2018

Summary of submissions

HDC CONSULTATION ON HEALTH AND DISABILTY RESEARCH INVOLVING ADULT PARTICIPANTS WHO ARE UNABLE TO PROVIDE INFORMED CONSENT

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Executive summary

This report summarises the public submissions made in response to the Health and Disability Commissioner Consultation Document: *Health and disability research involving adult participants who are unable to provide informed consent (24 February 2017).* The focus of the consultation was on two fundamental questions: Are New Zealand's current laws regarding non-consensual research appropriate and, if not, how should they be amended? A series of five case studies followed by eight consultation questions were presented in the document and views were sought of consumers, those interested in the welfare of adults unable to consent, providers, and researchers. A total of 154 submissions from a variety of groups and individuals were received. A descriptive analysis was carried out to identify the key issues and highlight themes that cut across all case study and consultation question responses.

The underlying tension evident in the submissions was between the two philosophical positions of deontology and utilitarianism. Deontological views are that non-therapeutic research on the incompetent is never justifiable because it uses them as a means to others' ends. Utilitarian views are that scientific advances and the interests of future patients can justify involving incompetent participants in research even though the benefit is to others.[1] Extreme views were not at both ends of these positions; some people argued strongly that non-consensual research is *never* ethically justified, but no one argued for a completely utilitarian view that the greater good should be put ahead of the needs or rights of individuals. Instead, there is a strong sense of the need to find the right balance of restrictions and safeguards on research in this context in order to protect vulnerable consumers from harm and exploitation.

Right 7(4) of the Code states that providers may provide services if a consumer is not competent to make an informed choice 'where it is in the best interests of the consumer'. All Rights in the Code extend to participation in teaching or research (Right 9). Many people who made submissions thought that the best interests requirement is effective and appropriate for protecting consumers in both treatment and research situations. Others argued that it was designed for treatment situations where a person is unable to consent, but almost never applies in research (with the possible exception of single arm, Phase III drug trials). A strongly held view was that the best interests test is a barrier to non-interventional types of research, including audit, which have relatively low levels of risk to participants. It therefore restricts the development of evidence-based care, preventing improvements in care for high-needs populations. Protection for these groups is needed, but there should be provision to allow for more research than at present. 'Best interests' is too high a threshold for research, and there should be more emphasis on recognition of an individual's will and preference, as well as minimum risk, burden, and benefit thresholds.

Circumstances that lead to people being unable to give consent to participation in research vary. They include acute and possibly temporary incapacity (e.g., in emergency or intensive care situations), progressive illnesses (e.g., severe dementia and Huntington's disease), and long-term and/or permanent disabilities (e.g., some intellectual disabilities). Mechanisms widely thought to be lawful for gaining consent to participate in research have been delayed consent in acute care contexts and substitute or proxy consent more often in long term contexts.

[1] Manning, J. (2016). Non-consensual clinical research in New Zealand: Law reform urgently needed. *Journal of Law and Medicine, 23*(3), 516–530.

Submissions were divided on the consultation questions about more permissive use of consent by substitute. Consent by substitute is not always practical in acute, time-sensitive contexts, and acute care clinicians were inclined to think that researcher-clinicians should be the decision-maker about participation. Others, however, thought that never appropriate due to their conflict of interest. In general, there was support for the idea that authorised representatives should be able to consent to participation in research on behalf of an adult who is unable to consent. Others thought that family and whānau should be consulted on any such decision. Some thought that substitute consent violates the principle of consumer autonomy, and that other forms of consent such as supported decision-making and participatory processes were preferable and more consistent with non-binary views of capacity.

A common theme throughout the submissions was of the need to address wider system issues concerning the governance and operation of research ethics committees before amendments to legislation were made. Many submissions raised concerns about the reduction in protection for research participants owing to changes to Health and Disability Ethics Committees (HDECs) in recent years. The system was described as unclear, confusing, contradictory, and fragmented and, although assumed, optimal safeguards do not fully exist even for competent participants. Although there was wide support for a change in the law to require ethics committee approval of research with adult participants unable to give consent, there was extensive comment that cautioned against changes to the Code without a parallel review of the functionality and composition of the committees. Ideally, there should be a national specialised committee to review research proposals involving non-consenting participants, as well as the establishment of ongoing monitoring and reporting processes on the ethical conduct of each study. It was thought that once strong ethics committee safeguards are in place to protect participants, fewer specific legal restrictions would be necessary.

Several submitters suggested that New Zealand law is out of step with other countries and overly restrictive and protectionist. One submitter argued that a research ethics paradigm that focuses only on the dangers of research is distorted and we need to aim for a balance, not a myopic focus on risk. It was argued that adults unable to consent are currently *protected by their exclusion* from participation in research when they could be *included but protected* with robust safeguards. Amendments to current New Zealand laws should be aligned with similar jurisdictions, particularly those of Australia, the United Kingdom, and the United States.

Amendments to the Code were suggested although a few submitters thought the Code should be seen as a coherent whole and individual Rights within it should not be changed in isolation. Suggestions for change included altering the best interests criterion to 'best-equal interests' (meaning participants would be no worse off) or introducing risk/burden thresholds. Other suggestions were to have separate Rights in the Code for research and for treatment. Several submissions suggested that cultural issues needed to be incorporated into the Code, including indigenous views about research, and the collection and retention of human tissue and DNA. There was wide agreement that the same laws should apply to all health and disability research and not just that done by service providers.

Amendments to the wider legislative framework were suggested. At present, the Protection of Personal and Property Rights (PPPR) Act 1998 prohibits authorised representatives (welfare guardians and EPOAs) from agreeing to participation in 'medical experiments' unless to save life or prevent serious risk to health. More permissive use of consent by substitute would require amendment to this legislation.

Introduction

In February 2017, the Health and Disability Commissioner called for public submissions on a Consultation Document: *Health and disability research involving adult participants who are unable to provide informed consent*. The focus of the consultation document was on two fundamental questions: Are New Zealand's current laws regarding non-consensual research appropriate and, if not, how should they be amended? A series of five case studies followed by eight consultation questions were presented in the document. They were produced in both standard and Easy Read format and included a series of questions and a submission form. The case studies were examples of different research scenarios and asked people their views about whether the research should be permitted, under what circumstances, and whether they would want the research to go ahead with themselves as a participant in such a study. These were designed to give some indication of the situations in which people thought research with people unable to consent might be more or less acceptable. The consultation questions set out the specific issues on which the Commissioner was seeking public input.

The consultation document was available on-line and in hard copy and was mailed or emailed to all those on the Health and Disability Commissioner's (HDC's) mailing list comprising 371 individuals, groups or institutions, although 65 were returned due to incorrect addresses. A total of 154 submissions from a variety of groups and individuals were received. Twenty-four used the Easy Read form either on-line or by post, 106 used the standard template, and 26 did not use either template to write their submissions. It is not possible to say reliably what proportion came from individuals, groups or institutions since the form did not specifically ask for this information. Respondents who provided details included District Health Boards, the National Ethics Advisory Committee (NEAC), the Chairs of the Health and Disability Ethics Committees (HDECs), the Health Research Council Ethics Committee, the Ministry of Health, Universities, Research institutes, the Ombudsman, the Human Rights Commission, PHARMAC, Hāpai Te Hauora, Ngā Hau e Whā, various health professional College groups and regulatory bodies, a variety of consumer groups, the New Zealand Disability Support Network, Auckland Women's Health Council, Palmerston North Women's Health Collective, Age Care, Age Concern, Grey Power, Alzheimer's New Zealand, IHC, Awareness Canterbury, the Nathaniel Centre, the Blind Foundation, individual clinicians, lawyers, and private individuals.

An independent researcher carried out a descriptive analysis using qualitative data analysis software (NVivo) to identify themes for each question, as well as themes that cut across all case study and consultation questions. The summary of submissions is descriptive with the aim of capturing the range of views. The consultation is not itself research, and the sample should not be considered representative. Caution has been exercised about how widely held the different views are; these are complex issues and not everyone answered all the questions. Figures show the count of responses for yes/no/unsure questions as well as the non-response rates. Some respondents wrote general comments rather than specifically answering each question. Caution is needed in interpreting the numbers reported in the figures because at times a 'yes' response essentially meant the same as a 'no' response. An example is consultation question 1.1 which asked, 'Do you believe research should ever be allowed to proceed with adult participants who are unable to consent?' Most people qualified their answer in some way to discuss safeguards that should be in place, that is, 'Yes, but only if there are safeguards', and 'No, unless there are safeguards'. Thus, simply looking at the figures could be misleading.

Quotes from the submissions are used to illustrate the points made and are in italics. These are at times composite quotes from more than one respondent.

Overview of themes

Protection

A consistent underlying theme throughout the submissions concerns the appropriate protection of people who are unable to give informed consent to participate in health and disability research owing to temporary, progressive, or permanent incapacity. Views ranged along a spectrum of deontological views that say it is never justifiable to use someone who is unable to consent in non-therapeutic research, through to utilitarian views that argue that there are circumstances in which non-consensual research is justified even though the benefit is to others. There was, however, a strong sense of trying to find the right balance of restrictions and safeguards that will protect vulnerable consumers from harm and exploitation.

Advances in knowledge

Right 7(4) of the Code of Health and Disability Services Consumers' Rights (the Code) requires that participation in research must be in 'the best interests of the consumer'. A strongly held view was that the best interests test is an unnecessary barrier to non-interventional types of research, including audit, which have relatively low levels of risk to participants. It therefore restricts the development of evidence-based care, preventing improvements in care for high-needs populations in both acute (e.g., emergency and intensive care) and long-term contexts (e.g., dementia care, intellectual disability, mental health).

Rights

The right to give informed consent to participation in research was acknowledged as fundamental to the Code and is reflected in the bioethical principle of autonomy. Only a few respondents said that research should never take place without informed consent by the participants, and a widely held view was that the right to participate in research must be protected. It was argued that adults unable to consent are currently *protected by their exclusion* from participation in research when they could be *included but protected* with robust safeguards.

Safeguards

Ethics committees play a crucial role in the protection of participants through their approval of research and study protocols. Many respondents raised concerns about how effectively ethics committees are able to carry out this role. Concern was also expressed about the impact of changes to the Standard Operating Procedures (SOPs) of the HDECs in recent years. Respondents reported confusion within the research sector about appropriate review processes and a perceived lack of consistency. Better safeguards were recommended to increase researcher accountability and establish monitoring and reporting processes on the ethical conduct of each study (e.g., the consent processes used to enrol individuals into a study). There should also be a national specialised committee to review research proposals involving non-consenting participants. Any amendments to the Code or to legislation to broaden the criteria for non-consensual research must coincide with a review of the functionality and composition of the ethics committees.

Summary of responses to the case studies

In Part IV of the consultation document a series of five case studies were presented that illustrate some types of research that could not proceed without the participants' informed consent under New Zealand law. Each case study began with a closed question that required a Yes/No/Unsure answer. These answers are collectively shown in Figure 1. Bearing in mind that the numbers could be misleading, they appear to suggest that people are generally more comfortable with case studies A, B and C, but much less so with case studies D and E.

