

**Report of the 1999 Workshops on the  
*National Statement on Ethical Conduct in  
Research Involving Humans***

**NHMRC**

National Health and Medical Research Council

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## FOREWORD

The 1999 workshops on the *National Statement on Ethical Conduct in Research Involving Humans* were very successful. There was an overall increase in registrations by approximately 70% on the previous workshops, held in 1995. Such an undertaking could not have been conducted without assistance from a large group of people.

I would like to congratulate all of the State Convenors for their contributions towards the success of the workshops. In particular, I would like to thank:

- Professor Robin Watts, for her role as the AHEC Coordinator for the workshops and as a workshop presenter;
- Associate Professor Colin Thomson, for his excellent presentations on the *National Statement*, and for his contribution to the Brisbane workshop;
- Members of the Australian Health Ethics Committee and the National Health and Medical Research Council, for their contributions and attendance; and
- State and Territory Health Departments, for their financial contributions.



Professor Donald Chalmers  
Chair  
AHEC

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## INTRODUCTION

In August 1999, the Australian Health Ethics Committee (AHEC), a principal committee of the National Health and Medical Research Council, conducted a series of national workshops about the newly-released *National Statement on Ethical Conduct in Research Involving Humans*. Workshops were held in all capital cities and in Alice Springs.

The objectives of the workshops were to

- Provide participants with an overview of the *National Statement*, including how the document differed from its predecessor; and the implications of the new document for researchers, Human Research Ethics Committees (HRECs), and participants in research.
- Provide participants with the opportunity to explore the impact of the *National Statement* within particular State or Territory health research environments, and to formulate strategies and recommendations for the future.
- Provide participants with the opportunity to discuss and seek input on issues in relation to the operation of their own HRECs.

The *National Statement on Ethical Conduct in Research Involving Humans* was developed by AHEC, and endorsed by the Australian Vice-Chancellors' Committee, the Australian Research Council, the Australian Academy of the Humanities, the Australian Academy of Science and the Academy of the Social Sciences in Australia. The Academy of Technological Sciences and Engineering also provided its support, as did the Ministers for Health and Aged Care, Industry, Science and Resources, and Education and Youth Affairs.

It is the most comprehensive *statement* on the ethical principles of research involving humans to be produced in this country. Australia is only the second country in the world, after Canada, to have national guidelines on human research.

## PROGRAM

A broad program was developed for the workshops, which is listed on the following page. This program was modified by the Convenor of each workshop, to reflect issues specific to their State or Territory.

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## WORKSHOP PROGRAM

TIME	SESSION
8.30 - 9.30am	Registration
9.00 - 9.10am	Welcome
9.10 - 10.10am	Overview of the <i>National Statement</i>
<b>Morning Tea</b>	
10.40am - 12.45pm	Exploration of the major themes and implications for HRECs, researchers, research participants and others (small groups) Plenary session: issues and questions arising from the small groups
<b>Lunch</b>	
1.45 - 2.45pm	Case studies: application of the <i>National Statement</i> to specific research ethics issues
<b>Afternoon Tea</b>	
3.15 - 4.30pm	Expert panel response to issues and problems

DATE	WORKSHOP	GUEST SPEAKER
18 August	Melbourne	Professor Andrew Glenn, Chair of the Joint Working Party on the <i>National Statement</i>
19 August	Sydney	Professor Andrew Glenn
20 August	Hobart	The Hon Judith Jackson MLA, Tasmanian Health Minister
23 August	Perth	The Hon John Day MLA, WA Health Minister
24 August	Adelaide	The Hon Dean Brown MP, Vic. Minister for Human Services
25 August	Darwin	Mr Steven Balch MLA, Member for Jingili
26 August	Alice Springs	Associate Professor John Wakerman, Chair of the Central Australian Institutional Ethics Committee
26 August	Brisbane	Dr Robert Stable, Director General, Queensland Health
27 August	Canberra	Mr Michael Moore MLA, ACT Health Minister

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## 1: EVALUATION

### 1 Workshop Preparations

Flyers were distributed widely to advertise the workshops to human research ethics committees, institutions, researchers, members of Council and the Medical Research Committee and to community organisations with an interest in research. The method of advertising was questioned by a few participants, who noted the predominance of the medical profession and HREC members participating in the workshops. Notable was the low number of young researchers, non-medical and non-HREC participants such as sociologists, psychologists and anthropologists.

Workshops were organised and conducted in Melbourne, Sydney, Hobart, Perth, Adelaide, Brisbane, Darwin, Alice Springs and Canberra. Alice Springs and Darwin were additional workshops to previous years. The program for each workshop was structured to encourage participants to become familiar with the new *National Statement*. Some States varied the program to accommodate local conditions.

A suggestion to improve workshop preparations is to explore other avenues to advertise workshops to appeal to a wider audience, especially in the field of social sciences.

### 2 Workshop Registrations

The organisation of venues and catering for the workshops, and the process for registrations and the mail-out of the pre-reading packages was contracted to Australian Convention and Travel Services (ACTS). Participants who registered early evaluated this service very well. Those who registered late evaluated the service poorly for several reasons: loss of booking; not receiving the pre-reading package; and the inability to attend workshops due to over-booked workshops or closure for further bookings. Communication difficulties were also generated by having three separate groups (State Coordinators, AHEC Secretariat and ACTS) involved in the organisation of the workshops.

An overall increase in registrations by approximately 70% since the last series of workshops in 1995 was higher than anticipated, resulting in over-registrations at most workshops.

On registration, workshop participants was sent a pre-reading package that consisted of:

- A copy of the *National Statement*
- 7 case studies
- a welcome letter

The majority of participants who received the pre-reading package early found the pre-reading package to be of excellent quality and informative.

The following table displays the increase in registrations per venue. The numbers exclude members of the AHEC and the Secretariat.

**Table 1: Participant registrations and % increase in registrations**

	Venue								
	Sydney	Melbourne	Hobart	Perth	Adelaide	Darwin	Alice Springs	Brisbane	Canberra
1999	136	218	43	116	139	58	30	161	77
1995	102	127	22	71	80	N/A	N/A	130	34
% increase	33.3%	71.65%	95.5%	63.4%	73.75%			24%	126.5%

The high demand for registrations and the increased attendance by participants at the 1999 workshops indicate their success.

Suggestions for improving the registration process include:

- Providing a registration deadline;
- Including an option to register for workshops by email; and
- Booking small group sessions at the time of registration.

### **3 Workshop Participants**

Participants were predominantly researchers, members of HRECs, academics and staff from institutes. Students represented 6.4% of participants. This information was obtained from the registration data provided by ACTS.

A large late registration trend resulted in late pre-reading packages being sent that were either not received before the workshops, or received at short notice, which limited participants' reading and understanding of the *National Statement* and therefore their ability to fully participate in the workshops. This caused some frustration among some of the participants.

Overcrowding at some of the venues impacted on participants' comfort, small group discussions and dynamics, and noise levels. Some participants needed to stand for the main sessions.

To assess participants' satisfaction of the workshop program a questionnaire was distributed at the workshops and completed by participants. The majority of participants found the workshops to be very helpful and requested the workshops be held more frequently.

Informal feedback received by AHEC members, Secretariat and State coordinators via verbal comments from participants, indicated satisfaction and appreciation for the structure and content of the workshops. The following tables display participants' response to various parts of the workshop program.

**Table 2: Presentation of the *National Statement***

Venue	Excellent	Very Helpful	Helpful	Not Helpful	Poor
Melbourne	24%	49%	25.5%	1.5%	
Sydney	18%	55%	25%	2%	
Hobart	52%	26%	19%	3%	
Perth	15%	49%	33%	1.5%	1.5%
Adelaide	4%	42%	50%	4%	
Darwin	14.5%	29.5%	44%	12%	
Alice Springs					
Brisbane	21%	45%	28%	4%	2%
Canberra	15.5%	44%	34.5%	3%	3%
<b>Totals</b>	<b>20.5%</b>	<b>42.5%</b>	<b>32%</b>	<b>3.5%</b>	<b>1.5%</b>

General comments:

The majority of participants were of the view that the presentation was very helpful. Feedback from one participant was that the presentation was a "very clear and concise overview. [It] reinforced aspects of the guidelines, and highlighted aspects of specific change/concern".

