HEALTH & DISABILITY COMMISSION RESEARCH SURVEY

Case Study A: Observational study measuring clearance of antibiotics during dialysis.

Dr A want to study how quickly antibiotics used to treat septic patients in Intensive Care Units are removed by dialysis. It is already known that most antibiotics are removed by dialysis to some extent, but the rate can vary. Consumers with severe sepsis often require dialysis therapy due to acute kidney injury. A special form of dialysis is used for these consumers in the ICU, but currently there is no information available regarding the rate at which that form of dialysis removes the antibiotics used to treat sepsis. If antibiotics are cleared by dialysis at a faster rate than expected, the sepsis could be undertreated.

Dr A proposes a study involving acutely septic patients in the ICU, who are unlikely to be able to provide informed consent owing to the impact of the sepsis. Dr A will not amend the treatment provided to the study participants – they would be provided with antibiotics and dialysis in the same way as they would outside of the study. However, Dr A would enrol the participants in his research and measure the changes in antibiotic concentrations during the participants' dialysis sessions. Changes would be measured by a number of tests, including urine and blood tests that would not otherwise be performed.

Information from the study would not affect the clinical management of the participants, and they would not benefit from the research. However, Dr A believes the data gather may lead to more accurate dosing of antibiotics for other septic patients in ICUs in the future.

A. If you were a patient with sepsis and unable to consent, would you want the research to go ahead with you as a participant?

Yes.

a) **There is no change in treatment envisaged whether the patient is in the programme or not;**
b) **Data from the urine and blood tests could provide valuable information for future treatments;**
c) **Routine urine and blood tests would be being carried out on such a patient anyway.** while extra information would be extracted.

Case Study B: Clinical trial comparing two products used following neurosurgery.

Dr B wants to compare the safety and effectiveness of two products used to achieve a watertight closure of patients' brain membranes following neurosurgery. Both products have already been clinically approved and are commonly used by surgeons. The current evidence does not indicate that either product is safer or more effective than the other, but no research has been conducted that directly compares the two products.

Dr B proposes to conduct a study on consumers undergoing neurosurgery, who would be randomly allocated to receive one of the two products. Dr B would then collect data about the safety and effectiveness of each product.

The consumers are mostly having surgery in relation to brain tumours and are likely to have reduced capacity to make a decision. Some of the potential participants may have brain injuries, cognitive impairments, intellectual disabilities, mental illnesses or be in intensive care. While some of the proposed participants may be able to provide informed consent, others will not have the capacity to do so. Dr B believes that both groups need to be included in the research in order to gather useful data that can be generalised to other consumers in the future.

* These comments were not included in my online submission.

Dr B intends to include consumers who are unable to give consent, and then seek 'delayed consent' from any consumers who regain the capacity to consent after the trial, If any of those consumers refuse consent after regaining capacity, their date will be removed from the study.

B.1 If you were having this surgery and unable to consent, would you want the research to go ahead with you as a participant?

Yes.

a) **With random selection of the product used in any particular situation, there is no violation of the patient by invasion or the introduction of another element into the surgery;**
b) **One or other product is routinely used already and the research is simply to compare the two in order to ascertain which is the more reliable and effective;**
c) **It is not as if the original surgery would be undone to implant the other product in the end.**

B.3 What are your views about 'delayed consent'?

That very much depends on what the consent is asked for. In this instance, personally I cannot see any problem with it, but I realise that many people are hypersensitive to any information about themselves or their treatment being shared with anyone.

Case Study C: Trial regarding care provided to consumers with severe dementia.

Dr C wants to study the care provided to rest home residents with severe dementia. Dr C Believes that conventional care for such consumers is task-focussed, concerned primarily with the consumer's physical needs and daily activities. Dr C things conventional care may be neglecting consumers' psychosocial needs, meaning that many consumers with dementia are spending many hours alone and emotionally distressed. Dr C thinks that part of the problem may be that a dementia diagnosis is treated as diminishing a consumer's personhood, leading staff to reduce their efforts to establish and maintain relationships with the consumer.

Dr C proposes a study that would randomly allocate consumers with severe dementia into two groups, each group receiving a different type of care. Group 1 would receive conventional care, which focuses on physical task-oriented practices and physical needs. Group 2 would receive 'interactive care', an alternative to conventional care that is intended to maintain personhood as dementia progresses. 'Interactive care' includes a greater focus on the psychosocial needs of the consumer. At this stage, there is very little evidence about the benefits or risks associated with 'interactive care'. However, Dr C Believes that the proposed study could supply evidence that would lead to improvements in the care provided to consumers with dementia.

It is not known whether the research would be in the participants' best interests. They would have to undergo additional assessments as part of the research, but the additional assessments could benefit the participants if the increased contact with the researchers was beneficial to them, or changes in their condition were picked up that would not otherwise have been noticed. On the other hand, there is a risk that some participants may find the additional contact distressing.

The proposed trial would take place over four months. Researchers would assess the participants' agitation levels, psychiatric symptoms and quality of life before and directly after the trial period, and then again four months after the conclusion of the trial.

* These comments were not included in my online submission.

The fact that a consumer has dementia does not necessarily mean that he or she is unable to provide informed consent. Some may be capable of providing informed consent with appropriate support, or they may have intermittent periods when they are able to provide consent to participate in the research. Dr C also proposes to include in the study consumers who are not able to consent.

C.1 If you were a person with dementia and unable to consent, would you want to be a participant in this research?

Unsure.

a) **I am unsure how the 'quality of life' would be assessed;**
b) **I am also doubtful as to just how one would go about obtaining consent under these circumstances. Even someone supposedly rational might have difficulty in appreciating the object of the exercise;**
c) **What is the measure of 'severe dementia'?**
d) **How would the research benefit current patients? ***
e) **What might be the consequences of a patient's being selected for Group 2 and then at the end of the research period perhaps returning to conventional practices? How damaging could that be? ***
f) **Surely the kind of care provided in Group 2 should be the norm, not the exception. ***

Case Study D: Clinical trial regarding use of adrenaline

Dr D wants to study the use of adrenaline in the treatment of cardiac arrest. Adrenaline has been used as a routine treatment for cardiac arrest for over 50 years, but its safety and efficacy have not been tested fully. Several previous studies suggest that while adrenaline may help to restart the heart initially, it may also lower overall survival rates and increase brain damage. While these studies have led to significant concerns about whether adrenaline could be harming consumers, the body of evidence is not yet strong enough to change current practice.

Dr D proposes a large clinical trial to gather further information. The trial would be randomised, double-blind and placebo-controlled. This means that some of the participants would receive adrenaline and some would receive a placebo (in this case, salt water). During the trial, neither the participants nor the paramedics would know who was being given adrenaline and who was being given salt water.

No consumer undergoing treatment for cardiac arrest would be able to provide informed consent to participate in the study, so Dr D proposes to enrol consumers in the trial without obtaining consent. She considers that the research is important to ensure the best outcomes for consumers who have cardiac arrests in the future, and that it cannot be conducted on consumers who are able to provide consent.

To deal with this issue, Dr D suggests an 'opt-out' process for consent. Consumers not wishing to be enrolled in the study would be able to opt out by requesting a bracelet with 'NO STUDY' engraved on it. Awareness of the study would be raised through a public information campaign.

D.1 If you suffered a cardiac arrest, would you want to be part of the study?

No.

a) **I might be the one who received the salt water!** (tongue in cheek!)
b) **The body of evidence does not support the research as yet.** - obviously.
c) **Of course, if I am dead, there is no answer to the dilemma because it might not** have ~~have~~ been the adrenaline which caused my departure.

* These comments were not included in my online submission.

d) How many of the public would be able to understand the aforesaid 'public information campaign'? *

D.3 What are your views about the proposed 'opt out' process?

a) At what stage would you ask someone whether or not he/she wanted to take part in the research?
b) A heart attack does not usually pre-warn the patient of its imminent arrival or severity, so the patient could well be unconscious (or dead! *) anyway.

Case Study E: Clinical trial of drug for people with Down syndrome.

Dr E wants to investigate whether a particular drug will improve the cognitive and learning abilities of people with Down syndrome. He proposes a randomised, double-blind, placebo-controlled study. This means that some of the participants would receive the study drug and some would receive a placebo (for example, a sugar pill). During the trial, neither the participants nor the researchers would know what was receiving the drug. Participants would be required to undergo regular six-hour assessment visits to check their progress.

The study drug has already been tested on people without Down syndrome. That research provided some information about the possible risks and side-effects of the drug, including that, for some participants, it increased the incidence of contemplating suicide. However, there may be other risks or side-effects that have not yet been discovered. In particular, the effects of the drug on people without Down syndrome may be different from those on people with Down syndrome.

It is not known whether the drug will have the desire effect on cognition or learning (or any other beneficial effects). However, it is likely that even if the drug did lead to an improvement in cognition for the research participants, the effect would be temporary because the drug would not be available to participants after the conclusion of the trial.

Some adults with Down syndrome may be capable of providing consent if given appropriate support and information. Those consumers could then be enrolled in the study in accordance with ordinary consent principles. Dr E proposes also to enrol participants who are not able to give consent because the effects of the drug on those participants may be different. Dr E proposes to consult with family/whanau/ caregivers and, if they express objections, those participants will not be enrolled.

E.1 Do you think people with Down syndrome who are unable to give informed consent should be part of this research?

No.

a) The desired benefits to the patient have not been proved.
b) The possibility of suicidal thoughts following administration of the drug in other studies.
c) The fact that the drug would not be available following the research period.
d) The chances of damaging the cognition and learning abilities the participants already have could be quite high. *
e) Has enough thought been given to the possible consequences of withdrawing the drug should it prove beneficial to the participant? *

* These comments were not included in my online submission.

E.3 Do you think the propose consultation with family/whanau/caregivers gives sufficient protection for participants who are unable to give consent?

No.

a) **No family member is able to know absolutely what the person concerned, if fully cognitive and 'normal', would choose.**
b) **Family would be imposing on the Down syndrome person their own perception of the advantages/disadvantages of the drug to the person.**

FURTHER QUESTIONS AROUND RESEARCH AND CONSENT

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent? If yes, please state the reasons why. If no, please state the reasons why not.

Yes.
As in the first two case studies, there are times when an unconscious patient's response to a particular treatment can provide valuable information for future treatment of the condition.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.

a) **There should be no invasion of the person by physical means.**
b) **There should be no change in treatment just to provide answers – only results should be assessed.**
c) **Lessons from the 'Unfortunate Experiment' should be kept in mind.**

1.3 Do you think the same laws should apply to all health and disability-related research?

Yes.
Purely academic research smells of the 'Unfortunate Experiment'. If anything, it should be under more stringent conditions than those apply to health care or disability services providers.

Dissent.

Some people who are unable to make an informed choice to participate in research may be able to express dissent or refuse the procedures involved, for example by way of facial expressions indicating pain or fear.

2.1 Should the law state expressly that, irrespective of the person's level of competence, any expression of dissent or refusal to participate in research must be respected?

Yes.

*** These comments were not included in my online submission.**

You never know just how much a person who appears to be unconscious hears and understands. If there is any possibility that the person is uncomfortable with the proposed treatment/research programme, it should definitely not be carried out.

Delayed consent.

In some jurisdictions, researchers may be permitted to carry out research on a person who is temporarily unable to give informed consent provided the researcher obtains delayed (retrospective) consent from the participants after they regain the ability to consent. Delayed consent is not permitted under New Zealand law.

3.1 Do you think the law should be changed to allow researchers to obtain delayed (retrospective) consent to research after incompetent participants regains competence to consent?

Unsure.

It is too easy retrospectively to presume the patient has consented. After all, the research has already been done, so there is precious little the patient can do about it.

Alternative participants.

The NEAC guidelines require that studies should not be performed with vulnerable groups if the studies can be performed with other groups. However, this ethical standard is not a legal requirement.

4.1 Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons?

Yes.

a) **I wonder what research which is proposed on incompetent people could not actually be done on competent people.**
b) **If the research cannot be carried out on competent persons, it seems like using the incompetent as guinea pigs.**

Interests of others to be taken into account.

There are different possible criteria about the people who might benefit from research conducted with other people as participants. Examples of such criteria are requirements that the research:

- Be permitted only if it may benefit others who have the same or a similar condition to the participant;
- Be connected to the impairing condition that prevents the participants from being able to provide consent;
- Be intended to provide knowledge of the causes or treatment of the impairing condition that prevents the participants from being able to provide informed consent;
- Be intended to contribute to significant improvement in scientific understanding of the incapacity suffered by the participants.

Given that in most research on incompetent participants any benefits for participants are uncertain, but the outcomes may benefit others:

*** These comments were not included in my online submission.**

5.1 Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?

No.

a) **It is using the person as a guinea pig.**
b) **The criterion as it stands is 'in the patient's best interests' – in this case, it would be other people's best interests.**

Ethics committee approval.

An option for change would be to make ethics committee approval mandatory in all cases where the research involved adult consumers who are unable to provide informed consent. This requirement could be introduced independently, or in addition to other criteria.

6.1 Do you think researchers should be required by law to btain ethics committee approval before conducting health and disability research with adult participants who are unable to give consent?

Yes.

a) **Given the human propensity to push the boundaries, it would be all too tempting to assume that the proposed research is in the patient's best interests.**
b) **There has to be sound ethical control of all such ventures.**

Ways to assess the advantages and disadvantages of participation by incompetent consumers in research.

7.1 Do you think the current best interests test, which requires that the consumer would be better off participating in the research than not participating, strikes an appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed?

No.

a) **If the researcher is the one making the decision that participation is in the best interests of the patient, this is patently open to abuse. Of course the researcher would think that.**
b) **The researcher would have to be able to prove the advantage 'beyond reasonable doubt'.**
c) **The definition of 'advantage' and 'disadvantage' would need to be clearly set out.**

7.3 Please state the reasons you formed this view.

Being of advanced years, I have seen too much of the ways human beings with an axe to grind can skew information to bolster up their theories so they can get permission/approval for their schemes.

*** These comments were not included in my online submission.**

Who decides?

8.1 Do you think there should be any change made to New Zealand law regarding *who* decides whether an incompetent consume will be enrolled in a study?

No.

8.2 Do you think there should be any change made to the roles played by the various possible decision-makers under current New Zealand law?

No.

EPOAs and welfare guardians

Should EPOAs and welfare guardians ever have a part to play in deciding whether an incompetent consumer is enrolled in a study?

Unsure.

If yes, in what circumstances should EPOAs and welfare guardians be involved in decision-making? *Please select all that should apply or provide comment below if you prefer:*

- In all cases where an EPOA or welfare guardian is available?
- Only when particular criteria are met?
- Only where circumstances require that an urgent decision is needed?
- Only when other possible decision-makers are unavailable? (Please specify which decision-makers)

Where an EPOA or welfare guardian is involved in decision-making, what role should he or she have? *Please choose any of the options that you think should apply, or provide comment if you prefer.*

- Consulted by decision-maker?
- Power to veto consumer's participation in the research? ✓
- Provide or withhold consent on behalf of the consumer?
- Other?

Family/whanau

Should family/whanau ever have a part to play in deciding whether an incompetent consumer is enrolled in a study?

Unsure.

If yes, in what circumstances should family/whanau be involved in decision-making? *Please select all that should apply, or provide comment below if you prefer.*

- In all cases where family or whanau is available?
- Only when particular criteria are met?
- Only where the circumstances require than urgent decision is needed?
- Only when other possible decision-makers are unavailable? *Please specify which decision-makers.*

*** These comments were not included in my online submission.**

Where family/whanau is involved in decision-making, what role should they have? *Please select all that should apply, or provide comment below if you prefer.*

- Consulted by decision-maker?
- Power to veto consumer's participation in the research? ✓
- Power to withhold consent on behalf of the consumer? ✓
- Other?

Provider not involved in the research (eg consumer's responsible clinician or GP)

Should a provider not involved in the research ever have a part to play in deciding whether an incompetent consumer is enrolled in a study?

No.

If yes, in what circumstances should a provider not involved in the research be involved in decision-making? *Please select all that should apply, or provide comment below if you prefer.*

- In all cases where a provider not involved in the research is available?
- Only when particular criteria are met?
- Only where the circumstances require than at urgent decision is needed?
- Only when other possible decision-makers are unavailable?

Where this person is involved in decision-making, what role should he or she have? *Please select all that should apply, or provide comment below if you prefer.*

- Consulted by decision-maker?
- Power to verto consumer's participation in the research?
- Provide or withhold consent on behalf of the consumer?
- Other?

8.4 Who do you think should be the final decision-maker when making a decision as to whether to enroll an incompetent person in a research project? Set out below are some options.

- EPOA or welfare guardian?
- Family/whanau?
- Provider no involved in the research?
- Researcher?
- Other?

Please rank the decision-makers you chose in order of preference from 1 being your most preferred to 5 being your least preferred. If you prefer a decision-maker other than those listed, please indicate the decision-maker.

- EPOA or welfare guardian? ( )
- Provider not involved in the research? ( )
- Family/whanau? ( )
- Researcher? ( )
- Other? ( )

Please provide any other comments you wish to make about the decision-makers.

Final comments

* These comments were not included in my online submission.

Please add any comments or final suggestions you wish to make.

This is a very contentious issue and I would probably have to ponder it for some times yet, but in general I would err mostly on the side of incompetent patients not being involved in research without consent. The exceptions would be Case Studies 1 & 2.

*** These comments were not included in my online submission.**

HDC Consultation

Health and disability research involving adult participants who are unable to provide informed consent

Consultation response form

The right to make an informed choice and give informed consent before receiving health or disability services, including participating in research, is the cornerstone of New Zealand's Code of Health and Disability Services Consumers' Rights (the Code). The maxim "nothing about us without us" is an essential part of the culture of New Zealand's health and disability sector.

In some circumstances it is appropriate and lawful to provide health or disability services to a consumer without consent. An example is the provision of emergency life-saving treatment to an unconscious patient. However, it is more complex to decide whether it is appropriate to include a person who cannot give consent to be a subject of research. At present in New Zealand, research on a person who is unable to give consent can take place only if participation in the research is in **that person's best interests**.

Currently, non-consensual research that is not intended to provide a benefit to an individual participant but nevertheless may provide important information of benefit to others cannot proceed because it does not meet the standard of being in the participant's best interests.

This consultation will focus on two fundamental questions: are New Zealand's current laws regarding non-consensual research appropriate and, if not, how should they be amended? Please note that this consultation is limited to research involving **adult** consumers.

To provide us with your comments, either:

a) complete the form online; or

b) print the form, record your answers on the form and return it to PO Box 11934, Wellington 6142. Add additional pages if you wish to do so.

You do not need to answer all of the questions for your responses to be considered by the Commissioner. Leave blank any questions that you do not wish to answer.

Case Study A: Observational study measuring clearance of antibiotics during dialysis

Case Study A questions

A.1
If you were a patient with sepsis and unable to consent, would you want the research to go ahead with you as a participant?

Yes/~~No~~/~~Unsure~~ yes

A.2
Please give the reasons you formed this view.

(1) Because the actual and hypothetical interests of all N.2 ers are best served by the advancement of all knowledge, especially medical knowledge.

(2) Because contrary to your assumptions, my personal best interests are advanced by the best interests of other people being advanced.

Case Study B: Clinical trial comparing two products used following neurosurgery

Case Study B questions

B.1
If you were having this surgery and unable to consent, would you want the research to go ahead with you as a participant?

Yes/~~No~~/~~Unsure~~ yes

B.2
Please give the reasons you formed this view.

Because it is safe to assume that an ethical person would want to serve the interests of others.

B.3
What are your views about "delayed consent"?

I would like to be informed of the results of the research, out of interest.

"Delayed Consent" (retro-active consent?) seems to be an oxymoron. The idea needs more discussion.

Case Study C: Trial regarding care provided to consumers with severe dementia

Case Study C questions

C.1
If you were a person with dementia and unable to consent, would you want to be a participant in this research?

Yes/~~No/Unsure~~ Yes

C.2
Please give the reasons you formed this view.

Same as before

Case Study D: Clinical trial regarding use of adrenaline

Case Study D questions

D.1
If you suffered a cardiac arrest, would you want to be part of the study?

Yes/~~No/Unsure~~

D.2
Please state the reasons you formed this view.

Same as above

D.3
What are your views about the proposed "opt out" process?

– Since the outcome of the trial is not known it would be distressing to be faced with the choice, I would prefer not to know, but again I would like to know what the outcome of the trial was.

– Some people opting out of the trial may have the potential to skew the result.

Case Study E: Clinical trial of drug for people with Down syndrome

Case Study E questions

E.1
Do you think people with Down syndrome who are unable to give informed consent should be part of this research?

~~Yes~~/No/~~Unsure~~

E.2
Please state the reasons you formed this view.

If the drug works it would be quite unethical to withhold it after the trial is finished.

E.3
Do you think the proposed consultation with family/whānau/caregivers gives sufficient protection for participants who are unable to give consent?

~~Yes~~/No/~~Unsure~~

Because of the reasons given in E.2

E.4
Please state the reasons you formed this view.

Consultation questions

Consultation Question 1

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent?

If yes, please state the reasons why. Yes – because the default position should be assumed to be a desire to do the morally right thing – ie. to help advance medical knowledge.

If no, please state the reasons why not.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.

Research should not be allowed on ~~adults~~ people unable to give consent if there is a foreseeable chance of harm.

The Code provisions relate to health and disability research conducted only by a health care or disability services provider. Research relating to health and disability issues is also conducted by non-providers, for example, some academic research. Given that such research is outside the jurisdiction of the Commissioner:

1.3 Do you think the same laws should apply to all health and disability related research?

Yes/~~No~~/~~Unsure~~

1.4 Please make any general comments you have about question 1.3.

The consistency requirement of the logic of ethics requires that like cases should be treated alike.

Dissent

Some people who are unable to make an informed choice to participate in research may be able to express dissent or refuse the procedures involved, for example, by way of facial expressions indicating pain or fear.

Consultation Question 2

2.1 Should the law state expressly that irrespective of the person's level of competence any expression of dissent or refusal to participate in research must be respected?

~~Yes~~/~~No~~/Unsure

2.2 Please give reasons for your answer.

The problem is that interpretation of a person's non-verbal behaviour is very subjective. Issue needs more study. For example how do you distinguish an adverse response to research from an adverse reaction to a vaguely artistic medical procedure? (or unattractive)

Delayed consent

In some jurisdictions, researchers may be permitted to carry out research on a person who is temporarily unable to give informed consent provided that the researcher obtains delayed (retrospective) consent from the participants after they regain the ability to consent. Delayed consent is not permitted under New Zealand law.

Consultation Question 3

3.1 Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence to consent?

~~Yes~~/~~No~~/Unsure

3.2 Please give reasons for your answer.

Delayed consent seems to me to be a contradiction in terms. The issue requires more discussion.

Alternative participants

The NEAC guidelines require that studies should not be performed with vulnerable groups if the studies can be performed adequately with other groups. However, this ethical standard is not a legal requirement.

Consultation Question 4

4.1 Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons?

~~Yes/No/Unsure~~

4.2 Please make any further comments you have about question 4.1.

It is an ethical requirement in itself that we ought not put unreasonable stumbling blocks in the way of advancing medical knowledge.

Interests of others to be taken into account

There are different possible criteria about the people who might benefit from research conducted with other people as participants. Examples of such criteria are requirements that the research:

- be permitted only if it may benefit others who have the same or a similar condition to the participant
- be connected to the impairing condition that prevents the participants from being able to provide consent
- be intended to provide knowledge of the causes or treatment of the impairing condition that prevents the participants from being able to provide informed consent
- be intended to contribute to significant improvement in scientific understanding of the incapacity suffered by the participants.

Given that in most research on incompetent participants any benefits for participants are uncertain, but the outcomes may benefit others:

Consultation Question 5

5.1 Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?

~~Yes/No/Unsure~~

5.2 Please give reasons for your answer.

Because it is an ethical obligation on everyone equally to do what they can, within reason, to advance medical knowledge.

If the answer to question 5.1 is yes:

5.3 If the proposed research may or may not benefit the incompetent participants, but may benefit others, should there be criteria about the group of people that it is intended to benefit?

Yes/~~No~~/Unsure

5.4 If the answer to 5.3 is yes, please indicate the criteria that you think should apply and indicate the order of importance of the criteria with 1. being the most important and 5. being the least important.

1. Should not be to benefit cosmetic surgery
2. should not be to benefit sexual competance
3. should not be to benefit fertility research
4.
5.

Any others?

The relief of suffering should be given priority over the increase of pleasure.

Ethics committee approval

An option for change would be to make ethics committee approval mandatory in all cases where the research involves adult consumers who are unable to provide informed consent. This requirement could be introduced independently, or in addition to other criteria.

Consultation Question 6

6.1 Do you think researchers should be required by law to obtain ethics committee approval before conducting health and disability research with adult participants who are unable to give consent?

Yes/~~No~~/Unsure

6.2 Please give reasons for your answer.

Ethics committees vary in quality and tend to put obstacles in the way of research. The whole issue needs further thought and discussion.

Ways to assess the advantages and disadvantages of participation by incompetent consumers in research

Consultation Question 7

7.1 Do you think the current **best interests** test, which requires that the consumer would be better off participating in the research than not participating, strikes an appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed?

~~Yes~~/No/~~Unsure~~

If you answered "No" to question 7.1, please answer question 7.2.

7.2 If research were to be permitted to proceed without the consent of adult incompetent participants, what criteria/tests do you believe should be used to assess the advantage and disadvantage to the participants?

The "best interests" test sets the bar too high. "No foreseeable danger of serious harm or death" would be a better test.

7.3 Please state the reasons you formed this view.

Because we ought not put stumbling blocks in the way of medical research. We also have a duty to protect incompetent people from harm. (Competent people, on the other hand, can volunteer to take risks)

Who decides?

Consultation Question 8

8.1 Do you think there should be any change made to New Zealand law regarding *who* decides whether an incompetent consumer will be enrolled in a study?

Yes/No/Unsure

8.2 Do you think there should be any change made to the roles played by the various possible decision-makers under current New Zealand law?

Yes/No/Unsure

8.3 If you answered "Yes" to question 8.1 and/or 8.2, please complete the table below about possible decision-makers and the roles you believe they should play in decision-making. Please note that you may consider that a combination of decision-makers is appropriate (either to play different roles in the decision-making process or to make decisions in different circumstances).

Person who could have a role in decision-making (X)	Should X ever have a part to play in deciding whether an incompetent consumer is enrolled in a study?	If yes, in what circumstances should X be involved in decision-making? i.e., a) In all cases where X is available? b) Only when particular criteria are met (e.g., that the study is to be conducted for the purpose of saving the consumer's life or preventing serious damage to the consumer's health)? c) Only when other possible decision-makers (please specify which decision-makers) are unavailable? d) Only where the circumstances require that an urgent decision is needed (see, e.g., Case Study D)? e) Other? *Please choose the letter(s) for any of the options above that you think should apply, or provide comment if you prefer.*	Where X is involved in decision-making, what role should he or she have? i.e., a) Consulted by decision-maker? b) Power to veto* consumer's participation in the research? c) Provide or withhold consent on behalf of the consumer? d) Other? *Please choose the letter(s) for any of the options above that you think should apply, or provide comment if you prefer.* *A veto means the right to refuse or reject permission for an incompetent consumer's participation in research.
EPOAs and welfare guardians	Yes/No/Unsure		
Family/ whānau	Yes/No/Unsure		
Provider not involved in the research (e.g., consumer's responsible clinician or GP)	Yes/No/Unsure		
Researcher	Yes/No/Unsure		
Other (please name):	Yes/No/Unsure		

8.4 Who do you think should be the **final** decision-maker when making a decision as to whether to enrol an incompetent person in a research project? Set out below are some options.

- EPOA or welfare guardian
- Family/whānau
- Provider not involved in the research (e.g., the consumer's responsible clinician or GP)
- Researcher
- Other

Please rank the decision-makers you chose in order of preference from 1. being your most preferred to 5. being your least preferred. If you prefer a decision-maker other than those listed, please indicate the decision-maker.

1.

2.

3.

4.

5.

8.5 Please provide any other comments you wish to make about the decision-makers.

You should exercise extreme care that you don't put unnecessary stumbling blocks in the way of medical research.

9. Please add any final comments or suggestions you wish to make.

Your primary ethical obligation is to advance the most important medical interests of the 2nd Party. A second obligation is to protect the vulnerable from harm.

(This questionnaire is badly designed. These inked areas, for example, would have been better left clear.)

Thank you for your contribution to this consultation.

HDC, with the assistance of the Expert Advisory Group, will review all of the submissions received. The Commissioner will then consider those submissions and decide whether to recommend any changes to the current law. If any change to the Code is recommended, further consultation will be conducted.

Please state your

Name:

Organisation:

Retired Public Servant.

HDC will publish a report after the consultation period has ended. All submissions that you make on this consultation are subject to the Official Information Act 1982. If you consider that all or part of your submission should be treated as confidential, please state this clearly when making your submission and indicate which of the grounds within the Official Information Act for withholding information you believe apply. HDC will take your views into account when determining whether or not to release information. Please note that any decision by HDC to withhold information is able to be reviewed by the Ombudsman.

HDC Consultation

Health and disability research involving adult participants who are unable to provide informed consent

Consultation response form

The right to make an informed choice and give informed consent before receiving health or disability services, including participating in research, is the cornerstone of New Zealand's Code of Health and Disability Services Consumers' Rights (the Code). The maxim "nothing about us without us" is an essential part of the culture of New Zealand's health and disability sector.

In some circumstances it is appropriate and lawful to provide health or disability services to a consumer without consent. An example is the provision of emergency life-saving treatment to an unconscious patient. However, it is more complex to decide whether it is appropriate to include a person who cannot give consent to be a subject of research. At present in New Zealand, research on a person who is unable to give consent can take place only if participation in the research is in **that person's best interests**.

Currently, non-consensual research that is not intended to provide a benefit to an individual participant but nevertheless may provide important information of benefit to others cannot proceed because it does not meet the standard of being in the participant's best interests.

This consultation will focus on two fundamental questions: are New Zealand's current laws regarding non-consensual research appropriate and, if not, how should they be amended? Please note that this consultation is limited to research involving **adult** consumers.

To provide us with your comments, either:

a) complete the form online; or

b) print the form, record your answers on the form and return it to PO Box 11934, Wellington 6142. Add additional pages if you wish to do so.

You do not need to answer all of the questions for your responses to be considered by the Commissioner. Leave blank any questions that you do not wish to answer.

Case Study A: Observational study measuring clearance of antibiotics during dialysis

Case Study A questions

A.1
If you were a patient with sepsis and unable to consent, would you want the research to go ahead with you as a participant?

Yes/~~No~~/~~Unsure~~

A.2
Please give the reasons you formed this view.

The research is just observation

Case Study B: Clinical trial comparing two products used following neurosurgery

Case Study B questions

B.1
If you were having this surgery and unable to consent, would you want the research to go ahead with you as a participant?

~~Yes~~/No/~~Unsure~~

B.2
Please give the reasons you formed this view.

The doctors would be able to seek consent from my family who have an enduring power of attorney

B.3
What are your views about "delayed consent"?

Rubbish. Consenting after the fact is not consent.

Case Study C: Trial regarding care provided to consumers with severe dementia

Case Study C questions

C.1
If you were a person with dementia and unable to consent, would you want to be a participant in this research?

Yes/No/~~Unsure~~

C.2
Please give the reasons you formed this view.

This is why I have an EPoA.