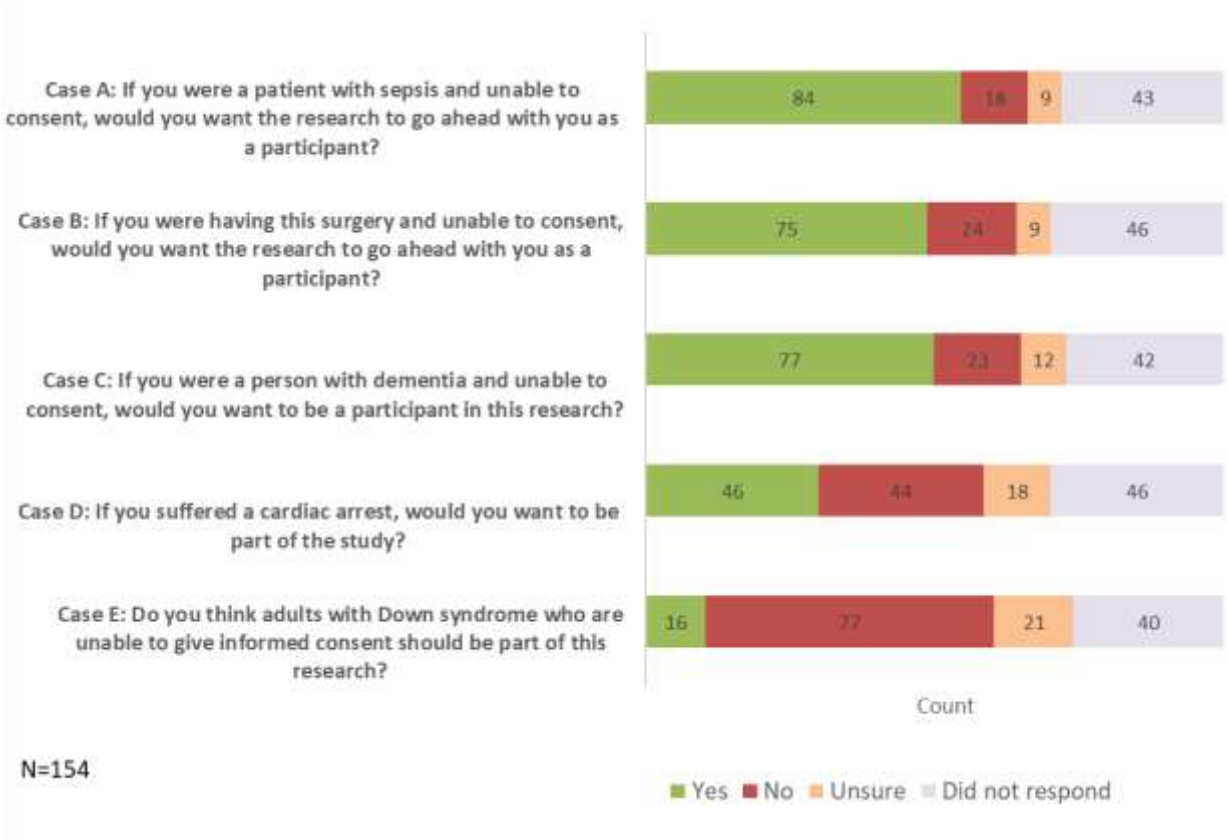

Figure 1: Yes/No/Unsure answers to all case studies

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

Case study A involved determining how quickly antibiotics used to treat septic patients in ICU are removed by dialysis. If antibiotics are cleared by dialysis at a faster rate than expected, the sepsis could be undertreated. Acutely unwell septic patients are unlikely to be able to provide informed consent. All study participants would receive standard treatment with some additional testing and monitoring (blood and urine tests). There are no anticipated benefits to patients in the study. Figure 2 shows that of the 111 people who responded to this case study, 84 agreed that they would want this research to go ahead with them as a participant if they could not consent, 18 said 'no', and 9 were 'unsure'.

Figure 2: Case study A

The reason most often mentioned for agreeing that the research should go ahead was the societal benefits from the research in the form of improved healthcare, and the importance of having evidence-based treatments. The topic of study was thought to be *of paramount importance* and was typically seen as *knowledge gained that would help future patients*. Some personalised the future benefit to themselves or their children:

> *I would want to contribute to the increasing body of knowledge so that if I or my children develop sepsis in the future we are further ahead, and they have an even greater chance of surviving.*

Some considered the situation to be like organ donation, stating:

> *In the same way as I am a nominated donor in the case of accidental death, I would like to benefit others in the case of illness.*

Several people thought the research should go ahead because it was observational and did not involve anything other than the usual treatment. They might also benefit from the additional monitoring, although extra testing could be uncomfortable or painful. Most thought that there was minimal risk or burden to the patient:

> *The tests will be able to be gathered through the normal routes of testing and are unlikely to harm me.*

These views need to be balanced with Māori cultural beliefs associated with the additional collection and use of tissue which *present risks for participants in this project.* A condition of participating was that the respondent would want *samples taken to be disposed of after the research and not redistributed or retained like the HeLa cells were.* Another condition of participation was that *the people doing [the research], do it with respect.*

Others suggested that the research was *only a small step more invasive than audit* which is routine in hospital environments and *a compulsory part of practice for maintenance of medical registration.* It was noted that studies such as this one:

> *… are the drivers for clinical excellence in hospitals and there is evidence that such hospitals achieve better outcomes for their patients.*

Some thought it unethical if observational research in the ICU were not possible because it provides evidence for the best treatment of patients:

> *It seems inconsistent that to collect data in a manner which would be consistent with treatment interventions for research is deemed unethical when a physician can order such tests in the interests of the patient. Especially, given in this case, the data gathered benefits the patient (identifying how much antibiotic loss) and the body of knowledge as a whole.*

The most common reason given by those who thought that the research should not go ahead was that it violated the principle of informed consent and/or was of no benefit to the patient:

> *As I am unable to give informed consent and the research would not be of any benefit to me, I should not be enrolled in this or any research study or clinical trial.*

On the other hand, and in the context of this case study, another stated that *anonymised data should be allowed to be collected, without informed consent as currently defined.*

Suggestions were made to find alternative competent participants; however, owing to it being improbable that sufficient consenting adults could be found owing to the impact of the sepsis, there were concerns that *the resulting sampling bias would significantly undermine the power of the study to produce meaningful results.*

A few suggested that delayed or retrospective consent would be appropriate once capacity is regained. Data collected from the patient could be withdrawn from the study should consent be withheld. A condition would be that whilst the patient is incapacitated, informed consent could be obtained from next of kin, a support person, or anyone holding EPOA, although not everyone agreed that others should decide on their behalf. As an indicator of what a participant might have wished, someone else suggested:

> *The researcher could look to see whether I am an organ donor as a measurement of whether I am happy for the blood tests to occur without giving explicit permission.*

Only a few people were 'unsure' about the study going ahead but were reassured that routine clinical management would be provided. Although the information collected could inform their care, they did have concerns about the additional tests required. Along with scientific peer review, ethical approval would be the safeguard, ensuring that the study was sound and *valuable for all consumers, whether they could consent or not.*

However, the study as described *would not benefit the person*, and an ethics committee could therefore approve only with consenting adults. An HDEC response was that:

> *However minimal the risks, the additional tests cannot currently be deemed as in the individual's 'best interest' — i.e. the participants are not better off by being in the study, although future patients are likely to benefit from the knowledge gained. Therefore, under current law an [ethics committee] could approve the study only with consenting adults.*

That said, a different ethics committee response stated that *they would approve the study* because there is *no foreseeable harm and it addresses an important research question*.

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

Case study B involved comparing the safety and effectiveness of two products that were already clinically approved and commonly used by surgeons following neurosurgery. Participants would be randomised to one of the two products. Some participants would not have the capacity to provide informed consent prior to surgery, in which case 'delayed consent' would be used (asking people for their consent when or if they regain capacity). Figure 3 shows that 75 of the 108 respondents said 'yes' to participating in this research without consent, while 24 said 'no', and nine were 'unsure'.

Figure 3: Case study B

People who said 'yes' they would want the research to go ahead typically cited the societal benefits of the research and the potential for healthcare improvement. They mentioned the importance of being able to help others, including a sense of responsibility towards the group of which they are a part:

> *I would not want the opportunity to learn from my illness to be wasted.*
>
> *An ethical person would want to serve the interests of others.*

Some people raised the issue of disadvantage to certain groups if research with them is prohibited:

> *If people who are unable to consent are excluded, then those with more severe disease will be excluded which will disadvantage an already impoverished group. People with lower educational levels or lower socioeconomic group present later and more severely. Excluding those groups disadvantages them as they are not forming part of the result.*

It was pointed out that patients have a right to a reasonable standard of care, but that that right has a corresponding obligation for clinicians, which is *to conduct research to find out what the standard of care should be, rather than rely on surgeon preference (which could be influenced by the company selling the product).*

A number commented that the research did not pose any additional risk to patients other than the potential risks of data handling and was *effectively a clinical audit and could even be done as a retrospective analysis.* It was simply comparing two treatments that were already in standard use:

> *No risks, so reasonable to proceed without any consent. I could opt out of use of health information later.*
>
> *The surgeon could choose which product to use anyway.*

A small number of respondents thought that comparing two standard treatments through randomisation was not risk free as there may be good reason for a clinician to choose one product over another, including it being the most familiar:

> *There are several reasons why any surgeon cho[o]ses to use particular products and the reasons may impact upon the outcomes in different patients operated on by different surgeons. If*

> *patients are randomised, a surgeon may end up using a product s/he is less familiar with or has less confidence in.*

Some people believed there were direct benefits for research participants: *I know patients in trials get better follow up, so I would benefit from that regardless of the product outcomes*. Others thought the study to be *at the margins of best interest* and there were *insufficient benefits to incapacitated patients that would outweigh their right to provide informed consent*.

A number who responded 'no' to the study going ahead were opposed in general to research without consent.

> *People have the right to choose what happens to them. It is important that research respects people's dignity.*
>
> *People have the right to refuse.*
>
> *Research should only include people who can give their consent before the surgery.*

A few people commented that the research was unnecessary, had little scientific merit, did not control for variables, and either did not need to be done or the research could be done in a way that removed the need for delayed consent:

> *The same information could be obtained through enrolling competent consenting patients undergoing elective surgery in which case clinical trials on incapacitated/incompetent patients should not be considered.*

Others thought there was inadequate justification for including non-consenting adults and they would want *reassurance that there is a need to use non-consenting participants in the study in order to answer the research question*.

Some questioned whether the study answered a genuine research question, and wanted assurance that safeguards would be in place established through formal ethics committee review. Responding on behalf of an ethics committee, approval for the trial involving incompetent adults would need to be based on the following:

- *Independent peer review from a surgeon not involved in the study*
- *Justification of incompetent persons*
- *Bio-statistical evidence regarding the minimum number of inclusions to generate a reliable result that was not confounded by the random element of different surgeons*
- *Reasonable steps to ascertain the views of persons interested in the welfare of incompetent persons; enrolment into the study would proceed only if it were consistent with those views*
- *Details of the constitution of the independent data safety group.*

Similar to responses to case study A, some thought that others such as family, next of kin, support person, or anyone holding EPOA, could consider their wishes and agree on their behalf if they were incapacitated. The *collective wish of families in certain cultures* was highlighted, and in the case of some Pacific families (fa'a Sāmoa), *the matai of the family or the local minister should be included in the ultimate decision*. Ideally these conversations would have been documented ahead of time:

> *Should include documented discussion with next of kin or Power of Attorney. Taking part should be in accordance with patients' wishes and how they would respond if able to give consent.*

Determining the patient's wishes ahead of time would be key as there may well be compelling reasons why a person would not have consented, such as:

> *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/suppl[i]er or manufacturing process or materials used … or simply did not want to take part in research for personal or cultural reasons.*

Delayed consent

Case study B included a question that asked for views about delayed consent, meaning those unable to give consent due to incapacity could give consent after the trial if or when they regained capacity. If consent was refused at that point, their data would be removed from the study. Some respondents thought this would be an acceptable approach, given the research design:

> *I am comfortable with the proposed process for delayed consent. Only relates to whether the patient's data is included in the research data set. Patient would not decide which product was used in any event.*

Some thought it was a pragmatic solution to allow the research to be carried out, particularly as participants could have their data withdrawn from the study later:

> *Doctors could approach family to consent on behalf of patient. Patient can consent for future use of the data upon recovery.*

Delayed consent was described by some as supporting the autonomy of participants by informing them and empowering them to withdraw if they chose:

> *Does respect participants' autonomy to some extent as they are informed they have been involved in a study and that they have the power to withdraw.*

> *It is respectful of the participants to give them the opportunity to consent. Delayed consent means they can opt out of the study and ask for their withdrawal from ongoing research involvement and potentially for withdrawal of their data. It provides a framework for the participants to be fully informed about what has happened when they were not competent and ask questions about this.*