A few participants felt this session was unnecessary because they had already read the *National Statement* or, that the session could have been shorter.

A small minority of participants stated that they were unclear about the aim of this session.

**Table 3: Plenary Sessions**

Venue	Excellent	Very Helpful	Helpful	Not Helpful	Poor
Melbourne	11.5%	40%	34.5%	14%	
Sydney	2%	36%	53%	4.5%	4.5%
Hobart	7%	45%	31%	7%	10%
Perth	1.5%	47.5%	46%	5%	
Adelaide	4%	23%	58%	15%	
Darwin		44.5%	47%	8.5%	
Alice Springs					
Brisbane	7.5%	37.5%	50%	2.5%	2.5%
Canberra	6.5%	35.5%	58%		
<b>Totals</b>	<b>5%</b>	<b>39%</b>	<b>47%</b>	<b>7%</b>	<b>2%</b>

**Table 4: Case Studies**

Venue	Excellent	Very Helpful	Helpful	Not Helpful	Poor
Melbourne	8.5%	32.5%	39.5%	12.5%	7%
Sydney	15%	36%	40.5%	8.5%	
Hobart	26.5%	50%	20.5%	3%	
Perth	9%	41%	40%	6%	4%
Adelaide	5%	45%	45%	5%	
Darwin	18%	42.5%	34.5%	2.5%	2.5%
Alice Springs					
Brisbane	9%	18%	50%	20.5%	2.5%
Canberra		31%	62%	7%	
<b>Totals</b>	<b>11.5%</b>	<b>37%</b>	<b>41.5%</b>	<b>8%</b>	<b>2%</b>

General comments:

The success of the case study and plenary sessions were evaluated by participants on the experience of the facilitators and their ability to focus the group on the topic.

Sessions that were rated 'excellent' or 'very helpful' were because the sessions were 'well chaired', or 'salient issues' were raised, or 'good discussion' occurred, or discussions were 'well focussed' on the topic.

Sessions that were rated 'not helpful' or 'poor' by participants were due to the facilitator's 'lack of clear guidance', or were 'inadequately prepared', or the facilitator dominating the session, or pushing their own agenda, or 'giving a lecture'. Some groups apparently deviated from the topic by focussing on the research details rather than the ethical issues; it is 'important that the facilitators are instructed to stick to ethical issues, not details of research study applications'. Sometimes the discussion was not related to the new *National Statement*. For example, 'we wandered far from the *Statement*. As such the opportunity to scrutinise the *Statement* was largely lost'.

Some participants requested 'a protocol rather than a broadly worded case study' that would be presented to an HREC. For example, 'we spent a lot of time trying to figure out what they meant and what they were doing so that we could then identify the issues'.

**Table 5: Expert Panel**

<b>Venue</b>	<b>Excellent</b>	<b>Very Helpful</b>	<b>Helpful</b>	<b>Not Helpful</b>	<b>Poor</b>
Melbourne	22%	49%	24.5%	3%	1.5%
Sydney	16.5%	30%	51.5%	2%	
Hobart	7%	38%	48%	3.5%	3.5%
Perth	6.5%	37%	50%	6.5%	
Adelaide		24%	76%		
Darwin	6%	22%	50%	22%	
Alice Springs					
Brisbane	12.5%	20%	55%	10%	2.5%
Canberra	16%	39%	35.5%	6.5%	3%
<b>Totals</b>	<b>11%</b>	<b>32%</b>	<b>49%</b>	<b>7%</b>	<b>1%</b>

General comments:

Quite a few participants felt that the workshops raised more questions than could be answered.

#### **4 General Comments**

Overall, the workshops were a success, judged by the positive feedback provided by participants on their evaluation forms. The majority of participants rated the program sessions as either 'helpful' or 'very helpful'.

Most participants appreciated:

- the breadth of input by participants, who drew upon their broad experience and expertise;
- hearing differing perspectives;
- networking;
- informal discussions;
- exchanging ideas;
- discussing the complexity of ethics;
- the overview of the *National Statement*;
- becoming familiar with the new *National Statement*;
- meeting other HREC members;
- the very comprehensive coverage of a large amount of information; and
- the joint exploration of issues.

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It was noted that many of the same suggestions for improvements for future workshops for the 1995 workshops were echoed in the 1999 workshop evaluations. The following is a summary of similar comments taken from the 1995 workshop report:

- workshops should be less clinically oriented;
- it would be desirable for there to be greater heterogeneity in participants, and session facilitators. It would be desirable for more researchers to be involved;
- there was a general desire on the part of participants at all the workshops for more opportunity for discussion;
- the workshops themselves were considered valuable opportunities for networking. To build on the opportunity, circulation of the names and addresses of participants was requested; and
- there was a call for similar workshops to be conducted more frequently.

Other suggestions for improving the 1999 workshops included:

- Better-prepared facilitators;
- Two facilitators per group to ensure a balance of views;
- Smaller groups for group discussions;
- NHMRC publication bookshop;
- More legal information including Therapeutic Goods Administration/regulatory requirements;
- Larger venues, and for all the sessions to be held on the same level;
- Better set up for morning and afternoon teas to avoid long queues;
- Seats designated for the disabled and consideration for the deaf;
- Separate rooms for each small group session;
- Divide groups into separate categories eg. new HREC members and experienced members or, HREC members, participants and researchers;
- Follow up of main issues identified;
- Invite Indigenous health board members eg. Miwatj, Tiwi and Maningrida;
- Organisers to have some prepared questions to stimulate and direct discussion;
- Better use of microphones; and
- Public symposium on bioethics for the general community.

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## 2 PRESENTATION OF THE NATIONAL STATEMENT ON ETHICAL CONDUCT IN RESEARCH INVOLVING HUMANS

Availability: Printed copies available from NHMRC.

Text is available and can be printed from the NHMRC Ethics Web page:

[www.nhmrc.gov.au/ethics/statemen.htm](http://www.nhmrc.gov.au/ethics/statemen.htm)

### ***National Statement***

- Why it was developed.
- How it was developed.
- Activities to which it applies.
- Approval processes it specifies.
- Principles to be applied.

### **Why it was developed**

- International developments, especially since 1945, eg Helsinki Declaration.
- Australian NMHRC *Statement* on Human Experimentation since 1966.
- NHMRC policy: institutional ethics committees a condition of research funding (1985).
- ARC recognition of need for research ethics code.
- 1996 recommendation of review of NHMRC *Statement*.

### ***National Health and Medical Research Council Act 1992***

- Section 7(1)(a)(v) authorises NHMRC to issue guidelines & advise community on matters relating to ethical issues relating to health.
- Section 8 requires NHMRC, in acting under section 7(1)(a)(v) to issue guidelines for the conduct of medical research involving humans.

### ***National Statement:***

- Contains guidelines and advice on matters relating to ethical issues in health, and
- Contains guidelines on the ethical conduct of research, including medical research, involving humans.

### **Purpose of *Statement***

- Protection of the welfare and rights of participants involved in research.
- National reference point for ethical consideration relevant to all research involving humans.