Case Study D: Clinical trial regarding use of adrenaline

Case Study D questions

D.1
If you suffered a cardiac arrest, would you want to be part of the study?

Yes/~~No/Unsure~~

D.2
Please state the reasons you formed this view.

Because I'd take the risk in the hope of surviving.

D.3
What are your views about the proposed "opt out" process?

Case Study E: Clinical trial of drug for people with Down syndrome

Case Study E questions

E.1
Do you think people with Down syndrome who are unable to give informed consent should be part of this research?

~~Yes~~/No/~~Unsure~~

E.2
Please state the reasons you formed this view.

I can't imagine such a scenario would ever arise

E.3
Do you think the proposed consultation with family/whānau/caregivers gives sufficient protection for participants who are unable to give consent?

Yes/~~No/Unsure~~

E.4
Please state the reasons you formed this view.

Most welfare guardians can be relied on to act ethically

Consultation questions

Consultation Question 1

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent?

If **yes**, please state the reasons why.

If **no**, please state the reasons why not.

It all depends on the nature of the research. Most researchers are - however - self serving.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.

The Code provisions relate to health and disability research conducted only by a health care or disability services provider. Research relating to health and disability issues is also conducted by non-providers, for example, some academic research. Given that such research is outside the jurisdiction of the Commissioner:

1.3 Do you think the same laws should apply to all health and disability related research?

Yes/No/Unsure

1.4 Please make any general comments you have about question 1.3.

Not all research is the same

Dissent

Some people who are unable to make an informed choice to participate in research may be able to express dissent or refuse the procedures involved, for example, by way of facial expressions indicating pain or fear.

Consultation Question 2

2.1 Should the law state expressly that irrespective of the person's level of competence any expression of dissent or refusal to participate in research must be respected?

Yes /~~No/Unsure~~

2.2 Please give reasons for your answer.

My son cannot talk but he can express his feelings

Delayed consent

In some jurisdictions, researchers may be permitted to carry out research on a person who is temporarily unable to give informed consent provided that the researcher obtains delayed (retrospective) consent from the participants after they regain the ability to consent. Delayed consent is not permitted under New Zealand law.

Consultation Question 3

3.1 Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence to consent?

~~Yes/No/Unsure~~

3.2 Please give reasons for your answer.

I've already said I feel delayed consent is nonsense

Alternative participants

The NEAC guidelines require that studies should not be performed with vulnerable groups if the studies can be performed adequately with other groups. However, this ethical standard is not a legal requirement.

Consultation Question 4

4.1 Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons?

Yes/~~No/Unsure~~

4.2 Please make any further comments you have about question 4.1.

Interests of others to be taken into account

There are different possible criteria about the people who might benefit from research conducted with other people as participants. Examples of such criteria are requirements that the research:

- be permitted only if it may benefit others who have the same or a similar condition to the participant
- be connected to the impairing condition that prevents the participants from being able to provide consent
- be intended to provide knowledge of the causes or treatment of the impairing condition that prevents the participants from being able to provide informed consent
- be intended to contribute to significant improvement in scientific understanding of the incapacity suffered by the participants.

Given that in most research on incompetent participants any benefits for participants are uncertain, but the outcomes may benefit others:

Consultation Question 5

5.1 Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?

~~Yes~~/No/~~Unsure~~

5.2 Please give reasons for your answer.

Much research has little benefit for the patients it is intended for

If the answer to question 5.1 is yes:

5.3 If the proposed research may or may not benefit the incompetent participants, but may benefit others, should there be criteria about the group of people that it is intended to benefit?

Yes/No/Unsure

5.4 If the answer to 5.3 is yes, please indicate the criteria that you think should apply and indicate the order of importance of the criteria with 1. being the most important and 5. being the least important.

1.

2.

3.

4.

5.

Any others?

Ethics committee approval

An option for change would be to make ethics committee approval mandatory in all cases where the research involves adult consumers who are unable to provide informed consent. This requirement could be introduced independently, or in addition to other criteria.

Consultation Question 6

6.1 Do you think researchers should be required by law to obtain ethics committee approval before conducting health and disability research with adult participants who are unable to give consent?

Yes/~~No/Unsure~~

6.2 Please give reasons for your answer.

Because some researchers need reining in.

Ways to assess the advantages and disadvantages of participation by incompetent consumers in research

Consultation Question 7

7.1 Do you think the current **best interests** test, which requires that the consumer would be better off participating in the research than not participating, strikes an appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed?

Yes/~~No/Unsure~~

If you answered "No" to question 7.1, please answer question 7.2.

7.2 If research were to be permitted to proceed without the consent of adult incompetent participants, what criteria/tests do you believe should be used to assess the advantage and disadvantage to the participants?

7.3 Please state the reasons you formed this view.

Who decides?

Consultation Question 8

8.1 Do you think there should be any change made to New Zealand law regarding *who* decides whether an incompetent consumer will be enrolled in a study?

~~Yes~~/No/~~Unsure~~

8.2 Do you think there should be any change made to the roles played by the various possible decision-makers under current New Zealand law?

~~Yes~~/No/~~Unsure~~

8.3 If you answered "Yes" to question 8.1 and/or 8.2, please complete the table below about possible decision-makers and the roles you believe they should play in decision-making. Please note that you may consider that a combination of decision-makers is appropriate (either to play different roles in the decision-making process or to make decisions in different circumstances).

Person who could have a role in decision-making (X)	Should X ever have a part to play in deciding whether an incompetent consumer is enrolled in a study?	If yes, in what circumstances should X be involved in decision-making? i.e., a) In all cases where X is available? b) Only when particular criteria are met (e.g., that the study is to be conducted for the purpose of saving the consumer's life or preventing serious damage to the consumer's health)? c) Only when other possible decision-makers (please specify which decision-makers) are unavailable? d) Only where the circumstances require that an urgent decision is needed (see, e.g., Case Study D)? e) Other? *Please choose the letter(s) for any of the options above that you think should apply, or provide comment if you prefer.*	Where X is involved in decision-making, what role should he or she have? i.e., a) Consulted by decision-maker? b) Power to veto* consumer's participation in the research? c) Provide or withhold consent on behalf of the consumer? d) Other? *Please choose the letter(s) for any of the options above that you think should apply, or provide comment if you prefer.* *A veto means the right to refuse or reject permission for an incompetent consumer's participation in research.
EPOAs and welfare guardians	**Yes/No/Unsure**		
Family/ whānau	**Yes/No/Unsure**		
Provider not involved in the research (e.g., consumer's responsible clinician or GP)	**Yes/No/Unsure**		
Researcher	**Yes/No/Unsure**		
Other (please name):	**Yes/No/Unsure**		

8.4 Who do you think should be the **final** decision-maker when making a decision as to whether to enrol an incompetent person in a research project? Set out below are some options.

- EPOA or welfare guardian
- Family/whānau
- Provider not involved in the research (e.g., the consumer's responsible clinician or GP)
- Researcher
- Other

Please rank the decision-makers you chose in order of preference from 1. being your most preferred to 5. being your least preferred. If you prefer a decision-maker other than those listed, please indicate the decision-maker.

1. EPoA or welfare guardian.
2. Family
3.
4.
5. Researcher

8.5 Please provide any other comments you wish to make about the decision-makers.

I may be unfair to researchers but some may go too far in their efforts to complete a project successfully.
I have found the medical profession are as diverse as any other group with some self seeking and unconcerned about welfare of patients with intellectual disabilities.

9. Please add any final comments or suggestions you wish to make.

I feel the way you have conducted this consultation does not give me confidence that you will get a cross section of parents of intellectually disabled people. Your advertisement was in a news paper (few people read them) in small print (easily over looked and your consultation document would be hard for many to read.
Do you know about the TPPPA Act?

Thank you for your contribution to this consultation.

HDC, with the assistance of the Expert Advisory Group, will review all of the submissions received. The Commissioner will then consider those submissions and decide whether to recommend any changes to the current law. If any change to the Code is recommended, further consultation will be conducted.

Please state your

Name:

Organisation:

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HDC Consultation

Health and disability research involving adult participants who are unable to provide informed consent

Consultation response form

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In some circumstances it is appropriate and lawful to provide health or disability services to a consumer without consent. An example is the provision of emergency life-saving treatment to an unconscious patient. However, it is more complex to decide whether it is appropriate to include a person who cannot give consent to be a subject of research. At present in New Zealand, research on a person who is unable to give consent can take place only if participation in the research is in **that person's best interests**.

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This consultation will focus on two fundamental questions: are New Zealand's current laws regarding non-consensual research appropriate and, if not, how should they be amended? Please note that this consultation is limited to research involving **adult** consumers.

To provide us with your comments, either:

a) complete the form online; or

b) print the form, record your answers on the form and return it to PO Box 11934, Wellington 6142. Add additional pages if you wish to do so.

You do not need to answer all of the questions for your responses to be considered by the Commissioner. Leave blank any questions that you do not wish to answer.

Case Study A: Observational study measuring clearance of antibiotics during dialysis

Case Study A questions

A.1
If you were a patient with sepsis and unable to consent, would you want the research to go ahead with you as a participant?

Yes

A.2
Please give the reasons you formed this view.

It is an observational study and does not change the treatment protocol.

Case Study B: Clinical trial comparing two products used following neurosurgery

Case Study B questions

B.1
If you were having this surgery and unable to consent, would you want the research to go ahead with you as a participant?

Yes

B.2
Please give the reasons you formed this view.

Both products are certified as safe and seemingly of equal merit. There's minimal risk of harm until proven otherwise. One product may be proven to be superior over the other under particular clinical circumstances.

B.3
What are your views about "delayed consent"?

I do not agree with delayed consent. There are risks of drug-induced confusion, and bias determined by a good or bad outcome. It is a "slippery slope" argument that undermines the code's fundamental principles of personal autonomy, protection of vulnerable people and transparency of providers.

Case Study C: Trial regarding care provided to consumers with severe dementia

Case Study C questions

C.1

If you were a person with dementia and unable to consent, would you want to be a participant in this research?

No

C.2

Please give the reasons you formed this view.

I wouldn't want to run the risk of personal distress from additional assessments. I would have said "yes" if the research design ensured I was immediately withdrawn on signs of distress.

Case Study D: Clinical trial regarding use of adrenaline

Case Study D questions

D.1

If you suffered a cardiac arrest, would you want to be part of the study?

Yes

D.2

Please state the reasons you formed this view.

Continuing clinical practice suggests use of Adrenaline preserves life although there are risks. But, the risk profile and effectiveness does need to be clarified for future care.

D.3

What are your views about the proposed "opt out" process?

I support the opt out process as an essential feature of the study design.

Case Study E: Clinical trial of drug for people with Down syndrome

Case Study E questions

E.1
Do you think people with Down syndrome who are unable to give informed consent should be part of this research?

No

E.2
Please state the reasons you formed this view.

The proposed beneficial effects are stated as only transitory. Vulnerable people are being used here!! The study design puts prospective societal interests over the best interests of vulnerable people which is not acceptable. There's no long term personal benefit, only a projected thesis that there might be a long term societal benefit. There are risks of suicidal thoughts.

E.3
Do you think the proposed consultation with family/whānau/caregivers gives sufficient protection for participants who are unable to give consent?

No

E.4
Please state the reasons you formed this view.

Lay family, whanau and caregivers may not appreciate the full ethical implications of the trial. The risks to participants compared with hypothesized long term societal outcomes may not be grasped against the seduction of the prospect of a chemical cure for cognitive deficits. Family are not always the closest confidants to the participant.

Consultation questions

Consultation Question 1

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent?

If **yes**, please state the reasons why.

Yes. The Code should be a "living document" in both law and application. However, the fundamental principles of personal autonomy, protection of vulnerable people and "do no harm" must be preserved against influences such as pecuniary interests and pseudo-

science. Ethical research within strict parameters, that can elucidate beneficial societal outcomes is justified in order to make overall progress, but, not at the expense of protecting the best interests of vulnerable persons.

If **no**, please state the reasons why not.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.

Strengthen ethical imperatives and guidelines and ensure National consistency; across public and private research, so far as that is possible. Australian, English and Scottish laws and guidelines reflect useful principles. Researchers be obliged to show that, on the balance of probabilities, the enquiry process will not be antithetical to the subjects' interests.

Ensure protocols cover disability research. Funding and infrastructural elements of disability research often differ from those of Health, while the complexity and demography of disability is changing with the aging population and advances in birth care.

The Code provisions relate to health and disability research conducted only by a health care or disability services provider. Research relating to health and disability issues is also conducted by non-providers, for example, some academic research. Given that such research is outside the jurisdiction of the Commissioner:

1.3 Do you think the same laws should apply to all health and disability related research?

Yes

1.4 Please make any general comments you have about question 1.3.

Consistency in the law and public codes is critical to avoid confusion. The public deserve to be informed on, what is known and proven on the one hand, and what is speculative and commercial on the other. Pecuniary interests and selective "truth telling" about the findings of science can be persuasive in molding public lobbying and political opinion. Academic institutions are not immune from such influences.

Robust and authenticated evidence and local trials is needed to guide Code development, along with the nature and volume of complaints and commentaries from consumers. Successive Commissioners have served the public well in this regard.

Dissent

Some people who are unable to make an informed choice to participate in research may be able to express dissent or refuse the procedures involved, for example, by way of facial expressions indicating pain or fear.

Consultation Question 2

2.1 Should the law state expressly that irrespective of the person's level of competence any expression of dissent or refusal to participate in research must be respected?

Yes

2.2 Please give reasons for your answer.

Any expression of descent must be respected. Its authenticity, in terms of personal autonomy, cannot be questioned.

Delayed consent

In some jurisdictions, researchers may be permitted to carry out research on a person who is temporarily unable to give informed consent provided that the researcher obtains delayed (retrospective) consent from the participants after they regain the ability to consent. Delayed consent is not permitted under New Zealand law.

Consultation Question 3

3.1 Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence to consent?

No

3.2 Please give reasons for your answer.

I do not agree with delayed consent. There are risks of drug-induced confusion, researcher influence and bias determined by a good or bad outcome. This is a "slippery slope" argument that undermines the code's fundamental principles of autonomy, protection of vulnerable people and transparency of providers.

Alternative participants

The NEAC guidelines require that studies should not be performed with vulnerable groups if the studies can be performed adequately with other groups. However, this ethical standard is not a legal requirement.

Consultation Question 4

4.1 Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons?

Yes

4.2 Please make any further comments you have about question 4.1.

Reasons for using incompetent persons in research must be justified and be at the heart of the research hypothesis. Vulnerable persons must never be used as a "soft touch" in research.

Interests of others to be taken into account

There are different possible criteria about the people who might benefit from research conducted with other people as participants. Examples of such criteria are requirements that the research:

- be permitted only if it may benefit others who have the same or a similar condition to the participant
- be connected to the impairing condition that prevents the participants from being able to provide consent
- be intended to provide knowledge of the causes or treatment of the impairing condition that prevents the participants from being able to provide informed consent
- be intended to contribute to significant improvement in scientific understanding of the incapacity suffered by the participants.

Given that in most research on incompetent participants any benefits for participants are uncertain, but the outcomes may benefit others:

Consultation Question 5

5.1 Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?

No

5.2 Please give reasons for your answer.

This is a slippery slope provision open to all manner of interpretation that may increasingly threaten the Code's principles.

However, societal interests may be served by permitting research involving incompetent people if:

that work is to benefit others with the same or similar conditions; or,

contribute to significant improvements in the scientific understanding of the incapacity sustained by participants.

If the answer to question 5.1 is yes:

5.3 If the proposed research may or may not benefit the incompetent participants, but may benefit others, should there be criteria about the group of people that it is intended to benefit?

Yes

See 5.2 above.

5.4 If the answer to 5.3 is yes, please indicate the criteria that you think should apply and indicate the order of importance of the criteria with 1. being the most important and 5. being the least important.

1.

2.

3.

4.

5.

Any others?

Ethics committee approval

An option for change would be to make ethics committee approval mandatory in all cases where the research involves adult consumers who are unable to provide informed consent. This requirement could be introduced independently, or in addition to other criteria.

Consultation Question 6

6.1 Do you think researchers should be required by law to obtain ethics committee approval before conducting health and disability research with adult participants who are unable to give consent?

Yes

6.2 Please give reasons for your answer.

Ethics Committee(s) are most likely to add consistency to provisions that allow incompetent people to be involved in research while preserving the principles of the Code. They are also more likely to be able to offer the Commissioner advice based on applications that could lead to future Code modifications as required.

Ways to assess the advantages and disadvantages of participation by incompetent consumers in research

Consultation Question 7

7.1 Do you think the current **best interests** test, which requires that the consumer would be better off participating in the research than not participating, strikes an appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed?

Unsure

I don't get the question? See 5.2, 6.1 and 6.2 responses.
If you answered "No" to question 7.1, please answer question 7.2.

7.2 If research were to be permitted to proceed without the consent of adult incompetent participants, what criteria/tests do you believe should be used to assess the advantage and disadvantage to the participants?

7.3 Please state the reasons you formed this view.

Who decides?

Consultation Question 8

8.1 Do you think there should be any change made to New Zealand law regarding *who* decides whether an incompetent consumer will be enrolled in a study?

Yes

8.2 Do you think there should be any change made to the roles played by the various possible decision-makers under current New Zealand law?

Yes

8.3 If you answered "Yes" to question 8.1 and/or 8.2, please complete the table below about possible decision-makers and the roles you believe they should play in decision-making. Please note that you may consider that a combination of decision-makers is appropriate (either to play different roles in the decision-making process or to make decisions in different circumstances).

I believe Ethics Committee(s) and/or close confidants ought to be enabled to have a role in deciding whether it is right for an incompetent person to participate in the research. Families are not always the most "in tune" with the incompetent person for reasons of history and empathy.

Person who could have a role in decision-making (X)	Should X ever have a part to play in deciding whether an incompetent consumer is enrolled in a study?	If yes, in what circumstances should X be involved in decision-making? i.e., a) In all cases where X is available? b) Only when particular criteria are met (e.g., that the study is to be conducted for the purpose of saving the consumer's life or preventing serious damage to the consumer's health)? c) Only when other possible decision-makers (please specify which decision-makers) are unavailable? d) Only where the circumstances require that an urgent decision is needed (see, e.g., Case Study D)? e) Other? *Please choose the letter(s) for any of the options above that you think should apply, or provide comment if you prefer.*	Where X is involved in decision-making, what role should he or she have? i.e., a) Consulted by decision-maker? b) Power to veto* consumer's participation in the research? c) Provide or withhold consent on behalf of the consumer? d) Other? *Please choose the letter(s) for any of the options above that you think should apply, or provide comment if you prefer.* *A veto means the right to refuse or reject permission for an incompetent consumer's participation in research.
EPOAs and welfare guardians	**Yes/No/Unsure**		
Family/ whānau	**Yes/No/Unsure**		
Provider not involved in the research (e.g., consumer's responsible clinician or GP)	**Yes/No/Unsure**		
Researcher	**Yes/No/Unsure**		
Other (please name):	**Yes/No/Unsure**		

8.4 Who do you think should be the **final** decision-maker when making a decision as to whether to enroll an incompetent person in a research project? Set out below are some options.

- EPOA or welfare guardian
- Family/whānau
- Provider not involved in the research (e.g., the consumer's responsible clinician or GP)
- Researcher
- Other

Please rank the decision-makers you chose in order of preference from 1. being your most preferred to 5. being your least preferred. If you prefer a decision-maker other than those listed, please indicate the decision-maker.

1. Provider not involved in the research.
2. persons who, in an everyday sense, are closest and most intimately connected to the participant.
3. EPOA/welfare guardian.
4. Family/Whanau.
5. Researcher.

8.5 Please provide any other comments you wish to make about the decision-makers.

Must be informed, independent and close to the well-being and assumed preferences of the participant.

9. Please add any final comments or suggestions you wish to make.

Publicity and updates on the Commissioner's concerns, work and decisions would help us all understand more fully the dilemmas that abound in health and disability matters.

Thank you for your contribution to this consultation.

HDC, with the assistance of the Expert Advisory Group, will review all of the submissions received. The Commissioner will then consider those submissions and decide whether to recommend any changes to the current law. If any change to the Code is recommended, further consultation will be conducted.

Please state your

Name:

Organization:

Individual,disabled person.

HDC will publish a report after the consultation period has ended. All submissions that you make on this consultation are subject to the Official Information Act 1982. If you consider that all or part of your submission should be treated as confidential, please state this clearly when making your submission and indicate which of the grounds within the Official Information Act for withholding information you believe apply. HDC will take your views into account when determining whether or not to release information. Please note that any decision by HDC to withhold information is able to be reviewed by the Ombudsman.

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April 26, 2016

Mr Anthony Hill
Health and Disability Commissioner
PO Box 11934
Wellington 6142

Dear Mr Hill

Re: Health and Disability research involving adult participants who are unable to provide informed consent

Thank you for seeking feedback from the Australian and New Zealand College of Anaesthetists (ANZCA) on the above consultation. As you may know, ANZCA, which includes the Faculty of Pain Medicine, is responsible for the training and examination of anaesthetists and pain medicine specialists, and for the standards of clinical practice in New Zealand and Australia. ANZCA's mission is to serve the community by fostering safety and high quality care in anaesthesia, perioperative medicine and pain medicine. One of ANZCA's strategic priorities is to advance standards through training, education, accreditation and research.

The New Zealand National Committee of ANZCA has reviewed the above consultation. Overall, ANZCA commends you for examining the issue of whether New Zealand's current laws about non-consensual research are appropriate. Research is integral for informing evidence-based care. Without research, improvements in quality of care for patients would not be possible. It is important that adult participants who cannot provide consent are able to benefit from research. It is also important that the rights of these vulnerable patients are protected with adequate safeguards.

ANZCA's responses to selected consultation questions are set out in appendix one.

Thank you once again for the opportunity to comment. If you have any questions or would like further information, please contact (Senior Policy Adviser) in the first instance at .

Yours sincerely

Dr Gary Hopgood
Chair, New Zealand National Committee

Appendix one: ANZCA responses to selected consultation questions

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent?

Yes, ANZCA considers there are scenarios where research should be allowed to proceed with adult participants who are unable to provide informed consent. As acknowledged in the consultation paper, research with such participants could enable significant improvements in health and disability services, and may provide valuable information about the conditions that cause patients to have diminished or total loss of capacity.

Informed consent is a critical aspect of the Code of Health and Disability Services Consumers' Rights, under Right 7. However, allowing research in participants who cannot provide informed consent may strengthen the ability of health practitioners to fulfil other aspects of the Code such as *Right (4): Right to Services of an Appropriate Standard* and *Right (6): Right to be Fully Informed*.

Research is integral to setting professional standards and developing services that minimise potential harm and optimise quality of life for consumers. Research outcomes are also essential to adequately inform patients and their families about their condition; options available for treatment; and the risks, benefits and expected outcomes of each treatment option. A careful balance needs to be struck between protecting the rights of vulnerable patients unable to provide consent, and allowing research in some scenarios with appropriate safeguards, so that quality of care can continue to improve for this cohort. It may even be unethical to withhold the benefits of research from disadvantaged groups of the population.

Also, as recognised in section 4.4.2 and 4.5.3 of *Australia's National Statement on Ethical Conduct in Human Research*, people unable to provide consent to research should be entitled to participate in research, for altruistic reasons.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.

Although ANZCA supports allowing research to proceed with adult participants who are unable to provide informed consent, strong safeguards must be in place to protect the rights of this vulnerable group. ANZCA supports the following criteria extracted from an article by Professor Grant Gillett (2015)[1] that any research should include:

i) Ethics committee oversight that is robust and dynamic so that what we do to our patients – both in established therapy and experimental treatment – meets the standards of a duty of care properly reflective of scientific evidence and a dedication to patient wellbeing

[1] Gillett, G.R. Intensive care unit research ethics and trials on unconscious patients. Anaesth Intensive Care 2015; 43 (3): 309-312.

ii) External scientific review to ensure what is being proposed in such a trial will see that appropriate existing standards of care are upheld for all trial participants

iii) Solid pre-clinical data to exclude any known harm and support a real prospect of benefit for a new experimental therapy

iv) A commitment to trialling new treatments against best-standard regimens.

ANZCA also considers that consent could be provided by an appropriate surrogate such as someone with Enduring Power of Attorney. Family members should also assist clinicians and researchers to understand whether the patient would likely give consent to participating in the proposed research if competent to do so.

1.3 Do you think the same laws should apply to all health and disability related research?

Yes, ANZCA considers the same laws should apply to all health and disability related research, regardless of whether the research is conducted by a health care or disability services provider, or by a non-provider such as an academic institution. The law should protect the rights of all research participants. There should not be a different standard of legislative protection depending on who is conducting the research.

2.1 Some people who are unable to make an informed choice to participate in research may be able to express dissent or refuse the procedures involved, for example, by way of facial expressions indicating pain or fear.

Should the law state expressly that irrespective of the person's level of competence any expression of dissent or refusal to participate in research must be respected?

No, ANZCA does not consider it would be appropriate to state the above in law. The nature of a patient's disability or condition may make it difficult to approach them even for non-research purposes, or to provide an intervention or treatment such as taking a blood sample, getting them to swallow medication, taking their blood pressure and so on. The law could be unintentionally limiting if it stated that any expression of dissent or refusal to participate in research must be respected. It is likely that defining "any expression of dissent or refusal" in a meaningful way would be difficult.

ANZCA supports the sentiment outlined in the College of Intensive Care Medicine's submission that in the context of ICU care, it would be difficult to interpret a transient expression of fear or discomfort as a specific unwillingness to participate in research.

However, as described in section 1.2, appropriate safeguards to protect patients must be in place, including: ethics approval; external scientific review of the proposed research; data supporting a low risk of harm and a real prospect of benefit; and comparing trial treatments against best-standards regimens. An EPOA or family members should be involved in decision-making about participation in research.

3.1 Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence to consent?

ANZCA does not consider that "delayed consent" is possible. If there has been an active intervention (for example administration of a product) retrospective consent is not possible. Decisions on whether a patient should be included in research should therefore be based on the criteria described in section 1.2, rather than an assumption that "delayed consent" may be provided. After an incompetent participant regains competence, they must be informed that the research has occurred, and be free to withdraw from ongoing research and decline the use of data gathered during the period of incompetence.

4.1 Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons?

ANZCA considers it reasonable that researchers should demonstrate that research of a similar nature cannot be carried out on a competent person, before research on an incompetent person is permitted. However, it is important to recognise that there may be circumstances where it is necessary to conduct research on incompetent persons, to ensure that the results of the research are applicable to and can benefit that population group. If incompetent patients are completely excluded from research by this provision, they may not have access to the benefits of such research. Results cannot always be extrapolated from a competent to an incompetent population due to pathophysiological differences associated with the underpinning diseases process rendering the person incompetent.

5.1 Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?

ANZCA considers that research that may or may not benefit the individual, but which may benefit other people, should be permitted. However, this should not take the form of research with no potential to benefit the research population. It would not be reasonable to use the incompetent population as a test population for therapy to be applied elsewhere or to other groups.

There are potential benefits of being involved in research in general, aside from the intervention that is being trialled. Gillett (2015)[1] highlights that patients involved in research are often better cared for due to the careful monitoring that is required for good clinical research. Facilities involved in research are also more likely to be grounded in evidence-based care. It is therefore common, in research rich environments, for outcomes in control groups to demonstrate improved outcomes compared to non-research environs, reflecting this elevated standard of care.

5.3 If the proposed research may or may not benefit the incompetent participants, but may benefit others, should there be criteria about the group of people that it is intended to benefit.

Yes, as described above, safeguards are needed to ensure the research is relevant to the participants involved. ANZCA considers the Mental Capacity Act 2005 (England and Wales) sets out sensible criteria for permitting research that benefits others. Section 31 (5) and (6) state:

5. The research must

a. have the potential to benefit P without imposing on P a burden that is disproportionate to the potential benefit to P, or

b. be intended to provide knowledge of the causes of treatment of, or of the care of persons affected by, the same or a similar condition.

6. If the research fits within paragraph (b) of subsection (5) but not within paragraph (a), there must be reasonable grounds for believing-

a. that the risk to P from taking part in the project is likely to be negligible

b. that anything done to, or in relation to P, will not –

i. interfere with P's freedom of action or privacy in a significant way, or

ii. be unduly invasive or restrictive

6.1 Do you think researchers should be required by law to obtain ethics committee approval before conducting health and disability research with adult participants who are unable to give consent?

Yes. ANZCA considers that ethics committee approval should be the minimum standard required by law when conducting research with adult participants unable to give consent. It will be necessary to have an independent body involved in deciding if the research is appropriate. This body should have an understanding of the nature of the research, and the patients involved.

7.1 Do you think the current best interests test, which requires that the consumer would be better off participating in the research than not participating, strikes an appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed?

No, ANZCA considers the present system is too restrictive and limits enrolment of patients in groups which need active research. The purpose of research is to find better ways of doing things for all patients, and without research there is no way of knowing whether current usual care is better or worse for the population. As acknowledged in the consultation paper, therapeutic studies are unlikely to satisfy the best interests test, because the risks and benefits of the intervention are incompletely known. If benefit is already confirmed, then it is likely the intervention in question would already be accepted as standard treatment rather than research.

When determining if research should proceed without the consent of incompetent adult patients, ANZCA considers criteria should include:

- the research is very unlikely to harm.

- there is a reasonable possibility of benefit.

No study can guarantee that the risk of an adverse event from any intervention is zero. What can be achieved is minimal risk. This of course cannot be quantified accurately but may be put into risk stratification bands (e.g. risk of serious adverse event <1%). It is unreasonable to put the bar as high as 'saving a patient's life', as few studies have this as a primary outcome. In terms of possibility of benefit, "inclusion benefit" should also be factored into determining if the research should proceed. As identified in the consultation paper, it is recognised that patients can receive indirect flow-on benefits from participating in research, including better monitoring and care, or more contact with clinicians.

Where comparative common use therapies are being researched, ANZCA considers equipoise should be a minimum. Where new therapies are being compared to old therapies, it would be reasonable to require compelling reason to believe benefit is likely - acknowledging that positive outcomes of most small trials are overturned if trialled on a large scale.

8.1 Do you think there should be any change made to New Zealand law regarding who decides whether an incompetent consumer will be enrolled in a study?

Yes, it would be reasonable to allow an EPOA to consent on behalf of an incompetent patient.

8.4 Who do you think should be the final decision-maker when making a decision as to whether to enrol an incompetent person in a research project?

EPOA or welfare guardian: ANZCA considers it appropriate for an EPOA or welfare guardian to decide whether an incompetent patient can be enrolled in a study, assuming the EPOA or welfare guardian had decision-making authority transferred when the patient was competent.

Family/whanau: ANZCA considers family should be consulted about enrolling an incompetent person in a research project, to help determine whether the patient would be likely to consent if able. The perspectives of the family should also be considered.

Provider not involved in the research (e.g. patient's responsible clinician, or GP): ANZCA considers the responsible clinician should be a key member of the team determining the propriety or otherwise of involving the patient in research. In different settings such as Intensive Care, the role of responsible clinician may be mobile across relatively short timeframes, transferring between clinicians. The role of all healthcare providers involved in the patient's care should be able to freely contribute to the decision making process in the best interests of the patient.

Researcher: The researcher must have a role in ensuring ethics approval is obtained; seeking independent scientific review of the study design; ensuring there is reasonable prospect of benefit/minimal risk of harm; and confirming equipoise when trialling against standard treatment. The researcher will naturally have a role in deciding whether a participant meets the eligibility criteria for the research. They should be responsible for ensuring informed consent where possible, (e.g. from an EPOA or welfare guardian) has been appropriately obtained.