However, another respondent thought that in this context, withdrawing data from the study was an extreme application of the autonomy principle and did not reflect the intention of the Code

> *… where no harms are expected or likely, and where the data may provide good benefits to all future patients ... While I note that this is a right that all study participants currently have under the Code, I think there is an implication that it is there for the protection of personal and sensitive data, rather than for data about medical benefits and harms.*

Not everyone agreed that people should be able to have their data withdrawn from the study later in a study that involved no harm:

> *Should inform patients what was done and the reason for it, but patients should not be able to withdraw data where no harm is expected or likely and the data may provide benefit to future patients and possibly that patient in the future.*

Another respondent suggested that the default position to participation should use an 'opt in' approach in preference to having to 'opt out':

> *If the researcher decides that participating in this research is in the best interests of a person and data is collected before they are able to give consent, the data should be added into the study if they say yes, rather than it being removed if they say no. The default position should not be that a person who has had their data collected without consent will agree to having the data used, but rather, that they will not agree to it.*

Respondents who disagreed with delayed consent described the concept as:

> *an oxymoron*
>
> *a euphemism for doing what you want and asking permission afterwards*
>
> *disingenuous semantics*
>
> *an irrational concept*
>
> *unlawful*

A phrase often used was that '*delayed consent is no consent'.* It is not possible to *say no to something that has already happened to you.* The only consent possible in the context of the case study is not retrospective consent, but *consent to remain in the research.* Delayed consent would *only be applicable in urgent and emergency situations. It should be seen as a last resort* and *only for observational study designs*. Delayed consent *is not appropriate for planned research.*

Others maintained that *research should only ever proceed with prior consent* and they could not foresee *any research circumstances where it would be justified*. There was a *danger of coercion*, of being *taken advantage of when vulnerable* and *maybe left with doubts about what was done.*

Given that not many patients have normal cognitive capacity early after neurosurgery, timing would be crucial to ensure that patients did not feel pressured or coerced into participation. For example:

> *If consent is sought too early after the surgery (i.e. very soon after the patient wakes up) then they may feel pressured by the situation and that they have to respond right away. This would lead to them not having enough time to properly consider all of the information and therefore not make a fully informed decision regarding their consent. If the delay is too long (i.e. after an amount of time that has allowed the patient to see that the treatment has worked) then there is the possibility of the patient feeling obliged to give their consent as a thank you to the doctor that treated them.*

Consideration would need to be given to patients who did not survive the surgery or regain competence:

> *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

In case study C, a doctor intends to randomly allocate patients with severe dementia into two groups to receive different types of care: conventional care and interactive care that includes a greater focus on the psychosocial needs of the patient. All participants in this study would receive, at least, standard care. Additional assessments would be involved to assess agitation levels, psychiatric symptoms, and quality of life. It is not known whether the research would be in the participant's best interests. Figure 4 shows that of the 112 people who responded to this question, 77 said that they would want to be a participant in the research, 23 said 'no', and 12 were 'unsure'.

Figure 4: Case study C

People who said 'yes' to participation in case study C were motivated by *altruism* and their desire to benefit others and improve future healthcare for dementia patients. They acknowledged that participation might not benefit themselves, but thought that the study was without significant risk and *it would be a good way of giving back*:

> *If my mental decline was such that I could not make decisions, then my basic philosophy is that I am happy for others to learn from whatever can be determined from my plight. It is part of my contribution to my fellows who may or may not suffer the same fate.*

The need to establish an evidence base to improve care was stressed and that would involve studying people with dementia who may not be able to provide consent. Not doing so would produce *'therapeutic orphans'* and would itself be unethical:

> *If it was not possible to undertake research in persons with dementia who are unable to consent, it would not be possible to establish any evidence-based medical practice for this common disorder, which would be in my view, unethical.*

Despite impaired capacity, some maintained that patients with dementia have the same rights as others and are entitled to contribute to society through participation in research:

> *Many of these patients would never be able to consent, but they are entitled to be involved in a study which may improve their quality of life and for patients with dementia in the future.*

The risk of harm to participants was generally thought to be low and some might even benefit from the intervention:

> *The new regime might be beneficial and is unlikely to cause harm.*

However, returning to conventional care at the end of the study if the programme could not continue was *questionable ethics*. Similarly, being assigned to the conventional care group when *they are used to something different just to see how it affects them could be mean and distressing.*

Some respondents were concerned about the distress the intervention and additional assessment (data gathering) might cause. There must be adequate protocols for removing participants from the research if they become agitated or distressed:

> *I would want the proviso built in that if the interactive intervention was causing me distress that the researchers would interpret that as non-consent and withdraw me from the project.*
>
> *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.*

The study protocol would require ongoing 'assent' from participants throughout the study. It would need to have *an appropriate threshold for stopping the study should there be evidence that the intervention was doing more harm than good* and to accommodate negative responses from participants to assessments:

> *For example, delaying assessment to another day if the individual is upset; two attempts at assessment before determining that the individual is negatively impacted by the research and therefore should cease to be researched in the study group.*

Furthermore, participants who were withdrawn from the study due to distress *should have their data included in the study.* That is, each person must be accounted for on an intent to treat basis and the impact on the research findings discussed.

Many respondents indicated that they would not participate in the study owing to the study design, and made recommendations for design improvement. The main recommendation was for a pilot study with patients capable of giving (supported) consent to assess the safety and efficacy of the new method of care before proceeding to study those unable to consent. 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.*

Another recommendation for study design was

> *to study ALL the patients with severe dementia in the rest home who are receiving traditional task-oriented care and then add psycho-social aspects to the care of ALL severely demented patients and measure any changes.*

However, if the focus is on those with more advanced disease, one respondent pointed out that *there are no alternative patient groups* to research to determine whether the intervention is beneficial.

Only a few respondents who indicated that they would not want to participate in this research thought so because it was inappropriate *to do any form of research on a person if they have not given consent*:

> *Vulnerable persons need to be protected from being enrolled in clinical trials or any research studies without their consent. There should be no exceptions made.*

More commonly, the suggestion was made to document a person's preferences about their involvement in research before their condition deteriorated, *that way I could make my own decisions about the type of research that I would want to take part in.* Some respondents thought an advance directive would be a suitable mechanism and *could be used for informed consent*:

> *[I]f the person had given an advance directive pre-severe dementia onset that they would be willing to participate in dementia studies, then they perhaps could be considered for enrolment.*

In the absence of a specific advance directive, consent should include discussion with family, next of kin, caregivers, legal representatives, or those legally authorised (e.g., EPOA), and research only undertaken if they believe the patient would have consented were they able:

> *Consent should include discussion with family or care givers to ensure such research was only undertaken if they believe the patient would have consented were they able to. Written consent from their Attorney or approval of next of kin to include the patient in the study should also be obtained.*

A comment was made that these measures aim to protect the person who has dementia, but family members too are vulnerable:

> *I have also become aware that family members of those who are unable to consent to taking part in research studies are also vulnerable when placed in the position of being asked to consent to their relative being enrolled in a research study.*

The role of ethics committees to protect all those involved in the research process and ensure the study was properly conducted was mentioned by many:

> *It would be absolutely necessary to seek formal ethical approval before commencement as well as establishing clear processes and protocols for the intervention to stop if there is perceived harm to people involved.*
>
> *I would want reassurance, verified by a review by an ethics committee, that any such harms would be monitored and, if noted, this would result in termination, (or at least, appropriate modification), of my involvement.*

Responding on behalf of an ethics committee, approval for a study such as this would be based on the following:

> *Any approval would be based on sufficient evidence that any residual risk of distress during study assessments would be no greater that the risk of distress in residents during routine interaction with rest-home staff, and would also be subject to the following [summarised] provisions:*
>
> - *That the benefits of person-centred care outweigh the risks*
> - *Peer reviewed evidence of the benefit of the intervention in an equivalent setting with competent (e.g. mild dementia) participants*
> - *Provision of evidence of the researcher's suitability to undertake the study*
> - *Participants would be informed of their involvement in the study, their decision making was supported, and that any indication of dissent was taken as a refusal to participate*
> - *Detail of the study procedures, assessment measures, and evidence of independent peer review*
> - *Data safety monitoring processes*
> - *An additional assessment point mid-way through the trial period*
> - *The views of persons interested in the welfare of the participants and obtaining their informed agreement for participants if enrolment in the study is in line with these.*

At present, researchers conducting research with incompetent participants must do so in the 'best interests' of the patient. In this case study, any potential benefit to participants is unknown and there is no benefit to those in the conventional care group. Changes to the Code would be required:

> *In this case it is clear that best interest is too high a bar and might be lowered to allow research with minimal risk or best-equal interest, so long as all other appropriate safeguards (including ethics committee review) were in place.*

Under existing law, authorised representatives (welfare guardians or EPOAs) may consent to participation in medical research but only if it might save the person's life or prevent serious damage to health. It was suggested that the law could be amended to allow consent in the following way:

> *In this case it would be helpful if a legally authorised representative was allowed to provide consent on behalf, and if a minimal risk threshold (i.e. does not involve devices or new or inappropriate drugs) were applied.*

Case study D: Clinical trial regarding the use of adrenaline

Case study D aims to test the use of adrenaline in the treatment of cardiac arrest. Adrenaline has been used routinely for over 50 years to treat cardiac arrest, but its safety and efficacy have not been tested. The study would be a randomised, double-blind and placebo-controlled trial meaning some patients would receive adrenaline and some would receive salt water. Neither paramedics nor participants would know who had been administered adrenaline or salt water. No consumer undergoing treatment for cardiac arrest would be able to give consent, so the researcher proposes to use an 'opt-out' process for consent in which awareness of the study would be raised through a public information campaign. People would need to wear a bracelet saying they did not want to participate.

Figure 5 shows that responses to this question were more evenly split than in the previous case studies, with 46 people saying 'yes' to participation, 44 saying 'no', and 18 'unsure'.

Figure 5: Case study D

Reasons for saying 'yes' to participating in this research were mainly related to the societal benefits from better health care:

> *The benefits of conducting a trial of this nature clearly outweigh the risks and the collateral benefits to society far outweigh any potential or perceived threat to individual patient autonomy.*

Several people mentioned altruistic motives for participating to benefit others:

> *Being part of a pioneering study means exercising courage without being sure I am going to benefit [and] I hope others will benefit.*

There could also be future benefit to the individual who participates:

> *People who survive cardiac arrest may suffer another cardiac arrest in the future and would therefore benefit directly from participation.*

Although some respondents thought *the benefits of the trial outweighed any risks,* many comments centred on the potential risks of the trial and was their main concern, particularly since *the potential harm appears to be life-threatening.* The dilemma lay between wanting the research to be done because of its importance for improving treatment, but concern about the level of risk:

> *Most people would not want emergency treatment withheld for research purposes, but also would want emergency treatment to be informed and based on good information.*

> *I am also very aware that at present we do not have all the answers, and that there are many treatment interventions commonly utilised in emergency medicine that do not have an evidence base for their use other than 'historical' tradition and which therefore, may actually be harmful.*

Some thought it would be unethical not to conduct the research:

> *In this setting the participants are dead and therefore the potential for harm by being in the research is minimal (being in the research will not make you 'more' dead) … If there is concern that the current treatment with adrenaline may increase this bad outcome it is imperative that research is done to determine the truth.*

Others thought the research to be unethical because the comparative treatment was a salt water placebo:

> *The doctor wants to give some people the medicine and others no medicine to see which group gets better. Is it even ethical not to treat patients who are having a cardiac event knowing it might result in death?*

People expressed concern about the research design, and various suggestions were made to improve the scientific validity of the study, such as *comparing alternative agents with adrenaline*, or *comparing adrenaline with a lower dose of adrenaline*, or *doing an animal study first.*

Questions were asked about the study protocol, such as:

> *Would the study be aborted if the people receiving salt and water die off faster?*
>
> *If adrenaline started my heart, but salt water didn't, what would be the next step if I was on this trial?*
>
> *How would paramedics proceed if they don't know exactly what [drugs] they're dealing with?*

A few thought delayed consent would be appropriate:

> *It is important to inform patients afterwards that they have been involved in a study.*

One person thought that this research was OK only if there was an explicit 'no treatment' advance directive. However, the person wondered *at what point the advance directive would kick in?* Another said, *I have considered having 'do not resuscitate' tattooed on my chest.*

Others highlighted the importance of evidence of treatment efficacy:

> *The issue is why this hasn't already been resolved (after 50 years!), not whether people should or shouldn't be studied without consent.*
>
> *Standard care is not necessarily best care and we need to look at the efficacy of adrenaline in cardiac arrest. I think an opt-out method of consent is not required.*

The 'opt-out' process

Regarding the proposed opt-out process and public awareness campaign, most people thought it *risky, entirely unsuitable, seriously flawed, stupid, and should not be considered a form of consent:*

> *People should not be placed in the position where they have to opt out of something that could have serious ramifications if they forget or don't get around to doing so.*
>
> *They may change their mind in 'the moment' even if wearing the 'no study' bracelet.*

Given potential negative outcomes, there was considerable caution about taking on what they saw as a high level of risk without seeking *explicit* consent that involved *opting in and not out of research*:

> *Not having a bracelet on would not mean people consented. It would just mean those wearing it didn't consent.*

Furthermore, *some people may want to opt-out but not want to wear a bracelet*, they might find it *stigmatising,* and *you could not assume a person not wearing a bracelet has consented*. The onus was on people to withdraw — a standard not even applied to organ donation in New Zealand.