(Preamble)

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## **How it was developed**

### **Section 8(2)**

Guidelines for conduct of medical research involving humans must be issued precisely as developed by the Australian Health Ethics Committee

### **Section 12**

Requires 2 stage public consultation and regard to be had to submissions

### **Section 35(4)**

Requires guidelines developed by AHEC and issued by NHMRC to be tabled in each House of Parliament within 15 sitting days of their issue

### **Public consultation**

1st stage: late 1996 -1997

129 submissions 1178 pages

2nd stage: July - September 1998

204 submissions 960 pages

### **April 1998 - June 1999**

AHEC + working party

### **October 1998 - June 1999**

Joint Working party, representing ARC, AVCC, Academies of Humanities, Science, Social Science & Technical Sciences and Engineering

### **June 1999**

Endorsement by ARC, AVCC and learned academies

28th: issue by NHMRC

30th: tabled in Commonwealth Parliament

## **Activities to which it applies**

### **Research**

- definition elusive, eg "systematic investigation to establish facts, principles or knowledge"
- key feature: results valid for facts like those researched
- lists of activities can over or under include
- quantity, diversity and emerging genres

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**Research involving humans Includes:**

- data from records
- oral testimony
- informed cooperation in eg cultural context
- observed activities
- testing of responses to devised conditions
- invasive testing of new therapies
- Traditional distinctions inadequate, eg
  - therapeutic/non-therapeutic
  - clinical/non-clinical
  - pure/applied
- Participants include
  - those the focus of research, and
  - those on whom research impacts

**What an HREC Should Review****An activity**

- aimed to establish or confirm facts, principles or knowledge
- where human involvement
- has potential for infringing basic ethical principles relevant to research  
(Preamble)
- institutions need to develop criteria for activities that their HRECs will review
- *National Statement* basis for those criteria
- variation of criteria among institutions may occur

**Approval processes****Institutional responsibilities:**

- Establish & resource Human Research Ethics Committee (HREC)
- Set terms of reference
- Accept legal responsibility

Non-affiliated researchers to have projects approved

**Human research ethics committees**

- Primary role to protect welfare and rights of research participants
- Member's responsibility to decide independently whether conduct of research proposal will so protect participants

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### **Human research ethics committees – membership**

- a chairperson
- two lay people, a woman and a man
- one with knowledge of & current experience in research regularly considered by the HREC
- one with knowledge of & current experience in professional care, counselling or treatment
- one who is a minister of religion or serves similar role in community
- one who is a lawyer
- Membership to equip HREC for all aspects of all research received, eg appoint medical practitioner, statistician
- Maintain diversity & institutional/non-institutional balance
- Appointment for institutions

### **Transitional arrangements**

- Committees established before the *Statement* and in existence after shall continue as if established under *Statement*
- Persons appointed before *Statement* taken to have been appointed under *Statement* till 31 December 1999
- HRECs to conform to *statement* from 1 January 2000

### **Human research ethics committees – meetings**

- all members to receive papers & have opportunity to attend
- chair to be satisfied that views of minimum membership received if not all present
- decisions by general agreement: more time where any member not satisfied participants protected
- HREC may invite researcher to attend
- HREC may seek expert advice, no conflict of interest
- No member conflict of interest
- HREC must approve all participant documentation

### **Researcher to disclose:**

- funding & any affiliation/financial interest
- relevant ethical considerations.

Institution, not HREC, normally communicates with research sponsor

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### **Human research ethics committees – monitoring**

- for institutions and HRECs
- frequency & type reflect risk to participants
- minimum annual reports
- HREC may recommend other mechanisms
- HREC must require report of:
- anything that might warrant review of ethical approval
- early discontinuance of research

### **Human research ethics committees – complaints**

- Institution to establish complaints mechanism
- HREC to nominate person to receive complaints
- If unresolved, referral from HREC to institution's complaints process
- Complaints information to participants
- Institution to establish mechanism for researcher complaints

### **Human research ethics committees – procedures**

- Advocates and interpreters
- Expedited review for minimal risk research
- Recording of decisions
- Suspension or discontinuance of research
- Compliance reports to NHMRC

### **Multi-centre research**

#### **HRECs may:**

- communicate with other HRECs
- accept scientific assessments
- adopt reasons & decisions of other HRECs
- adopt procedures to avoid duplication
- agree on monitoring responsibilities
- Researchers may agree to primary ethical & scientific assessment by one institution & copies of approvals to others who may accept primary HREC approval
- Inform each HREC of all sites, disclose previous & pending HREC decisions

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## **Principles to be applied**

### **Ethics**

- integrity of researchers (*Joint NHMRC/AVCC Statement and Guidelines on Research Practice*)
  - respect for persons
  - beneficence
  - justice
- (Belmont Report 1978) (Preamble)
- communities and individuals
  - dynamic cultural diversity
  - scientific quality of research proposal
  - law and ethics

### **Principles of Ethical Conduct (in first part), apply**

- to all human research to which *Statement* applies
- to interpretation of subsequent parts of *Statement*

### **Principles of Ethical Conduct (Section 1 of *Statement*)**

- Integrity
- Respect for persons
- Beneficence
- Justice
- Consent
- Research merit and safety
- Ethical review and conduct of research

### **Integrity = commitment to**

- search for knowledge
- principles of research conduct
- honest & ethical conduct of research
- dissemination & communication of results (Section 1.1)

### **Respect for persons = regard for:**

- welfare,
- rights,
- beliefs,
- perceptions,
- customs, cultural heritage,
- both individual and collective
- of research participants (Section 1.2)

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Research to be so designed that respect for dignity and well being of participants takes precedence over expected benefits to knowledge (Section 1.4)

**Beneficence = researchers' responsibility to minimise risks of harm or discomfort to research participants (Section 1.3)**

**Justice requires**

- fair distribution of benefits and burdens of participation in research
- avoidance of unfair burden of participation
- fair recruitment exclusion and inclusion
- no non-essential discrimination in selection of participants (Section 1.5)

**Justice recognises**

- that burden/benefit proportion will vary, eg
- in clinical research, risks of participation balanced by possible benefits
- in non-clinical research, absence of benefits balanced by absence of all but minimal risk

**Consent:**

- required for participation (some exceptions)
- information about purpose, methods, demands, risks, discomforts, outcomes
- voluntary, by self, or one with lawful authority for those lacking competence
- may refuse, without reasons
- research design clearly establish participant consent
- no coercion, inducement, influence that may impair voluntary choice
- Some research ethically acceptable without consent, eg de-identified data, observation in public, anonymous survey
- freedom to withdraw consent: be informed about consequences

**Research merit and safety = research to be**

- justified by potential contribution to knowledge
- based on current literature, prior research
- designed to balance risks of harm to participants with likely benefits
- conducted by those with experience & competence, using appropriate facilities & resources

**Ethical review and conduct =**

- no research involving humans until HREC approval
- suspend/modify where risks disproportionate to benefits
- stop involvement if harm likely
- results normally published, open to scrutiny, public knowledge, available to participants

- 
- privacy, confidentiality & cultural sensitivity in personal information to be respected
  - keep information of clinical significance to allow follow-up
  - overseas research to conform to *Statement* and relevant law

### **Types of research participants**

- Children and young people (Section 4)
- Those with intellectual or mental impairment (Section 5)
- Those highly dependent on medical care (Section 6)
- Those in dependent/unequal relationships (Section 7)
- Collectivities (Section 8)
- Aboriginal & Torres Strait Islander People (Section 9)

### **Children & Young People**

#### **Only where**

- question important (research merit)
- their participation indispensable (justice)
- study method appropriate (research merit)
- physical, emotional & psychological safety (beneficence)

#### **Consent from**

- child/ young person where competent **and**
- either parent/guardian (but exceptional circumstances)
- or organisation/person required by law (respect for persons & consent)
- HREC not to approve (& no consent to) research contrary to child/young person's best interests (beneficence)

#### **Intellectual/mental impairment**

- HREC weigh potential benefits & undue burden (justice)
- Consent from person where competent or guardian/lawful authority (respect & consent)
- HREC not approve (& no consent to) research contrary to person's best interests (beneficence)

#### **Highly dependent on medical care**

- emergency care
- intensive care
- neonatal intensive care
- terminal care
- impaired capacity for communication
- unconscious

- 
- HREC may approve without prior consent on conditions (approval)
  - gravity of condition, invasive measures & increased risk (beneficence)
  - capacity for consent compromised (respect & consent)
  - risks of coercion, undue burden (respect & justice)

**HREC may approve without prior consent if:**

- not contrary to interests of patient
- research therapeutic
- risks no more than treatment & condition
- reasonable possibility of benefit over standard care
- inform as soon as possible with option to withdraw

**Where prior consent possible, HREC to be satisfied that:**

- Information process avoids factors that may impair understanding
- Dependency of patients/relatives on medical personnel does not affect decision

