations including Fitzroy Legal Service, the Health Issues Centre, Women Against Rape, Feminist Lawyers and the Prostitutes Collective of Victoria. She has been a member of two hospital ethics committees and is a correspondent for the medical journal “The Lancet”.

News for HREC’s

HRECs and Public Accountability

HRECs and their institutions will have received and considered AHEC’s proposed policy on public access to information about HRECs. The development of that draft policy reflects a recognition that openness and transparency in the ethical review of research involving humans contributes to public confidence in that process.

AHEC believes that HRECs have an important role in fostering a culture of public awareness of such research, its goals and methods and the reasons for and focus of ethical review. HRECs may choose to consider sympathetically requests for people to attend their meetings as observers or to speak to community groups about the ethical review of research.

AHEC is aware that some HRECs publish their own annual reports, contribute to their institution’s annual report, and/or have information on a website. This transparency is applauded and AHEC encourages all HRECs to consider these avenues for providing information to the Australian community.
AHEC would value receiving copies of HREC annual reports and advice of examples of websites containing HREC information.

**Blood / tissue samples for research**

AHEC is aware that, with increasing frequency, research participants are being asked to consent to the taking of samples of human tissue or blood for present and future research use without being fully informed of the nature of that future use. Consent forms that seek approval for a future use, without adequately specifying that future use, raise a number of questions:

- Can consent conform to the requirements of paragraphs 1.7 – 1.9 of the National Statement if the participant does not know fully the future intended use?
- Could requiring consent to unspecified future uses, as a condition of participation, be coercive contrary to paragraph 1.10 of the National Statement?
- What control will the participant and researcher have over the sample(s) in the future?
- Will samples be de-identified and is this in the best interests of the participant?

Further, paragraph 15.8 of the National Statement authorises HRECs to decide to waive the requirement for consent to research with human tissue in certain circumstances. These include the need to decide when a research project is an extension of, or closely related to, a previously approved research project.

Other issues that may need consideration are:

- The basis on which tissue banks are established, the rules of their operation and how commercial interests are addressed.
- Costs associated with obtaining sample(s).
- Potential for identifying non-paternity that participants may unwittingly discover.
- The global nature of information transfer and the potential for breach of privacy.

Responses to these questions need to be considered carefully by each HREC and their institutions. It is for them to decide what conditions need to be satisfied before proposals for collection of tissue for research are approved.

Where consent is to be sought for such research, an HREC needs to be satisfied that sufficient information is provided to meet the requirements of paragraphs 15.4-15.7 and, where there will be genetic research, paragraphs 16.9-16.11, of the National Statement. Examples of the matters that an HREC might consider relevant include:

- Whether the sample will be destroyed on completion of the research;
- Whether the use of the sample could reveal non-paternity or non-maternity;
- Whether the sample will be used and stored in an identifiable, potentially identifiable or de-identified form;
- Whether the consent will permit the sample to be used for future research related to the initial study and/or future unrelated research;
- Whether participants will be advised if further research is conducted;
- Whether participants will receive results of the research, with or without counselling;
- Whether participants’ medical advisors are to be informed of the study results that relate to participants’ families;
- Whether identifying genetic information will be released to a third party, including family members with or without consent.

The use of a separate information sheet and consent form for the tissue study where it is associated with other research, such as a pharmaceutical drug study, can be an effective response to concerns about coercion.

Where consent is to be waived, HRECs need to be satisfied that all of the elements of paragraphs 15.8 and, where applicable 16.13, are satisfied.
Dr Wooldridge referred AHEC’s report “Scientific, ethical and regulatory considerations relevant to cloning of human beings” to a Parliamentary committee of inquiry in August 1999. The terms of reference for the review were simply to review AHEC’s report. The Standing Committee on Legal and Constitutional Affairs (the “Andrews Committee”) took written and oral submissions from interested parties over a two-year period. The final report was tabled in September 2001, some two years after commencement of the review.

The Report contains 15 recommendations. Of these, 12 involve the Commonwealth legislating to: regulate human cloning and stem cell research; ban the cloning of humans for reproductive purposes; and establish a national licensing body to regulate any research involving the isolation, creation and use of embryonic stem cells. The remaining recommendations: seek AHEC involvement in monitoring scientific developments in this area; call for an independent review of the human research ethics committee system; and require all Commonwealth departments to seek advice from the licensing body on any issue relating to the use of human reproductive material, embryonic stem cell research or cloning research.

AHEC is preparing a response to this report, which will become part of the response of the NHMRC.

The report of the Andrews Committee is available on the web at:

Contact: Ian Denley 02 6289 9802

Recent AHEC Progress

Guidelines approved under Section 95A of the Privacy Act 1988

The NHMRC Guidelines approved under Section 95A of the Privacy Act 1988 (s95A Guidelines) will come into effect from 21 December 2001, in line with the implementation of the Commonwealth Privacy Amendment (Private Sector) Act 2000.