On the other hand, some thought the opt-out process to be *ethically sound, reasonable*, and would *stimulate discussion about medical research in emergency situations*.

Either way, it was viewed by most as an expensive and impractical way of getting informed consent that was likely to disadvantage people with poor health literacy, low socioeconomic status, or with English as a second language. Consequently, data quality could be compromised:

> *The data would not be representative because people with advantages, good health literacy, and most likely better health, would opt out leaving a pool of potential participants skewed towards the disadvantaged.*

> *I don't have confidence that the public awareness campaign would be effective and that the 'No Study' is a decision that people want to make prior to it happening to them.*

A small number of respondents thought opt-out by individuals was not necessary as ethics committee approval *to protect patients' interests is more important:*

> *If the study is in the public interest and approved by an ethics committee, opt-out is not required.*

However, the view of the Health and Disability Ethics Committees (HDECs) concerning the opt-out innovation was that they did not consider the consent process to be properly informed:

> *We do not consider the opt-in consent protocol (indicated by not wearing a study issued 'opt-out' bracelet) to be sufficiently robust evidence that consent is informed. Even after a very large (and expensive) public information programme …*

Responses from all ethics committees were similar in their desire for further clarification about the study and for justification, particularly as it involves a placebo arm rather than a comparison with an alternative agent. One committee was clear that *the study as described is seriously flawed and would not be accepted by the Ethics committee*; and another said, *[W]e would be prepared to allow this study if we were satisfied about [poorer outcomes from previous studies and the safety of the proposed protocol, including genuine 'equipoise' in the argument for and against adrenaline].*

In the view of the HDECs, approval would not be given for this study because of the current law regarding best interest, that is, *the withdrawal of standard of care cannot be proven as best interest. Nor might it meet any future best-equal interest or minimal risk threshold.*

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

In case study E, a doctor wants to investigate whether a particular drug will improve the cognitive and learning abilities of people with Down syndrome. The trial will be a randomised, double-blind, placebo-controlled study, meaning that some participants will receive the study drug and some will receive a placebo (sugar pill). Neither the participants nor the researchers will know who is receiving the drug. Regular six-hour assessments will be required for all participants. Possible side effects of the trial drug are increased suicidal ideation. The drug has not yet been tested on people with Down syndrome and will not be available to participants at the end of the trial even if there are beneficial effects. Some potential participants will not have the capacity to give consent to be in the trial, and the researcher intends to consult with family/whānau/caregivers about whether they should participate or not.

The previous case studies asked whether respondents thought that the research should go ahead or whether they would agree to participate in the research proposed. The questions for case study E, however, differ from the other case studies by asking whether people think that adults with Down syndrome who are unable to give informed consent should be part of the research. Figure 6 shows a high level of discomfort with the proposed research, with only 16 respondents saying 'yes', 77 saying 'no', and 21 being 'unsure'.

Figure 6: Case study E

Reasons for saying 'yes' to adults with Down syndrome who are unable to consent being part of this research included the potential of the drug to improve the quality of life for people with Down syndrome. It was therefore necessary for clinical trials to take place with this group of people provided they had the support of their family. Technically, a doctor could *prescribe the trial drug off-label for a patient with Down syndrome as part of their license to practice 'the art of medicine'.* Such a situation strengthened the need for research to determine the risks and benefits of the drug.

Some people thought that those who were unable to consent have the same rights as others to participate in research that might benefit themselves or others *(excluding them would be discriminatory)* provided sufficient safeguards were in place governed by ethics committees, and they were unlikely to be harmed by participating:

> *I believe their population group should not be left out of medical advances that could improve their quality of life. If these advances are to take place, their population group needs to participate in research.*

The study could benefit some participants directly, albeit temporarily. A few thought the risks to be small and able to be managed if carers and whānau were made aware of the risk of suicidality and knew what to look for: *These patients are usually well supervised, so any suicide risk should be controlled.* There was much to be gained for people with Down syndrome and for their carers; it was worth the risk of side effects.

A number of people questioned the study's underlying *deficit approach to Down syndrome, which is not a medical condition, and should not be treated by medication* to make them *more 'normal'*. Many were uneasy about the level of risk. There was concern that if people were unable to consent *they would also be unable to articulate or understand suicidal thoughts and feelings* if they occurred. The *double-blind design made this particularly problematic because neither the researcher nor the caregivers would know if the participant had received the drug or not*.

Others were worried about the unknown effect of the drug on physical health problems common in Down syndrome *such as poor immune function, congenital heart defects and epilepsy; it would be unethical to risk side-effects that would further compromise their quality of life.*

For most respondents, the study *risks were more than minimal* and outweighed what were *mostly speculative benefits.* These are *vulnerable* participants and the study *exploitative*. It *puts prospective societal interests over their best interests*. The burden of participation was *onerous and intrusive*:

> *In participants who are unable to give consent, which are presumably those with fairly severe forms of Down syndrome, six-hour assessments could be very stressful.*

Most respondents thought it unfair and highly irregular for there to be *no continued access to the product if the trial proves beneficial.* That said, with genuine uncertainty as to the drug's effectiveness, it was ethically and medically unsafe to trial it without direct informed consent. With no clear benefits to participants, most people thought the research should be performed only on those who can give informed consent: *[The study] is simply not OK.*

A better study design would be to *demonstrate benefit to patients with Down syndrome who can consent, and then it may be reasonable to perform another trial in those unable to consent.* A data safety committee could review the interim results and perhaps consider those who cannot consent.

Respondents thought that the law should protect vulnerable people and set a benefit threshold very high and risk threshold very low for all research subjects. A number noted the long history of exploitation of disabled people for medical research. Weakening Right 7(4) of the Code

> *is likely to increase the risk of exploitation of people with learning disabilities and allow researchers to carry out clinical trials on people who cannot consent.*

Consultation with family/whānau/caregivers

Respondents were asked whether they thought that the consultation proposed with family/ whānau/caregivers in case study E gave sufficient protection for participants who are unable to give consent. Responses were fairly evenly split between 'yes' (n=39) and 'no' (n=42); and 19 were 'unsure'.

People who said 'yes' thought it essential to consult with the family of a person with Down syndrome. They *can be trusted, know them best*, *have their interests at heart,* and they *can speak for them.* Family/whānau *are generally excellent advocates, genuinely interested in the wellbeing of the person, and fierce defenders of people's rights.* Caregivers should be consulted, and if they are responsible for making medical decisions they should be able to make decisions about research, as they do overseas:

> *I think that family/whānau would be able to make an informed decision for these types of patients as they would be making those informed decisions for them in every other aspect of their life as well.*

Others who were less sure thought it would depend on how well they knew the individual, their experience in such matters, and the character of the person with Down syndrome. That said, if a person is unable to give informed consent they are unlikely to have expressed their views about participation, so it is difficult to see what families would base consent on.

People who said 'no' thought that family members may be swayed by thoughts of a possible cure or improvements in learning that could (temporarily) reduce their burden of care. There is also *a high level of vulnerability of service users and families may feel obliged to be helpful. It is coercive and unsatisfactory.*

Some people said that a good research process that protects vulnerable people requires more than consultation with family. While family should be asked for assent, they did not think that *other people have the right to make this decision for someone else considering the risk involved*. It felt like *the patient's rights are being taken away* and it is *not certain that family/whānau/caregivers have the best interests of the participants at heart:*

> *Large sectors of the disabled population are treated like the property of their 'caregivers' and family.*

Many challenged the legal status of family members to give consent for others:

> *Only designated and activated EPOA or welfare guardian should be used to obtain consent.*

Even as an authorised representative, *the PPPR Act does not allow someone to consent to experiments for another. If the legislated means of substituted consent does not allow it, then an 'informal' system should not either.*

A response from an ethics committee was as follows:

> *If allowed by law, we would be satisfied with the proxy consent by a legally authorised representative of an adult Down participant, if they had sufficient information presented in lay language for making an informed decision. Assent of the Down participant is of course also required.*

Summary of responses to the consultation questions

In Part V of the consultation document a series of eight general questions were asked about whether the law should remain as it is or be changed, what factors or criteria should be taken into account when considering whether incompetent adults should be research subjects, and who should be the decision-makers. Each consultation question began with a closed question that required a Yes/No/Unsure answer. These data were incomplete for some questions and have not been included.

1. Should research ever be allowed to proceed with adult participants who are unable to provide informed consent?

Figure 7: Should research ever be allowed to proceed with adult participants who are unable to provide informed consent?

The first consultation question asked whether research should ever be allowed to proceed with adult participants who are unable to provide informed consent. Most of the people who answered this question thought that research should be allowed. Figure 7 shows that 84 of 126 said 'yes', while 26 said 'no', and 16 were 'unsure'. However, these figures are likely to be misleading as most people qualified their answer to discuss safeguards or to stipulate certain conditions.

People who answered 'yes' said so because of the need to improve treatments and patient outcomes. It was pointed out that current treatments may be doing just as much harm as the proposed study treatments, *so we need to do research to ensure we harm patients less in future*. Allowing research in patients who cannot consent would support other parts of the Code, such as the Right to Services of an Appropriate Standard (Right 4). People have the right to the best treatment, and sometimes the need for research will *override the risk of enrolling individuals without consent.* The current treatment/research situation is illogical:

> *It does not make sense that clinicians are allowed to give potentially harmful or expensive treatments that have not been shown to be beneficial in high quality studies, while at the same time we are not able to conduct studies which would demonstrate whether these treatments are beneficial or not.*

Furthermore, some thought that people have a right to participate in research and should not be excluded from the benefits of participating or from contributing to the community by participating in research. There should *not be unnecessary limits on the opportunities to gather robust, evidence for policy and practice.* However, *studies should be for the public good and not the benefit of commercial entities.*

Caveats were applied in almost all instances of support for research to proceed with adults who are unable to consent. Examples of qualified support included: the need for direct benefits to participants, benefits outweigh risks, adequate safeguards, there is appropriate proxy consent, rigorous ethical review, solid pre-clinical data, peer review, questions cannot be answered another way, does not affect existing treatment or care, relates to the condition experienced by the participant, people can withdraw later, and the type of study. Low or minimal risk, non-invasive, non-intervention, observational research was most frequently mentioned as suitable. Clinical trials or randomised controlled trials were thought too risky and required active consent. Studies should *ideally demonstrate equipoise or evidence of benefit.*

Other caveats included some limited and very strictly controlled circumstances where there is direct benefit to the participant that no other opportunity would provide, or a person might otherwise die.