**Dependent or unequal relationships**

**Examples:**

- chronic conditions/disabilities & carers
- students & teachers
- employees & employers, supervisors
- HREC satisfied that consent voluntary (respect)
- Researcher assure that no discrimination etc will follow refusal (justice)

**Aboriginal and Torres Strait Islander people**

- NHMRC interim guidelines under review
- Review to involve Joint Working Party, ie NHMRC, ARC, AVCC and learned academies

**Types of research**

- Involving Ionising Radiation (Section 10)
  - reference to radiation guidelines
- Assisted reproductive technology (Section 11)
  - Reference to Assisted Reproductive Technology guidelines
- Clinical trials (Section 12)
- Innovative therapy (Section 13)
- Epidemiology (Section 14)
- Human tissue samples (Section 15)
- Genetics (Section 16)
- Involving deception, concealment or covert observation (Section 17)

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### **Clinical trials**

- Testing whether drug, procedure, device in fact improves health
- Mainly biomedical but any therapy
- Pharmaceutical drugs and devices standards for good clinical research practice

### **HREC to be satisfied about:**

- clarity & validity of aims & research question (research merit)
- balance of risks & benefits (justice)
- methodology on recruitment, sample size (merit)
- safety (respect & beneficence)
- TGA requirements
- International Conference on Harmonisation (ICH) requirements
- no placebo if effective treatment available
- HREC review ethical aspects of budgets, eg. capitation, researcher payments, costs to institutions/participants
- payments not to influence consent/findings
- relevant disclosure of budget
- funding to be adequate

### **Adequate Compensation arrangements**

Researcher to:

- disclose \$ associations
- reporting of adverse, events, protocol changes, new information that may affect ethical status of trial
- early discontinuance
- tracking of device trial participants

### **HREC to determine review to suit drug/device and degree of risk**

May be unethical to continue trial if:

- deviations from protocol,
- unexpected severe side effects,
- one treatment so much better or worse that some participants disadvantaged

Data recording to

- comply with AS4400
- preserve confidentiality
- comply with Federal/ State law
- enable trace participants where biological materials used

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### **Innovative therapy**

- Innovation part of clinical practice (integrity)
- Systematic investigation of innovation to determine efficacy & safety = clinical research
- Clinical research requires HREC approval

### **Epidemiological research**

Distinguished from public health surveillance

Data categories:

- identified
- potentially identifiable
- de-identified

HREC satisfied that

- complies Federal/State privacy policy/law
- researcher skilled & adequate facilities
- record access to researcher only
- scientifically acceptable result disclosure

### **Consent for use of identified/identifiable data**

HREC satisfied that

- collection etc complies law/AS4400
- participants not disadvantaged
- no use beyond protocol
- new use requires new protocol
- for establishing linkage, then coded

HREC can approve access without consent when consent process cause unnecessary anxiety or prejudice scientific value & no disadvantage to participants

OR

impossible in practice due to age, quantity accessibility

AND

interest in research outweighs to substantial degree interest in privacy

- Storage of data to be secure
- Preserve confidentiality in consolidated data
- Published results not identify participants & respect cultural sensitivities
- New clinical knowledge disclosed to health authorities & where possible to participants/medical advisers

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### **Human tissue**

- Samples include diagnostic, statutory, archives & research
- *Statement* excludes fetal, reproductive & tissue from autopsy
- Institutions to develop policies on research with tissue related to source, nature, cultural sensitivity, reason for collection, purpose of research
- full information to donor for consent
- professional removal
- appropriate secure storage
- confidentiality/privacy in recording storing, release of data
- accountability (respect for persons)

### **Consent for use generally required**

- voluntary
- specific to research purpose
- informed on project and
- whether samples to be stored
- Consent generally required for new research use of stored research samples
- Consent required if clinical or archived samples to be used in research that may lead to harm, benefit or injustice to donor

### **HREC may waive consent: regard to**

- any existing consent
- justification for no consent
- privacy protection & de-identification
- risk to privacy of person
- related to other research
- commercial exploitation
- relevant law
- confidentiality to be maintained where samples gained in professional relationship
- minimum identification
- if health relevant information, HREC may require procedures to identify/follow up

### **Genetic research**

#### **Ethical issues arise from**

- genetic information affecting relatives
- family participation in research
- not all relatives want to know
- genetic information can stigmatise

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**Social significance & consequences of genetic research**

- HRECs satisfied no contestable values assumed (scientific merit)
- Balance contribution to knowledge & risk of harm (justice)

**Privacy/confidentiality**

- to be protected in stored information
- specify whether identified/identifiable/de-identified
- risk family identification with de-identified
- consequences for future research of storing de-identified data
- identified info to any others (including family) only with consent
- no transfer to other researchers unless
  - both collaborating on HREC approved research
  - participants not identifiable (HREC may approve exception)

**Consent from participants on being informed:**

- they may refuse
- how privacy protected
- whether data identified/identifiable/de-identified
- if health related information possible
- whether feedback on outcomes & respect choice not to know
- participant consent to informing family
- whether family info needed for research
- participant consent to approach relatives
- if research may detect non-paternity
- if genetic material has uses beyond research
- about intent to store genetic info/material for further research
- if genetic material to be disposed
- that free to withdraw consent, & dispose of genetic material
- collectivity consent may be needed

**Consent for use of stored genetic material**

HREC may waive consent, regard to

- any existing consent
- justification for no consent
- privacy protection & de-identification
- risk to privacy of person
- related to other research
- commercial exploitation
- relevant law

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- institutions to develop/publish policies about use of genetic material for research
  - if health related info about identified person, counselling etc as if clinical setting
  - information/counselling to those asked to consent to genetic research

### **Involving deception**

- Deception, concealment of purpose, covert observation contrary to respect for persons
- Exceptional circumstances where research cannot be conducted without deception, concealment of purpose or covert observation

### **HREC may approve if satisfied that**

- full information would compromise validity
- extent of deception defined
- no suitable non-deceptive alternatives
- no increased risk to participants
- prompt disclosure & de-briefing after participation
- participants may withdraw data
- research/community relationship not corrupted

### **Privacy**

- information privacy research focus
- confidentiality from agreement: privacy broader
- legal regulation of information privacy using Information Privacy Principles
- Commonwealth agencies may infringe IPPs in HREC approved medical research (Section 95 guidelines under review)

### **HREC to be satisfied that:**

- research complies with Federal/State law
- privacy personal info protected, IPPs as standard
- IPP risk of breach, use Section 95 guidelines
- consent for use of personal info on registers
- HREC may allow personal info in linkage studies

### **Intellectual property**

#### **Where commercial exploitation intended:**

- disclosure of researchers' interests to HRECs
- consent of participants

NHMRC/AVCC guidelines on scientific practice & intellectual property

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### 3 CASE STUDIES

Seven case studies were used in the workshops. They were developed by members of the Australian Health Ethics Committee, and were aimed at making workshop participants more familiar with specific sections of the *National Statement*. The following table matches the case studies with the relevant sections of the *National Statement*.