Guidelines issued by the Office of the Federal Privacy Commissioner (OFPC) will also be important for ensuring privacy is protected in the conduct of research generally. OFPC Guidelines are available from www.privacy.gov.au.

The s95A Guidelines will need to be applied by HRECs when reviewing research, statistical or health service management proposals that involve the collection, use or disclosure of identifying health information where consent is not sought from the individual concerned. HRECs should note that the review of health service management proposals is only required where it is proposed to undertake an initial collection of health information without consent.

From 19th December 2001, the Guidelines will be on the NHMRC web site at www.nhmrc.gov.au. AHEC will send all HRECs a copy of the guidelines in January 2002. AHEC will also provide information on the details to be recorded by HRECs when reviewing proposals using the s95A Guidelines. This information will be important for annual compliance reporting purposes and will feed into the larger evaluation of the Commonwealth privacy legislation, which is to be undertaken in two years.

Given the complexity of the new private sector privacy legislation and the added responsibilities of HRECs under the s95A Guidelines, it will be essential that AHEC properly monitors and evaluates the operation of the s95A Guidelines.

The AHEC Privacy Working Group is currently developing a brief plain-English document on privacy regulation in Australia. This document will outline the critical factors for researchers and HRECs to consider in deciding when and how to apply the Commonwealth privacy legislation and associated guidelines when preparing and reviewing research proposals. The document will also briefly highlight relevant State/Territory legislation.

AHEC is also proposing to hold a series of national workshops in the first half of 2002 focussing on privacy.

Contact: Nerida Lawrentin 02 6289 9848
Australian Health Ethics Committee review of the NHMRC Ethical guidelines on assisted reproductive technology (1996)

In September 2001 AHEC established a working party to review the 1996 Ethical guidelines on assisted reproductive technology. The review is to be completed in the current triennium. A round of public consultation has been completed and the working party is considering a range of issues including:

- the strengths and weaknesses of the guidelines;
- emerging issues in assisted reproductive technology including research on embryos and the development and use of stem cells derived from embryos;
- practices currently prohibited which should be either no longer prohibited or should remain prohibited;
- practices that have emerged since the 1996 guidelines and which should be either prohibited or authorised;
- whether guidance on clinical practice and on research should be separate or combined in one set of guidelines; and
- the role of HRECs in reviewing proposals for clinical practice and/or research.

Contact: Ian Denley 02 6289 9802

2002 National Workshop Series

AHEC has commenced work on the next series of workshops with privacy as the focus. Information will be sent to HRECs and posted on the website as it comes to hand.

Contact: Francine Kelly 02 6289 9801

Protection of Human Genetic Information Inquiry

In the last Bulletin, it was reported that AHEC is conducting an inquiry jointly with the Australian Law Reform Commission into the protection of human genetic information. The issues paper for this inquiry has been released and can be downloaded from www.alrc.gov.au. Printed copies are available at no charge from the ALRC, 131 York Street, Sydney or (02) 9264 6333.

Public consultations have been held in Melbourne, Hobart, Perth, Adelaide and Brisbane. Further consultations in other capital cities and regional centres will be conducted early in the New Year. Information about consultation venues and dates can be obtained from www.alrc.gov.au.

AHEC encourages HRECs to examine the issues paper and to consider making submissions to this important inquiry.

Other useful information

The NHMRC Gene and Related Therapies Research Advisory Panel

The Research Committee, a principal committee of the NHMRC, established the Gene Therapy Committee in June 1993. This committee was renamed the Gene Therapy Research Advisory Panel in 1997 and has recently been renamed the Gene and Related Therapies Research Advisory Panel (GTRAP).

Part of GTRAP’s role is to assist HRECs in their assessment of research proposals involving human somatic cell gene therapy and related issues, including xenotransplantation. HRECs give the final approval and monitor gene therapy studies under their jurisdiction.

HRECs have been advised not to approve studies involving xenotransplantation without GTRAP input. National guidelines for xenotransplantation are presently being formulated by the NHMRC, however, GTRAP will continue to advise HRECs on xenotransplantation research proposals until those guidelines are developed.

Further information about GTRAP’s membership and work program can be found at http://www.nhmrc.gov.au/research/gtrap.htm.

Contact: Helen Willimott 02 6289 9806
Continuing our series of questions and answers from the 2001 workshops.

**Question:** If a patient withdraws from a clinical trial, is it ethical to continue to collect information from the patient medical record for the purposes of the trial?