It was pointed out that the wider system would need to be strengthened to protect consumers, especially ethics committee oversight processes. Specific examples of greater protection or needed safeguards included (in summary):

> *HDEC, and health organisation approval, as well as SCOTT [Standing Committee on Therapeutic Trials] approval for medications or devices not approved in New Zealand; Independent ethics committees (not appointed by the institution in which the study is being done); independent data monitoring committees; respect for participants' rights under the Convention on the Rights of Persons with Disabilities [CRPD]; participating institutions are properly resourced to conduct the research; ethical imperatives and national guidelines are strengthened; consistency across public and private research; and development of protocols to cover disability research.*

People who said 'no' to participation without consent thought *the right to informed consent is too precious to trifle with* and it *was inappropriate to do any form of research on a person if they have not given consent.* However, as above, low risk or minimal risk studies might be appropriate, and if there is potential benefit to the patient:

> *Some such research has a good prospect of providing a direct individual benefit to the person, and providing the potential risks are minimal, should be able to proceed with the informed consent of a personal representative and subject to strong safeguards.*

However, people should be protected from abuse and exploitation and the current law needed to be strengthened. Financial incentives to enroll patients must be avoided for this vulnerable group:

> *Studies sponsored by commercial entities in which clinicians are paid (per participant or otherwise) to enrol participants should not be allowed to enrol incapacitated participants. In this setting the clinicians should definitely not be the decision makers with respect to enrolling participants.*

1.2 General comments about the circumstances/restrictions that should apply

The need to balance the right to participate in research with the principle of informed consent to ensure *maximum protection for vulnerable disabled people* who are unable to consent would require a range of *very strong safeguards* to be in place, rather than *specific restrictions*. The right to participate in research must be protected:

> *Not allowing research to proceed unless the participant is able to provide informed consent unnecessarily limits opportunities to learn about the lives of adults with [intellectual] disability and gather the information needed for robust, evidence-based policy and practice.*

The safeguards mentioned included consultation and proxy/substitute consent processes, the role of ethics committees, and how the Code could be strengthened.

Respondents said that researchers need to actively consult with the family of patients and *where a legal option for consent can be obtained then this should be sought, otherwise a medical consultant (not involved in the research) in consultation with whānau should be sought.* When researcher and clinician are the same this can be a conflict of interest, although other people thought it might offer more protection because the clinician has the patient's best interests in mind.

In contrast to consent by substitute and considerations of best interests, *s*upported decision-making was raised by several respondents and *applies to disabled people who have persistent, impaired decision-making capacity as a result of significant intellectual, cognitive or communication impairment.* It involves a supporter or advocate who knows the person well and supports the person to make decisions according to their will and preference. Supported decision-making sometimes *makes use of advance directives written prior to losing capacity*:

> *Supported decision-making is a model where others are involved in decision-making, alongside a person who requires support to make decisions ... decisions are also made based on the person's will and preference. [It] is in-line with the UNCRPD (Article 2, General Comment No.1). Supported decision-making rejects substitute decision-making and the concept of 'best interests'.*

There were also indigenous concerns held internationally about *the individualistic vs community-based decision-making process in providing consent for research and the growing interest in issues of indigenous data sovereignty in research.*

The role of ethics committee approval was stressed by most respondents and was necessary for all research involving adults who are unable to consent. Consideration should be given to the appropriate level of ethics committee approval (HDEC, University, or District Health Board) and there should be a higher level of oversight than for other research that included monitoring and follow-up to ensure adherence to the ethics committee's conditions. Specialised committees may be necessary for this type of research. Standard risk thresholds were needed and these were thought to be more relevant than the current best interest standard.

There needed to be flexibility provisions in any changes to the law so that ethics committees could deal appropriately with the variety of study designs and their unique circumstances:

> *We need a legal framework that allows ethics committees to consider the best approach to use for the unique circumstances of each individual clinical trial. Sometimes this will be fully informed consent prior to trial enrolment before the patient becomes unwell; sometimes it will be consent from a family member prior to enrolment; sometimes it will be provision of information and the opportunity to opt-out of participation or to opt-out of use of a patient's information once competence is recovered.*

Ethics committees also have the following responsibility:

> *To ensure that research should only be conducted in an institution with strong research governance, clear reporting frameworks, that each researcher has GCP [Good Clinical Practice] certification, transparency regarding research activities, protocols and outcomes.*

A legally binding, detailed regimen of strong safeguards was suggested, *preferably enacted in primary legislation (such as the Protection of Personal and Property Rights Act 1988), or in additional*

separate Code rights applicable to non-consensual research. These safeguards include the need for: *prior consent where possible; a statutory requirement for HDEC satisfaction with the trial design; respect for dissent; a requirement for informed consent of a legal representative; scientific grounds to support expectations of participant benefit; minimal risk and burden; and no financial incentives.*

1.3 Should the same laws apply to all health and disability related research?

The Code provisions relate to health and disability research conducted only by a healthcare or disability services provider. Research relating to health and disability issues is also conducted by non-providers, for example, some academic researchers. Some research is therefore outside the jurisdiction of the Commissioner. Respondents were asked whether the same laws should apply to all health and disability research.

Figure 8: Should the same laws apply to all health and disability research?

Almost all people who answered this question thought that the same laws should apply to all health and disability research. Figure 8 shows that 97 said 'yes', 6 said 'no', and 15 were 'unsure'. The question did not clarify what the 'same law' might be, so respondents have interpreted it variously to mean the Code, or to mean some other law.

The main theme throughout the responses was that participants should all be protected regardless of who is doing the research, the status of the researcher, or whether the researcher's employer is a healthcare provider or an academic or research institution: *no-one should be exempt:*

> *There is no reason to discriminate on the basis of the status of the researcher. The issue concerns the rights and interests of the consumer. The right to consent applies to participants, regardless of the status of the researcher. From a research participant's perspective what is the difference who the researcher works for?*

It was pointed out that the National Ethics Advisory Committee (NEAC) guidelines *apply to everyone doing research and the law should reflect and enable those principles*. Concern was raised about *the large volume of sponsored research* which reinforced the need for clear and fair laws that would protect vulnerable people: *Any disparities in the legislation would likely be exploited to further dehumanise and annex such people.*

One respondent referred to gaps in the current research governance landscape in which non-health professional researchers can legally avoid ethics review in some circumstances, leaving participants, especially non-consenting participants, unprotected and without a clear avenue for complaint:

> *Coverage gaps exist and provide uncertainty for researchers, participants, and regulators. These gaps could be rectified by changes to proposed primary legislation 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.*

Other comments were that *academic research should also be within the jurisdiction of the Commissioner* and participants should have his *protection.* Academic research already *typically has considerable ethical review attached to it which includes complying with national standards such as HDC Codes, as well as laws of the land.* That said, if the Code applied to all research, a lot of academic social science research would be restricted placing even more barriers to research on disability issues.

Another thread throughout the responses was for consistency in application of the 'rules' as they applied to gaining patient consent to reduce confusion and improve transparency:

> *[At present] the Code precludes health and disability providers from conducting scientifically rigorous, low-risk, low-burden social research, and creates a sense of unease for researchers who are not subject to the Code and are therefore legally able to pursue such research.*

However, the rules should *not be determined by the research team*. There should be a unified approach, but with flexibility to cater for different types of research.

For most respondents, the Code should apply to all research and all people with disabilities, even those *not currently being 'treated' as patients*. Others thought that the HDC mandate should only apply to interaction with services or if the research is part of treatment.

There are other wider system issues that need to be strengthened, such as treatment of harm arising from research that is covered by ACC:

> *Since the 1992 changes to the Act, 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.*

2. 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.

Figure 9: 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?

Most respondents agreed that it is important to support people to express a view as far as they are able and to respect that view as dissent to participate in the research. Figure 4 shows that 77 said 'yes', the law should expressly state the requirement to respect indications of dissent, 16 said 'no', and 30 were 'unsure'.

People who responded 'yes' said so because some *people who have communication difficulties related to disability or cognitive impairment, communicate by way of body-language or behaviour.* These signals need *to be recognised as dissent and the intervention stopped*. A person who knows the individual well (the family) *should interpret and guide researchers about how a person expresses dissent.* Although not able to give informed consent, signs of dissent indicate some level of cognitive awareness and should be acted upon, particularly if indications of distress are clear and unequivocal. After all, people who are competent to consent have the right to withdraw from research, and the expression of dissent from someone who is not competent should be similarly respected as exercising their right to withdraw. It is too easy *to ignore indications of dissent* and *too easy to abuse people who do not speak*. The law should

> *expressly state that irrespective of the person's level of competence any expression of dissent or refusal must be respected.*

People who were unsure about a change to the law reported their difficulty interpreting expressions and gestures and their intent. These behaviours may have been present prior to enrolment in research or be a broad indication of overall physical discomfort unrelated to the research:

> *Impaired persons may demonstrate those expressions simply by being out of their usual environment, or in the presence of strangers, due to the acute condition they are suffering, or by associating a medical setting with painful things like blood tests. So how would we know that it is the research they are apparently objecting to?*

A number of respondents were from intensive care clinical settings: *I can think of instances in ICU where no research would be done if we went off facial expressions alone.* These respondents thought it difficult to distinguish standard treatment-related dissent (which must sometimes be provided) from research-related dissent:

> *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.*

While this group would withdraw a noticeably distressed patient from study-related interventions, they thought *it would be difficult to standardise what is considered an expression of dissent, because it would depend on the situation.* There were many comments about the difficulty of legally defining meaningful thresholds of distress. The introduction of a distress threshold could 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.*

People who were clear that the law should not expressly have this provision thought that it is too dependent on the situation and may relate to illness rather than the informed wish of a patient. Dissent must be sustained and consistent, and every effort should be made to ameliorate distress. Some thought that people who cannot consent cannot make a choice, and that if the research will be of benefit, it should go ahead.

Rather than amending the law, it is probably more appropriate for this issue to be addressed by the ethics review process*. 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*. 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.*

3. 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. Delayed consent is not permitted under New Zealand law, because the events have already taken place.

Figure 10: Should the law be changed to allow researchers to obtain delayed consent to research after incompetent participants regain competence to consent?

Figure 10 shows that the yes/no responses to this question were almost evenly split, with 49 people saying 'yes', the law should change to allow delayed consent, 52 saying 'no', and 22 being 'unsure'.

Respondents supporting a change in law to allow delayed consent thought that this was appropriate for *observational rather than interventional studies*, where there was *possible benefit to the participant (and not commercial entities)* and *low likelihood of harm*. Others thought it only appropriate for the ongoing use of data. Delayed consent supports principles of autonomy, participation, and dignity, and is more consistent *with informed consent being an ongoing agreement rather than a one-off agreement*. There should be initial proxy consent from family/whānau/caregivers if possible. Without delayed consent, *the comparison of therapies where there is equipoise between treatments could be missed.*

Others who supported a law change thought it was *vitally important* that delayed consent remained a method of being able to recruit patients into a trial for research in emergency or intensive care settings. There are otherwise *no other options for time critical treatment/research*:

> *Potentially new lifesaving therapies can be tested when consent cannot be obtained (e.g. the REVERSE-AD trials led to the introduction of dabigatran reversal as an accepted therapy).*

In these circumstances it was pointed out that family members are not immediately available (nor is it necessarily appropriate to approach them for consent at this time) and *the researcher is charged with weighing risk and benefit on behalf of the participant and [enrolling them in the study]. That is acceptable.* The only alternatives are *not doing the research or doing it without consent.* Respondents said that patients should *not be denied the opportunity to contribute to knowledge* and that *denying them the opportunity to participate introduces a selection bias into studies towards those who are less unwell*. One respondent said:

> *I have worked on studies that used delayed consent so I'm not sure if it is actually not permitted by law. My experience from patients is positive, especially because the study was of direct benefit to them.*

Several people said that delayed consent studies already happened in New Zealand, with very low rates of subsequent denial of consent to use information. A number of respondents expressed

surprise that delayed consent is not permitted under New Zealand law, and thought the best interests provisions in the Code were sufficient. *So, the current law is being ignored by both ethics committees and researchers* and it should be made possible in the law under specific circumstances deemed appropriate by an ethics committee:

> *In view of the uncertainty I think it would be a high priority for this [the law] to be clarified with the express provision of delayed consent.*

People who were less sure of the need for a change in the law could see some circumstances where delayed consent would be appropriate, such as very low risk studies that primarily involved the collection of anonymised data. Other conditions might be for treatment that patients would be receiving anyway, and they would give informed consent when recovered for ongoing monitoring. Under these circumstances there should be a reasonable belief that the patient would want to participate.