<b>Case Study number</b>	<b><i>National Statement</i> Section &amp; Name</b>
<b>1</b>	<b>Sections:</b> <ul style="list-style-type: none"><li>• 1 Principles of ethical conduct, and</li><li>• 17 Research involving deception of participants, concealment or covert observation.</li></ul>
<b>2</b>	<b>Sections:</b> <ul style="list-style-type: none"><li>• 3 Multi-centre research,</li><li>• 14 Epidemiological research,</li><li>• 15 Use of human tissue samples, and</li><li>• 16 Human genetic research.</li></ul>
<b>3</b>	<b>Section</b> <ul style="list-style-type: none"><li>• 16 Human genetic research.</li></ul>
<b>4</b>	<b>Sections:</b> <ul style="list-style-type: none"><li>• 1 Principles of ethical conduct, and</li><li>• 13 Innovative therapy or intervention.</li></ul>
<b>5</b>	<b>Sections:</b> <ul style="list-style-type: none"><li>• 2 Human Research Ethics Committees, and</li><li>• 3 Multi-centre research.</li></ul>
<b>6</b>	<b>Sections:</b> <ul style="list-style-type: none"><li>• 1 Principles of ethical conduct,</li><li>• 2 Human Research Ethics Committees,</li><li>• 4 Research involving children and young people,</li><li>• 5 Research involving persons with an intellectual or mental impairment, 6 Research involving persons highly dependent on medical care,</li><li>• 7 Research involving persons in dependent or unequal relationships, and</li><li>• 8 Research involving collectivities.</li></ul>
<b>7</b>	<b>Sections:</b> <ul style="list-style-type: none"><li>• 1 Principles of ethical conduct,</li><li>• 2 Human Research Ethics Committees,</li><li>• 4 Research involving children and young people,</li><li>• 5 Research involving persons with an intellectual or mental impairment,</li><li>• 6 Research involving persons highly dependent on medical care,</li><li>• 7 Research involving persons in dependent or unequal relationships,</li><li>• 8 Research involving collectivities, and</li><li>• 12 Clinical trials.</li></ul>

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## CASE STUDY 1:

### **Research involving deception of participants, concealment or covert observation**

As part of a program aimed at reducing the harmful effects of alcohol, research is being conducted on the educational effectiveness of a training program for hotel bar staff. The research is being conducted in two widely separated sections (of comparable profile) of a large metropolitan city. Participants in one group will receive an intensive training program involving a variety of adult learning strategies while the participants in the other group only attend one half hour didactic lecture. This particular study is being conducted by a student.

One of the means proposed to test the effectiveness of the educational program is the use of individuals below the legal age to attempt to purchase liquor. Participants in the study will not be informed of this evaluation strategy. The data collectors will be briefed to ask for an alcoholic drink or purchase liquor in a normal manner. If questioned or challenged they are to leave the premises or liquor outlet immediately without indicating they are involved in this study. In case they are questioned by the police, the data collectors will be provided with a letter indicating that their actions are required as part of an approved study. The police have indicated support for the study.

In the section on ethical considerations, the proposal argues that benefits to the community, from the perspective of both individual and population health, of reducing drinking in adolescents e.g. trauma, outweighs ethical concerns related to the need to conduct the research in this manner. Names of the businesses, proprietors or employees will not be recorded. Only aggregated data will be reported.

## Issues to be considered in Case Study 1

Main components of the research proposal	Elements of the main components	Ethical issues and relevant sections of <i>National Statement</i>
'Research' proposal	<ol style="list-style-type: none"> <li>1. Evaluation of an educational intervention</li> <li>2. Student proposal</li> </ol>	<ul style="list-style-type: none"> <li>• Does this proposal meet the definition of 'research'?</li> <li>• Should it come to an HREC?</li> <li>• See Preamble pp.5-7.</li> <li>• Research merit and safety. See Section 1.15.</li> </ul>
Consent	<ol style="list-style-type: none"> <li>1. Data collectors will attempt to entrap bar staff</li> <li>2. Employees will be unaware and remain unaware of study i.e at no time will they be advised they have been included in the study, even after the data collector has purchased liquor or been refused service.</li> </ol>	<ul style="list-style-type: none"> <li>• See Section 17 in <i>Statement</i>.</li> <li>• Does this study:               <ol style="list-style-type: none"> <li>a) constitute an exceptional circumstance whereby it can not be conducted without using an approach considered unethical, and if so:</li> </ol> </li> </ul>
Data collection	<ul style="list-style-type: none"> <li>• Data collectors will be advised that they are being asked to undertake an illegal act but that the police will not pursue the matter if evidence of being employed in the study is produced.</li> </ul>	<ol style="list-style-type: none"> <li>b) does the study satisfy the requirements listed in Sections 17.2 (a)–(g)?</li> </ol> <ul style="list-style-type: none"> <li>• Minors (or any individual) being asked to entrap others.</li> </ul>
Benefits of the research	<ul style="list-style-type: none"> <li>• Proposal argues that benefits to the community from a public health perspective outweigh ethical concerns related to the need to conduct the research in this manner.</li> </ul>	<ul style="list-style-type: none"> <li>• See 'Research merit and safety' and Section 1.14.</li> <li>• Weighing of public interest</li> </ul>
Recording and reporting of data	<ul style="list-style-type: none"> <li>• Names of businesses, proprietors or employees will not be recorded.</li> <li>• Only aggregated data will be reported.</li> </ul>	<ul style="list-style-type: none"> <li>• Privacy issues</li> </ul>

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## CASE STUDY 2:

### **Research involving multicentre studies, epidemiology, human tissue and human genetics research**

#### **Predictors of low birth weight (background)**

Low birth weight is considered an important predictor of long term health problems (such as diabetes, coronary heart disease) in the individual. We would like to examine possible risk factors that may be influencing the known higher frequency of low birth weight in some subgroups of the population such as teenage mothers, specific ethnic groups. These include smoking in pregnancy, use of non-injected drugs, poor nutrition, domestic violence, infection, income, prior pregnancy loss (miscarriages and abortions), and a specific genetic marker ('LBWG1').

#### **Case/control study methodology**

In order to determine how these risk factors affect the outcome, it is necessary to contact a random sample of mothers of term (at least 37 weeks gestation), low birth weight, non- malformed babies and an age matched control group with normal weight babies and assign a postal questionnaire. These babies would be one to two years old. The random sample will be selected from the data held in the Perinatal Data Collection Unit, a mandatory reporting system for every birth in the State. Information on many of the variables of interest are available from there, as is the hospital of birth of the baby. The hospitals will be provided with the questionnaires to send to the selected sample of women. Questions will refer to the proposed risk factors and current health status of the child. Included with the questionnaire will be a consent form for permission to access their medical record in order to validate or supplement aspects of the information on the questionnaire. This will help with the problem of recall.

There will be **record linkage** to the newborn screening laboratory database to identify the blood spot taken on the baby at the time of birth, the Guthrie spot. The appropriate samples will then have a laboratory test that will reveal whether the baby has the genetic abnormality of interest known to predispose to low birth weight.

All of the results will be analysed using logistic regression to determine the influence of each of these predictors on the outcome and will identify if particular population subgroups are more at risk than others.

## Issues to be considered in Case Study 2

Main components of the research proposal	Elements of the main components	Ethical issues and relevant sections of <i>National Statement</i>
Multiple HREC approval required	From: a) Institutions housing the registers and tissue banks b) All hospitals required to send out questionnaires	See Section 3.  See Sections 14, 15 or 16 for all below.
Selection of cases and controls from central register	Mandatory State-based register with identified information	Waive consent to extract random sample data (See Section 14.4)
Contacting sample	Questionnaires sent by participating hospitals at which births occurred	<ul style="list-style-type: none"> <li>• Consent for women to participate. Does completion of the questionnaire obviate the need for consent form?</li> <li>• Is the questionnaire intrusive / harmful?</li> <li>• How much attempt at follow-up of non-respondents is made?</li> </ul>
Questionnaire data collection	Sensitive, retrospective data.	<ul style="list-style-type: none"> <li>• Appropriateness of questions to be asked in questionnaire?</li> <li>• Willingness to provide accurate data – data quality?</li> <li>• Raises anxieties?</li> </ul>
Access to medical record information	Consent form sent with questionnaire	Consent required from woman (See Section 14.2c)
Record linkage (to newborn screening data)	Use of identified data in these clinical databases	<ul style="list-style-type: none"> <li>• Consent for linkage?</li> <li>• How is matching to be done?</li> <li>• If data are to be used in coded form, who holds the code?</li> </ul>
Genetic testing	Blood taken for clinical purposes	<ul style="list-style-type: none"> <li>• If data are to be used in coded (15.6)</li> <li>• Could test be done on de-identified material? (YES)</li> <li>• Any implications for child? NO – low birth weight already occurred (see Section 16.11)</li> </ul>
Provision of research results	<ul style="list-style-type: none"> <li>• Group data – identification of population subgroups eg. teenagers, ethnic groups.</li> <li>• Personal genetic test results.</li> </ul>	<ul style="list-style-type: none"> <li>• Is feedback possible?</li> <li>• Is feedback requested?</li> <li>• Usefulness and originality of findings?</li> </ul>

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## CAST STUDY 3:

### **Scenario for Human Genetic Research**

#### **Background**

It has been shown recently that mutations in two genes, BRCA1 and BRCA2, can create susceptibility to breast and ovarian cancer.