9. Please add any final comments or suggestions you wish to make

ANZCA recommends the Health and Disability Commissioner should refer to the International Conference on Harmonization's *Guideline for Good Clinical Practice E6*. This is a tripartite agreement between the USA, EU and Japan about drug research and setting ethical, documentation and other research standards.

HDC Consultation

Health and disability research involving adult participants who are unable to provide informed consent

Consultation response form

The right to make an informed choice and give informed consent before receiving health or disability services, including participating in research, is the cornerstone of New Zealand's Code of Health and Disability Services Consumers' Rights (the Code). The maxim "nothing about us without us" is an essential part of the culture of New Zealand's health and disability sector.

In some circumstances it is appropriate and lawful to provide health or disability services to a consumer without consent. An example is the provision of emergency life-saving treatment to an unconscious patient. However, it is more complex to decide whether it is appropriate to include a person who cannot give consent to be a subject of research. At present in New Zealand, research on a person who is unable to give consent can take place only if participation in the research is in **that person's best interests**.

Currently, non-consensual research that is not intended to provide a benefit to an individual participant but nevertheless may provide important information of benefit to others cannot proceed because it does not meet the standard of being in the participant's best interests.

This consultation will focus on two fundamental questions: are New Zealand's current laws regarding non-consensual research appropriate and, if not, how should they be amended? Please note that this consultation is limited to research involving **adult** consumers.

To provide us with your comments, either:

a) complete the form online; or

b) print the form, record your answers on the form and return it to PO Box 11934, Wellington 6142. Add additional pages if you wish to do so.

You do not need to answer all of the questions for your responses to be considered by the Commissioner. Leave blank any questions that you do not wish to answer.

Case Study A: Observational study measuring clearance of antibiotics during dialysis

Case Study A questions

A.1
If you were a patient with sepsis and unable to consent, would you want the research to go ahead with you as a participant?

Yes/~~No/Unsure~~

A.2
Please give the reasons you formed this view.
In this case blood poisoning must be addressed as soon as possible. The infection will not disappear with the help of nature alone but increase & spread through the body. I would engage all the help from the experts I could obtain.

Case Study B: Clinical trial comparing two products used following neurosurgery

Case Study B questions

B.1
If you were having this surgery and unable to consent, would you want the research to go ahead with you as a participant?

Yes/~~No/Unsure~~

B.2
Please give the reasons you formed this view.
It is only by trial & error one can pick the right course of product to take. I trust the medical team concerned would make an informed decision quickly.

B.3
What are your views about "delayed consent"?
Delayed consent will the danger of picking the less effective product

Case Study C: Trial regarding care provided to consumers with severe dementia

Case Study C questions

C.1
If you were a person with dementia and unable to consent, would you want to be a participant in this research?

Yes/~~No/Unsure~~

C.2
Please give the reasons you formed this view.

If my care was to consist of improving my health and of giving me a feeling of being "safe" among "friends" it does no longer alone in this empty place full of "unknown" faces & strange happenings

Case Study D: Clinical trial regarding use of adrenaline

Case Study D questions

D.1
If you suffered a cardiac arrest, would you want to be part of the study?

Yes/~~No/Unsure~~

D.2
Please state the reasons you formed this view.

I would welcome any attempt to start the heart beating again.

D.3
What are your views about the proposed "opt out" process?

Does opt out mean give in & do nothing? If so I feel I would give it to other sufferers who would be younger or who would have more responsibilities than me & try any means to help the heart do its job.

Case Study E: Clinical trial of drug for people with Down syndrome

Case Study E questions

E.1
Do you think people with Down syndrome who are unable to give informed consent should be part of this research?

Yes/~~No~~/Unsure

E.2
Please state the reasons you formed this view.

People with Downs syndrome live in a different world. I feel uneasy at taking any liberties with that world but I do not know enough about Downs syndrome to make a true comment

E.3
Do you think the proposed consultation with family/whānau/caregivers gives sufficient protection for participants who are unable to give consent?

Yes/~~No~~/Unsure

E.4
Please state the reasons you formed this view.

Most family/whanau/caregivers have a deep love of their charges, but again I am uneasy about challenging that love in such a trial.

Consultation questions

Consultation Question 1

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent?

If yes, please state the reasons why. If the adult is comatosed this research should take place as quickly & as carefully as possible
If ~~no~~, please state the reasons why not.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.

The patient should at all times be monitored thoroughly and at any sign of deterioration the research should be held over

Thank you for your contribution to this consultation.

HDC, with the assistance of the Expert Advisory Group, will review all of the submissions received. The Commissioner will then consider those submissions and decide whether to recommend any changes to the current law. If any change to the Code is recommended, further consultation will be conducted.

Please state your

Name:

Organisation:

HDC will publish a report after the consultation period has ended. All submissions that you make on this consultation are subject to the Official Information Act 1982. If you consider that all or part of your submission should be treated as confidential, please state this clearly when making your submission and indicate which of the grounds within the Official Information Act for withholding information you believe apply. HDC will take your views into account when determining whether or not to release information. Please note that any decision by HDC to withhold information is able to be reviewed by the Ombudsman.

Right 7(4) consultation

Response on behalf of the University of Otago's Bioethics Centre

This response represents the views of: Dr Angela Ballantyne, A/P Lynley Anderson, A/P Neil Pickering, Dr Ben Gray, Dr Jeanne Snelling, Mrs Sandy Elkin, Dr Mike King, Prof. Jing-Bao Nie, Dr Simon Walker.

We would like to thank the HDC for initiating this important consultation and for the clear and accessible consultation document. In particular we appreciated the careful selection of interesting case studies.

Consultation Question 1: *Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent?*

Justice: The importance of evidence-based clinical care for vulnerable populations

Clinical care should be evidence based. As a matter of justice, all classes of patients deserve good evidence to inform their clinical care. Some classes of patient have a condition that impairs their capacity to consent either permanently or for a critical period of time (dementia, unconscious). If clinical care is offered during this period, we should facilitate mechanisms for developing evidence to inform this care. Inevitably this will entail some form of research. Conservative research ethics paradigms that restrict research with these groups may further entrench their vulnerability by denying them access to the standard of evidence-based clinical care that other, non-vulnerable groups, expect. This is unjust.

Part of our reluctance to enrol un-consenting patients in research derives from the history of clinical research. In many jurisdictions the fundamental principles of research ethics (autonomy, beneficence, justice) were developed in response to shockingly unethical research with un-consenting patients, for example the *Nuremberg Code* in response to Nazi research with people deemed "unfit" and prisoners of war during WWII; the US *Belmont Report* in response to the Tuskegee Study and the NZ *Cartwright Inquiry* in response to the "unfortunate experiment". These cases are useful reminders about the potential dangers of research. But a research ethics paradigm that focuses only on the potential dangers of research is distorted. We should not be blind to the great advances in modern medicine that we benefit from as a result of medical research. Research regulation requires a balancing of the interests of current and future patients; and a balance of potential benefit relative to potential harm.

It is also worth noting that New Zealanders have an ethical obligation to contribute fairly to the global production of new medical knowledge. It would amount to free riding if New Zealanders were to adopt innovative treatments for these groups of patients, without bearing any of the risk or burdens associated with the research.

Promoting the interests of vulnerable consumers

The Right 7(4) consultation document represents the focus on 'risk minimisation' rather than 'balance'. The document is framed by two 'key principles' (p8-9) which include 'consent' and

'protection'. There is no mention of the benefits of research in this opening section. We believe the overarching ethical framework for research with adults unable to consent should be 'promoting the interests of vulnerable consumers'. This approach would acknowledge the benefits of medical knowledge to consumers as a group, the risks of non-evidence based clinical care (where evidence is weak or lacking) and the risks and potential benefits for individual consumers participating in a research study. The research ethics framework should facilitate access to the benefits of medical knowledge while preventing undue harm. We need to aim for balance and avoid a myopic focus on risk.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.

Yes we think such research with adults unable to consent should be permitted. We prefer a risk threshold standard in place of a best-interest standard. For therapeutic research (where there is potential for individualised benefit for the participant) we believe that risks should be minimised as far as possible and that risks should be proportional to the benefits of the research (both to the research subjects and future patients). Non-therapeutic studies must involve no more than minimal foreseeable risk to the consumer and must not involve more than minimal discomfort. A 'minor increase over minimal risk' may be permitted when the social value of the study is especially high.

All research involving adults unable to consent should be approved by a research ethics committee. Risk benefit assessment and peer-review of the protocol is especially important in non-consensual studies.

Consent by an EPOA holder, or if there is none, a doctor not involved with the study would be appropriate. Researchers should consults with family, whānau or others who advise as to the values of the potential participant in relation to research participation.

Consultation Question 2: *Should the law state expressly that irrespective of the person's level of competence any expression of dissent or refusal to participate in research must be respected?*

Where possible the assent (acceptance of the procedures involved in the study) of the potential participant must be sought and their dissent (refusal of the procedures involved in the study) should be respected. We believe this is in accordance with spirit of the Right 7(3) Code of Rights which states that "Where a consumer has diminished competence, that consumer retains the right to make informed choices and give informed consent, to the extent appropriate to his or her level of competence."

Interpreting expressions of dissent may be difficult. Non-compliance with the research protocol may be an expression of dissent, or it could be an expression of anger, frustration, confusion or an involuntary movement. What might count as dissent for a given study population, and who will judge this, should be discussed with the ethics committee during ethical review.

Consultation Question 3: *Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence to consent?*

We do not think that 'retrospective' consent is a useful conceptual tool, what does it mean to consent to something that has already happened? We do however think that when the participant regains competence their consent should be sought to (1) continued participation in the study or on-going research related follow-up; and (2), if the study is complete, for permission to use the research data collected while the participant was incompetent (an ethics committee should be able to waive this second requirement on the grounds of the scientific validity of the study in some circumstances).

Consultation question 4: *Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons?*

The NEAC vulnerable test is essential: the research should only be carried out with people who lack capacity if it is essential to the purpose of the research and the equivalent research could not be carried out with people able to consent. We do not believe that there should necessarily be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons. But researchers should satisfy the research ethics committee that this standard has been met. Peer-review will be especially important in this context.

Consultation Question 5: *Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?*

Yes we believe that non-therapeutic research with adults unable to consent should be permitted in some circumstances. We believe the overarching ethical framework for research with adults unable to consent should be 'promoting the interests of vulnerable consumers'. 'Vulnerable consumers' includes both participants and non-participants.

We prefer a risk threshold standard in place of a best-interest standard. Non-therapeutic studies must involve no more than minor increase over minimal foreseeable risk to the consumer and must not involve more than minimal discomfort. Note that the new 2016 CIOMS international research guidelines permit *a minor increase above minimal risk* in non-therapeutic studies if the social value of the study is high. The social value of the study refers to the potential for other people (future patients') to benefit from the research. We think it would be advantageous to have New Zealand guidelines consistent with these international standards.

<u>CIOMS revisions</u>

The Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World health Organization (WHO) released the revised version of their influential "International Ethical Guidelines for Health-Related Research Involving Humans"[1] in late 2016. Guideline 16 relates to "Research Involving Adults Incapable of Giving Informed Consent." CIOMS states that:

[1] International Ethical Guidelines for Health-related Research Involving Humans, Fourth Edition. Geneva.

1. For research interventions or procedures that have the potential to benefit adults who are incapable of giving informed consent, the risks must be minimized and outweighed by the prospect of *potential individual benefit*.

2. For research interventions or procedures that have *no potential individual benefits* for participants, two conditions apply: the *necessary* data cannot be obtained without participation of persons who are incapable of giving informed consent; and the risks must be minimized and *no more than minimal*.

3. When the *social value* of the studies with such research interventions and procedures is compelling, and these studies cannot be conducted in persons who can give informed consent, a research ethics committee may permit *a minor increase above minimal risk*. (p61-62)

Note that CIOMS has taken a minimal risk threshold approach, rather than a 'best interests' approach. The CIOMS position is more liberal than the NZ status quo in that it allows a research ethics committee to approve research that present a "minor increase above minimal risk" to adults incapable of providing informed consent, where there is no potential for individual benefit to the research subject, on the grounds of the social value of the research (i.e. benefit to patients not enrolled in the study).

Q5.3 If the proposed research may or may not benefit the incompetent participants, but may benefit others, should there be criteria about the group of people that it is intended to benefit?

We support the first criteria that research be permitted only if it may benefit others who have the same or a similar condition to the participant; in so far as this is interpreted to be equivalent to the NECA (Interventional Guidelines 2012) requirement P 5.30 that research with vulnerable groups should ensure that the study "asks questions that matter to the participant's community, and the answers should benefit the community"; and that "studies should not be performed with vulnerable groups if they can be adequately performed with other groups".

We think the remaining potential criteria are too restrictive.

Consultation Question 6 *Do you think researchers should be required by law to obtain ethics committee approval before conducting health and disability research with adult participants who are unable to give consent?*

We believe that it should be a legal requirement that research with adult participants who are unable to give consent undergoes independent review by an accredited ethics committee. We believe this is the best way to facilitate high quality research that protects vulnerable participants. It may also allow monitoring and auditing of the prevalence of this research, which is an important ethical safeguard.

Consultation Question 7: *Do you think the current best interests test, which requires that the consumer would be better off participating in the research than not participating, strikes an*

Council for International Organizations of Medical Sciences (CIOMS); 2016.

appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed?

We disagree with the best interest standard and prefer a risk threshold standard. We consider the best interest standard is not conducive to permitting research in the majority of cases and inhibits the development of high quality evidence based care. We consider a risk based threshold would better protect the rights of consumers.

2. Can randomisation ever be in a patient's best interests?

One objection to RCTs with a patient who is unable to consent is that elements of the patient's care would be directed by chance; they would be randomly allocated to receive one of the test interventions. This element of randomness seems intuitively objectionable and contrary to the best interest standard. One might ask "how can a doctor, charged with acting in the patients best interests, allocate their care according to chance?" However, we think it is easy to underestimate the degree to which different doctors have preferred treatments and different DHBs follow different treatment protocols. Often this variability is due to a lack of compelling evidence showing one approach to be preferable to others. I may well receive different advice about how to manage back pain, or when to take antibiotics, depending on which GP I see. One study in Canada showed a 15-fold variation in the chance of a patient having their care withdrawn under the care of different ICU consultants.[2] The variability involved in a carefully controlled clinical trial may well be less than that experienced by patients in a non-research setting.

Where there is clinical equipoise it can conceivably be in a patient's best interest to be randomised. If it is a placebo controlled trial with a new treatment, the placebo arm benefits from not experiencing the risks of the new treatment and the treatment arm benefits from any therapeutic effect. Both arms benefit by having a robust study.

[2] Garland A, Connors AF. Physicians' influence over decisions to forego life support. J Palliat Med. 2007 Dec;10(6):1298-305.

Cases

Case Study A: Observational study measuring clearance of antibiotics during dialysis

This is a non-therapeutic observational study with no prospect of direct benefit to participants but no foreseeable harm to patients either. It addresses an important research question. We would allow this study.

Case Study B: Clinical trial comparing two products used following neurosurgery

This is a comparative effectiveness study of two approved and commonly used products. We would be prepared to allow this study. We would however like to see further justification of the physiological difference between the proposed non-consenting patient group and other patients able to consent. The justification for using vulnerable non-consenting adults relies on the relevance of the research to this particular group, and the inability to derive similar knowledge from less vulnerable groups.

The "delayed consent" process (if/when the patient regains capacity they can choose to have their data removed from the study within a reasonable timeframe) seems appropriate in this case, as per our answer to question 3.

Case Study C: Trial regarding care provided to consumers with severe dementia

We would be prepared to allow this study. No participants are receiving less than standard care. There needs to be good evidence that the trial intervention has genuine potential as an improved standard of care. We would like to see participant 'assent' in this case, and a procedure for removing participants from the study if they show signs of distress.

Case Study D: Clinical trial regarding use of adrenaline

We would be prepared to allow this study if we were satisfied on the two following issues:

- We would like to know more about the previous studies suggesting poorer outcomes with standard practice (number of studies, quality, and overall evidence for this position). We would need to be satisfied that there was well founded doubt about the safety of the standard protocol and equipoise between the two arms. Peer-review would be important in assessing the quality of this evidence.
- In addition, it is unclear why Dr D needs to conduct a 'large trial'. Given the life and death context, an incremental research protocol where several smaller studies are conducted might be more prudent.

The proposed 'opt-out' process is quite innovative, but we are sceptical about the ethical, legal and pragmatic status of this option. It will be interesting to see how many people take up this option in the UK study.

Case Study E: Clinical trial of drug for people with Down syndrome

We would not be prepared to allow this study as currently described because the study fails to meet the minimal risk threshold.

1. There is no evidence that this is a high priority research question for the Down syndrome community. We would need to see further evidence of engagement with the Down syndrome community and some evidence that they see this as a valuable potential product.

2. There are serious concerns about the safety profile of the drug.

3. The potential benefit to participants is limited because there is no post-trial access to the product. This also raises the question of whether there would be reasonable access to the product, if successful, for the broader Down syndrome community (in terms of product approval in NZ and cost).

4. There is inadequate justification for the use of a vulnerable population in this case. What evidence is available to show that the drug will work differently in a person with Down Syndrome? The drugs should be adequately tested in consenting non-vulnerable patients prior to testing in a vulnerable population (unless there is high potential social value of the research to the vulnerable community, which we don't see in this case).

HDC Consultation

Health and disability research involving adult participants who are unable to provide informed consent

Case Study A

A.1 I would not want to participate in this research.

A.2 It is unethical and verges on something akin to Herbert Green watching the natural progression of CIN 3 with limited or no intervention.

Case Study B

B.1 Unsure

B.3 I think delayed consent is farcical. If a person regains capacity and refuses consent, the treatment won't be undone even if the data is removed from the study.

Case Study C

C.1 I would have to question why this is research, especially when it may be best practice elsewhere. However I would probably want to be a participant.

C.2 Hopefully I might have been in a position to give advance consent via an advance directive. Interactive care sounds like a better option than task focused care.

Case Study D

D.1 No, give me the adrenaline thanks.

D.3 What are your views about the proposed "opt out" process?

I think the 'opt out' process is seriously flawed and totally unworkable in the real world situation.

Case Study E

E.1 No

E.2 Harm from the drug has already been identified. I would have to question why the research was even being proposed. It seems unethical and undermines the personhood of these adults with Down Syndrome. Whose interests are being served?

E.3 The question is essentially academic since I am opposed to the research. But in other research scenarios it may be necessary as an extra safeguard to consult with someone who knows each participant but is independent of the family.

Consultation Question 1

General Comments

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent?

Yes, in limited circumstances, when it is in that person's best interests and/or where the prospective participant has signalled their consent in an advance directive.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.

I would give consideration to widening these circumstances in the future, if it can be demonstrated that in any research the protection of research participants is truly paramount.

It has been deeply concerning over recent years to see the shift in priorities for Health and Disability Ethics Committees (HDECs). The streamlining of these committees' operating procedures appears to have been driven more by researcher interests and/or by the potential to generate more economic benefits for the country. The protection of research participants appears to have become a much lesser consideration.

It is interesting to note that when the draft NZ Health Research Strategy was released last year for consultation, it was devoid of any mention of the unethical research at National Women's Hospital (NWH) that led to the Cartwright Inquiry. I would have expected it to be a fundamental grounding point of such a strategy given its significance to health care and health research in this country.

After all it was the failure of the ethics processes and the power of the medical hierarchy within NWH at the time that allowed unethical research to continue for so long. This was despite repeated attempts by other doctors to have the research stopped given their strong evidence that women were being harmed. It wasn't until the consumers exposed the extent of those harms in an article in the Metro magazine that authorities took notice and took action

There was minimal comment in the draft strategy on Ethics Committees other than they were part of *research infrastructure* and ethics processes needed to be enhanced *to ensure effective protection of research participants while operating an efficient process for approving research proposals*. It was noted *protection of participants is particularly important for disadvantaged or vulnerable population groups such as many disabled people*.

Improving ethics and regulatory systems was an additional theme emerging from the submissions on the NZ Health Research strategy – there was *a strong call to make ethics central to the New Zealand Health Research Strategy in order to improve protection for research participants, ethics around data and samples, regulation of medical devices and management of conflicts of interests*. It is yet to be seen if this will be taken on board in a meaningful way.

Adding to this uncertainty around Ethics Review and the Ethics Committee environment is the recent announcement that the Ministry of Health has placed a temporary hold on recruitment to the National Ethics Advisory Committee (NEAC). The temporary hold on vacancies within the current Committee is in place while the Ministry undertakes a review of NEAC's activities in respect to its role in research in New Zealand, aligned with the release of New Zealand's first Health Research Strategy later this year. This includes a review of the oversight of both NEAC

and the four national Health and Disability Ethics Committees, the Advisory Committee on Assisted Reproductive Technology and the Ethics Committee on Assisted Reproductive Technology.

1.3 Do you think the same laws should apply to all health and disability related research?

Yes, I think so.

Consultation Question 2

Dissent

2.1 *Should the law state expressly that irrespective of the person's level of competence any expression of dissent or refusal to participate in research must be respected?*

Yes

2.2 Upholds person's autonomy and personal choice

Consultation Question 3

Delayed Consent

3.1 *Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence to consent?*

No

3.2 It would create a legal precedent. It would risk undermining and/or compromising the concept and integrity of informed consent and be open to manipulation/exploitation. Incompetent participants would be even more vulnerable/less safe.

Consultation Question 4

Alternative participants

4.1 *Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons?*

Yes

Consultation Question 5

Interests of others to be taken into account

5.1 *Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?*

Unsure

This needs more discussion within the disability community in particular – especially with research that is low risk, low burden.

Consultation Question 6

Ethics committee approval

6.1 *Do you think researchers should be required by law to obtain ethics committee approval before conducting health and* disability research with adult participants who are unable to give consent?

Yes

6.2 The conduct of science has not always been ethical, including on human subjects, as we have seen in NZ and elsewhere in the world. Research on very vulnerable people needs to be of high ethical, legal and scientific standards. Researchers and all other stakeholders that may be involved need to be mindful of and transparent about conflicts of interest.

Consultation Question 7

Best interests test

7.1 *Do you think the current best interests test, which requires that the consumer would be better off participating in the research than not participating, strikes an appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed?*

For the most part, yes. May be an exception if the interests test was neutral and there was low risk, low burden.

Consultation Question 8

Who decides?

8.1 Do you think there should be any change made to New Zealand law regarding who decides whether an incompetent consumer will be enrolled in a study?

Unsure

8.2 Do you think there should be any change made to the roles played by the various possible decision-makers under current New Zealand law?

Unsure

This aspect needs more discussion. There are mixed views on possible decision-makers. For the most part Welfare Guardians and EPOAs are likely decision-makers, but it is acknowledged they may not always be the best placed/best person to make the decision.

Final Comments

This has been a difficult issue to consider. I have been keen to see the issues around the legality of research on patients who are unable to give informed consent clarified. However, until we have a research environment that is strong on ethical review, has the protection of research participants as paramount and has zero tolerance of unethical behaviour, I find myself erring on the side of caution and supporting the status quo meantime.

Consumer

From: " >
Date: 30 April 2017 at 3:21:29 PM NZST
To: "Rose Wall" < >
Subject: HDC CONSULTATION

Hello Rose,

My apologies for not sending this earlier.

.

So have typed out my contribution. This was a most in-depth paper to contribute to and the most interesting I have been involved in for some time.
Thank you for the opportunity. I am sure with all the feedback it will answer some questions.

Kind Regards

HDC CONSULTATION
Health and disability research involving adult participants who are unable to provide informed consent.

Case Study A:
Observational study measuring clearance of antibiotics during dialysis.
A1. Yes
A2. I do think this would be appropriate as it is most rare (currently) that there are not many participants available. It is paramount that we endeavour to research the outcome or learn more about the type of antibiotics that will assist sepsis. As our immunity to antibiotics is diminishing and scientists/ researchers require current information to enable further research to be developed.

Case Study B
B1. If you are having surgery and unable to consent, would you want the research to go ahead with you as a participant?
Yes
B2 . I would want to include my family in the decision and why the research is important to the study. The benefits require to be fully explained. The importance of family in certain cultures and the collective wish to be involved in the ultimate decision.
B3. I agree with delayed consent as the participant or family may wish to discuss this fully and is so dependent on the nature of the operation.
As well as in Pacific culture, E.G. the Matai (SAMOA)of the family may be included and or the local Minister. This is dependent on the family. Pacific Health groups would have current knowledge on various communities in NZ.

There is a difficulty in e.g. Pacific communities that enduring powers of authority etc.,are not known to them and they may give consent and not understand the benefits of research.

Case Study C
Trial regarding care provided to consent, would you want to be a participant in this research?
C1. If you were a person with dementia and unable to consent, would you be a participant in this research?
Yes
C2. This research would be of benefit to many as our population ages and families are exposed and there is minimal understanding to how this occurs and what we can do to prevent or manage dementia. Increasingly there are many younger people experiencing dementia. A comparison with participants who have symptoms of pending dementia would be beneficial.

Case Study D
D1. If you suffered cardiac arrest, would you want to be part of a study?
Yes
D2. I am influenced by cardiac arrests that occur in young people, one recently at the gym I attend. As well as Pacific and Maori are prone to rheumatic fever which can affect their heart in latter years i.e. valves. I am sure that many participants from this community and mainstream NZ's receive information from their doctors or surgeons on a one to one basis. This does not provide an understanding before cardiac arrest occurs.
D3. What are your views about the proposed "opt out " process?
Participants should have a say in this process.

E1. Do you think people with Down Syndrome who are unable to give informed consent should be part of this research?
Unsure
This is complex as the parent together care -givers consent or non-consent does not reflect the persons wishes.
E3. Do you think the proposed consultation with family/whanau/caregivers gives sufficient protection for participants who are unable to give consent?
Unsure.
There are many Down Syndrome participants who are able to provide consent. Consultation with family etc., should have an independent person on behalf of the Down Syndrome person whether the agreement /non agreement is understood and delivered fairly.
E4. As noted above there are Down Syndrome persons who are capable of making decisions and their choice and/or consent should be considered carefully.

Consultation Questions
1.1 Do you believe research should be allowed to proceed with adult participants who are unable to provide informed con sent?
Yes
The benefits of research are important to society and the future of our communities.
1.2 If you think such research should be allowed, please make general comments about restrictions that you think should apply.

All involved in non-informed consent research should have the credentials, understanding of the people and conditions to ensure that there is no misuse of the process. I am particularly concerned for those in the Pacific community who have difficulty with process language. Not all require assistance, some are vulnerable in view of their health and lower socio-economic circumstances.

1.3

Yes

1.4 The principles of the code should apply to all those(including academic) who are involved in related H&D research.

2.1

Yes

2.2 Dissent or refusal should be given to the participant being interviewed. Many will have the capacity to understand the research to be undertaken.

3.1 Yes

3.2 The research to be undertaken will be of importance to all.

It is of utmost importance that the research is explained to the participant when they regain competence.

4.1

Yes

In the first instance, this standard should be a legal requirement.

If currently this is heeded by researchers and is covered under the NEAC guidelines , and working within legal parameters, it may not be required to place all ethical standards in law.

5.1 Yes

5.2 I am more then inclined to say yes. I am also conscious of the participant/individual. If this will surely benefit the wider community this research should proceed. The process should include approval from an expert adviser and in some circumstances family, should this be practicable.

5.3

Yes,

5.4

1. All research undertaken of participants should in all be anonymous and protect their identity.
2. Peer review on outcomes by relevant groups, It may be necessary to obtain permission from Ethics Committee in certain circumstances
3. Those people who will immediately benefit from the research undertaken
4. Those who may have contributing factors to the specific research
5. Specific ethnic groups who have a tendency towards specific outcomes
6. Medical groups to ensure new and tested outcomes are distributed to patients.

6. Ethics committee approval

6.1 Unsure

6.2 It would depend on the circumstances and the type of research to be undertaken. In some cases it would be appropriate where the principles of consent are considered fair, and balanced for the rights of the individual.

In other cases to obtain approval may mean that opportunities are lost.

7.Ways to asses the advantages and disadvantages of participation by incompetent consumers in research.

7.1 Yes

Question 8.
8.1 Do you think there should be any change made to New Zealand law regarding who decides whether an incompetent consumer will be enrolled in a study?
YES
8.2 Do you think there should be any change made to the roles played by the various possible decision makers under current NZ law?
YES
8.3
Person who could have a role in decision making X

A combination of family, guardians and those involved in the research are equally important to each other to derive information on the participant and the research required to be undertaken. It may be useful to bring representatives together to discuss the research. Or alternatively seek the feedback from decision makers on an individual basis this research. There may be concerns where the family or EPOA's should be concerned in all cases.
8.4 Who should be the final decision maker ?

Other: EPOA/ family member with information from feedback as noted above.

8.5 If English is a second language a person who can translate should be involved. A person or family member adversed with the understanding of the specific culture. There may be religious and cultural reasons that research cannot proceed. There are industrial chaplains involved in hospitals and there role may be useful to the participant and act as an independent person .

I do think there is onus on the research organisations or appropriate organisations to discuss the subject in the public arena so various and future participants have some knowledge of the subject. Communication to wider sector and ethnic groups is required. Open up the discussion and utilise respected people in the academic, medical to discuss with the public.

9. Some families do not have EPOA which is not known in some communities and this can be difficult to give consent.
10. Name : Organisation: .

To:
Cc:
Bcc:
Subject: Fw: NEAC response to HDC consultation on Right 7(4)

From: NEAC@moh.govt.nz
To: hdc@hdc.org.nz
Date: 01/05/2017 12:07 p.m.
Subject: NEAC response to HDC consultation on Right 7(4)
Sent by:

Good afternoon

Please find attached a submission, on behalf of the National Ethics Advisory Committee, on the review of Right 7(4) of the Code of Rights.

Kind regards

Neil Pickering
Acting Chair
National Ethics Advisory Committee

NEAC HDC Response Final.docx

HDC Consultation – NEAC Response

Summary of NEAC's work reviewing the Guidelines

Until recently NEAC was undertaking a comprehensive review of its *Ethical Guidelines for Observational Studies* and *Ethical Guidelines for Intervention Studies*. These guidelines set out the ethical requirements that must be met when undertaking health and disability research, whether or not that research requires review by an ethics committee.

The main objectives of the review were to ensure the guidelines were fit for purpose and consistent with other relevant guidance. The guidelines were also being updated to address ethical issues associated with innovative practice and developments in research methods and emerging topics such as data linkage. NEAC's view is that all health and disability research conducted within New Zealand will impact on Mâori, and the new guidelines should incorporate Mâori ethical concepts and principles throughout the document.

A key area of focus for the review has included reviewing guidance on informed consent, particularly retrospective consent and consent for incompetent participants and vulnerable groups.

NEAC notes that its new draft ethical research guidelines state all research must comply with domestic legislation, reading as follows:

NEAC's National Ethical Standards are subject to legal constraints. While the National Ethical Standards can impose on researchers a higher standard than the law in terms of how they conduct research, they should not be read to suggest that research can ethically be conducted in a manner that is otherwise contrary to legal constraints.

A fuller summary of NEAC's work reviewing the Guidelines is available on its website (http://neac.health.govt.nz/review-neac%E2%80%99s-ethical-guidelines-research-and-related-activities). An announcement on the current status of NEAC is also available on its website (http://neac.health.govt.nz/announcement-national-ethics-advisory-committee). The Ministry of Health has advised that all work NEAC was undertaking on authoring the new ethical research guidelines should stop, effective from 13 April 2017.