Respondents who did not support a law change thought that delayed consent was *open to abuse, coercion* and *manipulation of vulnerable consumers*, or *the well-intentioned assumptions of researchers.* They reiterated that *consent after the fact is not consent* and *makes a mockery* of the principle of informed consent. It is also *absurd to assume that all patients have altruism and would consent on the basis of contributing to the greater good.* Some conceded that *it would only be acceptable for lifesaving procedures.*

Some respondents made it clear that the phrase 'delayed consent' *offered no meaningful choice*. They thought it was misleading, and consideration should be given to *more accurate alternative phrases such as 'consent for ongoing participation' and 'consent for use of data until withdrawal'.* These phrases capture the intent of the researcher more clearly, *avoids the person feeling coerced to consent retrospectively*, removes *the uncertainty around deleting data if consent is not subsequently given*, maintains *the integrity of the concept of informed consent*, and *deals with the problem of consent if the patient dies* or never (re)gains the capacity to consent. These phrases do not, however, *readily apply to people with intellectual disability who are unlikely to be regarded as competent in the future.*

4. 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.

Figure 11: Should there be a legal requirement for researchers to show that research of a similar nature cannot be carried out on a competent person?

The responses to question 4.1 suggest that most people thought that there should be a legal requirement to show that research of a similar nature cannot be carried out on a competent person. Figure 11 shows that 71 respondents said 'yes', 28 said 'no', and 21 were 'unsure'. These numbers appear to provide clear support for a change to the law, but there is significant overlap between yes/no/unsure responses. For example, 'yes, not sure if this needs to be a legal requirement'.

Positive responses to a law change indicated that there should definitely be maximum safeguards enshrined in law to protect vulnerable people from being used as research *guinea pigs*. It was thought to be *an easy-option* to use incompetent participants and *grossly unfair to involve someone who can't consent if there are others who can*. Very early phase trials

> *should not be considered at all in non-consenting adults, neither should the burden of research be shifted to other vulnerable groups, such as children (whose parents can provide consent on their behalf).*

Some thought that there is no point having ethical standards with no legal basis, and it is a feature of all overseas legal models. The legislation should state a principle that incompetent subjects can be used in research only when competent subjects cannot be used:

> *It should be impossible to do research of comparable effectiveness on individuals who are not able to consent to participation. This is required to prevent individuals who lack capacity being used as research subjects when it would be possible to recruit competent subjects. It is a feature of all of the overseas models, EU Regulation 2015, art 31.1.(e), MCAs 31(4), AISA s 51(1).*

Other responses indicated agreement in principle, but *it may not be required to place all ethical standards in law*. Ethics committees should *require a researcher to show research of a similar nature cannot be carried out on competent people before research on incompetent people is considered.* Relevant evidence to justify the importance of the research was thought to be *more important tha[n] ensuring a trial on competent patients first*. There are some clinical circumstances in which research of a similar nature cannot be adequately carried out on competent persons first:

> *An example here would be the treatment of life-threatening influenza treated in Intensive Care during a pandemic influenza. By the time research of a similar nature was undertaken in competent less sick persons the pandemic may well have finished with an unnecessary loss of life due to the inability to undertake research in the most critically ill patients during the pandemic.*

Respondents indicated that the application of a blanket-rule law change to all research might be valid for some intervention studies, but research on those who are able to consent may not be relevant or transferable to other sub-populations: *Therapies of use in the critically ill should be proven to work on the critically ill*. Similarly, research about disability *should be carried out on a disabled group*. Respondents thought there should be caution about assuming that research on competent populations is applicable to non-competent populations. Any law change should not create more barriers to research that will benefit vulnerable populations, nor is it justifiable to exclude incompetent people from participating in research.

It was pointed out that a change in the law could lead to funding being wasted or cause delays to important research. On the other hand, *delay is preferable in order to amass sufficient consenting subjects to undertake the research rather than rely on incapacitated/incompetent subjects.*

5. Interests of others to be taken into account

The current law in New Zealand takes account of the interests of only the incompetent research participant and not the interests of others, such as other people with the same condition. Most respondents thought that research that may or may not benefit incompetent research participants should be permitted if it may benefit others. Figure 12 shows that 70 said 'yes', it should be permitted, 30 said 'no', and 20 were 'unsure'.

Figure 12: Should research on an incompetent participant be permitted if the research may or may not benefit the individual participant, but may benefit other people?

People who said 'yes', research on incompetent adults should be permitted if it benefits others (even if it may not benefit the individual) also thought there needed to be sufficient safeguards in place to protect participants. As well, they thought it was important for research to take place with this group in order to improve future care.

Respondents who said 'yes' had a high expectation that *all* or at least *most people* (able and unable to consent), *if given the opportunity, would normally consent to research for altruistic reasons* due to *a natural wish to try and help treat others.* Assuming sufficient safeguards are in place,

> *it is reasonable that all patients should be expected to participate in clinical research. [After all], health care is funded from the public purse in New Zealand.*

It was pointed out that the advancement of knowledge and improvements in care are dependent on the participation of patients in research, and it is *because of the risks that other people have taken in the past that we benefit and I see no problem with carrying this forward. How are we to make improvements for the benefit of everyone if we don't do this?* People with disabilities or who are incapacitated are *no different* in this respect *than patients who are able to give consent who do so for a study that may not directly benefit them.* These groups should not be excluded from participation in research:

> *If we do not study incompetent patients, we cannot be expected to improve their care.*

Not everyone took a utilitarian position, and others thought that the interests and rights of the individual should always come first. People who said 'no' to the interests of others being taken into account thought that *value judgements were being made on behalf of the incompetent person* when *their integrity and interests should come first*:

> *Utilitarianism becomes very problematic when it becomes an obligation on others indifferent to the wider good. Considerable erosions of liberty and autonomy here.*

These respondents expressed considerable disquiet about the rights of incompetent individuals being *sacrificed* for the future benefit of others if there is no personal benefit to themselves:

> *This type of utilitarian logic is behind some of the most unethical research conducted, including the Willowbrook hepatitis studies. Vulnerable people who cannot give consent should not be used as test subjects for research to benefit others. The risks of exploitation are far too great.*

Respondents who said that they were unsure thought that *research to provide wider benefit may be taken into account, provided these interests cannot override the interests, rights and welfare of an individual participant*. It was pointed out that *the Declaration of Helsinki permits minimal risk research where the research benefit is not applicable to the individual*.

Others, however, said that as a general rule, clinical research is *never primarily intended to benefit its participants* but *to improve management of future people with the same conditions.* It should not be conflated with expectations of individual benefit. *To require research, particularly observational research and research comparing different treatments or a treatment and a placebo, to benefit every individual participant in the research is in many instances going to be an impossibility.*

For people to agree that the interests of others could be taken into account, safeguards would be needed to protect adults unable to consent (see also Consultation Question 1). An important inclusion mentioned from the Adults with Incapacity (Scotland) Act 2000 requires that the researcher make a compelling case of significant societal benefit. Suggested wording would be that

> *the ethics committee must be satisfied by credible evidence that the research will contribute through significant improvement in the scientific understanding of the adult's incapacity to the attainment of real and direct benefit to the adult or other people having the same incapacity, and that the research cannot be done on capacitated people.*

A number of respondents cited the Council for International Organizations of Medical Sciences (CIOMS) research guidelines which *has taken a minimal risk threshold approach rather than the '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 presents 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).*

There were opposing views about the validity of 'inclusion benefits' which refers to the benefits thought to accrue to research participants from being enrolled in a study. Two respondents cited Gillet (2015), who *highlights that patients involved in research are often better cared for due to the careful monitoring that is required for good clinical research.* Furthermore:

> *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.*

On the other hand, where some level of risk is involved and if the benefits are only due to inclusion, this respondent considered the research to be unacceptable:

> *If a project goes beyond observational research and involves intervention and the benefit is only an 'inclusion' benefit some level of risk is involved, then the answer is a categorical NO [to research being permitted].*

5.3 Should there be criteria about the group of people the research is intended to benefit?

Figure 13 shows that 45 said 'yes' there should be criteria, 16 said 'no' to any criteria, and 15 were 'unsure'. There was a high non-response rate to the question; over half (n=78) did not respond. The question asked, '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?

Figure 13: 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?

Question 5.4 asked those who had replied 'yes' to 5.3 to 'indicate the criteria they thought should apply [to the group of people that the research is intended to benefit]' and indicate the order of importance of the criteria with 1 being the most important and 5 being the least important. Forty-two 'yes' or 'unsure' respondents attempted this question but provided only general criteria about carrying out research on adults who are unable to consent. Examination of the replies to this question added nothing new.

6. 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.

Figure 14: Should researchers be required by law to obtain ethics committee approval before conducting H&D research with adult participants who are unable to give consent?

Most people thought that the law should change to make ethics committee approval mandatory. Figure 14 shows that 112 said 'yes', 4 said 'no', and 9 were 'unsure'. It was not always clear from the responses whether the requirement should apply to all research, only health and disability research, that done by providers, or only to cases where the research involves adult consumers who are unable to provide informed consent. There seemed to be some confusion between the issue of approval of an overall study by an ethics committee and the process of consent for individuals to participate in a study.

With those caveats in mind, almost all respondents thought that mandatory ethics committee approval would provide protection and safeguards for people who are vulnerable:

> *Because the ethics committee is independent of the researcher, they are able to protect the interests of the participant, and ensure safeguards are in place.*

There was expectation of a higher level of protection for participants in this type of research than for competent participants, *to avoid exploitation, abuse*, and *experimentation*. All animal research requires ethical approval and should also for humans who cannot give consent. Respondents thought that ethics approval would ensure that all research is *open and transparent* with *universal application of standards*. For maximum benefit from research, the results need to be disseminated and *few studies can now be published without prior formal ethical approval anyway.* Mandatory ethics approval would be consistent with international practice as *all overseas models require it*.

Some respondents, however, thought that ethics committee approval might not be required for low-risk studies. Institutional review might be sufficient for observational or audit studies, case studies, and conference presentations:

> *This would allow progress to be made at a much faster pace, without any negative impact on the participants.*

The position of some respondents was that ethics committees should not ever approve unconsented research, but that if it is allowed, ethics approval should be the minimum requirement. One person indicated a preference for a High Court decision.

A law change was not supported by a few on the basis that decisions about research ethics *should be ethically driven rather than legally driven*:

> *Every 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 the ethical approval should come from.*

Making ethics committee approval mandatory, however, would require robust and transparent ethics committee processes. Not all respondents were confident that ethics committees provide adequate protection to adults unable to consent to participation in research. For example, despite the law, ethics committees do already approve such studies:

> *[T]here have been forty medical studies in New Zealand since 2006 that included non-consenting 'participants' and … these studies were approved by ethics committees.*

A number felt strongly that the ethics framework in New Zealand needs to be clarified and strengthened, particularly if any changes were to be made to Right 7(4) of the Code:

> *Any change to Right 7(4) should also include a parallel review of the functionality and composition of NZ ethics committees.*

Changes to the Standard Operating Procedures (SOPs) of the HDECs over recent years have *resulted in a deeply concerning shift away from protection of consumers and proposed research subjects, towards expediting research.* The changes in 2012 reduced the number of HDECs 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.* Other types of research are no longer eligible for full HDEC assessment, giving rise to confusion within the research sector about appropriate review processes and a perceived lack of consistency:

> *In many parts of New Zealand there is great confusion as to who to go to, to obtain appropriate ethical review. We believe that all studies should undergo some sort of review but that there will be varying levels of review required depending on the type of study. Urgent clarification is required on this issue and should be applied consistently across the country.*

At present, the SOPs state that the level of qualification in which a student researcher is enrolled determines whether the research will be reviewed by HDEC or an institutional committee. For example, *master's level research goes to institutional ethics committees, but PhD research goes to HDECs, although both levels can undertake very invasive human tissue research or psychologically distressing studies.* Acknowledging the need *to aim for balance and avoid a myopic focus on risk,* it was thought that the criteria for studies requiring HDEC review would be better assessed on a risk-rated basis than on a level of university education.