#### **The Research Proposal**

- To collect pedigrees, clinical information, DNA and tissue samples from families with familial breast cancer at multiple sites around Australia and to transfer these research resources to a central repository.
- To screen the collected and stored DNA for mutations in the BRCA1 and BRCA2 breast cancer susceptibility genes. It is intended to define the frequency of BRCA1 and BRCA2 mutations in Australians with familial breast and/or ovarian cancer, to define the variety of mutations present, to correlate each type of mutation with the risk of developing cancer and to try to identify environmental/lifestyle factors which influence risk.
- To store the pedigrees, clinical information, DNA and tissue samples as a national and international resource for future research by the proponents and other researchers.

### Issues to be considered in Case Study 3

<b>Main components of the research proposal</b>	<b>Elements of the main components</b>	<b>Ethical issues and relevant sections of <i>National Statement</i></b>
Definition of families of interest (inclusion criteria)	Four or more first or second degree relatives with breast or ovary cancer on the same side of the family AND Four or more unaffected living first or second degree female relatives of a person who has had breast cancer	<ul style="list-style-type: none"> <li>• Participants will include women who have had cancer and women who have not had cancer.</li> <li>• The women will have a family history of breast +/- ovary cancer.</li> </ul>
Ascertainment of families	Through familial cancer clinics, to which women have been referred for <u>clinical care</u> . The women may have had cancer or not had cancer. Both groups will have a family history of breast +/- ovary cancer.	<ul style="list-style-type: none"> <li>• Identify and address the clinical needs of the women. Give precedence to these needs over the wish to carry out research.</li> <li>• Ask the women for permission for a member of the research team to make contact to invite them to participate in the research. See Section 16.10(g)</li> </ul>
Obtain consent		<ul style="list-style-type: none"> <li>• Obtain consent to participation in the research in general, and to any particular aspects of the research which require specific consent (see below). See Section 16.9, 16.10 and 16.12</li> </ul>
Contacting other family members		<ul style="list-style-type: none"> <li>• Consent from woman of first contact to approach relatives. See Section 16.10(g)</li> <li>• Ways of approaching relatives eg. through woman of first contact, other family member, GP, letter. See Section 16.10(g)</li> <li>• Obtaining consent from relatives to present the research proposal to them.</li> <li>• Obtaining consent from the relatives for the research.</li> </ul>
Data collection	<ul style="list-style-type: none"> <li>• Confirmation of diagnoses.</li> <li>• Documentation of pedigree.</li> <li>• Lifestyle questionnaire.</li> </ul>	<ul style="list-style-type: none"> <li>• Are there circumstances when obtaining consent from relatives is not necessary? For example:             <ul style="list-style-type: none"> <li>• To record &amp; retain pedigree information provided by the woman of first contact, or</li> <li>• To confirm a diagnosis from a cancer register. See Section 16.13.</li> </ul> </li> <li>• From whom to seek consent to confirm diagnoses.</li> <li>• Appropriateness of questions to be asked in questionnaire.</li> </ul>

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**Issues to be considered in Case Study 3 (continued)**

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<b>Main components of the research proposal</b>	<b>Elements of the main components</b>	<b>Ethical issues and relevant sections of <i>National Statement</i></b>
DNA and tissue collection	<ul style="list-style-type: none"> <li>• Blood for preparation and storage of DNA/RNA.</li> <li>• Breast tissue – cancer tissue, normal tissue removed at prophylactic mastectomy.</li> </ul>	<ul style="list-style-type: none"> <li>• Consent. See Sections 16.12, 16.10(i), (j) and (k), 16.11 and 16.5.</li> <li>• Clinicians advising about prophylactic mastectomy should be independent of the researchers.</li> </ul>
Genetic testing		<ul style="list-style-type: none"> <li>• Consent. See Sections 16.10(b), (c), (d), (e), (h).</li> <li>• Counselling prior to testing if can be, and are to be fed back.               <ul style="list-style-type: none"> <li>• Implications for future health.</li> <li>• Implications for future offspring.</li> <li>• How non-paternity will be dealt with if the research reveals it.</li> <li>• Flagging that the researchers will ask the participant to share clinically significant information with relevant family members. See Section 16.15</li> <li>• Respecting the wish of a participant to not receive result. See Sections 16.10(d), 16.16.</li> <li>• Privacy of result – in general and with regard to family. See Sections 16.3, 16.4, 16.5, 16.7 and 16.8.</li> </ul> </li> </ul>
Central storage of research materials (clinical information, pedigrees, DNA, tissue and test results).		<ul style="list-style-type: none"> <li>• Consent to store. See Sections 16.10 (j and k), 16.12, 16.16.</li> <li>• Storage in identified, coded or de-identified form. See Sections 16.5 and 16.10(b).</li> <li>• Duration of storage. See Sections 16.10(j).</li> <li>• Destruction at end of storage period. See Sections 16.10 (k).</li> <li>• Where stored, who is responsible, and how to contact them.</li> <li>• Privacy of research materials – who will have access to it in identified form. See Sections 16.8 and 16.10(j).</li> </ul>

**Issues to be considered in Case Study 3 (continued)**

<b>Main components of the research proposal</b>	<b>Elements of the main components</b>	<b>Ethical issues and relevant sections of <i>National Statement</i></b>
Access to research materials by researchers.		<ul style="list-style-type: none"> <li>• Consent for future research, including specific but broad ranging research. See Sections 16.10(j).</li> <li>• Commercial value of research materials.</li> <li>• Ethical review prior to access for research – HREC determines whether the requirement for consent can be waived and whether access is in potentially identifiable or de-identified form. See Sections 16.10(j), 16.12, 16.13.</li> </ul>
Access to research materials by research participants.		<ul style="list-style-type: none"> <li>• Is access possible? See Sections 16.10 (i and l).</li> <li>• Under what circumstances will it be provided?</li> <li>• Reserve sufficient DNA to meet clinical needs of the family.</li> </ul>
Release of information to third parties.		<ul style="list-style-type: none"> <li>• With written consent. See Sections 16.10 (e and i).</li> </ul>
Database linkage	<ul style="list-style-type: none"> <li>• Known about at time of consent.</li> <li>• Possibility arises at a later date.</li> </ul>	<ul style="list-style-type: none"> <li>• Consent.</li> <li>• How is matching to be done?</li> <li>• If data is to be used in coded form, who holds the code?</li> <li>• Waive the requirement for consent? See Section 16.13.</li> </ul>
Provision of research results	<ul style="list-style-type: none"> <li>• Group data.</li> <li>• Personal genetic test results.</li> </ul>	<ul style="list-style-type: none"> <li>• Is feedback possible? See Section 16.10(d).</li> <li>• Is feedback requested? See Section 16.10(d).</li> <li>• How will feedback be provided and by whom? See Section 16.5.</li> </ul>

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## CASE STUDY 4:

### **Innovative Therapy**

In your position as Chair of your hospital's Research Ethics Committee, you are approached by a surgical colleague who is interested in developing a new surgical procedure for patients with primary hyperparathyroidism in whom surgical correction of the disorder is indicated. The standard procedure for this condition is surgical exploration of the neck by an experienced parathyroid surgeon leading to identification of all (usually four) parathyroid glands and removal of the gland or glands identified as being abnormal. This procedure is successful in 95% of cases. The surgeon's proposal is to use a new form of scanning which can identify the abnormal gland in most cases, and indicate its anatomical location quite precisely. The gland can then be removed using a "key hole" procedure causing the patient minimal discomfort and having less chance of interfering with the function of the remaining parathyroid glands. A further advantage is seen to be the lessening of hospital stay, and could perhaps even come to be done as day surgery.