NEAC's submission

NEAC's responses to the consultation questions are based on the collective view of the committee, given work to date on the new ethical research guidelines.. This view reflects the stage NEAC reached reviewing the Guidelines, and may have changed as work progressed.

NEAC's response will cover the consultation questions, but not the case study questions.

Responses to Consultation Questions

Consultation Question 1

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent?

Yes.

NEAC's position is that, subject to legal requirements, people who lack competence to consent to participation in research must not be inappropriately excluded from research.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.

Research proposals should be considered on a case-by-case basis. Different ethical principles will apply in different situations, with varying levels of relevance and importance.

If a person is not competent, either permanently or temporarily, to decide whether to participate in a research project, then in order to become a participant in research, NEAC considers the following conditions must be met:

- The researcher should make all reasonable efforts to identify any prior consent or refusal to participate in research (whether general or specific) and give effect to any such decision.
- The researcher involves participants who lack the competence to consent on their own behalf to the greatest extent possible in the decision-making process.
- If the person dissents then this must be respected and overrides any consent given by an individual legally entitled to decide on that person's behalf.
- Where an individual is legally entitled to decide on behalf of that person, the researcher seeks and maintains consent from that individual.
- The researcher must be able to demonstrate that:
    - the research question can be addressed only with participants who are from this group
    - when the research involves minimal risk, the research has the potential to provide benefits to the participants or the group to which they belong
    - when the research involves more than minimal risk, the research has the potential to provide benefits to the participants or the group to which they belong.
- If the person becomes competent during the course of the research, then the researcher must promptly seek the participant's consent as a condition of continuing participation.

1.3 Do you think the same laws should apply to all health and disability related research?

Yes.

1.4 Please make any general comments you have about question 1.3

NEAC's guidelines apply to everyone doing research. Laws should reflect and enable ethical principles, which are the same regardless of who is doing research.

2.1 Should the law state expressly that irrespective of the person's level of competence any expression of dissent or refusal to participate in research must be respected?

Unsure. There needs to be more clarity about what is meant by 'dissent' in the consultation document.

2.2 Please give reasons for your answer.

As a general principle, dissent should be respected. NEAC's position is that a person's dissent must be respected, and overrides any consent given by an individual legally entitled to decide on their behalf.

However, the law needs to be general enough to take account of proposed research projects on a case-by-case basis. What constitutes dissent could be context-dependent, and should be considered in the ethical review of a research proposal.

There is a risk involved in formalising what counts as an expression of dissent. For example, an expression of discomfort may not be dissent, and it could be difficult to tell if somebody is upset about an intervention that would take place regardless, or the research.

3.1 Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence to consent?

No.

3.2 Please give reasons for your answer.

NEAC considers there to be two issues at play in this question: whether it is appropriate to conduct research on people unable to consent, and then getting consent after they regain competence.

NEAC strongly believes the phrases 'delayed consent' or 'retrospective consent' should be avoided. It is not possible to get consent for something that has already happened. However, people should be *informed* of their involvement afterwards. If/when somebody regains capacity, their consent or dissent should be sought and respected for any future involvement in the research, and the use of their data.

Participants' initial involvement in a study must be able to be justified without any reference to obtaining consent later.

4.1 Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons?

Unsure

4.2 Please make any further comments you have about question 4.1

NEAC supports this as an ethical consideration (a researcher having to show research of a similar nature cannot be carried out on competent people before research on incompetent people is considered), and if it becomes a legal one it needs to be worded well. NEAC is concerned that this requirement could be too restrictive. The purpose of such a requirement should be to prevent the exploitation of vulnerable people, but it must also ensure that the opportunity for a particular group to participate in research is not closed off.

Law and ethics are not the same thing, but they need to enable each other to function. Legislating ethical principles is problematic. Legislation should be permissive of good ethical practice, but should not define it.

5.1 Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?

Unsure

5.2 Please give reasons for your answer

NEAC's position is that this is dependent on other characteristics of the research project. For example, NEAC's guidelines state that in this situation the research must be minimal risk. NEAC also notes that defining 'benefit' is problematic.

All research is of benefit to the wider population, as it generates knowledge that is used to improve health services and outcomes. Negative outcome research is as valuable as positive outcome research.

A large proportion of what is done in health care may have no impact on patients[1], therefore it is difficult to make a judgement about whether research will have a particular benefit. Researchers always have to guess whether there will be a benefit or not and this knowledge gap is often the reason why the research is being carried out in the first place.

In considering research participants, researchers also need to consider the risk posed to participants. This is a generic ethical consideration, and is not confined to any particular group of people. It is difficult to define what 'minimal risk' to participants is, and to determine what a valid indicator of minimal risk is.

In general, minimal risk posed to participants is a good condition of research participation. However, risks and benefits are always contingent and researchers cannot be certain at the outset that either will occur (as if this was known, there would be no need for research). Risks are prospective rather than known. It is always part of a researcher's responsibilities to consider potential risks and benefits to participants, and the balance between these.

When researchers are considering the balance between potential risks and benefits, they should take into consideration that incompetent participants are less able to take account of their own interests than competent participants are.

5.3 If the proposed research may or may not benefit the incompetent participants, but may benefit others, should there be criteria about the group of people that it is intended to benefit?

5.4 If the answer is yes, please indicate the criteria that you think should apply and indicate the order of importance of the criteria.

It could be problematic to be prescriptive about criteria for this group of people. NEAC would opt for a more encompassing restriction.

If generalisations from the findings may benefit other people that is ok. Being too prescriptive about who the research can benefit may unintentionally prevent some research from being done.

6.1 Do you think researchers should be required by law to obtain ethics committee approval before conducting health and disability research with adult participants who are unable to give consent?

No

6.2 Please give reasons for your answer

NEAC's position is that this consideration should be ethically driven, not legally driven.

More clarity is needed around what is meant by 'approval' and whether 'ethics committee' specifies any particular committee/s.

NEAC recognises there is a need for input from outside the research team when researchers cannot rely on the consenting process for participants to protect their own interests. NEAC considers every

[1] See for example, Demand Better! Revive Our Broken Health Care System *(Second River Healthcare Press, March 2011) by Sanjaya Kumar, chief medical officer at Quantros, and David B. Nash, dean of the Jefferson School of Population Health at Thomas Jefferson University.*

research project needs ethical review, but the level and formality of that is dependent on the nature of the research and participants. For example, in some cases formal ethical approval from an ethics committee might be required, while in other cases discussing ethical matters less formally with someone from outside the research team would suffice.

When research involves participants who are unable to consent, a higher level of ethical consideration is needed than if all participants in the same project were able to consent. However, there should not be a rigid requirement about what (if any) ethics committee this should go through. The law should not be too prescriptive about where that ethical approval should come from.

7.1 *Do you think the current best interests test, which requires that the consumer would be better off participating in the research than not participating, strikes an appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed?*

No

Whether or not the best interests test strikes the appropriate balance is dependent on the nature of the research project and participants. Different criteria and tests will be more appropriate in different research projects.

7.2 If research were to be permitted to proceed without the consent of adult incompetent participants, what criteria/tests do you believe should be used to assess the advantages and disadvantages to the participants?

7.3 Please state the reasons you formed this view.

The best interests test and threshold test are both problematic.

With the best interests test, the issue remains of determining what is in a participant's best interests. Often, uncertainty around this is the reason the research is being done – the research is to determine what intervention is in someone's best interests. A best interest test can often amount to a basic interests test, ensuring that participants are looked after 'well enough'. Meanwhile, a threshold test might produce the wrong answers.

Best interests tests and threshold tests relate to each other. In understanding best interests, one must start with some kind of threshold, and then move on to balancing interests if one concern is greater than others. Both tests must be taken into consideration, and applied in different scenarios.

When research is minimal risk, there is less need to balance the risks and benefits posed to participants, and vice versa. However, there are things other than risk to consider. For example, the impact the results of the research will have.

Question 8

Do you think there should be any change made to New Zealand law regarding who decides whether an incompetent consumer will be enrolled in a study?

Do you think there should be any change made to the roles played by the various possible decision-makers under current New Zealand law?

Who do you think should be the final decision-maker when making a decision as to whether to enrol an incompetent person in a research project?

Law in this area should align with other legislation. This issue does not pertain solely to research. NEAC believes there is a good case to review legislation in this area, and not a good case for research to be treated differently.

In the UK, the Mental Capacity Act 2005 was an attempt to address something that is not well covered in New Zealand laws. NEAC notes that under the Mental Capacity Act people have or are nominated a 'personal consultee'. These people give advice, not consent, which is an important distinction.

Consistent with NEAC's advice to the Minister on dementia, NEAC recommends supported (rather than substituted) decision-making systems where possible, based on the person's will and preferences, not what might be perceived as being in their best interests. A preference for supported decision-making means that representative decision-makers are appointed only as a last resort, and the will, preferences and rights of individuals' direct decisions.

It is good practice to involve people who know and care for the participant in the decision. However, this should not necessarily be a requirement.

HDC Consultation

Health and Disability research involving adult participants who are unable to provide informed consent

Submitted by: Health Research Council Ethics Committee		
Contact:	, email:	DDI:

Case Study Questions

The general position taken in respect of the series of presented case studies is that the NZ context tends to discourage rather than encourage the generation of further information that may have benefits to the wider patient population at some point in the future. Of course, each case should be judged on its own merits but with a fuller understanding of whanau dynamics and its wishes for their family member. Moreover, while the core notion of 'best interests' is important, there will be situations in which best practice is being applied but where also the opportunity for a research based action is available in a way that does not compromise the impact of conventional intervention. In these situations, the risk-benefit equation should be examined to see why research should not proceed. Matters to do with advanced care plans and other instructions on patient preferred intervention will also be a critical variable when discussing patient protection and research potential.

The diversity of the case studies illustrates the problem of being too definitive at a general level. For instance, it appears that while the procedures outlined for cases 1-4 protect patients, case 5 introduces more problematic elements. It is possible therefore to agree to the first four studies but not the fifth.

Concerns would arise where, as in case 5, there is evidence of increased risks associated with the treatment, combined with a lack of knowledge about whether it will have beneficial effects for the patient. The reasons given for enrolling patients unable to consent in this example are flimsy. Even with the consent of the family/whanau/caregivers, the ethical decision-making is fraught. General consent should allow for problem cases such as this one.

We have not commented specifically on the cases.

Consultation Questions

Consultation Question 1

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent?

Yes. If not, improvements in health outcomes will not occur in such patient groups, such as those who are in intensive care. The care we offer to patients should be evidence based. We want to be able to offer the best of care to all patients, but as a nation we cannot do this if the safety mechanisms are bound down too tightly, or where our system is too restrictive. We need to strike a balance between protecting our most vulnerable participants, with meeting the best interests of this group by being able to offer them the best of care available. Ethical review

processes in NZ ensure that safety of patients in these settings is not compromised by participating in research. There are several examples of simple trials of current best practice vs an alternative that have improved outcomes for such patients in NZ.

Having a blanket restriction on research in situations without consent seems unwise. The reasons for this are many-fold and apply to all forms of health and disability related research.

First, 'blanket restrictions' on research has the potential to generate an uneven spread of knowledge across a population. This in turn can lead to situations where interventions become increasingly based on 'tradition' and less based on systematically generated evidence. The obvious irony is that this could lead to situations where the current intent of Right 7(4) to protect vulnerable populations in fact does the very reverse because of the levels of risks levels associated with unsubstantiated interventions.

Second, restrictions on research in New Zealand potentially generates a reliance being placed on knowledge produced by other nations possibly – if the basis of our legal position is to be justified – with increased risk or reduced protection for the patients of these jurisdictions. Accordingly, acceptance of this knowledge for the purposes of modifying practice within the New Zealand context does then present an ethical question around the extent of our global contribution and responsibility.

Third, there is, in terms of allowing research on vulnerable populations in the broadest sense of the term, the view that we are underestimating the capacity of some segments of our population to give informed consent such as adults with Down syndrome.

Fourth, some commentators have argued that legal/ethical systems around research on human subjects have evolved over the time from ones that permitted exploitation to a state where protection was a prime focus (our current position) to a recent trend towards inclusivity. The implication is that the New Zealand context needs a rebalancing in a way that allows greater flexibility to do research in contexts involving vulnerable populations.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.

We do consider that such research should be allowed with some important restrictions including that all research on vulnerable groups must be reviewed and approved by an accredited research ethics committee. We also consider that all risks must be minimised and that risks should be proportional to benefits to either future patients or current participants. Where the study is non-therapeutic then risks should be minimal.

Where a legal option for consent can be obtained then this should be sought, otherwise the medical consultant (not involved in the research) in consultation with whanau should be sought.

<u>Consultation Question 2</u>

2.1 Should the law state expressly that irrespective of the person's level of competence any expression of dissent or refusal to participate in research must be respected?

We consider that it is difficult to make a generic response to this as level of competence can vary considerably. However, we consider that the assent of the participant should be sought wherever possible, and their dissent respected.

Consultation Question 3

3.1 Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence to consent?

We are very concerned about the usefulness and quality of delayed/retrospective consent. It may work out well if the patient retrospectively approves, but not if they disapprove of what has been done (even assuming that what has been done will not have ongoing negative effects on the patient). Even if the data can be removed from the study retrospectively, the patient would have every right to feel that their interests have been disregarded.

Consultation Question 4

4.1 Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons?

Yes. Research should only be carried out with those unable to consent only when it has met certain criteria. The researcher should demonstrate that carrying out such research meets the following:

1. It is central to the research to have it carried out on this group –
And,
2. the research is not able to be carried out on those with the capacity to consent.

This seems a reasonable position obviously because the generation of research information in contexts of lower risk is attractive.

Consultation Question 5

5.1 Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?

Yes. Such research should be permitted in limited circumstances. In these cases, protections must be put in place, such as minimised risks and discomfort. The CIOMS 2016 document Guideline 16 'Research Involving Adults Incapable of Giving Informed Consent' is helpful in this regard, stating that:

> 'For research interventions or procedures that have the potential to benefit adults who are incapable of giving informed consent, the risks must be minimized and outweighed by the prospect of potential individual benefit. For research interventions or procedures that have no potential individual benefits for participants, two conditions apply:
>
> - the interventions and procedures should be studied first in persons who can give consent when these interventions and procedures target conditions that affect persons who are not capable of giving informed consent as well as those who are capable, unless the necessary data cannot be obtained without participation of persons who are incapable of giving informed consent; and
> - the risks must be minimized and no more than minimal.
>
> When the social value of the studies with such research interventions and procedures is compelling, and these studies cannot be conducted in persons who can give informed

consent, a research ethics committee may permit a minor increase above minimal risk.' (p61-62)

This document permits an ethics committee to approve a slight increase in risk on a case by case basis.

5.2 Please give reasons for your answer.

The response to this question will require assessment on a case by case basis. However, the value of producing data and analysis that may inform improvements in patient management is high. The critical element will be whether the management of the 'incompetent' participant will be unreasonably compromised to adhere to the research design of any proposed research.

5.3 If the proposed research may or may not benefit the incompetent participants, but may benefit others, should there be criteria about the group of people that it is intended to benefit?

Yes. The important dimension will be that there is clarity around the segment of the population that any proposed research is likely to benefit. Such research would be acceptable if it benefitted a similar group as those that took on the burden of research.

5.4 If the answer to 5.3 is yes, please indicate the criteria that you think should apply and indicate the order of importance of the criteria with 1. being the most important and 5. being the least important.

1. People in a similar situation where there is no available evidence from other comparable studies on unable-to-consent patients.

2. Where there is evidence from animal and other studies that people with this damage might benefit from the proposed treatment.

<u>Consultation Question 6</u>

6.1 Do you think researchers should be required by law to obtain ethics committee approval before conducting health and disability research with adult participants who are unable to give consent?

Yes. This is an important safeguard.

6.2 Please give reasons for your answer.

It is important that research projects involving elements of complexity regarding the balance between risk and benefit be subject to broad ethical evaluation which is best done by an appropriately constituted and approved ethics committee.

Consultation Question 7

7.1 Do you think the current best interests test, which requires that the consumer would be better off participating in the research than not participating, strikes an appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed?

No. We think that the best interests test is too restrictive and does not allow us to improve the quality of care for those who cannot consent.

It becomes difficult when the consumer is unable to consent to the research. The 'best interests' test then changes its character, since the consumers'/patients' rights may be placed in jeopardy by proceeding. I think the whole situation should be reframed ethically, or we simply accept that the 'best interests' notion no longer applies.

7.2 If research were to be permitted to proceed without the consent of adult incompetent participants, what criteria/tests do you believe should be used to assess the advantage and disadvantage to the participants?

An approved ethics committee should be accorded the responsibility of deciding on the balance of risks and benefits in respect of each research proposal. Given the expertise and skill required to assess, this should possibly be decided by a single committee that is populated by a skill set able to decide.

Consultation Question 8

Law reform is critical for the protection of incapacitated participants and researchers in non-consensual research. The legality under current law is doubtful.

The barrier to the lawfulness of research involving incompetent participants is S 18 (1) (f) of the Protection of Personal and Property Rights Act 1988. The provision will need to be amended if research on non-consenting patients is to be lawful.

Changes to the Code of Rights which are regulations would be simpler not requiring parliamentary involvement. This would be by way of amendment to the Code. The Health and Disability Commissioner has the power to review any part of the Code at any time and make recommendations to the Minister of Health.

The reform will need to enable provisions for research to proceed when there will be no possibility of direct benefit or overall benefit to the incapacitated person. Safeguards are needed for the protection of people who are unable to consent for themselves or are unable to assess the risk and decide for themselves. Legally binding safeguards need to be initiated.

9. Please add any final comments or suggestions you wish to make.

The framing of the law in New Zealand seems overly protectionist potentially creating situations that put vulnerable populations at greater risk. Moreover, this current position appears to ignore the broader parameters described at 1.4 above that generates ethical concerns requiring an answer. A degree of relaxation or 'rebalancing' would provide the basis for an appropriate response to these ethical matters while clarifying the accountability and function of both the research and ethics communities. However, this is framed, the HRC EC recommends that change be made to the substance and philosophy underlying Right 7(4).

The Code around right 7(4) is Eurocentric in that it appears not to take into account or pay cognisance to either Te Ao Māori and the attitudes and values around research or the concepts of benefit and risk as perceived by Tangata whenua in the health context where notions of collective decision-making in the whanau setting are important. This is a serious shortcoming that requires attention.

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Introduction

The Health and Disability Ethics Committee (HDEC) Secretariat provide administrative and advisory support to the four HDECs and the Ethics Committee on Assisted Reproductive Technology. The Ethics Committees team sits within the Protection, Regulation and Assurance business unit of the Ministry of Health. In relation to ethics review processes, protection of study participants, regulation of clinical trials and conduct of health research, and assurance of an effective research eco-system is core business for the Secretariat and the five Committees we serve.

We are highly experienced in dealing with health and disability research, assessing and validating well over 600 new applications per annum, and advising the HDECs in their review and decision-making on these applications. We also process 32000 post approval items relating to ethics applications per annum such as progress reports, approval conditions and amendments. In addition to being practically experienced through our work, the Secretariat staff also have a range of relevant academic and personal experiences, including working with persons with disabilities, work as counsellors, and a number of staff with post graduate qualifications specialising in ethics. This combined with our specific experience of dealing with a wide range of research applications and having contact with participants, researchers, sponsors and ethics committee members gives us a unique perspective on health and disability research in New Zealand.

General Comment

The Secretariat notes that each research project is different, in considering thousands of applications no two are ever exactly the same. Each project presents different risks and benefits to participants and even small differences between two seemingly similar studies can mean that one is ethically acceptable while the other is not. All HDEC decisions are application specific: they are not precedent-setting. The Case Studies as presented in this consultation document contained very limited and simplified information and we attempted to respond to these as presented, avoiding making assumptions based on our own knowledge of research processes. As you will notice in our submission, each case was considered as a balance of risks and benefits to determine whether the study is ethical to proceed.

In our experience, the current Right 7(4) *best interests* test is unsuitable for consideration of the specific circumstances posed by research with adult participants unable to provide informed consent. Although this test may be suitable for treatment, when all decisions should be made based on the clinician's decision regarding what is best for the patient, this same test does not work well for research where it generally cannot be known whether participation is in the participant's best interest. A research hypothesis tests whether two alternative regimes are equal or one is better than the other – it tests the unknown using indicative information to frame the research question. A participant cannot know at the time of consent if the research will benefit him or her but they can consent to participate in a study, to take a risk to test the hypothesis. A Best Interests test can only test a person's support for a given [theoretical] approach.

Our submission provides detailed responses to each Case Study and Consultation Question with clear themes throughout in support of the need for change to the current regulations to more suitably account for the risks and benefits posed by each research project. For all applications, HDECs consider the risks and benefits of the project when determining whether it should be approved. This consideration is especially important in studies involving participants unable to provide informed consent as, usually (with participants who can consent for themselves) the decision whether to accept the potential risks of the study is made by the participant themselves, and this is clearly not possible with these studies. Although participants may have a poor understanding of risk, when they are able to provide their own consent the decision to take these risks is theirs to make. Autonomous decision-making is fundamental to our informed consent process in New Zealand and enshrined in law. In the case of adults unable to consent, someone else (such as the HDECs) must determine whether the risks of participation are acceptable in light of the expected benefits of the research and if the study should be allowed to proceed without consent. We note for children, the situation is different, as the law allows adults to assent to a child's research participation. The irony of this anomaly and the risk of vulnerability, is not lost on all of us working in this field.

Options Going Forward

The HDECs require a practical legal framework to work within that is suitable for the uncertain nature of research to ensure they are able to promote and protect the rights of all study participants and society as a whole, by allowing ethically acceptable high quality research and preventing ethically dubious research. New Zealanders expect a level of rigour and protection to be applied to all research endeavours in order to improve outcomes for our health and disability system, but to also ensure we do not repeat history and conduct *"unfortunate experiments"*.

This review of Right 7(4) offers an excellent opportunity to align New Zealand's regulations more closely with that of other relevant jurisdictions and allow limited research in certain circumstances with people unable to provide autonomous informed consent. The Secretariat supports a *best equal interest test*, where participation must have risks and benefits at least equal to non-participation. Some of our responses to the consultation questions are more aligned to supporting a *not contrary to best interest test*, where participation cannot be worse than non-participation as in other jurisdictions, but we recognise the differences between these tests and favour the best equal interest test. This approach would allow the HDECs more flexibility to consider the benefits and risks of each individual study and the effect on individuals and society at large, when determining if they should be able to proceed.

Case Studies:
Case Study A:

If you were a patient with sepsis and unable to consent, would you want the research to go ahead with you as a participant?
Unsure

A.2
Please give the reasons you formed this view.

Participants in this study will receive no benefit, despite there being potential incidental findings that show that a patient's sepsis is being undertreated. The Secretariat notes that it is not clear from the wording of the case study whether the tests mentioned are additional procedures that participants are undergoing (i.e. additional blood samples being taken) or additional tests being performed on samples collected as part of standard care.

In the case of the former above then there are a number of issues associated risks from additional testing procedures on patients when they will not benefit from the study. Invasive testing (the collection of bloods) and Māori cultural beliefs associated with the collection and use of tissue present risks for participants in this project.

A key aspect is that hypotheses are not facts, and, therefore, should not be considered benefits in concrete terms. Referring to the potential findings of a study as the main reason for inclusion is questionable and should not support the enrolment of patients into research without their consent.

If there are no additional medical procedures, and the study only involves analysis of data/samples collected as part of standard care, then this can change the landscape. Whilst the concerns around use of tissue remain there may be reasonable grounds for the study to proceed. Participants have little to no involvement in the project and future patients stand to benefit from the results. The potential for benefit to all sepsis patients here outweighs the relatively minor risks associated with the study.

However, other factors must be considered. The case study mentions that participants are unlikely to be able to provide informed consent. This implies that there may be a population of patients who can provide consent for this study. This raises the question of why the researcher could not perform the study in a consenting population. For example, if patients are unwell and their sepsis is getting worse but can still provide informed consent then it is worth asking why the researchers could not seek consent from patients before their condition deteriorated. However if consent cannot be obtained for a genuine reason then the study may still be acceptable.

The Secretariat also noted that a reason had not been provided in the case study as to why participants care could not be changed if it were found that they were being undertreated. If it would be possible for a participant's care to be improved by study results then the secretariat expects that this would be done, and could offer a benefit to participants. However, we accept that there may be a reason that individual participants' care could not be changed from study participation, for example if the results of the tests would not be available in time.

Case Study B: Clinical trial comparing two products used following neurosurgery

B.1
If you were having this surgery and unable to consent, would you want the research to go ahead with you as a participant?
Yes

B.2
Please give the reasons you formed this view.

This study involves randomizing participants to receive either of two standard care treatment in order to assess which treatment is better. This study poses no additional risk to participants (assuming that both treatments are routinely used) and has the potential to benefit future patients.

If participants in this study would receive either treatment at roughly equal rates regardless of the study we would question why this cannot be conducted as a retrospective review of patient notes. A number of reasons could be given regarding the reasons that it cannot be done retrospectively, including that the study requires additional testing or that they need to be sure similar patients get allocated to each treatment arm. The responses to these questions would impact our response to this question. For example, if the study requires additional testing this may increase the risk for participants, or if the treatment arms are not balanced in standard care we would question why this is and whether surgeons have reasons for using one treatment over another.

However, if this study does not involve additional invasive testing and in standard care patients are equally likely to receive each treatment, we would consider that this study does not pose any additional risk to participants (above standard care) and the researcher should be allowed to undertake this study given the potential to help future patients, if the results shows that one product is superior.

It should be noted that the reasons why this study cannot be done retrospectively, and whether it involves any additional testing, highlight serious concerns about the practicality of any guidance or law issued on this subject. These cases are highly variable and the nature of research means that benefit or level of risk cannot be guaranteed.

B.3
What are your views about "delayed consent"?

Delayed consent is not consent as you cannot freely choose to participate or not. You cannot say no to something that has already happened to you.

Seeking consent from participants for the use of their data is always advisable, so if this delayed consent is revised to be consent to ongoing inclusion in the study and the use of their data then this is beneficial and advisable.

Requiring consent to be sought, even if this must be obtained after initial study enrolment, is important as this forces a conversation to be had about the study with participants and/or their family members. A participant's right to withdraw data collected without their consent must be respected whenever possible.

We noted that an essential aspect to consider when making guidelines or regulations is when participants should be approached for their consent to ongoing participation in the study. We

believe that participants should be approached a soon as reasonably practical, when they have regained the ability to provide informed consent.

Additionally, the case of participants who die or do not regain the ability to provide informed consent must be considered. These participants never have the opportunity to express whether they wish to continue participating in the study or wish for their data to be withdrawn. Researchers should seek the views of the family and friends of these participants on whether a patient would want to participate (or allow their data to be used) in the study if they were able to provide their own informed consent. This is best practice and the views of these people should be respected when possible.

Case Study C: Trial regarding care provided to consumers with severe dementia

C.1
If you were a person with dementia and unable to consent, would you want to be a participant in this research?
No

C.2
Please give the reasons you formed this view.

This case study reads as though the two arms of the project are standard care versus the new unproven intervention without standard care. However, it could also be interpreted as standard care versus unproven intervention AND standard care. The first part of this response will respond to the former part interpretation with the latter responding to the second interpretation.

Under the former interpretation (that the study compares standard care to study treatment without standard care) the Secretariat believes that this project is not justifiable as presented. There is a lack of clear benefit to participants with the potential of direct harm both from the withdrawal of standard care and from an untried intervention in an already vulnerable population.

As previously stated, hypothetical benefits should not be used to enrol patients in a study without pre-existing evidence that can help gauge the risk/benefits to participants. The Secretariat notes that, in practice, the proposal of completely novel research designs or interventions happens very rarely. Interventions such as these are developed over time and tested incrementally. The move from a theoretical model to testing an intervention in participants is one that does not happen without some forms of evidence existing. Thus arguments can be made about the benefits or risks in more concrete terms. The Secretariat believe that it is important that the design and evidence base behind research is acknowledged.

If there is genuinely no pre-existing data about the efficacy of the program then performing a pilot study in dementia patients who can provide informed consent needs to be a seriously considered option. This way the safety and efficacy of the new method of care can be assessed. If the risks and benefits associated with participating in a study are purely hypothetical then the risks and benefits to participants cannot be determined with full certainty. In all cases where withdrawal of standard care is part of the design then there needs to be sufficiently compelling reasons for this withdrawal. Arguments for the withdrawal of care in cases where patients cannot consent also need at least the same amount of evidence, if not more.

Under the second interpretation above then the Secretariat's concerns remain but are diminished slightly by the knowledge that patients are receiving standard care regardless of study arm. The Secretariat holds that the difference between standard care versus unproven intervention or standard care versus unproven intervention *plus standard care* is significant.

Slight changes in the interpretation of the case studies, or the evidence presented in support of an application for such a study, can have a significant impact on the acceptability of a study. Considering applications for ethical approval involves a careful weighing of complex evidence regarding expected risks and benefits which is impossible to adequately do with the limited information provided.

Case Study D: Clinical trial regarding use of adrenaline

D.1
If you suffered a cardiac arrest, would you want to be part of the study?
No

D.2
Please state the reasons you formed this view.
This study involves withholding standard care from patients without their consent. The justification for this is that several previous studies have suggested that while standard care (adrenaline) may help initially, it may also lower overall survival rates and increase brain damage.

In reviewing this case study we considered that the previous studies being relied on to support conducting this study may be inconclusive or poorly designed. It is unclear from this case study the number and type of studies that exist in support or opposition of the use of standard care. Because this is unknown in the case study we cannot support withholding standard care from patients due to the lack of justification.

In reaching this decision we considered whether the average patient would be willing to consent to be in this study, if it were practicable to obtain consent. We determined that at a minimum a large number of lay people would not be willing to forgo standard care without substantial evidence against its use. Although this decision may be due to a therapeutic misconception, the idea that receiving something is generally better than receiving nothing, if they were able to provide informed consent these patients would be required to. If we expect that a large number would not consent to participate if given the opportunity then this study should not be conducted on these people without their consent.

If significant evidence existed demonstrating that standard care is more harmful than beneficial this study may be acceptable under the 'best interest' test, however, if enough evidence existed to meet this test it is likely to also be enough evidence to support changing standard care.

D.3
What are your views about the proposed "opt out" process?

'Opt-out consent' should not be considered a form of consent. 'Consent' involves a person giving permission for something to happen, with 'opt-out consent' no permission has been granted. The lack of a 'no' is not a 'yes'.

If consent is required, the onus is on the researchers to ensure all participants can understand what they are consenting to. With opt-out consent, the onus is on the patient to understand and opt-out of the research if they wish. However, there is no guarantee that all potential

participants have seen and understood the information about the study. Even in the best circumstances participants have difficulty understanding research and providing genuinely informed consent. You cannot assume that everyone recruited in to a non-consent study has seen and understood the opt-out information provided, and opted-out if they do not want to participate. Therefore, opt-out cannot be considered a form of consent.

Additionally, opt-out poses issues for individuals who are of low socioeconomic status or who have English as a second language. These people may not understand a public awareness campaign or face other barriers to their being aware of, and understanding, a project before then making a decision about whether or not they want to opt-out.

However, if a study is justifiable without consent then we consider it is desirable to offer opt-out consent. If possible, opt-out consent should be offered for any non-consensual study. The option to 'opt-out' is important for those individuals that are strongly opposed to participating in research. However, the use of opt-out should not imply a lesser requirement on non-consent studies, they should need to meet the same strict standards to be considered acceptable.