**Answer:** It should be made clear to the patient, at the commencement of a trial, what information regarding the patient will be collected. It should also be made clear to the patient what “withdrawing” from the trial means. Hence, the ongoing collection of information after the patient has withdrawn from a trial will be determined by the consent given by the patient at the commencement of the trial or at the time of withdrawal. In some circumstances it is legally permissible to use patient information without consent for the purposes of research if approval for this activity is given by the HREC. However, this situation can be easily avoided, and the welfare of the patient fully protected, by providing the patient with full information at the commencement of the trial and obtaining appropriate consent.

**Question:** Will the National Statement be updated in compliance with the new privacy legislation? Is there a possibility the Statement will exempt medical research from the legislation?

**Answer:** The National Statement will not be specifically updated to accommodate the Commonwealth Privacy Amendment (Private Sector) Act 2000 which will come into effect on the 21 December 2001, nor will it exempt medical research from the legislation.

Chapter 18 of the National Statement will continue to be the source of general guidance on the protection of personal information in the conduct of research. However, the NHMRC Guidelines under Section 95 of the Privacy Act 1988 (s95 Guidelines) and the new Guidelines approved under Section 95A of the Privacy Act 1988 (s95A Guidelines) are designed to protect the privacy of personal information in prescribed circumstances (essentially, where access to or use of information is proposed without consent) and form part of the Privacy Act 1988. The s95 Guidelines apply to medical research (involving Commonwealth held data). The s95A Guidelines apply to research, statistical and health service management activities (involving data held by the private sector organisations).

For further information about the new NHMRC Guidelines approved under Section 95A of the Privacy Act 1988 (s95A Guidelines), which will also come into effect on 21 December 2001, please refer to the article in this Bulletin under 'Recent AHEC Progress'.

The National Statement will be reviewed and revised in accordance with NHMRC policy on the review of guidelines ie. after five years.

**Question:** Recognising that HREC members spend many hours before and during a committee meeting, what are the issues relating to compensation, reimbursement or payment of HREC members?

**Answer:** HRECs members are appointed by, and act on behalf of, institutions. In accordance with paragraph 2.2 of the National Statement, “The institution or organisation must, when establishing an HREC, set out its terms of reference including its scope of responsibilities, relationship to non-affiliated researchers, accountability, mechanisms of reporting, and remuneration, if any, for members.” Consequently, it is the decision of individual institutions as to whether HREC members are remunerated for their contribution, for example, by payment of a sitting fee. It is recommended that, as a minimum, HREC members be reimbursed for expenses such as travel and parking. Anecdotal evidence suggests that currently a small number of Australian institutions pay a sitting fee to HREC members.
When deciding whether to provide payment that is more than reimbursement to HREC members, institutions would need to consider the respective status of employee and non-employee members and any potential for such payments to affect public perceptions of the integrity and independence of the ethical review of research.

**Future AHEC meetings for 2002**

The meeting dates for 2002 are as follows:

- 27-28 February
- 8-9 May
- 4-5 September
- 10-11 December

**Reference materials for HRECs**

The Australian and New Zealand Journal of Public Health recently published an article written by Dr Sandy Webb for AHEC "Consent for the linkage of data for public health research: Is it (or should it be) an absolute pre-requisite?" (2001 Vol. 25 No. 5). The abstract for the article is reproduced below.

Data linkage research is being conducted in an evolving and complex environment. The National Health and Medical Research Council’s Guidelines Under Section 95 of the Privacy Act 1988 and National Statement on Ethical Conduct of Research Involving Humans allow scope for such research to be legally and ethically acceptable, although conducted without consent. Although the Privacy Amendment (Private Sector) Act 2000 will extend privacy requirements into the private sector and into the areas of health statistics and health service management, it is vital that valid and useful public health research will be allowed to continue in a broadly similar framework.

New HREC members may find useful references to current NHMRC and ethical issues including past issues of this bulletin at our http://www.nhmrc.gov.au/ web-site.

**Letters to the Editor**

If there are issues that you would like to see discussed in future bulletins, please write or email to the AHEC secretariat. We would be happy to receive your questions, ideas or comments for consideration for publication.

Send to:

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Email to: ahec.nhmrc@health.gov.au

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For privacy enquiries - (02) 6289 9848
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**Commentary on the National Statement on Ethical Conduct in Research Involving Humans**

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The Human Research Ethics Handbook

Commentary on the National Statement on Ethical Conduct in Research Involving Humans

The Human Research Ethics Handbook is a major publication designed to assist Human Research Ethics Committees (HRECs) in their review of research proposals. It comprises three parts; a commentary on the NHMRC National Statement on Ethical Conduct in Research Involving Humans (1999), and two collections of writings by a number of authors, regarding legal and ethical issues, relevant to the review and conduct of research involving humans.

The Handbook will be of use not only to members of HRECs, but also to researchers, research participants, students, research administrators and the public generally in providing useful information and references on most topics relevant to the ethical conduct of research. The Handbook has been planned as a dynamic document that will be expanded and updated as appropriate.

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