Changes to the SOPs were thought to have been *driven more by researcher interests and/or by the potential to generate more economic benefits for the country.* To better protect research participants, suggestions were made for a fifth HDEC or a *'special ethics committee'* that is *separate and independent (from the existing HDECs) to be set up solely to consider research in these vulnerable incapacitated/incompetent adult cohorts.*

Notwithstanding the above-mentioned concerns and suggestions, some respondents indicated that *ethics committee approval was not, in itself, enough* because of the insufficient knowledge and experience of some members. It was pointed out that the case studies (A to E) provided in the Consultation Document *demonstrate that any methodological lack (or lack of information about methodology) can fundamentally alter the ethical considerations.* Committee members must therefore be *highly skilled, accredited and independent*. They must understand research methodology, the rationale for the research, be able to judge the robustness of the research, and understand the conditions and populations being studied:

> *We believe that key to such safeguards are highly and diversely-skilled ethics committees that include exploration of the scientific validity of a project under their scope.*
>
> *Many people on ethics committees know nothing of research, the standard of proof required for different disciplines, what may or may not be generated — and nor do many of them care to know.*

There was an expectation from respondents that research would have ongoing monitoring and review by ethics committees. However, the current research ethics system was described as *a high-trust system which relies largely on self-reporting [of problems]*. At present there is no mechanism for researcher accountability because *there is no national system for audit of compliance against conditions of ethics approval.* Some thought that building direct statutory requirements for ethics review into New Zealand law would therefore ensure that participants were properly protected by enabling effective management of the conduct of a study.

A few respondents pointed out that ethical conduct is as much a part of research integrity as the study justification, protocol, independent peer review, recruitment practices, and data safety monitoring. Responsibility for the safe ethical conduct of a research project lies with the *researchers' cognisance and ownership* of the ethical issues arising from their proposed research. The researcher's grasp of the issues should be addressed during the ethics review process as the committee examines *the different scenarios which may occur and the documented proposed enrolment procedures to address such scenarios.* Another respondent pointed out the researcher's responsibilities during the study when or if ethical issues arise that were not anticipated:

> *[I]t 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.*

One respondent observed that a sufficiently rigorous review process and researcher accountability might avoid the need to amend the law.

7. Best interests test

Respondents were asked in this section whether they thought that 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?

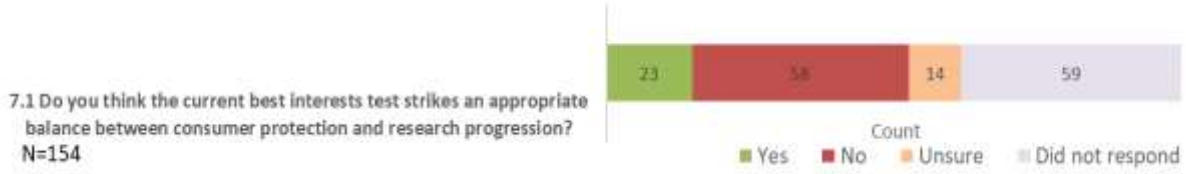

Figure 15: Do you think the current best interests test strikes an appropriate balance between consumer protection and research progression?

Most respondents to this question thought the 'best interests' test does not strike an appropriate balance between consumer protection and research progression. Figure 15 shows that 23 said 'yes' (there is an appropriate balance), 58 said 'no', and 14 were 'unsure'. There were a very high number of non-responses (over one-third) and considerable overlap between yes/no/unsure. The question asked at 7.2 was complex and required respondents to focus on criteria other than best interests that would bring more balance. Some people interpreted this question more broadly than just assessing advantage and disadvantage for people who are unable to consent.

7.2 Other than best interests, what criteria to assess participant advantage and disadvantage would be appropriate if research were to be permitted without the consent of adult incompetent participants?

Only people who answered 'no' to 7.1 were asked to provide criteria, although a number of people who said 'yes' provided criteria also. These people thought that best interests should remain the threshold in the Code because it is a reasonable test, although stronger protection is needed. Most people, however, thought that the best interests test is too high and places unnecessary restrictions on knowledge development (see 7.3).

The current best interests test does not provide for any consideration of the potential for advances in knowledge that may benefit other people. It was suggested that a remedy that would shift the focus from benefits to the individual to benefits to others could be achieved with only a minor change to the existing wording in the Code:

> *[E]ither 'best interests of **similar or related** consumer**s**', or even 'best interests of ~~the~~ consumer**s**'.*

Suggested examples for risk and benefits tests exclusive of best interests were:

- An identifiable potential benefit preferably guaranteed
- No risk or minimal risk or minimal foreseeable risk
- Very unlikely to harm and a reasonable possibility of benefit
- No greater risk of harm or benefit than if they didn't participate (i.e., not better or worse off)
- Minimum risk and burden thresholds, but not benefit
- Any harm would not be permanent or invasive.

Specific wording for a benefit threshold was made as follows:

> *There must be scientific grounds for expecting that the research would be likely to produce a real and direct benefit for the individual.*

Specific wording for minimal risk and burden thresholds were made as follows:

> *Whether or not there is an expectation that the research would be likely to produce a real and direct benefit for the individual, the research must entail no more than a minimal foreseeable risk or minimal foreseeable burden, discomfort, interference with the freedom or movement or privacy of the participant.*

The best interests test is complicated by different types of study designs and means that some otherwise valuable low-risk research is not possible. That is, it is usually impossible to demonstrate best interests for low-risk qualitative, observational, non-invasive, standard of care comparisons, or comparing two treatments that are already standard practice.

Although randomised controlled trials seem intuitively wrong if non-consenting adults are included, there is considerable variability in treatments provided based on clinician preference alone, and it is, perhaps, more appropriate to ask

> *whether it is better for a participant to be in the study and potentially receive an experimental treatment rather than not be in the study and just receive the gold standard therapy.*

In addition to the items above for risk thresholds, other more general criteria to permit research with adults unable to consent were suggested:

- Ethics committee approval
- Evidence of no harm from phase 1 or any other studies
- The research would be impractical on consenting subjects
- A research question of importance to the population being considered for inclusion
- Minimum numbers of incompetent persons enrolled
- Effective assent from nominated representatives of the individual
- Social value, real world answers, and likelihood of uptake by health services
- Responsive to participant needs identified during the research.

Disabled people with impaired decision-making or people who are temporarily incapacitated *should be given maximum protection from becoming the subject of non-consensual research if their will and preferences about research participation are unknown*. Unless the provider has tried to ascertain a person's wishes prior, it is unclear who decides what the best interests are of an adult who is not competent to give consent. Often a presumption of consent is made if the provider thinks the person would consent if competent. *The problem is that these decision-makers are considered to be ethical, are competent to decide what's best for the person, know their wishes, preferences and so on.* Researchers necessarily have a conflict of interest in this context and should never be the ones to determine the best interests of a proposed research subject.

7.3 Please state the reason you formed the view that the balance is not right

Many people thought that the best interests requirement in the Code is unreasonable and almost never applies in research. It is a barrier to research and restricts the development of evidence-based care, preventing improvements in care for high-needs populations. Protection for these groups is needed, but there should be provision to allow for more research than at present. New Zealand

should align with similar jurisdictions, particularly Australia, the United Kingdom, and the United States. The irony is

> *that there are times when there is a lack of evidence base for what is in the person's best interest and cases where research may benefit the person long term, and cases where the ethical harm of providing an unstudied intervention should outweigh the ethical harm of research.*

8. Who decides?

At present, if proposed research includes participants who are unable to consent for themselves, the decision as to whether an incompetent consumer can participate in the research will be made by an EPOA or welfare guardian (if the research is not a medical experiment, or if so, is for the purpose of saving the consumer's life or preventing serious damage to the consumer's health), the Court (if a personal order has been made), or the provider of health and/or disability services (who must determine that the conditions in 7(4) of the Code have been satisfied).

Question 8.1 asked whether there should be any change made to the law regarding who decides whether an incompetent consumer will be enrolled in a study. Figure 16 shows that 42 said 'yes' there should be a law change, 19 said 'no', and 24 were 'unsure'. Question 8.2 asked whether there should be any change made to the roles played by various decision-makers under current New Zealand law. Response numbers were similar to question 8.1. There was a high non-response rate to both questions; almost half did not respond.

Figure 16: Who decides?

Question 8.3 involved completing a table about possible decision-makers and the roles they could play in decision-making. Question 8.4 asked who the final decision-maker from a list of five possibilities should be, and to rank the decision-makers chosen in order of preference from 1 being the most preferred to 5 being the least preferred. Question 8.5 asked for further comments about decision-makers.

Those who responded appear to consider that EPOA or welfare guardians should be consulted and/or be able to consent or decline. The second most common choice was family/whānau, and most respondents felt that families should be consulted, but fewer felt that they should have the power to consent or the power to withhold consent. If family/whānau indicate that the person would likely object to participation, the research should not be conducted.

Some thought that EPOA or welfare guardians should have the power to veto, but the family should be consulted. Others thought that EPOAs or welfare guardians should not have the final say as they are not independent, although their views need to be taken into account.

Respondents noted that family members will often have the most relevant information about what a person's most likely choice would have been. In some cultures, it is customary for the family to have the right to decide on behalf of a family member, even if the patient has an advance directive and has specifically asked for something else. Ideally, the patient should decide whilst still able to do so whether they wish to follow customary practice or not. If there is no advance directive and no EPOA or welfare guardian, then the family should be the decision-makers. More consultation would be

necessary if the research is likely to make a significant difference to the patient's daily life or outcome; observational research would require less consultation.

In the case of research on people with severe intellectual disabilities or advanced degenerative conditions (such as dementia), the respondents commonly thought that the EPOA/welfare guardian should be the decision-maker. If there were no authorised representatives, then the family should make the decision. If, however, an EPOA exists, and there is time to seek their opinion, their consent should be regarded as similar to consent obtained directly from the patient.

However, equal weight should not be given to all family members, and the person's 'chosen' family member should be consulted rather than parents or siblings. This is particularly the case for people with mental health conditions.

There were other suggestions made such as the person's lawyer being involved if they had no EPOA, or there being a panel of competent experts to make the decision.

A number of clinicians felt that researchers/providers should be the decision-maker, as most research participation decisions for incompetent patients are made in the clinic or at the bedside. EPOAs, welfare guardians, and family members would be consulted if they were available. This was particularly so in ED research and some ICU research where there may not be time to consult others. Many thought it was unlikely that there would be an EPOA or welfare guardian in that situation, and in the ICU setting, independent other clinicians would not generally be available.

> *In an emergency situation to involve an EPOA/welfare guardian or whānau/friend/ family in a full informed consent process will be too time consuming and render the research useless. I consider that in emergency situations there should be a staged consent process where a potential participant indicates after the brief discussion with the researcher and treating clinician that they would or would not wish to participate in a research study that requires urgent enrolment with the opportunity for them to subsequently withdraw consent at any stage. This would give the people who are against any sort of research or the general concepts for the particular research study to express this. Observational studies that pose minimal risk to participants should not require consent.*

Depending on the type of study, the ranking of decision-makers is likely to be different. For example, the ranking exercise showed that in ICU, researchers will be high on the decision-making ladder, then consumers, then EPOAs/welfare guardians/families should be consulted. In a dementia-type trial, EPOA and family would rank higher. In this context, some respondents thought that the general practitioner (GP) should always be involved as they are an objective and informed advisor, which adds another layer of protection. They may be able to inform researchers of a patient's previous wishes but should not be able to consent or veto. Others thought that GPs should be consulted and have the power to veto participation. Decision-makers in a community context should be the GP, then family/whānau, then the researcher.