Case Study E: Clinical trial of drug for people with Down syndrome

E.1
Do you think people with Down syndrome who are unable to give informed consent should be part of this research?
No

E.2
Please state the reasons you formed this view.

In weighing and balancing the risks of this vulnerable group participating in such a study without consent, there is not enough evidence to show that the expected benefits outweigh the potential risks.

Participation in this study without consent could put the participants at risk of exploitation and could appear to place an unfair burden on them, should they not in any way benefit from being in the study:

- while this experimental drug has been tested for safety in healthy volunteers, the safety profile is not yet fully known or understood, and,
- results in the healthy volunteer group showed that some experienced suicidal tendencies after taking the drug, and,
- if there is a beneficial effect, the drug will not be made available to participants after the study and those in the placebo arm would not have a chance for any benefit (assuming the results showed a beneficial effect)

Potential participants should have the right to decide whether what is being proposed is an issue of significant importance to this group of people and in turn whether they wish to participate in a study addressing the issue.

This study could be conducted with only people able to provide informed consent, although this would only give limited results, and then if evidence is promising it may be able to be considered for people unable to provide informed consent. However, significantly more information and justification would need to be provided and carefully considered. This pilot study approach is a key part of assessing studies, particularly in a new population. If this was a pilot study then it is unacceptable that it is being conducted in a non-consenting population

when a consenting population, those who have Down syndrome but can provide informed consent, exist.

That the trial drug would not be available to participants after the study is unacceptable if it was beneficial. Participants who took the risks involved with study participation should have the option to continue in an extension study if the results are positive. The Secretariat feels that it is unacceptable to expose non-consenting participants to the risks of a study such as this without expectation of benefit to them. Additionally, the Secretariat feel that short term increased cognitive abilities may not be considered a benefit by all participants and would require further information regarding this.

E.3

Do you think the proposed consultation with family/whānau/caregivers gives sufficient protection for participants who are unable to give consent?

No. It is not certain that family/whānau/caregivers have the best interests of the participants at heart, or that they understand what they would have sufficient understanding of what would be in the participant's best interest. In this case the caregivers may feel that participation could temporarily reduce their burden of care and agree to participation, even if this may not be what the participant would want if they could adequately understand and express their own views. Other methods should be used to protect the rights of potential participants.

Consultation Questions:

Research in populations who cannot consent

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent?
If yes, please state the reasons why.
If no, please state the reasons why not.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.
Yes.

Some studies offer expected benefits to participants and must be conducted in participants who cannot provide informed consent. For example, if a study offered access to a drug that has conclusively shown to wake people from comas it would be unethical to not provide this treatment to them, and, assuming it was only available through the study, it would be justifiable to conduct this research on them. Another example could be a study drug that it showing very promising results in reversing dementia, it would be unethical to restrict these benefits to only the dementia patients who can provide their own informed consent. In these cases the risks from study participation are outweighed by expected benefit to each individual participant, as well as benefit to future patients from the results of the study. In both of these examples we assume that the expected risks to participants are minimal.

Other studies may not offer benefit directly to individual participants, but are expected to benefit future patients (from increased evidence). We believe these are justifiable if study participation does not increase risk to participants beyond standard care. For example, studies comparing two commonly used standards of care do not increase risk to participants as they would receive one of these standards of care regardless of study participation, and the results of the study will inform and improve future care.

Non-invasive observational studies are also justifiable as their results benefit future people without exposing participants to increased risk.

However, many variables impact a determination on whether a study is acceptable and ethics review should be required to assess each study on an individual basis. For example, the study may be very controversial (such as one that involved the use of embryonic stem cells) and there may be a reasonable expectation that many potential participants could be opposed to the study on religious or moral grounds. A morally or religiously controversial study may be more difficult to justify without consent.

Because of this, another essential factor to take in to consideration is whether potential participants can reasonably be expected to want to participate in the study if they were able to provide informed consent. In some cases this can be determined by consulting with the participants' family and friends, in other cases this may be impossible (such as if the participants are people suffering a heart attack). This means that a subjective decision must be made regarding whether most patients are likely to agree to participate in the study if they were able to provide informed consent. If patients would not consent to being in a study, if they were able to consent, then it is unjustifiable to conduct this study on people who are unable to consent.

Other factors that must be considered are potential bias, and how the participants' circumstances may impact their likely decisions (for example, patients at the end of life with

limited options may be more likely to consent to participation in a risky trial that had even a limited chance of benefit).

The exposure to significant additional risk by involvement in research must be justified by an expected benefit to the participant. However, if study participation only involves minimal risk, similar to that of non-participation, or no risk at all, then the threshold should be much lower and these studies should be able to proceed. The expected benefits of study participation should be at least equal to non-participation, and additional risk can only be justified by additional benefit to the participant themselves, this additional benefit should be agreed by a clinician independent from the research. Additionally, there must be an expectation that participants are unlikely to oppose the research in general terms, if this cannot be determined by consultation with their whānau (such as for an ICU study) then it should be agreed by an independent ethics committee that participation is unlikely to be overly morally or religiously controversial.

The decision about best interest or if potential participants are likely to want to participate should not be left up to the research doctors. These kinds of decisions must be independent from the research team and informed by evidence. The research team can be expected to have a bias towards their study and independent review can help determine if these benefits actually exist, assess the possible risks, and consider alternatives.

The Secretariat noted that a requirement for there to be some evidence of expected benefit, and information regarding expected risks, could pose issues for first in human trials. However, it would be a very unlikely situation for it to be impossible for early phase studies to be conducted in participants who can provide consent before moving on to participants who cannot consent, if it is warranted by the results of the early studies.

The Code provisions relate to health and disability research conducted only by a health care or disability services provider. Research relating to health and disability issues is also conducted by non-providers, for example, some academic research. Given that such research is outside the jurisdiction of the Commissioner:

1.3 Do you think the same laws should apply to all health and disability related research?
Yes

1.4 Please make any general comments you have about question 1.3.

People should have the same rights regardless of where they are when they participate in research or get treatment. The important factor is not where the study is being conducted, but that human participants are involved and should have their rights protected.

Currently, researchers could avoid the rules by conducting the research through a University or private research company and this leaves the HDECs at a loss to what requirements the researchers must meet. Committees often apply the HDC Code of Rights to all research, despite these cases where it does not technically apply.

Researchers often make mistakes regarding use the information, tissue, and make use of relevant materials in order to pursue their research endeavours. There is a natural tendency to see a positive value in all research and to want to accrue all information/tissue/biomarkers at your disposal to advance your study. The large volume of sponsored research means that there must be a clear and fair law applied to all research in New Zealand, especially when it comes to vulnerable people.

Vulnerable participants, including those unable to provide informed consent, should not be disqualified from participation but they should also not be experimented on unjustifiably.

The Secretariat noted that in New Zealand there is a generally accepted principle that all treatment harm will be covered by ACC, and this common view extends to research for most people, except since the 1992 AC Act changes, commercially sponsored trials under section 32 (that have been reviewed by an *approved ethics committee*) are exempt. It is imperative that the HDC has jurisdiction over all human health and disability research to ensure there is a parallel process for complaint and investigation of those harmed (a rare event fortunately), and that this jurisdiction should not be contingent on the setting, researcher, or institution.

Dissent

Some people who are unable to make an informed choice to participate in research may be able to express dissent or refuse the procedures involved, for example, by way of facial expressions indicating pain or fear.

Consultation Question 2
2.1 Should the law state expressly that irrespective of the person's level of competence any expression of dissent or refusal to participate in research must be respected?
Unsure

2.2 Please give reasons for your answer.

The question posed in 2.1 presents a heavy-handed approach to solving the complex issue of dissent. Whilst the law needs to protect the rights of those who are most vulnerable there also needs to be provision to address the practical issues faced by researchers. For example, what to do when patients have previously consented but now no longer have the capacity to provide this ongoing consent. Participants who gave consent while competent to do so should not have all signs of dissent considered to be withdrawal of consent to participate in research. However, explicit withdrawal of consent to research participation must always be respected.

For example, a trial comparing two standards of care, which the patient would otherwise receive one of, may not be able to run under this zero tolerance model as standard care must sometimes be provided even if there is dissent from the patient. In some cases study participation does not pose additional risks above standard care, and may provide additional benefits, in these cases it must be considered whether dissent would be respected if the treatment was being provided as part of standard care rather than a research project. Consent and dissent should be considered on a continuum and weighed against the associated expected risks and benefits.

Patients who cannot provide informed consent may have varied reasons for why they express dissent. For example, a patient might have a phobia of needles. If this person was participating in research which is truly beneficial for that person, i.e. there is pre-existing evidence for the efficacy of an intervention then any expression of dissent or refusal is extremely difficult to interpret in this context. An accumulation of dissent factors may signal withdrawal from a study but equally may signal that the procedure for the study needs attention/revisiting. It is a very nuanced area that the researcher must be trained to observe, record and deal with dissent and this forms part of the study conduct. As an aside, record keeping for research is at least as important as record keeping for treatment, as the data generated provides the evidence for benefit change, status quo, or harm. The Secretariat is concerned that the introduction of a threshold that expressly states that any expression of dissent should be respected and acted

on will lead to researchers excluding non-consenting participants from research as a way of safeguarding themselves against complaints. In turn, this may lead to a reduction in research into the serious conditions that render people incompetent.

Dissent to a certain aspect of a study or treatment should not always be considered as dissent to study participation or treatment generally. For non-consenting participants it would be wrong to misconstrue objections to the practical aspects of participation with withdrawal of consent to the research. The dissent may be an indicator that the participant does not want to be involved in the study, but it could equally be a temporary reaction to the procedure, not the research per se.

The study protocol should have clearly set out procedures for considering dissent that should take in to consideration the relative merits of the study, including benefits and risks to participants. In each case varying levels of dissent should be respected and the process for this in the protocol should be considered and approved by a suitable ethics committee.

Delayed consent

In some jurisdictions, researchers may be permitted to carry out research on a person who is temporarily unable to give informed consent provided that the researcher obtains delayed (retrospective) consent from the participants after they regain the ability to consent. Delayed consent is not permitted under New Zealand law.

Consultation Question 3
3.1 Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence to consent?
No

3.2 Please give reasons for your answer.

Delayed consent is not consent as the person cannot say no. Consent involves a person giving permission for something to happen, but in the case of delayed consent the thing has already happened, and the choice is not optional.

However, participants should be given the option to withdraw themselves and/or their data from the study if they were enrolled without their consent. Although this is sometimes called *delayed* consent this is a misrepresentation, the participant cannot be asked to consent to something that has already happened but they can consent to their ongoing participation in the study and/or the use of their already collected data. Study data should be considered participants health information, this information is very personal and must be treated respectfully.

To avoid confusion, the Secretariat recommends that a more appropriate phrase be used in place of 'delayed consent'. Typical phrases include 'consent for ongoing participation' and 'consent for use of data until withdrawal' are types of consents sought by researchers for patients who wish to continue or withdraw from a research once they are competent.

Alternative participants

The NEAC guidelines require that studies should not be performed with vulnerable groups if the studies can be performed adequately with other groups. However, this ethical standard is not a legal requirement.

Consultation Question 4

4.1 Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons?

Yes

4.2 Please make any further comments you have about question 4.1.

When there is no evidence to substantiate the claim that participation is in a population's best interests or that there are minimal risks to participation then research should be carried out in a consenting population first to establish that participation could be in a non-consenting participant's interest. The Secretariat is aware that this may result in some projects not being carried out or delayed. In the Secretariat's opinion, the changing research landscape, particularly with the advent of platform trial designs, means that this will not present a significant barrier to research in New Zealand. It is uncommon to have no pre-existing evidence for an experimental treatment/research procedure.

The Secretariat believes that first-in-human and other very early phase trials should not be conducted in participants unable to provide informed consent. People unable to provide informed consent are especially vulnerable and should not be exposed to unknown risks with no reasonable expectation of benefit. Early phase research is not supported by evidence surrounding the associated risks and benefits, this makes it difficult or impossible to justify conducting the research in people unable to consider the potential risks for themselves. Although it is important to conduct some research in people unable to provide informed consent the Secretariat believes that early phase studies can be at least piloted in participants able to provide their own informed consent, and this should occur before it is considered whether to include more vulnerable participants.

The Secretariat notes that it is important that preventing early phase trials in participants unable to provide their own consent does not lead to the burden of research being shifted to other vulnerable groups, such as children (whose parents can provide consent on their behalf).

Consultation Question 5

5.1 Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?

Yes

5.2 Please give reasons for your answer.

Yes, for low risk studies in which it can be shown that minimal harm will be done to participants and done in a group to which the results are relevant and or many improve treatment options. This is with the general caveat that if the research could be performed in a consenting population with the same outcome then it should not be performed in a non-consenting population.

Research performed in a non-consenting population that does not immediately benefit those patients should be beneficial to other persons with the same condition. That is, trials of no immediate benefit to patients should be reasonably expected to benefit others who have the same condition.

If the answer to question 5.1 is yes:

5.3 If the proposed research may or may not benefit the incompetent participants, but may benefit others, should there be criteria about the group of people that it is intended to benefit?

Yes

5.4 If the answer to 5.3 is yes, please indicate the criteria that you think should apply and indicate the order of importance of the criteria with 1. being the most important and 5. being the least important.

1. The research cannot be done in the group it is intended to benefit.
2. The risk to participants is minimal or non-existent.
3. The research cannot be done in people able to consent.
4. The participant is not indicating dissent or withdrawal to study participation (please see our earlier response to question 2.2 for detailed views on dissent).
5. This study is important and ethically sound in all other respects.

Any others?

Ethics committee approval

An option for change would be to make ethics committee approval mandatory in all cases where the research involves adult consumers who are unable to provide informed consent. This requirement could be introduced independently, or in addition to other criteria.

Consultation Question 6

6.1 Do you think researchers should be required by law to obtain ethics committee approval before conducting health and disability research with adult participants who are unable to give consent?

Yes

6.2 Please give reasons for your answer.

There is currently a high volume of applications being submitted to HDECs, over 600 are validated annually, and the number submitted is increasing rapidly due to the Government's stated policy objective to grow clinical trials and international co-operative agreements in science and health research. However, the number of research projects that are legally required to undergo ethics review is quite small (Human Tissue Act, Privacy Act, AC Act, HPCA Act are all tangential laws). By building the direct statutory requirements for ethics review into New Zealand law then the rights and wellbeing of vulnerable participants will be protected and the conduct of a study effectively managed (not just monitored). The system is a high-trust system and relies largely on self-reporting. There is no national system for audit of compliance against conditions of ethics approval.

The Secretariat notes that this question does not specify HDEC review, merely ethics review. The Secretariat supports this distinction in principle, as different projects can have different risk thresholds and the system for ethics review in place since 2012 is disaggregated and non-hierarchical. In our view it is should be strengthened to be more risk based rather than determined by an academic level of study for instance, (Masters research go to IECs, PhDs to HDECs) but for example, both levels can undertake very invasive human tissue research or psychologically distressing studies. Resource constraints suggest that attention for review should be applied on a risk–rated basis that works to provide assurance in the ethics eco-system and has synergies with overseas jurisdictions and is at an acceptable standard for international research purposes. For example, research involving no invasive procedures and merely the collection of data that is not normally collected (e.g. recording a participant's temperature) could be considered sufficiently low risk to not need HDEC approval, if it received suitable ethics review at a DHB or University level.

With the current research governance landscape researchers are legally able to simply not seek HDEC review in some circumstances. Moral imperatives and publishing requirements often dictate compliance but this is not always the case. When this happens HDECs are not sufficiently empowered to provide protections to participants, especially when they are non-consenting. Coverage gaps exist and provide uncertainty for researchers, participants, and regulators. These gaps could be rectified by changes to proposed primary legislation (such as the Therapeutic Products Bill), as well as clarity in The HDC Code that participants in health and disability research have an avenue for complaint that is not dependent on who conducts the research or where it is conducted, but that all study participants are as of right protected. We see the HDC as having not only an advocacy role but also an educative role in terms of health consumer rights and participation in health research. It is one further source of independent information to assist people to make an informed choice about research participation or about the bounds that safeguard non-consented research.

By legislating specifically for ethics committee review there is greater scope for the protection of patient rights as well as improving capture and linkages and clarity to those persons who might fall outside of Accident Compensation coverage. Any legislative changes need to ensure persons unable to consent and in studies are specifically covered for insurance purposes, either by private insurance or ACC.

Ways to assess the advantages and disadvantages of participation by incompetent consumers in research

Consultation Question 7
7.1 Do you think the current *best interest's* test, which requires that the consumer would be better off participating in the research than not participating, strikes an appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed?
No

If you answered "No" to question 7.1, please answer question 7.2.

7.2 If research were to be permitted to proceed without the consent of adult incompetent participants, what criteria/tests do you believe should be used to assess the advantage and disadvantage to the participants?

The nature of research means that participation in a study can almost never be decisively in a participant's best interest. Research is conducted due to a lack of evidence, and even if there is evidence to support the study treatment as superior to standard care it is difficult to argue that being randomised to a standard care control arm is better than receiving standard care outside of the study.

Generally, standard care is considered to be in a patient's best interests as it is, usually, substantiated by evidence. However, without comparing novel treatments to standard care we cannot improve medical care for these patients. The decision to compare a new treatment to standard care must carefully weigh the risks and benefits of such a treatment against the expected risks and benefits of standard care.

The Secretariat believes that certain kinds of research that require participants unable to provide informed consent are ethically acceptable and should be able to proceed, however many of these are prevented by their inability to meet the *best interest* test. For example, a study that compares two standards of care is important as it may be that one of these standards is preferable to the other, and the results would benefit future participants, however without research this conclusion could never be drawn. This study would not pose additional risks to participants (as they still receive standard care) but it would also not meet the *best interest* test as study participation is no better than standard care (as it is exactly the same).

Additionally, the current test does not allow for a *chance* of benefit to justify a study. For example, a study that compares standard care to standard care plus a treatment with substantial evidence supporting it (for example a better treatment that is not available in New Zealand) would be prevented under the current test. This study would be prevented as we cannot *know* that participants would receive a benefit as they may be randomised to the standard care arm and not receive the benefits of the study arm. However, the Secretariat believes that the expectation of benefit should be able to be considered when determining if a study should be able to proceed.

The *best interest* test fails to adequately consider risks and benefits and prevents studies that do not pose increased risk to participants and may benefit future patients. The current *best interest* test also prevents studies that investigates new treatments that are expected to be at least as good as standard care and may offer additional benefits with minimal additional risks. The Secretariat believes that the *best interest* test should be replaced by another method that allow consideration and balance of risks and benefits.

If the law began from the basis of medicine, first do no harm, and allowed committees to assess the level of risk and burden of being in a study then it would allow currently prohibited studies whilst not opening the door to unethical or damaging research. This would cover including non-consenting people in important 'low risk' observational studies where participation is not contrary to their best interest; as opposed to *in their best interest.*

This non-contrary research could be conducted in accordance with established ethical guidelines (ethical and clinical guidelines) and with ethical scrutiny. The Secretariat notes that such an approach would bring New Zealand in line with other jurisdictions.

7.3 Please state the reasons you formed this view.

As noted in above answers there are several types of projects that are currently prohibited by Right 7.4 that either have little to no patient involvement or are functionally identical to patient care but are made illegal due to them being research. Valuable trials that simply involve the collection of data from patients who are unable to provide informed consent but where inclusion cannot be made are considered as contrary to right 7.4. The outcomes of these trials could be of high value, as can be seen in case study A, and advance care for all people effected by a serious illness. But with the current restrictions this type of research simply cannot be performed in New Zealand.

The current law appears to take a narrow view on what constitutes research. Although the *best interest test* can be applied to certain intervention studies that are testing a hypothesis in a patient population, in other cases it is difficult to determine if the project meets the test and satisfies the code. The Secretariat notes that at times the current *best interest* test prevents ethical and important research, such as non-invasive observational studies that can never be in a participant's best interest but also do not expose them to additional risks, while allowing higher risk intervention studies when there is evidence that the study intervention is superior to standard care. These examples indicate that the current law is inadequate to protect patients' rights while allowing vital research to proceed.

Person who could have a role in decision-making (x)	Should X ever have a part to play in deciding whether an incompetent consumer is enrolled in a study?	If yes, in what circumstances should X be involved in decision-making? i.e., a) In all cases where X is available? b) Only when particular criteria are met (e.g., that the study is to be conducted for the purpose of saving the consumer's life or preventing serious damage to the consumer's health)? c) Only when other possible decision-makers (please specify which decision-makers) are unavailable? d) Only where the circumstances require that an urgent decision is needed (e.g., *Case Study D – adrenaline)*? e) Other? Please choose the letter(s) for any of the options above that you think should apply, or provide comment if you prefer.	Where X is involved in decision-making, what role should he or she have? i.e., a) Consulted by decision-maker? b) Power to veto* consumer's participation in the research? c) Provide or withhold consent on behalf of the consumer? d) Other? Please choose the letter(s) for any of the options above that you think should apply, or provide comment if you prefer. * A veto means the right to refuse or reject permission for an incompetent consumer's participation in research.
EPOAs and welfare guardians	**Yes**	The current rules for welfare guardians and EPOAs are satisfactory. The term medical experiment does need clarification, as not all research, intervention or observational, meets what might be considered this definition. In practice there are a variety of definitions for medical experiment, some consider that this only applies to intervention studies while others believe that it includes all research (such as non-invasive observational studies).	A person with EPOA or the welfare guardian should be consulted by the decision maker in order to better account for the likely views of the participant if they were able to provide their own informed consent (as per the current Right 7(4)(c). This would allow for families from different cultural or religious backgrounds to avoid physician paternalism if a study could meet their best interests medically but may not be in their best interests for these other reasons. In some time sensitive situations it may not be practicable to consult this person, however they should be consulted when possible
Family/ whānau	**Yes**	The family and whānau of participants (especially next of kin) should be consulted when available, regarding whether the	As above, consulting with friends and whānau can help guide the clinical

		participant would want to participate in the study if they were able to provide informed consent.	decisions to account for what the participant would want.
Provider not involved in the research (e.g., consumer's responsible clinician or GP)	**Yes**	Could be used to supplement the decision only. Additional information from a non-biased source. The views of the participant's GP may be especially useful as they may have a good understanding of what the participant would want.	
Researcher	**No**	The researchers can be expected to be bias towards their study. Although they can be involved in determining who is eligible for participation, another clinician not involved in the study should be responsible for making the decision to enrol each participant unable to consent, this decision should be based on as much (indicative) evidence as possible.	
Other (please name):	**No**	HDECs should not make this call as they are too removed from the decision process. HDECs should only establish that the study generally is ethical and able to proceed, but not specifically consider whether an individual participant should be enrolled in a study. The Secretariat supports supported decision making as a best practice, this would allow the views of clinicians, family, and the participant themselves to be considered, even if the participant is not competent to give formal consent.	

		participant would want to participate in the study if they were able to provide informed consent.	decisions to account for what the participant would want.
Provider not involved in the research (e.g., consumer's responsible clinician or GP)	**Yes**	Could be used to supplement the decision only. Additional information from a non-biased source. The views of the participant's GP may be especially useful as they may have a good understanding of what the participant would want.	
Researcher	**No**	The researchers can be expected to be bias towards their study. Although they can be involved in determining who is eligible for participation, another clinician not involved in the study should be responsible for making the decision to enrol each participant unable to consent, this decision should be based on as much (indicative) evidence as possible.	
Other (please name):	**No**	HDECs should not make this call as they are too removed from the decision process. HDECs should only establish that the study generally is ethical and able to proceed, but not specifically consider whether an individual participant should be enrolled in a study. The Secretariat supports supported decision making as a best practice, this would allow the views of clinicians, family, and the participant themselves to be considered, even if the participant is not competent to give formal consent.	

P.J. Bascand

Philippa Bascand
Manager
Ethics Committees

New Zealand
SOCIETY OF
Anaesthetists

28 April 2017

Mr Anthony Hill
Health and Disability Commissioner
PO Box 11934
Wellington 6142

Dear Mr Hill

Re: Health and disability research involving participants who are unable to provide informed consent

Thank you for seeking feedback from the New Zealand Society of Anaesthetists (NZSA) on the above consultation.

About the NZSA
The NZSA is a professional medical education society, which represents over 550 medical anaesthetists in New Zealand. Our members include specialist anaesthetists in public and private practice, and trainee anaesthetists. We facilitate and promote education and research into anaesthesia and advocate on behalf of our members, representing and championing their professional interests and the safety of their patients. As an advocacy organisation, we develop submissions on government policy and legislation, work collaboratively with key stakeholders, and foster networks of anaesthetists nationwide. The NZSA, established in 1948, also has strong global connections, and is a Member Society of the World Federation of Societies of Anaesthesiologists (WFSA).

Overview
Executive members of the NZSA have reviewed the consultation document and have also sought the opinion of members who are actively involved in research. All commend you for examining whether New Zealand's current law relating to nonconsensual research is appropriate. Without research and indeed without audit, in which healthcare systems and individuals routinely collect and pool significant amounts of anonymised data to enable the analysis of outcome according to patient, operator and institution risk[1], improvements in the quality of care for patients would not be possible.

The NZSA is a membership based organisation and we believe that it is important for members with a particular interest in this issue to have an individual voice, so that all points of view may be considered by the Commission. Accordingly, NZSA members' individual responses to selected consultation questions are attached (Appendix I and II).

As a Society, the NZSA supports research with adult participants who are unable to provide informed consent, provided there are strong safeguards in place to protect the rights of this vulnerable group. The NZSA, and the Australian New Zealand College of Anaesthetists

[1] Dennehy L, White S. Consent, assent, and the importance of risk stratification. BJA (2012) 109 (1): 40-46

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(ANZCA), support research with the following criteria, extracted from an article by Professor Grant Gillett (2015)[2]:

- Ethics committee oversight that is robust and dynamic so that what we do to our patients – both in established therapy and experimental treatment – meets the standards of a duty of care properly reflective of scientific evidence and a dedication to wellbeing.

- External scientific review to ensure what is being proposed in such a trial will see that appropriate existing standards of care are upheld for all trial participants.

- Solid preclinical data to exclude any known harm and support a real prospect of benefit for a new experimental therapy.

- A commitment to trial new treatments against best standard regimens.

The NZSA also recommends that the Commission refer to the International Conference on Harmonisation's Guideline for Good Clinical Practice E6. This was originally an agreement between the United States, the EU and Japan, which is now ratified by other countries. This guideline was created to ensure consistent standards for drug research and includes universal issues relating to practice and research.

Recommended papers
We would like to draw your attention to key points from various papers from recent anaesthetic publications as follows:

Consent, assent, and the importance of risk stratification. Dennehy L and White. BJA (2012) 109 (1); 40-46

I. Valid consent depends on patient voluntariness and the capacity to make a treatment decision based on the information provided

II. A person with capacity understands, remembers, and uses the information provided

III. Information should be provided to a standard which a reasonable patient would want to know in the patient's circumstance

IV. There are logistical and theoretical difficulties in delivering on each of these principles of consent

V. Information provision during the consent process inadvertently incentivizes data collection for perioperative outcomes research.

[2] Gillett, G R. Intensive care unit research ethics and trials on unconscious patients. Anaesthesia Intensive Care 2015; 43 (3): 309-312

This paper includes a discussion on the British Mental Capacity Act 2005, enforced since 1 April 2007. Patients who are not competent to make decisions about treatment are administered treatment, provided that it is necessary and in their best interests. "Best interests" must be determined by the treating clinician (or less commonly the Courts) in a nondiscriminatory manner, taking into account information outside the clinical episode, including for example, the patient's known wishes as previously expressed to relatives and other third parties. The Act recognises the legality of advanced decision making.

In New Zealand, the introduction of Advanced Life Care Planning has allowed advanced decision-making and should include decisions relating to research.

Ethics in Research. Bevan J C. Current Opinion in Anesthesiology 2007, 20:130-136.

This paper discusses the ethical principles adopted by the Universal Declaration on Bioethics and Human Rights (2005) including:

I. Consent
Any procedure or research is only to be carried out on a person with the prior, free and informed consent of the person concerned, based on adequate information (exceptions only under international human rights law). The person may withdraw consent at any time and for any reason without disadvantage or prejudice. For research in communities, additional agreement of community leaders or legal representatives is needed.

II. Persons without the capacity to consent
Authorization in accordance with best interest of the person concerned in accordance with domestic law. Research only carried out for direct health benefit to person or exceptionally when risk is minimal and research benefit is great.

Ethics of research for patients in pain. David Waisel. Current Opinion Anesthesiology. 2017, 30:205-210.

This review describes advances in rising and continuing ethical issues in pain research. Some of the issues focus directly on research, such as neonatal pain, while others focus on widespread ethical issues that are relevant to pain research, such as scientific misconduct, deception, placebo use and genomics. Key issues, which are relevant to this submission, are:

I. Neonatal pain management research for routine ICU procedures often uses placebo instead of other validated, non-pharmacologic methods for the control group. There are well recognized, long term behavioral harms to neonates of repeated painful stimuli, even of this nature.

II. Potential remedies to what appears to be increasing scientific misconduct include recognizing the warning signs of repetitive irreproducibility, scrutinizing data omissions, improving whistle blower protection and harshly sanctioning researchers, their mentors and institutions for scientific misconduct.

A crucial component of informed consent for research participants is the provision of written information. Generic templates are provided for Participant Information and Consent Forms (PICFs) by the Harmonisation of Multicentre Ethical Review Reference Group, which states that the language should be readily understood by a grade eight equivalent. Taylor and Bramley [3] found that the average grade level of patient information and consent forms for anaesthesia research exceeded the average literacy and comprehension of the general population in both Australia and New Zealand.

For all patients involved in research, and particularly those vulnerable patients reliant on others (such as family/whanau, EPOA, or legal representatives) to provide informed consent on their behalf, all information and consent forms must be understandable to the levels required by the Health Research Council of New Zealand and as recommended by the Harmonisation of Multicentre Ethical Review Reference Group.

Informed consent in psychiatry clinical research: a conceptual review of issues, challenges and recommendations. Gupta U and Kharawala S. Perspectives in Clinical Research 2012; 3.1; 8-17

Although not part of the anaesthetic literature, the NZSA recommends this paper as it discusses the issue of voluntarism, and details consent capacity assessment, proxy and surrogate consent and screening the decisional capacity of a participant. The paper also looks at various informational/educational techniques that may need to be considered to enhance the understanding of participants.

The distinction between research and audit

It is important for the legislation, as well as ethicists, to distinguish between audit and research. In current practice, there is often no distinction made between research, which tests a new way of doing something, from an audit which is simple observation and appraisal of results without making changes. The recent shift towards labelling all reviews of medical practice as research prevents the necessary methodical examination of patient outcomes. Therefore, we are unable to know our current results or to consider how to improve what we do. Not all studies which collect patient outcome information are correctly labelled as research: when results of normal, currently accepted therapies, or of different approaches in common use are monitored, this is an audit, not research. The ability to do regular audits is vital to maintain the high standards of medical practice for patients. The regular conduct of audits is mandated by the Medical Council of New Zealand for all doctors, as audits monitor clinical results and ensure that standards of practice are maintained and improved wherever possible. Audit results are usually anonymised aggregated patient information and where individual patient information is described, the patient's consent is required.