The surgeon has successfully trialed this procedure on one patient but one of his colleagues suggested that if he were to do any more, ethical approval should be obtained and hence he has approached you.

What should be your advice, and was it reasonable for the first operation to be carried out without ethical approval?

### **Issues to be considered in Case Study 4**

Firstly, please note that this scenario is hypothetical. A minority of experts might argue that the described "innovation" could be regarded as acceptable standard practice. The most relevant section of the *National Statement* is Section 13 (Innovative Therapy or Intervention). This section allows that some innovations may be introduced in the course of clinical practice, taking note that improvement in medical and perhaps particularly surgical care is dependent on the development of such innovations. In some jurisdictions, statements of ethical conduct specify innovations as research when particular numbers of subjects are involved, eg one or more, two or more, etc. The new NHMRC *National Statement* has chosen not to follow that path, but to recognise that innovations may be introduced as part of normal clinical practice but should be regarded as research, particularly when they are subjected to systematic investigation so as to determine safety and efficacy.

Your group may judge that the first operation was reasonable provided it was not a complete departure from recognised clinical practice or imposed unacceptable risks on the individual patient. It would be expected that the patient would have been given full information about the non-standard nature of the procedure and that consent had been given on this basis.

If the new procedure is now to be trialed systematically, it should be regarded as clinical research as specified by Section 13 of the *National Statement*. This means it must now comply with the provisions of Section 1, particularly parts 1.13 to 1.15

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dealing with research merit and safety, and 1.3 to 1.4, dealing with the balance of benefits and harms.

Particular attention in this setting is drawn to 1.13 and 1.15, relating to the need for clinicians undertaking innovative treatment to have fully researched the literature and to have available to them all the required facilities for systematic investigation if such is to be undertaken.

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## CAST STUDY 5:

### **Multi-centre Research**

Your hospital's Research Ethics Committee receives an application from the oncology research group in the Department of Cancer Medicine. The proposed study involves trialing a new approach to first-line therapy in patients with glioma, a malignant brain tumour. Usual first-line therapy involves debulking surgery followed by radiotherapy, but recurrences are common. Further radiotherapy is usually not possible, and the tumours respond poorly to usual chemotherapy regimens.

In a previous study, the investigators treated patients with glioma recurrences by further debulking surgery followed by insertion of a slow-release 'wafer', impregnated with either a cytotoxic drug or placebo, into the resulting brain cavity. The intention was to achieve high local concentrations of cytotoxic drug at the site of the tumour recurrence, whilst minimising systemic toxicity. The outcome of the recurrence study showed a statistically significant increase in median survival in the active versus placebo group, and the investigators now wish to test this approach as an added component of first-line therapy.

The investigators are members of a national oncology study group, and nine other centres are participating. The drug has been on the market for many years as a standard cytotoxic agent, and the pharmaceutical company has no interest in funding the study. The wafer manufacturer is providing the wafers impregnated with active drug and placebo, but is not providing any other support since it considers the market potential for this application to be very limited.

The investigators indicate the status of the application at the other centres as follows: Centres 3, 4, 7 and 9 — approved; Centres 2 and 8 — deferred; Centre 5 — rejected; Centres 1 and 6 — submitted.

Your scientific subcommittee (which provides expert assessments of clinical trials for the HREC) has expressed some concerns after consideration of the protocol. In the previous study, although there was an increase in the median survival time amongst those on active treatment, careful review of unpublished data requested from the applicants indicated that this group also had a significantly longer period of dependency on nursing home and hospice care. This information and its possible implications were not mentioned in the plain language information statement.

Your committee has serious reservations about the study itself, and about the informed consent procedures. However, the investigators insist that their approach represents a major advance in glioma therapy. They claim that delays in approval or rejection by the HREC would result in many of their patients being denied this valuable treatment, and a loss of kudos for their Department and for the Institution. They point out that they are already recruiting patients at a nearby private hospital, using the approval of another ethics committee.

How should your committee proceed? What are its obligations to communicate its concerns to other committees? Is it permissible to request copies of correspondence

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from other committees? If your committee rejects the study, or modifies the informed consent procedures, should your investigators be required to abide by your decisions at the private hospital as well?

### **Issues to be considered in Case Study 5**

The major concern here is that the cytotoxic drug may have caused local brain inflammation or neurotoxicity, resulting in increased functional impairment and dependency in the actively treated group. If so, survival time would be increased, but at the cost of significantly decreased quality of life. Note that one other committee has rejected the proposal.

On the other hand, is the scientific subcommittee correct in its interpretation of the unpublished data? Do the assessors on the subcommittee have the appropriate expertise? After all, the investigators (who should be experts themselves) do not appear to agree with them, and other committees have approved the study. It may be that the numbers in the first study were small, or that the apparently increased dependency was due to some other confounding factor, or was of minor clinical importance.

Then again, perhaps the investigators were blinded by their enthusiasm; and perhaps those committees that approved the proposal did not have access to appropriate independent expert advice.

**Discussion Point:** *Would this situation be better dealt with by (1) all participating HREC's having access to one another's assessors reports, or (2) getting together and soliciting a shared assessment by a group of appropriately qualified experts?*

It is clear that different committees considering the ethics of this proposal at the participating centres are reaching different conclusions, but their reasons are not known to one another.

**Discussion Point:** *Exchange of information between committees would clearly be helpful. Would this be a breach of confidentiality? How can it be done ethically and efficiently?*

Even with good communication between HRECs, uncoordinated responses could result in committees repeatedly changing their recommendations or requiring amendments as information trickles in from other centres.

**Discussion Point:** *Could a centralised system of ethical approval for multicentre studies overcome this? What are the pros and cons?*

This is essentially an investigator-initiated project using a marketed drug. It will be a CTN. There is no commercial sponsor, so the institution will be the sponsor and will carry the legal liability.

**Discussion Point:** *Would committees be prepared to accept the decision of another committee without having scrutinised the proposal themselves? If not, how else could committee responses be coordinated and harmonised?*

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## CASE STUDY 6:

### **Social Research**

A mature-age PhD student applies for ethical clearance for a project seeking an understanding of the development and rise of the consumer movement of people with psychiatric disabilities in a region.

There will be 100 semi-structured interviews with people with psychiatric conditions, family members, advocates, paid and unpaid carers, bureaucrats and providers. It is proposed to show how the status quo has developed, mistakes, and develop a model of best practice in consumer participation in health care decision making.

The researcher identifies as having 30 years involvement as a professional (psychologist) in the region, and having recently developed a psychiatric condition is keen to explore the other side. The researcher is semi-retired and proposes to use contacts derived via consumer and professional life in the region to do the interviews, which will touch upon the person's life experience, how they came to be involved in the mental health field and positive and negative experiences.

The application notes that it will build upon recent efforts in the mental health arena to utilise consumer input and perspectives. The literature search has revealed that little has been documented of the effects of particular approaches which utilise the discourse of consumer input, and that is an arena of constant change. Providers and consumers alike seem to have engaged in little written evaluation of different models, approaches and activities in an environment where many are busy grappling with change and apparent lack of resources.