Not all respondents agreed that clinicians should decide, because as researchers they have a conflict of interest. It was thought that

> *it is never the right of the researcher or medical professional to make the decision and they should have no say. Doctors already have too much influence over what is deemed to be in the best interests of consumers. Please don't give them any more freedom to do that.*

It was pointed out that although clinicians involved in research generally have the best understanding of the potential risks and benefits of participation, family are likely to rely on a clinician's judgement.

Some respondents thought that there should be less emphasis on ethics committees as decision-makers, whereas others ranked ethics committees higher than EPOA/welfare guardian:

> *Ethics committees should be able to make decisions about consent being waived and have a deferred consent process in certain situations for intervention or studies such as when immediate enrolment is required, equipoise exists between the treatments, and the research is in the public good.*

A change in the law to provide more protection to adults unable to consent to participation would be necessary as follows:

> *At present the researcher decides based on a best interest assessment and must seek the prior views of the consumer or consult with suitable persons. This is insufficiently protective of the person. They should be informed and able to participate to the extent of their capacity (assent) if they are unable to give informed consent. I consider there should be a legal requirement that an incapacitated person cannot be included in clinical research without the informed consent of a legal representative. To do this a statutory provision would be required to permit a guardian or personal representative to give informed consent. I prefer this to a veto model as in the MCA. Otherwise I consider that the family members should make the decision as they know the person best and are more likely to be able to predict what they want and would be motivated to protect them from harm.*

9. Other issues

Respondents were asked for final comments or suggestions. Issues not already covered in detail or that did not arise in the case studies or consultation questions have been summarised in this section. Areas of comment concern a range of issues: New Zealand's protectionist approach that is out of step with other countries; the primacy of autonomy; the conflation of treatment and research; conflict of interest; the confusion surrounding the law regarding consent by substitute/proxy; assessment of capacity and other forms of consent; different types of studies and level of risk; the best interests threshold; safeguards and ethics committees; and suggestions for changes to the Code.

There was feedback about the consultation document itself, namely that it had a focus on risk minimisation and was framed *by two key principles, consent and protection*. A number of respondents think that New Zealand's approach to research ethics has swung too far towards protectionism. A research ethics paradigm that focuses only on the dangers of research is distorted and *we need to aim for a balance not a myopic focus on risk.*

Groups of people considered to be vulnerable (e.g., adults unable to consent) are currently *protected by their exclusion* from participation in research when they could be *included but protected* with robust safeguards. Right 7(4) of the Code was thought to be out of step with other countries:

> *It is clear that Right 7(4) as it stands is not aligned with the World Medical Association Declaration of Helsinki — Ethical Principles for Medical Research Involving Human Subjects. The current position in New Zealand is also at odds with other jurisdictions including the UK and Australia, both of which allow research involving participants who are unable to give consent to proceed in a broader range of circumstances than in New Zealand.*

Better alignment with other countries would reduce confusion and facilitate cross-country research, as well as benefit patients who deserve the best possible treatment options, which can come only through well designed and executed clinical trials. Those who are critically ill and people *with dementia and intellectual disabilities are disadvantaged by not being included in research that has the potential to advance our knowledge of meeting their complex health needs and providing them with better health care services.* A few reiterated not only the right of all people to participate in research, but also the obligation or duty to participate to build a better future for all.

It was acknowledged that tension is created between the core bioethical principles of a*utonomy, beneficence, non-maleficence and justice* in the context of non-consensual treatment and research. However, the *Nuremberg Code and the Declaration of Helsinki have cemented autonomy as the most important principle:*

> *Failure to respect autonomy in the pursuit of the 'greatest good for the greatest number' has been at the heart of some of the worst historical atrocities in the name of advancing knowledge through research.*

The place of autonomy is a key issue arising from this consultation and is central to the deontological and utilitarian positions held by various respondents.

There is no distinction between treatment and research in Right 7(4) of the Code, which adds to the complexity of issues to do with non-consensual research. For many respondents, it is clear that

research is an integral part of medicine and cannot be considered a separate activity because of its relationship to evidence-based practice and quality improvement. Furthermore, patients need to expect requests to participate in research, which *should be seen as an ordinary part of treatment, especially in a tertiary hospital.* However, not all respondents thought that treatment and research are inseparable and they each require separate justification

> *… because research is not treatment, it should always be seen as distinct from clinical care, and therefore the ethical justification for research will be different.*

One respondent suggested that the Code should deal only with treatment and not with research at all:

> *I do not believe the Code needs to directly address research. I think that treatments are already covered in the normal policies of the Code, while research is covered by the ethics committees.*

Respondents pointed out the imbalance of power that arises from the conflation of research and treatment, which creates a conflict of interest for clinician/researchers who are recruiting patients to be participants in their own research:

> *Right 7(4) does not give any guidance on how to address any conflict of roles and the investigator could potentially decide whether to enrol the patient in the research in the absence of independent advice or oversight.*

Other conflicts of interests arise if *doctors and nurses are paid by drug companies or by another research team to recruit participants*.

While ethics committees stipulate the requirement for dual roles to be managed and transparent, there are potential gaps in protections for participants when there are no appropriate monitoring processes in place. Respondents suggested that ethics committee follow-up should be mandatory for all non-consensual research projects, but that it will require a specific mechanism to be created and funded:

> *A significant weakness of the current system of ethical review in New Zealand [is] that there is no mechanism for checking that a particular study is carried out according to the agreed ethical protocols. This requirement, we note, is stipulated in Paragraph 24 of the Declaration of Helsinki under the heading of Research Ethics Committees: 'The committee must have the right to monitor ongoing studies'.*

Responses indicated that changes to the SOPs for HDECs in 2012 have resulted in a reduction in protection for research participants, and some respondents made it clear that optimal safeguards are often assumed but do not yet fully exist, even for competent participants. Confidence in the current system of ethical review in New Zealand is needed, *and a determination must be made that the HDEC review committees are adequately resourced and adequately trained.*

Concerns were raised about the apparent confusion amongst researchers about the law regarding research with adults who can consent, cannot consent, assent, and proxy or consent by substitute. It is not well understood that the PPPR Act prohibits EPOAs from agreeing to participation in 'medical experiments' unless to save life or prevent serious risk to health.

Even when researchers are clear about the proper use of EPOA, it remains a problematic area especially in emergency medicine and in hospitals without policies for their use:

> *In my experience, even if they [EPOA] exist, they are rarely activated. My hospital also has no protocol for how I should validate them when they are presented. When vulnerable/trauma patients present to hospital we have no way of knowing they exist, who holds it or what it says. This needs to be fixed. Surely, they should be available on-line.*

The issues to do with consent by substitute for incapacitated adults in acute ED and ICU settings are substantially different for people with diminished or variably diminished capacity due to dementia, intellectual disability, or mental health problems. In these situations, assessment of capacity is not a binary choice and people may be able to make their own decisions:

> *Competence should not be seen as an 'all or nothing' concept but might be dependent on the type of decision to be made. What this means is that there may be competency to decide on some issues and not others, and this may also occur within varying time-frames.*

A wider range of forms of consent are needed, with *priority given to supported decision making over substituted decision making* and *aligns with the CRPD emphasis according to will and preference, so that preference is the bar rather than the assessment of capacity*. Participatory processes, particularly for dementia patients, avoids their exclusion from taking part in research and emphasises the need for consent throughout the research project:

> *A narrow focus on cognitively biased informed consent and to consent taking place at the beginning of projects is exclusionary for people with dementia. [Participatory processes are] a method for consent which enables people with dementia to take part in research projects, and on consent as a process that runs through the whole of a research project.*

A suggestion was also made for better use of *advanced care directives which should include a section on research.* However, blanket advance directives to participate in research is not appropriate and must be decided on a case-by-case basis:

> *Our view is that the decision to take part in research must be made on a case-by-case basis and following the provision of full information about the risks of the particular study.*

Although outside the scope of this consultation, the consequences of the inconsistencies in the current law with respect to consent-on-behalf are that some types of research are pushed onto children:

> *Even where the study does not meet best interest, it is lawful when conducted on children whose legal guardians/parents have given consent and where the child has lawfully provided assent to the level that is appropriate to them (as in Gillick competency). We observe that this is potentially pushing higher risk research in the direction of children, who are arguably more vulnerable than adults.*

Respondents pointed out the need to distinguish between research and audit. There are also different types of research, such as social science research, observational and interventional research, high risk and low risk research. While guidelines are needed to assess risks and benefits, the different risk levels of different types of research should be recognised:

> *While there is always an incremental risk in being part of research, this is sometimes negligible, perhaps no more than inconvenience, and it is inequitable to treat all research as though it was high risk clinical research.*

Despite general calls for a more standardised approach to ethical review, responses from ethics committees are that individual assessments take into account each project's differences:

> *[E]ach 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.*

One respondent was frustrated by low risk, observational research that uses existing data which *fully meets the requirements of the Health Information Privacy Code in all respects but is sufficient to trigger the need for a Health and Disability Ethics Committee review due to the technical presence of a non-consent issue.* The requirement to meet Right 7(4) of the Code in these circumstances was also questioned by HDEC:

> *We do not believe that evaluative or information-only research needs to meet Right 7(4) as it does not entail the 'provision of a service'. However, the use of health information does need to meet the Health Information Privacy Code, and in the case where its use is without consent we apply Clause 6.43 of NEAC's Observation Guidelines and Rule 11 of the HIP Code.*

Some respondents commented that the very high threshold of best interest in Right 7(4) of the Code prevents the advancement of knowledge in some cases: *a more moderate best-equal threshold would not only ensure that all participants were receiving best available care, but would also allow knowledge to progress, safely.* Researchers currently 'work around' the Right 7(4) requirement for best interests by arguing inclusion benefits such as *improved or more watchful care*. HDECs do not necessarily accept it as a justification until provided with evidence of the claim to best interest:

> *[We] do not accept outright the argument that participants in health research are always better off. The onus is on the researcher to prove legality of the trial as well as the benefit to participants.*

It is important to note that there were a number of respondents who considered that inclusion benefit arguments *should never be presented/weighted as a study benefit.*

The legitimacy of research that will benefit others with minimal, if any, benefit to the participants has been discussed in section 5. However, further comment was made about research that is part of an international study with results that will not benefit New Zealanders or where there is no hope of drugs being funded in this country: *I do not believe that New Zealand or New Zealanders should be a testing ground for experimental therapies/novel agents that will not be made available to New Zealanders.*

There was extensive comment that cautioned against changes to the Code without *a parallel review of the functionality and composition of NZ ethics committees.* Broadening the criteria for non-consensual research would be *unworkable and unsafe in the current context of ethical review.* The need for better protection for all research participants applied also to changes more permissive of consent by proxy:

> *The law should not be changed at this point in time to allow decision-making by others to consent incompetent persons to being enrolled in research within NZ until better protections are in place for all research participants.*

Notwithstanding these cautions, suggestions for changes to the Code were: to include all health and disability research, not just research done by providers; to better acknowledge *Te Ao Māori attitudes and values around research;* to insert *a research specific clause* allowing minimal risk research; and to amend to include *a best equal interest test where participation must have risks and benefits at least equal to non-participation.* The conflation of research with treatment in the Code is confusing

and *it would be useful to consumers, researchers, and ethics committees if research per se and treatment (which may include audit, clinical evaluation and quality assurance practices as part of good care and treatment) were distinguished within the Code.*

There was support for changes that would *allow for delayed consent and proxy consent in circumstances that warrant it*. Other recommendations were for a legal representative to give informed consent as a precondition of inclusion in research of an adult unable to consent:

> *(1) I now consider that the informed consent of a legal representative (nearest relative, caregiver or third party professional) should give informed consent as a precondition to inclusion of an incapacitated person, rather than merely being able to veto inclusion; and (2) I am more sceptical about whether it should be legally and ethically permissible to include incapacitated people in clinical research where there is no expectation that they could derive an individual personal benefit from inclusion.*

Finally, the review of Right 7(4) was thought to *offer 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.*