Summary

Thank you once again for the opportunity to provide feedback on this consultation. The NZSA believes that it is important that adult participants who cannot provide consent are

[3] Taylor H E, Bramley D E P, An analysis of the readability of patient information and consent forms used in research studies in anaesthesia in Australia and New Zealand. Anaesthesia intensive Care 2012; 40: 995-998

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able to benefit from research. As Atul Gwande suggests, we must "count something" to enable analysis of outcome according to patient, operator and institution specific risks.[4]

If you would like further information or have any questions please email:
president@anaesthesia.nz

Yours sincerely

David Kibblewhite

David Kibblewhite
President

[4] Gwande A. Better. A Surgeon's Notes on Performance, 2007 London Profile Books

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APPENDIX I:

HDC Consultation Response Form

Case Study A: An observational study measuring clearance of antibiotics during dialysis

A1. If you were a patient with sepsis and unable to consent, would you want the research to go ahead with you as a participant?

Yes

A.2 Please give the reasons you formed this view.

Blood and urine tests, even if additional, or not that invasive. If I'm in ICU septic they will be doing regular bloods anyway. The potential impact of sub-therapeutic levels of the AB in septic patients is an important one and even though it won't benefit me it may benefit someone in my position in the future.

Case Study B: Clinical trial comparing two products used following neurosurgery

B1. If you were having this surgery and unable to consent, would you want the research to go ahead with you as a participant?

Yes

B.2 Please give the reasons you formed this view.

If both products are in use then I would be equally likely to get either, even if not in the trial, depending on the surgeon preferences in the hospital I am being treated at. If one is shown to be better than the other, this would be beneficial for future patients. I would not agree if it was testing a new product that was not already in clinical use.

B.3 What are your views about "delayed consent?"

I think delayed consent is appropriate, although how long would you wait? If I regain capacity I would want to be involved in a discussion about the trial in the same way I would if I had capacity at the time of enrolment. I would be unlikely to withdraw, given that the data has already been collected, but I think it gives some autonomy back to the patient.

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Case Study C: Trial regarding care provided to consumers with severe dementia

C1. If you were a person with dementia and unable to consent, would you want to be a participant in this research?
Yes

C.2 Please give the reasons you formed this view.
Again, if a new model of care is proven to be beneficial that would be good. It seems to make sense that increased contact would be a good thing, but the study is looking at the negative impacts of such contact too. The goal of this is to improve the QAL of those with dementia; this can be hard to assess. It would be inappropriate to conduct such a study only with those that can consent, as that would skew the results. We are potentially denying this group of patients a better care model if it turns out to be better if we exclude them because they cannot consent.

Case Study D: Clinical trial regarding use of adrenaline

D.1 If you suffered a cardiac arrest, would you want to be part of the study?
Yes

D2. Please state the reasons you formed this view.
The evidence is weak, but adrenaline is a standard treatment. In my medical mind it is a great study, but if I had just had an arrest, I would want adrenaline, not saline. However, I think such a study would be one of the main benefits of allowing research on those unable to consent.

D3. What are your views about the proposed "opt out" process?
I don't think the opt out consent is appropriate. How can you ensure adequate coverage of the opt out bracelet? What if I forget to wear it on the day I have my arrest?

Case Study E: Clinical trial of drug for people with Down syndrome

E.1. Do you think people with Down syndrome who are unable to give informed consent should be part of this research?
No

E.2 Please state the reasons you formed this view.
I think there should be a trial first looking at the effects of the drug in those with Down's syndrome, to ensure there is no difference in effect. You could look at a small group who had capacity to consent. If this study showed no difference in effects/side effects compared to non-downs, then I would be happy with the original study to go ahead using those who cannot consent.

E.3 Do you think the proposed consultation with family/whanau/caregivers gives sufficient protection for participants who are unable to give consent?
Unsure.

E.4 Please state the reasons you formed this view
Taking into account family thoughts is valuable, especially if the family are intimately involved in the care of the patient, but it is not fail safe. The family may not always have the patient's best interests at heart.

Part 5 Consultation questions

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent? If yes, please state the reasons why. If no, please state the reasons why not.
Yes. This is a valuable group of patients who are currently missed from research when it could add important information.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.
There must be clear ethics discussion and guidelines around the study as is the norm anyway.

1.3 Do you think the same laws should apply to all health and disability related research?
Unsure

1.4 Please make any general comments you have about question 1.3
Potentially a wider base for abuse?

Dissent

2.1 Should the law state expressly that irrespective of the person's level of competence any expression of dissent or refusal to participate in research must be respected?
Unsure

2.2 Please give reasons for your answer.
If someone is clearly objecting and it is not necessary for their care, then you must respect their objection, however many patients will become agitated having tests and it may be unclear what they mean if unable to communicate. For example, a demented patient may refuse to go to the toilet, but that is clearly in their best interest.

Delayed consent

3.1 Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence to consent?
Yes

3.2 Please give reasons for your answer
It acknowledges my autonomy once I regain capacity, and informs me of the study I was involved in and gives me the choice about removing my data.

Alternative participants

4.1 Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons?
Yes

4.2 Please make any further comments you have about question 4.1
If this is not in place, it may mean that a researcher may use incompetent adults to perform a study as easier to get the numbers if they don't need to get consent.

Interests of others to be taken into account

5.1 Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?
Yes

5.2 Please give reasons for your answer.
This is the only way that the care of future patients can be improved

5.3 If the proposed research may or may not benefit the incompetent participants, but may benefit others, should there be criteria about the group of people that it is intended to benefit?
Yes

5.4 If the answer to 5.3 is yes, please indicate the criteria that you think should apply and indicate the order of importance of the criteria with 1. Being the most important and 5. Being the least important
Those with the same condition and similar demographics.

Ethics Committee Approval

6.1 Do you think researchers should be required by law to obtain ethics committee approval before conducting health and disability research with adult participants who are unable to give consent?
Yes

6.2 Please give reasons for your answer.
To prevent abuse, particularly because they cannot consent.

New Zealand
SOCIETY OF
Anaesthetists

Ways to assess the advantages and disadvantages of participation by incompetent consumers in research

7.1 Do you think the current best interests test, which requires that the consumer would be better off participating in the research than not participating, strikes an appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed?
Unsure

7.2 If you answered "No" to question 7.1, please answer 7.2. If research were to be permitted to proceed without consent of adult incompetent participants, what criteria/tests do you believe should be used to assess the advantage and disadvantage to the participants?
As long as there is no harm, it is okay to participate if no direct benefit to the patient, but there is a potential benefit to future patients.

Who decides

8.1 Do you think there should be any change made to NZ law regarding who decides whether an incompetent consumer will be enrolled in a study?
No

8.2 Do you think there should be any change made to the roles played by the various possible decision-makers under current NZ law?
Yes, if consent has to fulfil section 7(4) then it will exclude all incompetent patients from studies, as usually unable to say it is in the best interests of the patient. I think the emphasis should be no harm.

8.4 Who do you think should be the final decision maker when making a decision as to whether to enrol an incompetent person in a research project? Set out below are some options.
EPOA, researcher, care provider not involved in research, family/whanau.

New Zealand
SOCIETY OF
Anaesthetists

Appendix II:

Case Study A: An observational study measuring clearance of antibiotics during dialysis

A1. If you were a patient with sepsis and unable to consent, would you want the research to go ahead with you as a participant?
Yes

A.2 Please give the reasons you formed this view.
Observational study. Study will benefit the greater population and body of knowledge.

Case Study B: Clinical trial comparing two products used following neurosurgery

B1. If you were having this surgery and unable to consent, would you want the research to go ahead with you as a participant?
Yes

B.2 Please give the reasons you formed this view.
Both products already approved. No risk to patient and again allows increase in body of knowledge. Delayed consent is necessary especially if there are ongoing followup issues with respect to the study. Everyone who is in a trial without consent must be informed and placed in a position to relinquish their presumed consent if they become competent to do so. Delayed consent could also be called delayed non-consent and as such should be mandatory.

Case Study C: Trial regarding care provided to consumers with severe dementia

C1. If you were a person with dementia and unable to consent, would you want to be a participant in this research?
Yes

C.2 Please give the reasons you formed this view.
There is some evidence to support this hypothesis. Could perhaps include some measure of patient distress during assessments to reassure that the assessments are not causing harm. There is the potential for significant benefits of inclusion in this study and the harms, although relevant (distress etc.) are likely to be non-significant in nature as long as they are considered and mitigated for.

Case Study D: Clinical trial regarding use of adrenaline

D.1 If you suffered a cardiac arrest, would you want to be part of the study?
Yes

D2. Please state the reasons you formed this view.

However, this is difficult. One could argue that this is not experimental as adrenaline is already part of cardiac arrest therapy. This study would again contribute to a greater body of knowledge but ethics approval would be necessary.

D3. What are your views about the proposed "opt out" process?
I suspect the opt out option would be very difficult and expensive to administer.

Case Study E: Clinical trial of drug for people with Down syndrome

E.1. Do you think people with Down syndrome who are unable to give informed consent should be part of this research?
No

E.2 Please state the reasons you formed this view.
There seems to be very little potential benefit and in addition with support a significant group may be able to give consent. In addition, if the drug is successful to then make it unavailable seems questionable.

E.3 Do you think the proposed consultation with family/whanau/caregivers gives sufficient protection for participants who are unable to give consent?
No, I don't think that discussion with whanau is sufficient. In this situation, there is the ability to use the drug on those with Down syndrome who are able to consent, so there should not actually be a need to trial the drug on those who cannot consent.

Answers to Part 5

1.1 Yes, provided that the study is thought ethical and will add to the total body of knowledge in a beneficial manner. Many people like to be involved in such ventures as they want to "give back" to the community in some way.

1.2. The same rules should apply to all research; consistency is important.

2. Difficult and probably no. Many impaired people refuse treatment that is clearly of benefit to them. If there is a clear benefit from being included in a study, one could argue that it would be unethical to not include.

3. Yes, delayed consent may well be useful.

4. Yes

5.1 Yes. Legislating for all possible contingencies is probably impossible. However, agreeing on underlying ethical principles to guide the discussion of a well selected group who are empowered to make decisions on a case by case basis may be more useful.

New Zealand
SOCIETY OF
Anaesthetists

7. I like the concept of "balancing tests" but the two tests suggested still seem to be very limiting in what studies would ultimately proceed. I refer to the comments I made in Q5.

8.1 No

8.2 No

8.4 Hopefully, the final decision will be a consensus between all. However, if consensus cannot be reached, in my opinion the EPOA must have the final say.

3rd May 2017

Health and Disability Commissioner
PO Box 11934
Wellington 6142

Dear Sir / Madam

HDC Consultation Document
Health and disability research involving adult participants who are unable to provide informed consent

The Health IT Consumer Panel would like to thank you for the opportunity to contribute to this consultation. We also appreciate the extension of time allowing us to file a submission today.

The Health IT Consumer Panel was formed some eight years ago to provide advice and guidance to the National Health IT Board. Since the Board was disestablished in early 2016 the Ministry of Health has continued to engage with the Panel to provide input into various activities at national working group and governance group levels. The Health IT Panel is able to provide a diverse range of perspectives on a variety of health issues.

In responding to the consultation document we have provided some overarching comments and then specifically commented against the General Comments section within this document. We have chosen not to respond to the specific case scenarios.

Overarching Comments

As a Panel we believe that a lot of the questions put forward were too diverse, or too simplistic to provide a definitive response.

We have difficulty with the term "incompetent". Using the term "unable to consent due to (and having to name why)" is of more value and empowering, and (hopefully) encourages people to stop and think 'am I saying and doing the right thing?

We recently learnt the most frequent requests for research are about people in intensive care units. These people are mostly unconscious. But they often have loved ones who, if they could consider such research in the emotion of the situation, might say the patient would agree to the research if they were conscious and could do so. There must be a better word than "incompetent".

Any change to Requirement 7 (4) should also include a parallel review of the functionality and composition of NZ ethics committees.

General Comments

Consultation Question 1.1 and 1.2

We answered ‘unsure’ to this question.

There were factors to consider that cannot be addressed at this stage because of the uncertainty of not knowing what changes may be made to Right 7 (4) and other existing legislation, or the introduction of new legislation. If the research was not interventional and was low burden/low risk with Ethics Committee approval then we could potentially answer ‘yes’ to this question.

We would support status of best interest, where the research would be neutral in terms of harm versus benefit.

Consultation Question 1.3 and 1.4

If we were to answer yes to this question there would need to be an assurance that ALL research would go through authorised Ethics Comittees for approval.

If we were to answer no then those who can give informed consent are at a disadvantage.

Consultation Question 2.1 and 2.2

The group answered ‘yes’, the law should expressly state that irrespective of the person’s level of competence any expression of dissent or refusal must be respected. We noted however, that this is open to exploitation depending on who is interpreting the ‘expression’. There must be a high level of trust in the decision making and the decision maker.

Consultation Question 3.1 and 3.2

We did not think it was at all acceptable to obtain delayed or retrospective consent. It is neither ethical nor moral to perform research in the hope of obtaining retrospective consent. We provide the following in support of this decision:

- The research may be against the individual’s personal beliefs which won’t be known until after the fact
- The person dies before consent is obtained – how is the data then treated?
- The person feels coerced to consent retrospectively
- The uncertainty around the deletion of data collected if consent is not subsequently given
- Defining retrospective consent in law risks undermining the concept and integrity of informed consent

Consultation Question 4.1 and 4.2

We answered ‘yes for the most part’.

Common sense would need to prevail, and we reiterate that ANY research would need ethics committee approval. Again, any research approved would need to be low risk, low burden with no intervention.

We do raise the concern about research being conducted on the wider population group and translating the results to specific sub populations . Particularly relevant to this consultation is disability research and this is recognised in the analysis of submissions on the Draft New Zealand Health Research Strategy.

Consultation Questions 5.1 and 5.2

We have chosen not to answer this question. It is too difficult to answer without knowing the outcomes of consultation questions 1 and 2, and any subsequent law changes.

Consultation Questions 6.1 and 6.2

We answered 'yes' to this.

It is a moral obligation to ensure all research receives ethical approval whether the individual can consent or not. It also adds another layer of trust to the process.

Consultation Questions 7.1 and 7.2

We considered this question too hard to answer at the moment and support the status quo at the current time. This stance is adopted because we don't know what may be considered in the future.

Consultation Questions 8.1 and 8.2

We answered this as 'unsure' as a lot more thought needs to be given as to who can decide whether a person who is unable to give informed consent can be enrolled in a study. We indicate a concern about identifying person or people who could/would be best placed to be the decision-maker(s). Sometimes the Welfare Guardian or the EPOA or family members may not have the ability to sufficiently understand the decision and/or the consequences of the decision they are being asked to make; we are aware the Chief Ombudsman has stated publicly there is a shortage of people available to give reliable explanations of issues in plain language to those who may need such support.

Consultation Questions 8.4 and 8.5

We have not provided an answer to this question. We do not feel that it is possible to rank the order in which people are identified as final decision makers. We would support a multidisciplinary approach to decision making where the natural support members are included as equal partners in decision-making.

We would like to see any changes include support for the decision makers so there can be confidence in the quality of decision making.

We look forward to receiving feedback from you on our submission.

Yours sincerely

Stephanie Fletcher
Chair
Health IT Consumer Panel
M:
E:

4 May 2017

Consultation on Right 7(4)
Health and Disability Commissioner
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Dear Mr Hill

HDC consultation on health and disability research involving adult participants who are unable to provide informed consent

Thank you for providing the Medical Council of New Zealand with an extension of time to respond to your consultation on health and disability research involving adult participants who are unable to provide informed consent.

Your consultation paper was discussed at our Council meeting in April 2017, and Council members provided the following feedback:

Consultation Question 6
We consider question 6 of your consultation paper to be the key question to address in health and disability research involving adult participants who are unable to consent. These participants are often vulnerable. To safeguard their interests, it should be mandatory for researchers to obtain approval from an ethics committee before commencing their research. Ethics committees play a vital role in reviewing the research proposal and in helping to ensure that the research is conducted in a manner that is ethical and appropriate. It is important therefore that ethics committees evaluate research proposals carefully and comprehensively at the outset. As additional issues could arise in the course of conducting research with adult participants who are unable to give informed consent, it would be prudent in those instances for researchers to seek further input and guidance from the ethics committee to ensure that their research remains ethical and appropriate.

Consultation Question 8
Question 8 of your consultation paper asks who should decide whether an incompetent consumer should be enrolled in a study. This is a difficult issue, and we wondered if question 8 is something an ethics committee could address as part of its evaluation of a research proposal.

Consultation Question 3
In relation to question 3 of your consultation paper, we are ambivalent about whether the law should be changed to allow researchers to obtain delayed or retrospective consent after incompetent participants regain their competence to consent. If the law were subsequently changed to allow retrospective consent, participants who regain their competence must be given the option to withdraw their consent at any time during the course of the research if they no longer wish to be part of it.

I hope that our comments are helpful for your consultation. If you have any questions, you are welcome to contact the Council's Senior Policy Adviser and Researcher, I , on or at

Yours sincerely

Philip Pigou
Chief Executive

Ngā Hau E Whā Submission

Health and disability research involving adult participants who are unable to provide informed consent 7(4)

Thank you for the opportunity to submit on HDC research involving adult participants who are unable to provide informed consent 7(4)

Nga Hau e Wha welcomes ongoing discussion about the issues raised in this submission.

Case study 1: Observational research on people with a bad infection

- **Relates to people in ICU with sepsis being treated with antibiotics while having kidney dialysis**
- **Researchers want to measure how much antibiotics are in the person's body during dialysis sessions.**
- **These people cannot give informed consent.**
- **Their treatment will not change because of the research – they get antibiotics as usual**
- **They will have a number of tests, including urine and blood tests that would not otherwise be performed.**
- **Are the people better off in ICU from being in the research?**
- **Probably not unless there is an inclusion benefit**
- **So this research cannot go ahead under right 7(4)**

Response:

1. **This procedure is low risk because the person is already hooked up to a cannula which would involve less intrusion. This could allow the removal of blood and urine without any hardship to the patient.**

2. **However researchers would need to show what benefit the person would get from the research. A possible benefit to the person could be that antibiotics may be reduced or increased during the research thus preventing antibiotic resistance**

3. **Any proposed guidelines that define 'low risk observational studies' (as recommended by some bioethicists)[1] should be made open to regular and well informed public consultation.**

1 Virginia McMillan, NZ Doctor- http://m.nzdoctor.co.nz

Case 2. Questions about research on brain operations.

- **A person has to have a brain operation. There are two things doctors can use to make sure a person having brain operations is okay after the operation is over. No-one knows what works best. In this case study a doctor wants to do some research to find out which of the two things will work better for other people in the future to help them get better.**
- **In the study the doctor will give one person 1 thing and the other people a different thing. The doctor will be able to see which thing works best. The people can't say if they want to be included in the research or not.**
- **The doctor wants to get delayed consent for the research from some of the people after their brain operation is done.**

1. **Delayed consent is deferred to a time when the patient may or may not choose to give informed consent.**

2. **Once a person has been subjected to research in any form it is not possible to change that person's outcome or their position on informed consent.**

3. **What may work for one person may not work for others. It could therefore be as likely to harm the participant as heal them.**

4. **This is essentially the reason the Code was developed – to avoid just such a situation.**

Case 3 Research on people with brain disease

- **Sometimes people get a brain disease that makes it hard for them to remember and say what they think and feel. Alzheimers of dementia.**
- **In this case a doctor might want to do some research on the care given to these people. Some will get one form of care and others will get another form of care.**
- **The doctor will see if any of the people get better. No one knows if the people getting care will become better or worse by being involved in the research.**
- **The doctor does not know if the research will mean better care for people in the future or not. The research is trying to find this out**
- **Some of the people the doctor wants to do research on cannot give informed consent.**

1. **Using people with dementia as an example we could assume that a researcher may want to investigate in the following way: provide a high stimulus environment and see if it improves memory and recall in the group so treated.**
2. **This immediately becomes problematic in a small environment of a rest home as some will observe that not all are being treated alike.**
3. **If the group receiving such services does in fact improve there are big questions over what will happen to these people when the service ends. A true ethical dilemma.**
4. **The research could be done with people who are mild to mediate level dementia who can probably provide informed consent.**

Case study 4. Research on people who are having a cardiac arrest.

- **Cardiac arrest is when you have a problem with your heart and it stops working.**
- **Most of the time when a person's heart stops they are given medicine. No one knows if this works of not.**
- **Dr. D wants to study the use of adrenaline after the cardiac arrest – it has been used for many years but safety and efficacy have not been tested fully.**
- **Studies show that that while adrenaline might help to restart the heart initially but may lower survival rates and increase brain damage.**
- **He proposes a large clinical trial – some people would receive adrenaline and others would receive a placebo (saline).**
- **All get CPR as usual.**
- **Neither patients nor paramedics would know who was being given a placebo or adrenaline.**
- **Participants cannot consent.**
- **Outcomes important for the treatment of other people in future.**
- **Opt-out process for consent. People not wanting to be enrolled in the study would request a bracelet that says (NO STUDY) on it.**
- **Awareness of the study would be raised by a public information campaign.**

1. **This is alarming research but we are aware that it is currently being done in the UK which does not have a code like that in Aotearoa.**
2. **This is potentially life threatening research which would not be countenanced within the limitations of the current code 7(4)**
3. **We don't believe this should change.**
4. **The opt out process is not adequate to cover even basic eventualities. While people may be able to wear a bracelet it is hit and miss as to who would go about obtaining one. E.g. large numbers of people do not have a will despite it being well known that this is advisable. Not all people in a particular area at any given time are actual resident in that area and could have missed the publicity about the proposed research.**

Case study 5. Research on people who have Down syndrome

- **In this case study a doctor wants to do some research to find out if a medicine can help people with their learning. But the medicine may make some people with Down syndrome think sad things and want to hurt themselves.**
- **Some people in the research will receive the medicine. Some people who take part in the research will not get the medicine.**
- **This is so the doctor can see if the medicine is helping people with Down syndrome.**
- **Some people with Down syndrome will be able to give consent to take part in the research some people might not be able to give informed consent.**
- **The doctor wants people who can give consent and people who can't in his research.**
- **The doctor wants to be able to get informed consent from the family members or support workers of the people with Down syndrome who cannot give informed consent.**

1. **"But the medicine may make some people with Down syndrome think sad things and want to hurt themselves." This is ethically and medically unsafe and should only ever be tried on people after informed consent has been gained.**

2. **Family/whanau and support workers cannot legally give consent for a person not able to give it themselves.**

3. **As with most of these cases all of the following HDC Code Rights are breached if the research goes ahead as well as 7(4):**

Right 5. You have the right to be told things in a way you understand.

Right 6. You have the right to be told everything you need to know about your care and support.

Right 7. You have the right to make choices about your care and support.

Right 9. You have the right to decide if you want to be part of training, teaching or research.

Consultation Question 1

1.1. Do you believe that research should ever be able to proceed with adult participants who are unable to provide informed consent?
If yes please state the reasons why.
If no please state the reasons why not.

NO

Any proposed guidelines that define 'low risk observational studies' (as recommended by some bioethicists) should be made open to regular and well informed public consultation.

1.2. If you think such research should be allowed please make any general comments about the circumstances/restrictions that you think should apply.

The Code provisions relate to health and disability research conducted only be health care and disability providers. Research related to health and disability issues is also conducted by non-providers, for example, some academic research. Given that such research is outside the jurisdiction of the Commissioner:

1.3. Do you think the same laws should apply to all health and disability researchers?

Yes

1.4. Please make any general comments you have about question 1.3

Ethics committees are variable in their standards and rigor. Ethics around the use of health care and disability providers should match with those of academic researchers.

Dissent

Some people who are unable to make an informed choice to participate in research may be able to express dissent or refuse the procedure involved, for example, by way of facial expressions indicating pain or fear.

Consultation Question 2

3.1. **Should the law state expressly that irrespective of competence any expression of dissent or refusal to participate in research must be respected?**

Yes

3.2. Please give reasons for your answer.

Delayed Consent

In some jurisdictions researchers may be able to carry put research on a person who is temporarily unable to give informed consent provided that the researcher obtains delayed (retrospective) consent from the participants after they regain the ability to consent. Delayed consent is not permitted under NZ law.

Consultation question 3

3.1. Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence?

No

3.2. Please give reasons for your answer

Alternative participants

The NEAC guidelines require that studies should not be performed with vulnerable groups if the studies can be performed adequately with other groups. However this ethical standard is not a legal requirement

Consultation question 4

4.1

Do you think that there should be a legal requirement that, before research is permitted on incompetent persons the researcher must show that research of a similar nature cannot be carried out on competent persons?

Yes

4.2. Please make any further comments about question 4.1

Interests of others to be taken into account.

There are different possible criteria about the people who might benefit from research conducted with other people as participants. Examples of such criteria are requirements that the research:

- Be permitted only if it may benefit others' who have the same or similar condition to the participant
- Can be connected to the impairing condition that prevents the participants from being able to consent
- Be intended to provide knowledge of the causes or treatment of the participant, but may benefit other people.
- Be intended to contribute to significant improvements in scientific capacity

Given that in most research on incompetent participants any benefits for the participants are uncertain but the outcome might benefit others?

Consultation question 5

5.1 Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit others.

No

5.2 Please give a reason for your answer

There are no obvious benefits for the person who is subjected to the research.

Ethics Committee Approval

An option for change would be to make ethics committee approval mandatory in all cases where the research involves adult consumers who are unable to provide informed consent. This requirement could be introduced independently or in addition to the other criteria.

Consultation question 6

6.1 Do you think researchers should be required by law to obtain ethics committee approval before conducting health and disability research on adult participants who are unable to give consent?

Yes

6.2 Please give reasons for your answer.

1. **If there is no Ethics Committee oversight then presumable the research is not properly supervised to at least the minimum standards of the research community.**
2. **All ethics committees considering research-involving people with psychosocial disability should include at least two people with publicly disclosed lived experience of psychosocial disability.**

Ways to assess the advantages and disadvantages of participation by incompetent consumers in research

Consultation question 7

7.1 Do you think the current best interest test which required that the consumers would be better off participating in the research than not participating strikes an appropriate balance between protecting the rights of consumers who are unable to consent and allowing research to proceed?

No

If you answered no to question 7.1 please answer question 7.2

7.2If research was to be permitted without the consent of an adult incompetent participant what criteria/tests do you believe should be used to assess the advantage and disadvantage to the participants.

Where there is not 'a clear benefit to the person', Clinicians, Welfare Guardians and Family/whanau members should not be able to agree to any medical experiments on behalf of people with significant cognitive impairment (including persons with psychosocial disability), unless the person has previously provided consent when deemed fully competent. (EPOA or advance directive)

7.3 Please state the reason you formed this view?

Advance directives

EPOA

Who decides?

Consultation question 8

8.1 Do you think there should be any change to NZ law regarding who decides whether an incompetent consumer will be enrolled in a study?

No

8.2 Do you think there should be any change made to the roles played by the various possible decision makers under current NZ law?

No

The Ministry of Health should develop a strategy for the widespread introduction of the 'Health Passport' and for services to be mandated to complete this with all persons being discharged from hospital care.

Ministry of Health approved Advance Directive templates and the 'Health Passport' should include specific reference to whether a person does or does not consent to health and disability research.

1. **If a consumer has diminished competence, the consumer still has the right to make informed choices and give informed consent to the extent appropriate to their level of competence. For example, the fact that a consumer has an intellectual impairment does not necessarily mean he or she is incompetent to consent to all health and disability services. The level of competence necessary to consent to treatment which has a high degree of risk, complexity or may have serious consequences for the consumer will usually be different from the level of competence required to consent to minor, low risk procedures.**

Advance directives

2. **Where consumers are not competent to make an informed choice or give informed consent, a provider should first establish whether the consumer has a valid advance directive that covers the services proposed.**

3. **Right 7(5) of the Code provides "every consumer may use an advance directive in accordance with the common law" Advance directives enable consumers to indicate in advance their objection**

to, or prohibition of, treatment which would otherwise be provided. They may also specify the type of treatment they would wish to undergo should they become incompetent. A "do not resuscitate" (DNR) order is a type of advance directive (see separate fact sheet on DNR orders).

4. **An advance directive can only be made by a competent consumer; it cannot be made by a consumer's guardian, enduring power of attorney, parent, family member or clinician on their behalf.[1]**

8.3 If you answered yes to 8.1 and/or 8.2 please complete the table below about possible decision makers and the roles you believe they should play in the decision-making. Please note that you might consider that a combination of decision makers is appropriate (either to play different roles in the decision making process or to make decisions in different circumstances.

Table goes here

8.4 Who do you think should be the final decision maker when making a decision as to whether to enroll an incompetent person in a research project. Set out below are some options:

- EPOA or welfare guardian
- Family/whanau
- Provider not involved in the research(e.g. consumers responsible clinician or GP
- Researcher
- Other

Please rank the decision makers in order of preference from 1 being your most preferred to 5 being your least preferred.

1

2

3

4

5

If you prefer a decision maker other than those listed please indicate that decision maker.

Please provide any other comments you wish to make about the decision make

Question 9

Please add any final comments or suggestions you wish to make.

What we believe is missing

Māori and Pasifika

The research question lacks an understanding and a commitment to addressing the specific issues that affect Māori and Pasifika people when it comes to unconsented research.

Older people

Older people, who are most often likely to be impacted by such research, are missing from this research question as a specific population. Older people should have around them the support and infrastructure that they require to participate on an equal basis with others.

Tools for remedy

The research question needs to include a plan for new and/or improved mechanisms for remedy's to be developed and strengthened for breaches of this section of the code..

Appendix 1

UNCRPD

Article 15 prohibits torture and cruel, inhuman or degrading treatment or punishment, including medical experimentation without consent, on people with disabilities.

What needs to be done?

Freedom from torture and cruel, inhuman or degrading treatment or punishment is one of the most well established principles of international human rights law. Medical experimentation without consent was first recognized as a form of torture or cruel, inhuman or degrading treatment or punishment in the International Covenant on Civil and Political Rights, Article 7.

1) Psychiatric drugs and other invasive methods such as electroshock are inherently experimental and endanger the mental and physical capacities, autonomy and personality of an individual. Use of such methods without free and informed consent constitutes torture or cruel, inhuman or degrading treatment or punishment. The practice of forced, coerced or deceptive psychiatric interventions must be stopped immediately and criminally sanctioned.

2) Ensure that psychiatric interventions are not used for purposes of interrogation, coercion or intimidation, punishment, preventive measures, for any reason based on discrimination of any kind (these are the purposes of torture as defined in the UN Convention Against Torture, Article 1), or for any purposes relating to the convenience of third parties. Such use must be prohibited whether in psychiatric settings, prisons, residential services, facilities for children or older persons, or in any other setting.

3) Some psychiatric methods may be inherently inhuman and degrading, and should be banned. For example, direct electroshock makes the person experience the full force of the convulsion without anaesthesia, in addition to the brain-damaging effects of the shock itself, and it should be considered a form of torture or cruel, inhuman or degrading treatment, regardless of whether consent was sought or obtained.

Please note that Article 25 requires that health care be provided on the basis of free and informed consent. This may be a more direct basis for stopping forced, coercive and deceptive psychiatric interventions, but advocates should be aware that the freedom from torture and cruel, inhuman or degrading treatment or punishment is relevant and applicable.

Health and disability research involving adult participants who are unable to provide informed consent

Auckland Women's Health Council Draft Submission

Note:

The Auckland Women's Health Council submission is presented here as an MS Word document with all the text (including case studies) of the online submission form.