## Issues to be considered in Case Study 6

<b>Main components of the research proposal</b>	<b>Elements of the main components</b>	<b>Ethical issues and relevant sections of <i>National Statement</i></b>
Nature of Participants	<ul style="list-style-type: none"> <li>• There is a marked variation in dependency/capability of people with psychiatric conditions.</li> <li>• There is a need for consideration of those in acute care and whether or not they should participate.</li> </ul>	<ul style="list-style-type: none"> <li>• See Section 5.</li> <li>• See Sections 6 and 7.</li> </ul>
Different Participants	<ul style="list-style-type: none"> <li>• Difference between the situation and issues of the variety of participants.</li> <li>• Will young people participate?</li> </ul>	<ul style="list-style-type: none"> <li>• Is sensitivity to this shown in protocol?</li> <li>• Is there a need for young people to participate? See Section 4.</li> </ul>
Selection of Participants	<ul style="list-style-type: none"> <li>• There is a need for a protocol as to how participants will be selected.</li> <li>• Will it involve contact with a community/consumer organisation and/or how will participants be contacted and selected?</li> <li>• Will it guard against people feeling they have to participate?</li> <li>• Effective Consent?</li> </ul>	<ul style="list-style-type: none"> <li>• If a collectivity is involved consult Section 8.</li> <li>• Consult Sections 1.7-1.12</li> </ul>
Contacting participants	<ul style="list-style-type: none"> <li>• Will this involve in-patients, and if so, how will it be tackled?</li> </ul>	<ul style="list-style-type: none"> <li>• See Section 7.</li> <li>• Also worth asking why contact with in-patients would be required?</li> </ul>
Questionnaire and Participation	<ul style="list-style-type: none"> <li>• Is the approach sensitive?</li> <li>• Is there recognition of issues associated with such research in a small region/community, especially privacy/ confidentiality?</li> <li>• Is there a need for some participants to consult their treating practitioner prior to participating?</li> <li>• Equity of Participation.</li> </ul>	<ul style="list-style-type: none"> <li>• Appropriateness of questions to be asked in questionnaire?</li> <li>• Raises anxieties/intrusive?</li> <li>• Is best practice in social research being followed?</li> <li>• Is there a need for advocates/ interpreter participation? (See Sections 2.25-2.26)</li> </ul>
Provision of research results.	<ul style="list-style-type: none"> <li>• Identification of population subgroups eg. teenagers, NESB groups.</li> <li>• All research reported in a way that individuals cannot be identified</li> </ul>	<ul style="list-style-type: none"> <li>• Is feedback possible?</li> <li>• Is feedback requested?</li> <li>• Usefulness and originality of findings?</li> </ul>

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## CASE STUDY 7:

### **Clinical Trial Using a Placebo**

Patients with mild (type 2) diabetes (defined as having a fasting plasma glucose of 7.0 mm.mol/L) usually respond to a treatment regimen of diet, exercise and weight reduction. Some do require additional antidiabetic treatment.

For this group, a pharmaceutical firm has developed a new protein derived drug, which stimulates a rapid release of insulin (if short duration) from pancreatic cells. In animal studies, and in a small pilot study in humans, this drug, N17, appears to be safe, and it is now proposed to test its efficiency and safety in a randomised placebo controlled trial of 1000 patients.

Physician A has been offered supplies of different strengths of N17 and asked to recruit his type II diabetic patients to the study. To date, no side effects of the drug have been noted, but this cannot be guaranteed. Likewise the optimum dose for humans is unknown. The study is intended to determine whether addition of the drug to diet and exercise is of benefit, and if so in what strengths.

Patients will have the intent of the study explained to them. If they wish to take part, they will understand that they must continue their program of diet and exercise, but will, as well, take a tablet 30 minutes before each meal. They also know that there are 3 in 4 chances that their prescription is an untried new drug, which may or may not be of benefit to them, and a 1 in 4 chance that their prescription tablet is a placebo, lactose.

The drug will be supplied by the firm to the Hospital Pharmacy. Tablets will be in 3 strengths: 25mg, 50mg, 100mg and a placebo which looks the same will also be supplied. Patients who attend Doctor A in the Diabetic Clinic and wish to participate in the trial will be randomised to one of 4 groups. The Pharmacy will code the drug, and document the patients of each group. Neither patients, nor doctor, will know to which group each patient has been assigned.

The trial will last 24 weeks. Each patient will be seen every four weeks, and body weight and fasting plasma glucose measured and documented.

The Research Plan, Toxicology data, Patient Information Sheet and Consent Form have been submitted to the Hospital Ethics Committees of several Australian hospitals.

To this date, one large hospital, likely to recruit 300 patients, has approved the trial, though its Ethics Committee has asked what will happen if the drug turns out to be useful to some patients, and is then withdrawn after 24 weeks.

One other hospital, with a likely recruitment target of 80 patients will not do the trial, as its HREC considers the use of a placebo is unethical.

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## Issues to be considered in Case study 7

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<b>Main components of the research proposal</b>	<b>Elements of the main components</b>	<b>Ethical issues and relevant sections of <i>National Statement</i></b>
Nature of Participants	<ul style="list-style-type: none"> <li>• There is a marked variation in dependency/capability of people with psychiatric conditions.</li> <li>• There is a need for consideration of those in acute care and whether or not they should participate.</li> </ul>	<ul style="list-style-type: none"> <li>• See Section 5.</li> <li>• See Sections 6 and 7.</li> </ul>
Different Participants	<ul style="list-style-type: none"> <li>• Difference between the situation and issues of the variety of participants.</li> <li>• Will young people participate?</li> </ul>	<ul style="list-style-type: none"> <li>• Is sensitivity to this shown in protocol?</li> <li>• Is there a need for Young people to participate? See Section 4.</li> </ul>
Selection of Participants	<ul style="list-style-type: none"> <li>• There is a need for a protocol as to how participants will be selected.</li> <li>• Will it involve contact with a community/consumer organisation and/or how will participants be contacted and selected?</li> <li>• Will it guard against people feeling they have to participate?</li> <li>• Effective Consent?</li> </ul>	<ul style="list-style-type: none"> <li>• If a collectivity is involved consult Section 8.</li> <li>• Consult Sections 1.7 - 1.12.</li> </ul>
Contacting participants	<ul style="list-style-type: none"> <li>• Will this involve in-patients, and if so, how will it be tackled?</li> </ul>	<ul style="list-style-type: none"> <li>• See Chapter 7.</li> <li>• Also worth asking why contact with in-patients would be required?</li> </ul>
Questionnaire & Participation	<ul style="list-style-type: none"> <li>• Is the approach sensitive?</li> <li>• Is there a recognition of issues associated with such research in a small region/community, especially privacy/confidentiality?</li> <li>• Is there a need for some participants to consult their treating practitioner prior to participating?</li> <li>• Equity of participation</li> </ul>	<ul style="list-style-type: none"> <li>• Appropriateness of questions to be asked in questionnaire?</li> <li>• Raises anxieties/intrusive?</li> <li>• Is best practice in social research being followed?</li> <li>• Is there a need for advocates/interpreter participation? (See Sections 2.25 - 2.26).</li> </ul>
Provision of research results	<ul style="list-style-type: none"> <li>• Identification of population subgroups eg. teenagers, NESB groups.</li> <li>• All research reported in a way that individuals cannot be identified.</li> </ul>	<ul style="list-style-type: none"> <li>• Is feedback possible?</li> <li>• Is feedback requested?</li> <li>• Usefulness and originality of findings?</li> </ul>

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## APPENDIX 1:      OBTAINING COPIES OF THE                              NATIONAL STATEMENT

The *National Statement on Ethical Conduct in Research Involving Humans* can be downloaded from the NHMRC web site at:  
<http://www.nhmrc.health.gov.au/ethics/contents.htm>.

Copies can also be obtained at a cost of \$12.95 each from AusInfo, by telephoning 132 447 (toll-free number).

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## The National Health and Medical Research Council

The National Health and Medical Research Council (NHMRC) is a statutory authority within the portfolio of the Commonwealth Minister for Health and Aged Care, established by the *National Health and Medical Research Council Act 1992*. The NHMRC advises the Australian community and Commonwealth; State and Territory Governments on standards of individual and public health, and supports research to improve those standards.

The NHMRC advises the Commonwealth Government on the funding of medical and public health research and training in Australia and supports many of the medical advances made by Australians.

The NHMRC also develops guidelines and standards for the ethical conduct of health and medical research.

The Council comprises nominees of Commonwealth, State and Territory health authorities, professional and scientific colleges and associations, unions, universities, business, consumer groups, welfare organisations, conservation groups and the Aboriginal and Torres Strait Islander Commission.

The Council meets four times a year to consider and make decisions on reports prepared by committees and working parties following wide consultation on the issue under consideration.

A regular publishing program ensures that Council's recommendations are widely available to governments, the community, scientific, industrial and educational groups.

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- Nutrition
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- Sport/Injury
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