The following case studies illustrate some types of research that could not proceed without the participants' informed consent under current New Zealand law. Some of the studies are based on actual research applications made in New Zealand or overseas (although the details may have been simplified and/or altered), and some are hypothetical. The questions asked in relation to each case study are intended to help us understand what factors are important to you and where you believe the line should be drawn. It may help you to imagine that you or someone you care about is a potential participant in each study. Considering these examples may assist you to form your views about the consultation questions in Part IV.

You do not need to answer all of the questions for your responses to be considered by the Commissioner. Leave blank any questions that you do not wish to answer.

Case Study A: Observational study measuring clearance of antibiotics during dialysis

Dr A wants to study how quickly antibiotics used to treat septic patients in Intensive Care Units (ICUs) are removed by dialysis. It is already known that most antibiotics are removed by dialysis to some extent, but the rate can vary. Consumers with severe sepsis often require dialysis therapy due to acute kidney injury. A special form of dialysis is used for these consumers in the ICU, but currently there is no information available regarding the rate at which that form of dialysis removes the antibiotics used to treat sepsis. If antibiotics are cleared by dialysis at a faster rate than expected, the sepsis could be undertreated.

Dr A proposes a study involving acutely unwell septic patients in the ICU, who are unlikely to be able to provide informed consent owing to the impact of the sepsis. Dr A will not amend the treatment provided to the study participants — they would be provided with antibiotics and dialysis in the same way as they would outside of the study. However, Dr A would enrol the participants in his research and measure the changes in antibiotic concentrations during the participants' dialysis sessions. Changes would be measured by a number of tests, including urine and blood tests that would not otherwise be performed.

Information from the study would not affect the clinical management of the participants, and they would not benefit from the research. However, Dr A believes the data gathered may lead to more accurate dosing of antibiotics for other septic patients in ICUs in the future.

Case Study A questions

A.1: If you were a patient with sepsis and unable to consent, would you want the research to go ahead with you as a participant?

Yes/**No**/Unsure

A.2: Please give the reasons you formed this view.

The AWHC would like to make clear from the outset their philosophical opposition to conducting medical experiments, including within the auspices of clinical trials, on any New Zealanders without their fully informed consent, and these concerns apply to all case studies provided. That vulnerable groups of consumers can, and are, being exploited for research gain under the current law goes against the principles of the Nuremberg Code (1947), the founding document that gave rise to modern medical research ethics. It is clear that the law as it stands is sufficiently weak and uncertain as to allow "studies to proceed in relation to participants who are unable to consent if participation in the research is in their "best interests""* where the researcher is able to make the decision as to what constitutes in the patients "best interests".

The AWHC believes that absolutely no incapacitated/incompetent adults should be enrolled for medical experiments/clinical trials/research until there are sufficient protections and safeguards established in law that first and foremost protect their rights and interests, health and well-being.

The Nuremberg Code (1947) on medical experimentation on human subjects was followed by the Geneva Convention and then the Declaration of Helsinki formulated by the World Medical Association, of which the New Zealand Medical association was and is a member. The Declaration of Helsinki clearly states that:

- "while the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects";
- "some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm… All vulnerable groups and individuals should receive specifically considered protection."
- "participation by individuals capable of giving informed consent as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees."

Yet despite these existing protections, which New Zealand's Medical Association ratified, medical experimentation on competent women at National Women's Hospital occurred without their knowledge or consent in the 1960s and 70s.

Our Code of Health and Disability Services Consumers' Rights, while a step in the right direction, still allows for research on adults not capable of providing informed consent on the basis that the researcher decides it is in the consumer/patient's best interests. The AWHC does not believe that researchers are capable of making an unbiased decision that is truly in the best interests of the consumer/patient. In addition, it is the AWHC's view that the current Health and Disability Ethics Committees (HDEC) do not prioritise the protection of research subjects.**

Once an adequate ethical and legal framework is in place (including specific definitions of terms such as "minimal risk/burden", "benefits", "best interests", and who constitutes an authorised legal representative) further nationwide discussion involving all stakeholders, including patient and consumer advocates, should revisit the circumstances, if any, in which research involving vulnerable groups such as incapacitated/incompetent adults might be permitted.

If an adequate ethical and legal framework was established that provided sufficient protections for incapacitated/incompetent research subjects, including a Special Ethics Committee to oversee approval to such research proposals (see Consultation Question 9), the AWHC might take the following view on a research proposal such as described in Case Study A:

The research is relatively non-invasive in that it does not involve varying the treatment protocol, and there is very low level of risk involved. It involves the collection of data from urine obtained through dialysis that is already occurring. However, the case study text infers that further blood tests would be taken to provide data on antibiotic concentrations in the blood; blood tests that would otherwise not be performed. The

knowledge gained could improve treatment for future patients, and it seems that significant benefit to future patients may result. Informed consent must be obtained from next of kin or anyone holding Enduring Power of Attorney (EPOA) and the patient's informed consent when competence is regained. However, if the patient, upon reaching competence, withholds consent, data collected from that patient must be withdrawn from the study and destroyed.

* *Health and disability research involving adult participants who are unable to provide informed consent* consultation document.

** AWHC members have attended HDEC meetings over the last eight years, and three current Council members have been sitting members of various ethics committees.

Case Study B: Clinical trial comparing two products used following neurosurgery

Dr B wants to compare the safety and effectiveness of two products used to achieve a watertight closure of patients' brain membranes following neurosurgery. Both products have already been clinically approved and are commonly used by surgeons. The current evidence does not indicate that either product is safer or more effective than the other, but no research has been conducted that directly compares the two products.

Dr B proposes to conduct a study on consumers undergoing neurosurgery, who would be randomly allocated to receive one of the two products. Dr B would then collect data about the safety and effectiveness of each product.

The consumers are mostly having surgery in relation to brain tumours and are likely to have reduced capacity to make decisions. Some of the potential participants may have brain injuries, cognitive impairments, intellectual disabilities, mental illnesses or be in intensive care. While some of the proposed participants may be able to provide informed consent, others will not have the capacity to do so. Dr B believes that both groups need to be included in the research in order to gather useful data that can be generalised to other consumers in the future.

Dr B intends to include consumers who are unable to give consent, and then seek "delayed consent" from any consumers who regain the capacity to consent after the trial. If any of those consumers refuse consent after regaining capacity, their data will be removed from the study.

B.1: If you were having this surgery and unable to consent, would you want the research to go ahead with you as a participant?

Yes/**No**/Unsure

B.2: Please give the reasons you formed this view.

There is insufficient information provided in this case study; however, it appears that the same information could be obtained through enrolling competent consenting patients undergoing elective surgery (refer to Schiariti A.; Surg Neurol Int. 2014; 5: 171.), in which case clinical trials on incapacitated/incompetent patients should not be considered.

Randomising patients without their consent is unethical because, in many patients, there could be a necessary variance from what is best practice care for the surgeon involved. It is unclear from the information provided if the researcher, Dr B, is the surgeon who will perform the surgeries involved in the study. There are several reasons why any given surgeon chooses to use particular products and those reasons may impact upon outcomes in different patients operated on by different surgeons. If patients are to be randomised a surgeon may end up using a product s/he was less familiar with or had less confidence in and this could introduce an outcome bias.

It is clear from other similar research that this research could be undertaken in patients who are competent before surgery and as a starting point Dr B should undertake fully consented research on competent patients.

There are insufficient clear benefits to incapacitated/incompetent patients that outweigh their right to provide informed consent.

B.3: What are your views about "delayed consent"?

There can be no such thing as "delayed consent"; it is effectively an oxymoron. Asking for consent after the fact is like a child asking a parent for a biscuit after having eaten one; if the answer is no what happens? You can't change what has already occurred.

In observational studies it is possible to remove a subject's data from the results of the study, but in interventional research the outcomes of treatment will be the same. Where treatment or procedures in a study (particularly a randomised study) might vary from what would have happened in a non-study situation, once it has happened it can't be reversed. There may well be compelling reasons why a person would not have consented; they opposed randomisation or had a personal preference for a specific procedure or product to be used; there were ethical issues that concerned them about the manufacturer/suppler or manufacturing process or materials used… or simply did not want to take part in research for personal or cultural reasons. It goes without saying that if "delayed consent" is sought, then a subject's information and any data obtained must be removed, and if the follow-up is long term (beyond the regaining of competence) the subject should be withdrawn. The inclusion of people not competent to consent prior to the research should never be justified on the basis that "retrospective consent" can be sought.

In reality, the only consent that can be obtained in retrospect from a previously incapacitated or incompetent research subject is consent to remain in the research. It is simply disingenuous semantics to suggest that patients could provide delayed or retrospective consent.

Case Study C: Trial regarding care provided to consumers with severe dementia

Dr C wants to study the care provided to rest home residents with severe dementia. Dr C believes that conventional care for such consumers is task-focused, concerned primarily with the consumer's physical needs and daily activities. Dr C thinks conventional care may be neglecting consumers' psychosocial needs, meaning that many consumers with dementia are spending many hours alone and emotionally distressed. Dr C thinks that part of the problem may be that a dementia diagnosis is treated as diminishing a consumer's personhood, leading staff to reduce their efforts to establish and maintain relationships with the consumer.

Dr C proposes a study that would randomly allocate consumers with severe dementia into two groups, each group receiving a different type of care. Group 1 would receive conventional care, which focuses on physical task-oriented practices and physical needs. Group 2 would receive "interactive care", an alternative to conventional care that is intended to maintain personhood as dementia progresses. "Interactive care" includes a greater focus on the psychosocial needs of the consumer. At this stage, there is very little evidence about the benefits or risks associated with "interactive care". However, Dr C believes that the proposed study could supply evidence that would lead to improvements in the care provided to consumers with dementia.

It is not known whether the research would be in the participants' best interests. They would have to undergo additional assessments as part of the research, but the additional assessments could benefit the participants if the increased contact with the researchers was beneficial to them, or changes in their condition were picked up that would not otherwise have been noticed. On the other hand, there is a risk that some participants may find the additional contact distressing.

The proposed trial would take place over four months. Researchers would assess the participants' agitation levels, psychiatric symptoms and quality of life before and directly after the trial period, and then again four months after the conclusion of the trial.

The fact that a consumer has dementia does not necessarily mean that he or she is unable to provide informed consent. Some may be capable of providing informed consent with appropriate support, or they may have intermittent periods when they are able to provide consent to participate in the research. Dr C also proposes to include in the study consumers who are not able to consent.

C.1: If you were a person with dementia and unable to consent, would you want to be a participant in this research?

Yes/**No**/Unsure

C.2: Please give the reasons you formed this view.

The research should start with a pilot study among those patients capable of providing consent. Dr C is clear that "there is very little evidence about the benefits or risks associated with 'interactive care' " and dementia patients are a very vulnerable group. A pilot study among consenting patients would give Dr C sufficient information to assess levels of distress among participants in the "interactive care" group as well as any benefits that such care might ultimately afford the patients.

A well designed study undertaken with sufficient advance notice should be able to provide enough information to answer the question as to the benefits and risks of the intervention without including patients unable to provide informed consent.

In a situation in which there is a strong legal and ethical legislative framework that offers sufficient protections and safeguards for vulnerable groups, results from a cohort of participants able to provide consent ***might*** then form the basis for further research in which informed consent from next of kin or those with EPOA might be a valid approach to understanding the benefits and risks of intervention for those unable to consent. However, the results of a pilot study might deliver data that rules out intervention on the basis of risk versus benefit, in which case a highly vulnerable incapacitated/incompetent cohort would never need to be subjected to research of little or no benefit to them.

A further consideration is that frequent assessments in themselves might raise levels of frustration, anxiety or emotional distress in this highly vulnerable group of patients and it's clear that the researchers can't say that the research is in any way in the "best interests" of the patients.

Case Study D: Clinical trial regarding use of adrenaline

Dr D wants to study the use of adrenaline in the treatment of cardiac arrest. Adrenaline has been used as a routine treatment for cardiac arrest for over 50 years, but its safety and efficacy have not been tested fully. Several previous studies suggest that while adrenaline may help to restart the heart initially, it may also lower overall survival rates and increase brain damage. While these studies have led to significant concerns about whether adrenaline could be harming consumers, the body of evidence is not yet strong enough to change current practice.

Dr D proposes a large clinical trial to gather further information. The trial would be randomised, double-blind and placebo-controlled. This means that some of the participants would receive adrenaline and some would receive a placebo (in this case, salt water). During the trial, neither the participants nor the paramedics would know who was being given adrenaline and who was being given salt water.

No consumer undergoing treatment for cardiac arrest would be able to provide informed consent to participate in the study, so Dr D proposes to enrol consumers in the trial without obtaining consent. She considers that the research is important to ensure the best outcomes for consumers who have cardiac arrests in the future, and that it cannot be conducted on consumers who are able to provide consent.

To deal with this issue, Dr D suggests an "opt-out" process for consent. Consumers not wishing to be enrolled in the study would be able to opt out by requesting a bracelet with "NO STUDY" engraved on it. Awareness of the study would be raised through a public information campaign.

Case Study D questions

D.1: If you suffered a cardiac arrest, would you want to be part of the study?

Yes/**No**/Unsure

D.2: Please state the reasons you formed this view.

It is totally unethical to withhold a standard or best practice treatment from patients without their consent and, in particular, in a life or death situation, such as when a patient's heart has stopped beating. While the issue of whether or not the use of adrenaline leads to overall lower survival rates and increase in brain damage is an important one to research, there is insufficient information provided on the effects of not using adrenaline and using a placebo (which by definition is a non-therapeutic substance or treatment) instead. This research has absolutely no benefit for the subjects involved in the research and can only possibly benefit future patients. The threshold for benefit versus risk, in the case where consent cannot be obtained, must necessarily differ if those provided a treatment cannot weigh up the pros and cons and make an informed decision. In this case the benefits for the subjects are too low and the risks potentially too high.

AWHC objects in the strongest possible terms to this type of research in which subjects unable to consent may be randomised to not receive best practice care in a life threatening situation. It is hard to imagine any scenario in which such research could be considered ethical. In addition, as a double blind trial, the attending physicians would not know whether adrenaline or placebo had been given and will therefore have no idea the exact cause if the patient fails to respond to the treatment.

D.3: What are your views about the proposed "opt out" process?

An "opt out" process, in virtually any medical scenario, is highly problematic and is in no way a valid or ethical alternative to the provision of fully informed consent. It is predicated on the idea that 100% of the population that may be at risk of sudden cardiac arrest will be made sufficiently aware of their choices that they will be able to, and motivated to, make an informed decision to "opt out" or, by definition, choose to actively "opt in" by doing nothing. Given the known apathy of populations to exercise their mandated right to do such things as vote (a far less personally risky action than to choose to participate in research in a life-or-death situation), it is extremely unlikely that anything close to 100% of the "at risk" population would be reached in a public information campaign. Therefore, the probable low level of active decisions to "opt out" cannot be taken as tacit consent to participation in a medical experiment by the remaining (quite likely majority) of the "at risk" population.

Additionally, many of the at risk population simply do not know that they are at risk until they have such a medical event. People ignorant of their risk status would not be easily communicated with via a public campaign.

A further stumbling block to this proposal is that it would seem likely that few people would want or would be bothered to consistently wear an "opt out" bracelet.

The "opt out" idea is a highly disingenuous way of abrogating responsibility for the need to obtain informed consent from patients involved in potentially risky medical research. It has been acknowledged that it would be difficult if not completely impossible to obtain informed consent in the described scenario and the "opt out" solution is an unethical attempt to get around deservedly stringent regulations regarding the participation of human subjects in medical experiments.

Case Study E: Clinical trial of drug for people with Down syndrome

Dr E wants to investigate whether a particular drug will improve the cognitive and learning abilities of people with Down syndrome. He proposes a randomised, double-blind, placebo-controlled study. This means that some of the participants would receive the study drug and some would receive a placebo (for example, a sugar pill). During the trial, neither the participants nor the researchers would know who was receiving the drug. Participants would be required to undergo regular six-hour assessment visits to check their progress.

The study drug has already been tested on people without Down syndrome. That research provided some information about the possible risks and side-effects of the drug, including that, for some participants, it increased the incidence of contemplating suicide. However, there may be other risks or side-effects that have not yet been discovered. In particular, the effects of the drug on people without Down syndrome may be different from those on people with Down syndrome.

It is not known whether the drug will have the desired effect on cognition or learning (or any other beneficial effects). However, it is likely that even if the drug did lead to an improvement in cognition for the research participants, the effect would be temporary because the drug would not be available to participants after the conclusion of the trial.

Some adults with Down syndrome may be capable of providing consent if given appropriate support and information. Those consumers could then be enrolled in the study in accordance with ordinary consent principles. Dr E proposes also to enrol participants who are not able to give consent because the effects of the drug on those participants may be different. Dr E proposes to consult with family/whānau/caregivers and, if they express objections, those participants will not be enrolled.

Case Study E questions

E.1: Do you think people with Down syndrome who are unable to give informed consent should be part of this research?

Yes/**No**/Unsure

E.2: Please state the reasons you formed this view.

The risks are significant in a group of already highly vulnerable people, with limited or no benefit. It is clear that the benefits are not well understood and that if there were any, they would likely be short lived – what would be the effects on the adults with Down syndrome if they enjoyed improvements in cognition and learning ability only for those effects to dissipate once the drug was no longer administered? This surely amounts to a cruel punishment, and if the subjects are not competent enough to provide informed consent, how will they cope with an improvement and followed by a decline in their abilities? Given that clearly little is known about the adverse effects of the drug, and that many Down syndrome people have other physical health problems, such as poor immune function, congenital heart defect and epilepsy, it would be unethical to risk side-effects that would further compromise their quality of life without their informed consent.

It is entirely unethical to involve anyone without their fully informed consent, and a full and conscious knowledge of the risks and benefits, in research that may raise their risk of contemplating suicide. It is hard to imagine that any transient and short-lived cognitive benefit to Down syndrome adults could be perceived as balancing the risk of self-harm or even thoughts of self-harm.

E.3: Do you think the proposed consultation with family/whānau/caregivers gives sufficient protection for participants who are unable to give consent?

Yes/**No**/Unsure

E.4: Please state the reasons you formed this view.

Some of the issues that are raised in E2 above apply here: if the subjects are not competent enough to provide informed consent, how will they cope psychologically with the impacts of the research and administration then withdrawal of the drug (e.g. an improvement and followed by a decline in their abilities; or significant risks to their health and quality of life, such as increased thoughts of suicide) if another person sees fit to consent on their behalf?

The family/whānau of vulnerable patients/consumers are subject to potential coercion and duress. Most want what is best for their loved ones, but may not be best placed to make important decisions regarding research of which they may have little understanding, in particular when they harbour hope that improvement is possible when the prognosis is poor.

In this case study, while family/whānau may be swayed by thoughts of possible improvements to cognitive and learning abilities, the risks are still significant and the benefits insubstantial and ephemeral. While people with Down syndrome have a reduced mental capacity, many lead happy, productive, quality lives and this vulnerable group should not be viewed as experimental subjects by anyone and only they should have the right to provide informed consent for medical research.

In this part you will be asked whether you think the law should remain as it is or be changed. We would like to know what factors or criteria you think should be taken into account when considering whether incapacitated/incompetent adults should be research subjects, and who should be the decision-maker(s).

The case studies above may have helped you to form an opinion about whether our existing law draws the line in the right place and, if not, where you think it should be drawn. You may find it useful to refer back to them when considering the consultation questions below.

As stated above, please note that the questions in this paper are reproduced in the Consultation Response Form on the HDC website: *www.hdc.org.nz*. To provide us with your comments, please either complete the form online or print the form, record your answers on the form and return it to PO Box 11934, Wellington 6142.

You do not need to answer all of the questions for your responses to be considered by the Commissioner. Leave blank any questions that you do not wish to answer.

Consultation Question 1

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent?

If yes, please state the reasons why.

If no, please state the reasons why not.

As stated at the outset of this submission, the AWHC holds a philosophical opposition to conducting medical experiments, including within the auspices of clinical trials, on any New Zealanders without their fully informed consent. That vulnerable groups of consumers can, and are, being exploited for research gain under the current law* goes against the principles of the Nuremberg Code (1947), the founding document that gave rise to modern medical research ethics. It is clear that the law as it stands is sufficiently weak and uncertain as to allow “studies to proceed in relation to participants who are unable to consent if participation in the research is in their “best interests”” where the researcher is able to make the decision as to what constitutes ‘in the patients best interests’.

The AWHC believes that absolutely no incapacitated/incompetent adults should be enrolled for medical experiments/clinical trials/research until there are sufficient protections and safeguards established in law that first and foremost protect their rights and interests, health and well-being.

* Johnston, M.: Consent for drug trials on coma patients to be reviewed, New Zealand Herald, 15 December 2014.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.

In the event that sufficient protections and safeguards are established in law – legislation that first and foremost protect their rights and interests, health and well-being – in some limited and very strictly controlled circumstances, research involving incapacitated/incompetent adults might be permitted to proceed. If there is a direct benefit to the incapacitated/incompetent adult/s, and without research there would be no other opportunity for the incapacitated/incompetent adult/s to benefit (e.g. a new drug specifically for the condition that relates or contributes to their lack of ability to consent), and if the risks are significantly outweighed by the benefits, research might be allowed to proceed. However the most stringent safeguards must be applied and each case (research proposal) should be assessed on an individual basis. Observational studies are of lesser concern as such studies do not require any variation on best practice treatment of the research subjects; rather the collection and analysis of data that would can be routinely collected in the normal course of care and treatment for their health condition/s.

However, even observational studies raise issues of consent and whether or not it is culturally appropriate and sensitive for some patients to be included without their consent when they might hold different values and views around the collection, storage and use of personal data and human material such as blood, urine and tissue.

Where there is no direct benefit to the incapacitated/incompetent adult/s but to future patients in the same or similar situation, research might be allowed to proceed under strict ethical control (see Question 6.2) where there is also very limited or no risk involved, such as in the case of observational studies without variance from best practice care of the subjects, and where sufficient other safeguards (e.g. next of kin/EPOA consent and "retrospective consent" is obtained, notwithstanding submissions made in Question B3 above and 3.2 below) are in force. However, as discussed in Question A2, it is critical that clear definitions of terms such as "minimal risk", "burden", benefit" and "best interests" should be set out with no room for interpretation. Additionally, the person/s able to make an "in the patient's best interests" decision must be clearly defined, including that that person cannot be associated with the research, or directly benefit from the research, and should have knowledge of the patient, and their condition.

Specifically, research should only involve incapacitated/incompetent adults in the following circumstances:

1. That the research is observational and does not involve invasive procedures and does not involve any deviation from best practice care of the patients; that data will be collected in the course of the normal best practise care provided.
2. That the same research cannot be undertaken with adults capable of providing informed consent;

And/or

Research has already been undertaken in competent, consenting adults, and further research involving incapacitated/incompetent adults would significantly add to the body of knowledge AND benefit those patients or future patients with the same condition (subject to 3 below).

3. That the research is directly related to the condition/s that the incapacitated/incompetent adults have, and/or directly relates to the reasons they are incapable of providing informed consent.
4. That there is direct benefit for the research subjects and negligible risk, or that the benefit to the research subjects is significantly outweighed by the risks; that a research subject will benefit as much from being included in the research as not being included;

Or

There is no expected benefit for the research subjects but that there will be a significant benefit for future patients with the same condition, and the risk to the research subjects is negligible.

5. That the research does not involve “non-inferiority” research, and that benefits to the subjects are more than inclusion benefits.
6. That all proposed research is subject to approval by a “special ethics committee”. This committee would have a core membership including entirely independent medical ethicists, patient advocates, lay persons and medical/health/disability representatives, and for each proposal would include co-opted members such as entirely independent lay representatives and patient advocates with a special interest in the vulnerable group to be involved in the research, lay persons or ex-patients of a similar medical demographic to the proposed subjects (where possible), and medical/health practitioners with expertise in the vulnerable group to be involved in the research.
7. That, notwithstanding the submission made in Question 3.1 below, in all cases where “retrospective” or “delayed” consent from the incapacitated/incompetent adult is obtainable upon regaining competence, that consent is sought under the existing code (i.e. without coercion, duress, discrimination, harassment, or exploitation).
8. That all efforts are made through discussions with next of kin, EPOA or the patient’s regular health professional (e.g. GP, counsellor, etc.) to ascertain the incapacitated/incompetent adult’s attitude to participation in research or clinical trials, such that it may have been discussed explicitly or otherwise at a time when the subject was competent, to understand the views that the now incapacitated/incompetent adult may hold were they in a position to provide consent.
9. That any indication that the research subject does not consent, or appears to object, or shows signs of resistance before, during or after the research, they must immediately be withdrawn from the research.
10. That especially vulnerable groups of incapacitated/incompetent adults, such as those with permanently reduced mental capacity (e.g. Down Syndrome, dementia patients) with no likelihood of being able to ever provide consent are never to be involved in anything more than strictly observational studies in which there is no deviation from best practice care and no physical intervention.

The Code provisions relate to health and disability research conducted only by a health care or disability services provider. Research relating to health and disability issues is also conducted by non-providers, for example, some academic research. Given that such research is outside the jurisdiction of the Commissioner:

1.3 Do you think the same laws should apply to all health and disability related research?

Yes/No/Unsure

1.4 Please make any general comments you have about question 1.3.

The circumstances, role, employer or title of the person or group undertaking the research do not in any way at all alter the vulnerability of adults who are unable to provide fully informed consent to participate in experimental research. There should no difference in the application of any code of rights, legislation or safeguards regarding the recruiting and involvement of incapacitated/incompetent adults in any and all research and the foremost consideration should be the safety and well-being of the subjects/proposed subjects of the research. The same laws should apply to all research involving adults unable to provide informed consent!

Dissent

Some people who are unable to make an informed choice to participate in research may be able to express dissent or refuse the procedures involved, for example, by way of facial expressions indicating pain or fear.

Consultation Question 2

2.1 Should the law state expressly that irrespective of the person's level of competence any expression of dissent or refusal to participate in research must be respected?

Yes /No/Unsure

2.2 Please give reasons for your answer.

If there is any doubt whatsoever about the willingness of any research subject to participate or continue participating, the decision must err on the side of caution and the subject must never be enrolled in or must be withdrawn from the research.

When considering such vulnerable groups of adults, the threshold for participation must be especially high in order to ensure all such adults are protected to the fullest extent possible. In order to protect all potential research subjects, it may be that some who may have consented had they had the competence to do so are ruled out, but this is necessary to ensure that no person is included in research that would not have consented had they been competent to do so.

It is widely reported by health professionals working in the field, that unconscious patients can still have some awareness of what goes on around them, in particular through the sense of hearing. Likewise, conscious but impaired people, such as dementia patients or intellectually disabled people have many ways of expressing their dissent even if they are unable to verbalise it with the same degree of articulateness that a fully competent adult might. It cannot be assumed that a patient who cannot provide clear, audible or visible responses in the way that fully competent patients can, cannot express themselves in any manner at all or that they are entirely unaware of what is happening. To ignore subtle signs of distress or resistance risks refusing the patient the opportunity to express their lack of consent in the only way that is possible.

Delayed consent

In some jurisdictions, researchers may be permitted to carry out research on a person who is temporarily unable to give informed consent provided that the researcher obtains delayed (retrospective) consent from the participants after they regain the ability to consent. Delayed consent is not permitted under New Zealand law.

Consultation Question 3

3.1 Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence to consent?

Yes/**No**/Unsure

3.2 Please give reasons for your answer.

Although in earlier questions in this submission the AWHC has indicated that this should be sought and the decision respected and abided by, in general we have a philosophical objection to the concept of "delayed" or "retrospective" consent.

It is simply not possible to provide ***informed*** consent after the fact.

As stated in Question B3, there can be no such thing as "delayed consent" or "retrospective consent"; it is effectively an oxymoron. The consultation document states that "In New Zealand, delayed consent is not a

legally valid form of informed consent. It is not possible to provide informed consent retrospectively, because the events have already taken place, even if the consumer, upon regaining capacity, does not have an objection to having been included in the research."

There needs to be an alternative term that more accurately describes the situation where patients, on regaining competence, are informed that they have been participating in research without their consent and that they can withdraw and have their data withdrawn from the study.

In a few very limited cases the obtaining of this type of "retrospective" consent may be sufficient to right an incorrect assumption that the subject would have given consent had they been able to prior to the commencement of research. In a practical sense, if the research is entirely observational and the data can be removed from the study if the adult, once competent, withholds consent, that might seem to remedy the situation entirely. However, in some cultures the collection of data may represent a breach of their beliefs and the removal of data from the study insufficient to remedy the wrong.

The inclusion of people not competent to consent prior to the research should never be justified on the basis that retrospective consent can be sought. Only in life or death situations, where lack of action or treatment would likely lead to the death or serious further disability of a patient, should action be taken prior to obtaining consent, and research in itself is not a life or death situation.

It is also absurd to assume that all patients have some degree of altruism and would happily consent on the basis of contributing to the "the greater good". There are constant examples of the lack of altruism among many citizens, and those citizens are as likely to find themselves in situations in which they are incapacitated /incompetent as any citizen whose altruism is demonstrated. In addition, one person's altruism may not extend to happily consenting to research that may bring no direct benefit plus known or unknown risks, and unless consent is acquired while they are competent it is all but impossible for anyone else to know if that person would consent on the basis of "the greater good".

Alternative participants

The NEAC guidelines require that studies should not be performed with vulnerable groups if the studies can be performed adequately with other groups. However, this ethical standard is not a legal requirement.

Consultation Question 4

4.1 Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons?

Yes/No/Unsure

4.2 Please make any further comments you have about question 4.1.

It is imperative that if research involving incapacitated/incompetent adults is proposed, and considered, that absolute proof be provided by the applicant that:

- they have exhausted all possible means of obtaining the required data from enrolling competent participants;
- it is critical to undertake research in a specified group of incapacitated/incompetent adults in order to benefit the specific cohort of incompetent adults with the particular conditions associated with their inability to provide informed consent; and

- adequate preliminary studies have been undertaken in competent and consenting adults in order to establish the probable risks and benefits prior to any research involving incapacitated/incompetent adults being proposed.

The AWHC also believe that such an ethical standard be made a legal requirement. There seems little point in having ethical standards that have no legal support, cannot be enforced and rely entirely on researcher compliance.

It may be that, in some cases, obtaining informed consent from competent patients prior to the situation in which their condition or impairment renders them incapacitated/incompetent slows down the progress of the research. In this case research must be delayed in order to amass sufficient consenting subjects to undertake the research rather than rely on incapacitated/incompetent subjects. The primary concern here is, and must always be, the welfare, health and well-being and rights of the research subjects, not the convenience of the researcher or expediting his or her research.

Changes to the Standard Operating Procedures of the HDECs in 2012 has resulted in a shift away from protection of consumers and proposed research subjects towards expediting research. Issues of concern were raised in an open letter to then Minister of Health, Tony Ryall, by five bioethicists. Their concerns included a reduction in ECs from seven to four, leading to a reduced level of scrutiny of clinical trials, expeditious review by the chair, and some research not being reviewed at all in order to cope with the increased workload. As a result of the changes, research protocols for clinical trials that are categorised as low risk, also receive only expedited review by a committee chair.

There must be a shift back to making the welfare, health and well-being and rights of proposed research subjects the foremost issue for consideration in the HDEC approval process.

Interests of others to be taken into account

There are different possible criteria about the people who might benefit from research conducted with other people as participants. Examples of such criteria are requirements that the research:

- be permitted only if it may benefit others who have the same or a similar condition to the participant
- be connected to the impairing condition that prevents the participants from being able to provide consent
- be intended to provide knowledge of the causes or treatment of the impairing condition that prevents the participants from being able to provide informed consent
- be intended to contribute to significant improvement in scientific understanding of the incapacity suffered by the participants.

Given that in most research on incapacitated/incompetent participants any benefits for participants are uncertain, but the outcomes may benefit others:

Consultation Question 5

5.1 Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?

Yes/No/**Unsure**

5.2 Please give reasons for your answer.

As previously stated in this submission, the AWHC believes that absolutely no incapacitated/ incompetent adults should be enrolled for medical experiments/clinical trials/research until there are sufficient protections and safeguards established in law that first and foremost protect their rights and interests, health and well-being.

Even in the event that such legislation is enacted, insufficient information is provided in this document to adequately and definitively answer this question. Whether such research should be permitted would depend entirely on the nature of the research. As AWHC stated in question 1.2 above, the only research that we believe should be permitted in incapacitated/incompetent adults is that of an observational nature, in which there is no deviation from best practice care of the specific cohort of patients. It is accepted that such research is unlikely to benefit the research cohort, but may benefit future adults with the same impairing conditions.

If the requirement that only observational studies are permitted in incapacitated/incompetent adults is met then the answer to Question 5.1 might be yes.

However, if the proposed research goes beyond the observational and involves intervention, variation to best practice treatment, randomised controlled trials, non-inferiority trials, etc. and there is no benefit to the research subjects or the benefit is only an "inclusion" benefit, and inherently, because the research is interventional, some level of risk must be involved, then the answer is a categorical NO.

If the answer to question 5.1 is yes:

5.3 If the proposed research may or may not benefit the incompetent participants, but may benefit others, should there be criteria about the group of people that it is intended to benefit?

Yes/No/Unsure

5.4 If the answer to 5.3 is yes, please indicate the criteria that you think should apply and indicate the order of importance of the criteria with 1. being the most important and 5. being the least important.

1. The group that the research is intended to benefit have the same or a very similar condition to the research subjects.

2. That the research is directly related to the impairing condition that prevents the participants from being able to provide consent.

3. That the results of the research is intended to provide knowledge of the causes or treatment of the impairing condition that prevents the participants from being able to provide informed consent.

The AWHC holds serious concerns that any regulation that allows research on one particular group of vulnerable patients to be involved in research in order to ultimately benefit any future patients would be subject to regulatory creep. It is unacceptable and unethical to undertake research on one group of subjects in order to subsequently benefit an entirely different demographic group; for example, undertaking research on cognitive improvement in Down syndrome adults that is then used to benefit dementia patients instead, effectively treating the Down syndrome adults as a group of lesser importance or value – effectively as guinea pigs!

Any others?

Ethics committee approval

An option for change would be to make ethics committee approval mandatory in all cases where the research involves adult consumers who are unable to provide informed consent. This requirement could be introduced independently, or in addition to other criteria.

Consultation Question 6

6.1 Do you think researchers should be required by law to obtain ethics committee approval before conducting health and disability research with adult participants who are unable to give consent?

Yes/No/Unsure

6.2 Please give reasons for your answer.

Absolutely, ethics committee approval must be obtained! It is unconscionable that research involving incapacitated/incompetent adults not be subject to the same rigors of ethical approval to which any other research involving competent consenting adults is subject. While it might currently be possible for medical, health and disability research to go ahead without ethics committee approval because the researcher is not a health and/or disability services provider and is, for example, an academic, it is imperative that ethics committee approval be mandatory no matter the researcher or setting in which the research is to be carried out.

The AWHC believes that the ethical threshold for research involving incapacitated/incompetent adult research subjects must be much higher than that required for competent adults. Such vulnerable sectors of the community must be afforded greater protections than those groups of competent adults who can make decisions for themselves and be their own advocates.

The AWHC believes that the current Code of Rights and HDECs do not provide sufficient protection for vulnerable adults incapable of providing informed consent.

Right 7(4) of the Code explicitly applies to the provision of health and disability services, not research, although right 9 does say that all rights in the code extend to research. However, greater clarity regarding rights of incompetent/incapacitated adults within the code should be addressed irrespective of any other legislative provisions for the protection of incompetent/incapacitated adults.

The AWHC requests that a separate and independent special ethics committee (separate and independent from the existing HDECs) be set up solely to consider research in these vulnerable incapacitated/incompetent adult cohorts. This committee would have a core membership, including entirely independent medical ethicists, patient advocates, lay persons and medical/health/disability representatives, and for each individual research proposal would include co-opted members, such as entirely independent lay representatives and patient advocates with a special interest in the vulnerable group to be involved in the research, lay persons or ex-patients of a similar medical demographic to the proposed subjects (where possible), and medical/health practitioners with expertise in the vulnerable group to be involved in the research.

Ways to assess the advantages and disadvantages of participation by incompetent consumers in research

Consultation Question 7

7.1 Do you think the current best interests test, which requires that the consumer would be better off participating in the research than not participating, strikes an appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed?

Yes/**No**/Unsure

If you answered "No" to question 7.1, please answer question 7.2.

7.2 If research were to be permitted to proceed without the consent of adult incompetent participants, what criteria/tests do you believe should be used to assess the advantage and disadvantage to the participants?

As AWHC has already stated, its view is that only observational, non-interventional and non-invasive research should be permitted in incapacitated/incompetent adults.

The AWHC opposes the "best interests" test because the term "best interests" is ill-defined and open to significant variations in interpretation depending upon who is making the decision that a particular course of action is in the "best interests" of an incompetent/incapacitated patient.

In particular, this assessment should never be left to the researcher. The AWHC does not believe that researchers are capable of making an unbiased decision that is truly in the best interests of the consumer/patient. Researchers necessarily have a conflict of interest and should never be the ones to determine the "best interests" of a proposed research subject.

In addition, the concept of "minimal" or "negligible" risk or burden is also ill-defined, and a relative concept that may vary significantly depending on who is making the assessment, and the range of adverse effects or events or the degree of burden that may be suffered by the research subjects. It is also entirely possible for completely unforeseen adverse effects to be suffered by research patients, for example, the phase I trials of TGN1412 which "caused a near fatal systemic inflammatory response in all six healthy trial volunteers" (Eastwood, D.; Br J Clin Pharmacol. 2013 Aug; 76(2): 299–315.). AWHC oppose all first in man trials in incompetent/incapacitated adults for this reason (see Question 9). However, even phase II and III trials can be subject to unforeseen and potentially catastrophic adverse events, as evidenced by Case Study E in this consultation document in which there was an increased incidence of suicidal thoughts in previous trials. In another example, in a 1993 phase II clinical trial of Fialuridine, out of 15 patients in the trial, five died and two required liver transplants despite a pilot study of 43 of shorter duration revealing no serious adverse effects (Honkoop P., Drug Saf. 1997 Jul;17(1):1-7; and Attarwala H., J Young Pharm. 2010 Jul-Sep; 2(3): 332–336).

In the event that sufficient protections and safeguards are provided, and in the circumstances of the limited research that AWHC considers might be permitted (as set out previously in this submission) the decision regarding whether or not participation in the proposed research is in the "best interests" of the proposed subject should be made by an EPOA or authorised representative, and, an independent physician (not involved in the research) who has knowledge of the condition or impairment the subject has. As is set out in the Australian guidelines, if consent is provided by an EPOA or authorised representative that consent should be "witnessed by a person who has the capacity to understand the merits, risks and procedures of the research and is independent of the research team, and who knows the person and is familiar with his or her condition."

AWHC is of the view that there are no circumstances in which it is acceptable to impose risk or burden upon a research subject who has no opportunity or ability to weigh up the benefits and risks of their involvement in medical experimentation. Likewise, it is not acceptable to assume that a person is or would be sufficiently altruistically motivated to accept risk and burden of pain, discomfort or adverse effects of research with little or no benefit to themselves, 'for the greater good', unless this view has been explicitly expressed prior to their loss of competence to provide informed consent.

However, in the case of observational studies where it is argued that there are no risks or burden, the very least that is owed the incapacitated/incompetent subject is that people with sufficient knowledge of the

patient and the proposed research including its risk, benefits and likely outcomes make that decision on their behalf.

In summary, the criteria should be that the proposed research causes no disadvantage, discomfit, pain or adverse effect on the research subjects. In effect there should be no disadvantage to the patient notwithstanding the potential for breaching cultural beliefs as commented upon in Question 3.2 above; this is the only way in which it can be assured that an incompetent adult is not subject to harm that s/he has no ability to consent or object to.

With regard to benefit, inclusion benefit – that the research subject will receive better care and monitoring if they take part in the research than if they did not – should never be used in any risk:benefit assessment and never used as any form of justification for inclusion in the research.

7.3 Please state the reasons you formed this view.

Determining whether or not an incompetent/incapacitated patient should participate in research should never come down to a mathematical formula: that if perceived or expected benefit exceeds the expected risk or burden the patient should be included. The value placed on any benefit or degree of harm from burden, or an adverse event or outcome, is a qualitative as well as quantitative assessment that competent adults make when making an informed decision and it varies according to each individual's values, circumstances and beliefs.

Who decides?

Consultation Question 8

8.1 Do you think there should be any change made to New Zealand law regarding who decides whether an incompetent consumer will be enrolled in a study?

Yes/No/Unsure

8.2 Do you think there should be any change made to the roles played by the various possible decision-makers under current New Zealand law?

Yes/No/Unsure

Despite what researchers might believe about themselves, all manner of biases are reported in the medical literature and few if any medical researchers could be said to be entirely unbiased. Many biases are sub-conscious and to place the burden of decision making about what is or is not in the best interests of patients in the hands of a single, interested researcher leaves both the researcher and their research subjects open to harm. Dependent on the nature of the proposed research, a range of people, preferably with complete independence from the research and researcher, should be involved in the decision to involve incapacitated/incompetent adults in research.

Similarly, the decision should not be solely made by the family/whānau of the proposed research subject. In some circumstances, the proposal to enrol an incapacitated/incompetent adult in research may be because their condition or impairment is life threatening. In such situations the family/whānau will be under stress and may not be capable of making objective decisions; may not be in a position to ask the questions that the proposed subject might ask were s/he competent. Such stress may constitute being asked to consent under duress, in particular, if the prognosis for their loved one is poor.

8.3 If you answered "Yes" to question 8.1 and/or 8.2, please complete the table below about possible decision-makers and the roles you believe they should play in decision-making. Please note that you may consider that a combination of decision-makers is appropriate (either to play different roles in the decision-making process or to make decisions in different circumstances).

Person who could have a role in decision-making (X)	Should X ever have a part to play in deciding whether an incompetent consumer is enrolled in a study?	If yes, in what circumstances should X be involved in decision-making? i.e., a) In all cases where X is available? b) Only when particular criteria are met (e.g., that the study is to be conducted for the purpose of saving the consumer's life or preventing serious damage to the consumer's health)? c) Only when other possible decision-makers (please specify which decision-makers) are unavailable? d) Only where the circumstances require that an urgent decision is needed (see, e.g., Case Study D)? e) Other? *Please choose the letter(s) for any of the options above that you think should apply, or provide comment if you prefer.*	Where X is involved in decision-making, what role should he or she have? i.e., a) Consulted by decision-maker? b) Power to veto* consumer's participation in the research? c) Provide or withhold consent on behalf of the consumer? d) Other? *Please choose the letter(s) for any of the options above that you think should apply, or provide comment if you prefer.* *A veto means the right to refuse or reject permission for an incompetent consumer's participation in research.
EPOAs and welfare guardians	**Yes/No/Unsure**		
Family/ whānau	**Yes/No/Unsure**		
Provider not involved in the research (e.g., consumer's responsible clinician or GP)	**Yes/No/Unsure**		
Researcher	**Yes/No/Unsure**		
Other (please name):	**Yes/No/Unsure**		

AWHC finds the table in Q 8.3 above overly prescriptive and it does not allow sufficient flexibility for vastly differing circumstances of incompetent individuals that might be considered for inclusion in research. The decision making process should be necessarily more complicated than these questions allow for; decisions for individuals need to be made on a case by case basis rather than according to some algorithm.

8.4 Who do you think should be the final decision-maker when making a decision as to whether to enrol an incompetent person in a research project? Set out below are some options.

- **EPOA or welfare guardian**
- **Family/whānau**
- **Provider not involved in the research (e.g., the consumer's responsible clinician or GP)**
- **Researcher**
- **Other**

Please rank the decision-makers you chose in order of preference from 1. being your most preferred to 5. being your least preferred. If you prefer a decision-maker other than those listed, please indicate the decision-maker.

1. EPOA or welfare guardian
2. Independent patient advocate, perhaps appointed in the absence of an EPOA and/or where there is no competent next of kin
3. Family/whānau
4. Provider not involved in the research (e.g., the consumer's responsible clinician or GP)
5. Special ethics committee in exceptional circumstances (see question 6.2)

8.5 Please provide any other comments you wish to make about the decision-makers.

The AWHC opposes the veto option for deciding upon whether or not an incapacitated/incompetent adult is enrolled in research. Notwithstanding the AWHC's philosophical opposition to research involving incapacitated/incompetent adults, if there is to be such research there should be a specific responsibility placed on a person or people to provide consent. A veto is akin to an "opt out" option (see Question D3), and the gravity of such a decision to involve an incapacitated/ incompetent adult in research deserves more serious consideration by those involved in the decision making.

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9. Please add any final comments or suggestions you wish to make.

The AWHC has specific concerns about the involvement of incapacitated/incompetent adults in medical experimentation. While we understand the potential benefits of increasing knowledge on the conditions suffered by incompetent adults and the impairments that lead them to be in the position of being incapable of providing consent, the overriding concern must be for the health and welfare of the patient, not the acquisition of knowledge no matter how well intentioned that might be.

While it has reservations about even the least invasive observational research, the AWHC categorically rejects permitting the following types of research on incapacitated/incompetent adults:

- 1st in man or phase I clinical trials of any type;
- non-therapeutic trials, e.g. non-inferiority trials;
- any research in which known or expected adverse effects could possibly exceed any potential benefit to the research subjects;
- any research in which known or expected adverse effects may include death, permanent disability or impairment, or a worsening of the existing condition or impairment.
- any interventional research where the only or most likely benefit to the incompetent adult is an "inclusion benefit".

It is the AWHC's view that HDEC approval is insufficient protection for vulnerable research participants such as incapacitated/incompetent adults, and that a Special Ethics Committee (see question 6.2) must be set up to specifically consider research proposals that seek to involve such subjects. The AWHC notes that the current law does not require research carried out in New Zealand to have HDEC approval (although lack of approval does impose some limitations on research such as an inability to publish results) and that low risk

studies do not require approval. However, the threshold for what constitutes low risk must necessarily be much, much higher when considering research in such vulnerable groups as incapacitated/incompetent adults who cannot weight the risks and benefits for themselves and make informed decisions or advocate for themselves if and when anything goes wrong, and cannot withdraw their consent and withdraw from the research at will.

It must be accepted that, because of the unique vulnerabilities of incapacitated/incompetent adults and the need to protect them, the timeframes for approval or otherwise of research proposals must necessarily be different from research that involves competent participants. Longer lead-in times must be accepted (by researchers, sponsors such as pharmaceutical companies, and ethics committees) and timelines established to benefit and protect the research subjects rather than research being expedited for the convenience and benefit of the researcher/s.

In addition, the AWHC protests in the strongest possible terms the lack of real consultation with the community and patient advocates with regard to proposed softening of the laws and regulations to allow the enrolment of incapacitated/incompetent patients in medical research. In a letter to the AWHC by HD Commissioner, Anthony Hill, dated 7 November 2016, he stated that "it is likely that, in addition to inviting written submissions, my Office will organise and focus groups and/or public meetings to facilitate discussion of the issues raised by the consultation document. The exact details of the consultation process will be released concurrently with the consultation document". Despite this undertaking the AWHC has not seen any further evidence of the intention to do so.

Any proposal to involve vulnerable people in medical experiments without their explicit and informed consent contravenes the Nuremberg Code. Although the Declaration of Helsinki and our own Code of Health and Disability Services Consumers' Rights are watered down versions of the Nuremberg Code, they still protect the rights of incapacitated/incompetent adults, albeit with wording that is at times vague and open to interpretation. Any change that would allow or sanction medical experimentation on New Zealanders, especially our most vulnerable citizens, requires more than submissions on a consultation document that has had little media coverage. It is entirely likely that significant portions of the potentially affected sectors of our community and their family/whānau, and the health professionals who care for them, are entirely unaware of the existence of the consultation paper or the proposed changes to the Code.

The AWHC requests that further consultation, in particular something of the nature of a nationwide road show, public meetings and/or focus groups, be considered to elicit greater community comment and involvement in any changes to the Code and that any changes not be expedited at the expense of our most vulnerable citizens.

HDC Consultation

Health and disability research involving adult participants who are unable to provide informed consent

Consultation response form

The right to make an informed choice and give informed consent before receiving health or disability services, including participating in research, is the cornerstone of New Zealand's Code of Health and Disability Services Consumers' Rights (the Code). The maxim "nothing about us without us" is an essential part of the culture of New Zealand's health and disability sector.

In some circumstances it is appropriate and lawful to provide health or disability services to a consumer without consent. An example is the provision of emergency life-saving treatment to an unconscious patient. However, it is more complex to decide whether it is appropriate to include a person who cannot give consent to be a subject of research. At present in New Zealand, research on a person who is unable to give consent can take place only if participation in the research is in **that person's best interests**.

Currently, non-consensual research that is not intended to provide a benefit to an individual participant but nevertheless may provide important information of benefit to others cannot proceed because it does not meet the standard of being in the participant's best interests.

This consultation will focus on two fundamental questions: are New Zealand's current laws regarding non-consensual research appropriate and, if not, how should they be amended? Please note that this consultation is limited to research involving **adult** consumers.

To provide us with your comments, either:

a) complete the form online; or

b) print the form, record your answers on the form and return it to PO Box 11934, Wellington 6142. Add additional pages if you wish to do so.

You do not need to answer all of the questions for your responses to be considered by the Commissioner. Leave blank any questions that you do not wish to answer.

Case Study A: Observational study measuring clearance of antibiotics during dialysis

Case Study A questions

A.1

If you were a patient with sepsis and unable to consent, would you want the research to go ahead with you as a participant? **No**

A.2

Please give the reasons you formed this view.

This is an observational study and potentially not in my best interests. If I was in this situation I would not want to be a participant given the death rate is >50%. Sepsis is a serious medical emergency ranging from minor (signs & symptoms to organ dysfunction and shock).

In view of the specific circumstances of this case study I support the consumer centred system as outlined in Hill (2013). Of importance to me is whether my mental capacity is temporary, permanent or likely to return, but this is very subjective. The right to respect is paramount.

Some interesting facts from Australian Prescriber:

- renal impairment reduces the clearance of some drugs
- multiple comorbid illnesses and drug clearance by dialysis all complicate prescribing
- main considerations are renal clearance and therapeutic index.

My views on the sepsis issues and aligns with The Peoples Review (p19) in identifying one of two critical human rights issues in mental health clinical practice (*and comorbid conditions*), including:

- the tension between (compulsory treatment) and the rights to refuse treatment, to make an informed choice and to give informed consent

Case Study B: Clinical trial comparing two products used following neurosurgery

Case Study B questions

B.1

If you were having this surgery and unable to consent, would you want the research to go ahead with you as a participant?

Yes/No/Unsure

B.2

Please give the reasons you formed this view.

Given the controversy around surgical mesh, I would be against this research as a patient safety issue and patients should not be subjected to experimentation.

I cannot imagine that this case study would pass ethics approval. The two products should have been adequately tested at procurement stage so this issue does not arise.

In the Perth Declaration for Patient Safety, the WHO definition of patient safety is stated as "*a fundamental principle of health care. Every point in the process of care-giving contains a certain degree of inherent risk. Adverse events may result from problems in practice, products, procedures or systems. Patient safety improvements demand a complex system wide effort, involving a wide range of actions in performance improvement, environmental safety and risk management, including infection control, safe use of medicines, equipment safety, safe clinical practice and safe environment of care.*"

B.3 What are your views about "delayed consent"?

I feel there is no way back from the actions of the substitute decision maker/responsible clinician/researcher. The risk is on the patient to be a participant that might not be in their best interests

From a personal psychological perspective, I would be totally against delayed consent, and traumatised when I discovered the truth of what had been done without my knowledge or informed consent.

There are issues of "protection" vs "access" which rest on the model of respect for persons and self-determination. The Bioethics article also discusses the argument that ensuring access of all groups to experimental medical interventions for their conditions especially where existing therapies are inadequate.

Case Study C: Trial regarding care provided to consumers with severe dementia

Case Study C questions

C.1
If you were a person with dementia and unable to consent, would you want to be a participant in this research? **Unsure**

C.2
Please give the reasons you formed this view.

This is a case where an EPA would prevail and protect the patient's right to informed consent. Dementia is a group of related symptoms associated with an ongoing decline of the brain and its abilities. This includes problems with memory loss, thinking speed, mental agility, language, understanding, judgment.

Persons with dementia are daily concerned with supports necessary for provision of proper dementia care, and relates to the physical environment, the training and expertise of staff, the level of staffing and the use of antipsychotic drugs. (Office of the Seniors Advocate). This describes the life reality for these patients and has a huge contributory impact on their mental capacity and decision making.

Of course, a person is assumed to have capacity unless it is established they do not. I have seen dementia first hand in a relative and if that was my life reality I cannot see how capacity can be demonstrated and maintained during the life of the study as is required; and of course, afterwards as they directly must live with the consequences arising from the study.

Case Study D: Clinical trial regarding use of adrenaline

Case Study D questions

D.1
If you suffered a cardiac arrest, would you want to be part of the study?

No

D.2
The inherent risk of not receiving proper care resulting in my incapacitation or mortality is not in my best interests.

D.3
What are your views about the proposed "opt out" process?

I would be all for it but require more information about process, systems and security.

Case Study E: Clinical trial of drug for people with Down syndrome

Case Study E questions

E.1
Do you think people with Down syndrome who are unable to give informed consent should be part of this research? **Unsure**

E.2

Please state the reasons you formed this view.

"Adults with Down syndrome experience the same life events as other adults; however, they may need specialised services and supports to accomplish some things, …advocacy plays a continued part. The overarching themes of *freedom, self-determination, the right to education and medical care etc.*… and the *human, legal and civil rights* those without disabilities often take for granted." (Eidelman)

The Herts paper (cited in E.4) on Capacity to consent presents the view that "the perception that people with intellectual disabilities who cannot consent for themselves correlates with the status approach to the question which presupposes that certain individuals, by virtue of their status, are necessarily incapable of making legally valid decisions."

E.3

Do you think the proposed consultation with family/whānau/caregivers gives sufficient protection for participants who are unable to give consent? **No**

E.4

Please state the reasons you formed this view.

A University of Herts, UK paper outlines decision making by relatives and carers and states that "the practice of proxy decision making … is contentious and without foundation in law, especially in the domain of treatment refusal … the contestable assumption that relatives will determine what is in their relative's best interests."

Consultation questions

Consultation Question 1

1.1 Do you believe research should ever be allowed to proceed with adult participants who are unable to provide informed consent?

If **yes**, please state the reasons why.

If **no**, please state the reasons why not.

1.2 If you think such research should be allowed, please make any general comments about the circumstances/restrictions that you think should apply.

The Code provisions relate to health and disability research conducted only by a health care or disability services provider. Research relating to health and disability issues is also conducted by non-providers, for example, some academic research. Given that such research is outside the jurisdiction of the Commissioner:

1.3 Do you think the same laws should apply to all health and disability related research?

Yes/No/Unsure

1.4 Please make any general comments you have about question 1.3.

Dissent

Some people who are unable to make an informed choice to participate in research may be able to express dissent or refuse the procedures involved, for example, by way of facial expressions indicating pain or fear.

Consultation Question 2

2.1 Should the law state expressly that irrespective of the person's level of competence any expression of dissent or refusal to participate in research must be respected? **Yes**

2.2 Please give reasons for your answer.

No means no, no matter how it is expressed. Rights to refuse or withdraw consent are specific in legislation and The Code for a reason. My initial reaction is it would be a major morality debate, and I need to further seek knowledge on this.

Delayed consent

In some jurisdictions, researchers may be permitted to carry out research on a person who is temporarily unable to give informed consent provided that the researcher obtains delayed (retrospective) consent from the participants after they regain the ability to consent. Delayed consent is not permitted under New Zealand law.

Consultation Question 3

3.1 Do you think the law should be changed to allow researchers to obtain delayed or retrospective consent to research after incompetent participants regain competence to consent?

No

See B3 for my answer on delayed consent as a potential participant.

I need to give some more thought (and reading) to retrospective consent. This appears to be a similar question but I think it asks for views on the legality.

Alternative participants

The NEAC guidelines require that studies should not be performed with vulnerable groups if the studies can be performed adequately with other groups. However, this ethical standard is not a legal requirement.

Consultation Question 4

4.1 Do you think that there should be a legal requirement that, before research on incompetent persons is permitted, the researcher must show that research of a similar nature cannot be carried out on competent persons? **Yes**

4.2 Please make any further comments you have about question 4.1.

Research ethics in my view should support this legal requirement. Considerable protocols are around ethic committees and must extend their reach thought the work of its members.

Surely the proposed research should be put before relevant ethic committee before any field work commences, even precluding research arising that meets the scope or aim of the research.

Interests of others to be taken into account

There are different possible criteria about the people who might benefit from research conducted with other people as participants. Examples of such criteria are requirements that the research:

- be permitted only if it may benefit others who have the same or a similar condition to the participant
- be connected to the impairing condition that prevents the participants from being able to provide consent
- be intended to provide knowledge of the causes or treatment of the impairing condition that prevents the participants from being able to provide informed consent
- be intended to contribute to significant improvement in scientific understanding of the incapacity suffered by the participants.

Given that in most research on incompetent participants any benefits for participants are uncertain, but the outcomes may benefit others:

Consultation Question 5

5.1 Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people? **Unsure**

5.2 Please give reasons for your answer.

*I*f the answer to question 5.1 is yes:

If it may harm or disadvantage the patient the research should not be permitted in any case.

I question definition of "person centred care" (refer p32 consultation document – it is not included in the glossary of terms).

Martin (2012) in framing Right 7(4) in the second statement on p7 emphasises the consumer-centred provision as the clear requirement by law to first enquire into consumer's actual wishes.

5.3 If the proposed research may or may not benefit the incompetent participants, but may benefit others, should there be criteria about the group of people that it is intended to benefit? **Yes**

5.4 If the answer to 5.3 is yes, please indicate the criteria that you think should apply and indicate the order of importance of the criteria with 1. being the most important and 5. being the least important.

1. Informed consent of all parties

2. Best interests of all parties and their families who care for them (not necessarily as carer, but who actually care).

3. Criteria

4. Criteria

5. Criteria

Any others?

Ethics committee approval

An option for change would be to make ethics committee approval mandatory in all cases where the research involves adult consumers who are unable to provide informed consent. This requirement could be introduced independently, or in addition to other criteria.

Consultation Question 6

6.1 Do you think researchers should be required by law to obtain ethics committee approval before conducting health and disability research with adult participants who are unable to give consent? **Yes**

6.2 Please give reasons for your answer.)

See my answer to

Ways to assess the advantages and disadvantages of participation by incompetent consumers in research

Consultation Question 7

7.1 Do you think the current **best interests** test, which requires that the consumer would be better off participating in the research than not participating, strikes an appropriate balance between protecting the rights of consumers who are unable to give consent and allowing research to proceed? **Yes/No/Unsure**

If you answered "No" to question 7.1, please answer question 7.2.

7.2 If research were to be permitted to proceed without the consent of adult incompetent participants, what criteria/tests do you believe should be used to assess the advantage and disadvantage to the participants?

7.3 Please state the reasons you formed this view.

Criteria tests – advantage disadvantage

Who decides?

Consultation Question 8

8.1 Do you think there should be any change made to New Zealand law regarding *who* decides whether an incompetent consumer will be enrolled in a study?

Yes

8.2 Do you think there should be any change made to the roles played by the various possible decision-makers under current New Zealand law?

Unsure

8.3 If you answered “Yes” to question 8.1 and/or 8.2, please complete the table below about possible decision-makers and the roles you believe they should play in decisionmaking. Please note that you may consider that a combination of decision-makers is appropriate (either to play different roles in the decision-making process or to make decisions in different circumstances).

Person who could have a role in decisionmaking (X)	Should X ever have a part to play in deciding whether an incompetent consumer is enrolled in a study?	If yes, in what circumstances should X be involved in decision-making? i.e., a) In all cases where X is available? b) Only when particular criteria are met (e.g., that the study is to be conducted for the purpose of saving the consumer's life or preventing serious damage to the consumer's health)? c) Only when other possible decision-makers (please specify which decision-makers) are unavailable? d) Only where the circumstances require that an urgent decision is needed (see, e.g., Case Study D)? e) Other? *Please choose the letter(s) for any of the options above that you think should apply, or provide comment if you prefer.*	Where X is involved in decision-making, what role should he or she have? i.e. a) Consulted by decision-maker? b) Power to veto* consumer's participation in the research? c) Provide or withhold consent on behalf of the consumer? d) Other? *Please choose the letter(s) for any of the options above that you think should apply, or provide comment if you prefer.* *A veto means the right to refuse or reject permission for an incompetent consumer's participation in research.
EPOAs and welfare guardians	**Yes**	a)	c)
Family/ whānau	**Yes**	b)	c)
Provider not involved in the research (e.g., consumer's responsible clinician or GP)	**Unsure**	d)	a)
Researcher	**No**	e)	e)

Other (any other, or nursing staff):	**No**	e)	e)

8.4 Who do you think should be the **final** decision-maker when making a decision as to whether to enrol an incompetent person in a research project? Set out below are some options.

- EPOA or welfare guardian
- Family/whānau
- Provider not involved in the research (e.g., the consumer's responsible clinician or GP)
- Researcher
- Other

Please rank the decision-makers you chose in order of preference from 1. being your most preferred to 5. being your least preferred. If you prefer a decision-maker other than those listed, please indicate the decision-maker.

1.

2.

3.

4.

5.

8.5 Please provide any other comments you wish to make about the decision-makers.

The legal framework for proxy decision makers is not always clear.

the Principles for the Protection of Persons with Mental Illness and the Improvement of Mental Health Care. (24)

9. Please add any final comments or suggestions you wish to make.

I am appreciative of the fact that the HDC is focussing on The Code, but would ask that the Right to Health state legal obligations *(respect*, *protect* and *fulfilment)* as outlined in General Comment 14 (2000), are upheld alongside in a global perspective.

I am concerned for those vulnerable populations who find themselves in circumstances such as in the case studies who experience physical, psychological and social health domains which impact on their mortality and capacity to consent. "Those with multiple problems also face more significant comorbidities and cumulative risks of their illness," The American Journal of Managed Care (2006).

Thank you for your contribution to this consultation.

HDC, with the assistance of the Expert Advisory Group, will review all of the submissions received. The Commissioner will then consider those submissions and decide whether to recommend any changes to the current law. If any change to the Code is recommended, further consultation will be conducted.

Please state your Name:

Organisation:

HDC will publish a report after the consultation period has ended. All submissions that you make on this consultation are subject to the Official Information Act 1982. If you consider that all or part of your submission should be treated as confidential, please state this clearly when making your submission and indicate which of the grounds within the Official Information Act for withholding information you believe apply. HDC will take your views into

account when determining whether or not to release information. Please note that any decision by HDC to withhold information is able to be reviewed by the Ombudsman.