**Summary of submissions**

on the draft *Standard Operating Procedures for Health and Disability Ethics Committees*, and the draft HDEC application form

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# Background

In February 2010, the Health Select Committee opened an [inquiry](http://www.parliament.nz/en-NZ/PB/SC/BusSum/7/1/5/00DBSCH_INQ_9752_1-Inquiry-into-improving-New-Zealand-s-environment.htm) into improving New Zealand’s environment to support innovation through clinical trials. The inquiry considered ways to ensure:

* coordinated, nationwide approaches to clinical trials and performance measures;
* streamlined ethics approvals systems;
* national patient referral networks, and better ways to approve, establish and conduct clinical trials;
* removal of unnecessary barriers;
* and benefit to New Zealand patients through clinical trials, as well as the New Zealand innovation system, health system, and economy.

In June 2011, the Health Committee completed its inquiry and made a number of [recommendations](http://www.parliament.nz/en-NZ/PB/SC/Documents/Reports/e/8/2/49DBSCH_SCR5154_1-Inquiry-into-improving-New-Zealand-s-environment.htm) to the Government on how these goals could best be achieved, including how best to improve the operation of the health and disability ethics committees (HDECs).

In September 2011, the Government [accepted](http://www.parliament.nz/en-NZ/PB/Presented/Papers/6/2/f/49DBHOH_PAP21990_1-Government-Response-to-Report-of-the-Health-Committee.htm) most of the Health Committee’s recommendations, and announced a number of changes to the HDECs with effect from 1 July 2012. These changes included:

1. new procedural rules to better define the HDEC review process. These procedural rules would:
   * introduce timelines for both full review (35 days) and expedited review (15 days)
   * allow some clinical trials to be reviewed by the expedited review pathway, on the basis of risk
   * clarify and reduce the scope of HDEC review to allow a greater focus on higher-risk studies
   * more clearly define when amendments to approved studies themselves require review
   * reduce duplication between HDECs, SCOTT, and other parties to research, and clarify that the HDECs’ role is to check that research has been peer-reviewed (rather than doing this peer review themselves)
2. a shorter, simpler application form
3. an online application system
4. a reduction in the number and size of HDECs.

To give effect to these decisions, the Ministry worked with HDEC Chairs during September and October 2011 to develop draft procedural rules, called *Standard Operating Procedures for Health and Disability Ethics Committees* (or “SOPs for HDECs”), and a draft application form for HDEC review.

Drafts of these two documents were circulated to the National Ethics Advisory Committee (NEAC) and the Health Research Council’s Ethics Committee (HRCEC) in November 2011 for comment.

The two draft documents were made available on the current HDECs’ website ([www.ethicscommittees.health.govt.nz](http://www.ethicscommittees.health.govt.nz)) from 23 December 2011, along with a form for providing feedback on them. A number of key stakeholders were notified of the draft documents and the public submission process. The Ministry met in January with representatives of institutional ethics committees (IECs) and DHB research offices to discuss the draft documents.

The close-off date for submissions was 10 February 2012. Seven submissions were accepted after this date.

Ministry officials met with a representative of the New Zealand Law Society in March 2012 to discuss their submission, which had since been made public.

## Overview of submitters and submissions

A total of fifty-one submissions were received on the two draft documents, from a range of different stakeholders.

|  |  |  |
| --- | --- | --- |
| Source of submission | Number of responses | % of total responses |
| research organisation | 9 | 17.6% |
| academic institution/department | 7 | 13.8% |
| researcher | 6 | 11.8% |
| HDEC member | 5 | 9.8% |
| research sponsor | 5 | 9.8% |
| DHB office | 5 | 9.8% |
| consumer organisation | 3 | 5.8% |
| government body | 3 | 5.9% |
| IEC or IEC member | 3 | 5.9% |
| Māori review office | 3 | 5.9% |
| professional body | 2 | 3.9% |
| TOTAL | 51 | 100% |

At a high level, responses from different stakeholder types tended to be consistent with each other in some respects. Feedback from the clinical research community tended to be most in favour of the draft SOPs and form, and tended to focus on suggestions for minor technical changes. On the other hand, feedback from academic institutions, consumer organisations and institutional ethics committees (IECs) tended to be more critical of the draft documents, and to suggest that more comprehensive changes were need to them.

The chart below shows the number of responses received on each section of the draft SOPs and form.

## Feedback on government decisions

As explained in the consultation documents, the SOPs and application form are designed to give effect to the Government’s decisions on HDECs following the Health Committee’s clinical trials inquiry. However, a number of submitters commented on the substance and process of these Government decisions, and on the Health Select Committee inquiry itself. As a result, in some submissions it was not always clear whether a given comment related to the Government decisions, on one hand, or to the Ministry’s proposals for how these decisions might best be implemented, on the other.

Comment from submitters on the Government’s decisions on HDECs tended to focus on the need to maintain the quality of the HDEC review process (and, in particular, to ensure that participants continue to give informed consent, and that participant and researcher trust in the system is maintained); manage workload appropriately between HDECs and other parts of the research sector; and involve Māori appropriately in the research approval process.

Many submitters saw specific risks in areas such as:

* the separation of procedural guidance on the HDEC review process from the ethical standards that apply to health and disability research
* the centralisation of the submission process
* the future role of HDECs in ensuring scientific quality of research
* the separation of local research governance issues from HDEC review
* a reduction in the scope of HDEC review, and the number and size of HDECs
* the introduction of timeframes for review.

# Feedback on draft *SOPs for HDECs*

This section summarises feedback received about the draft Standard Operating Procedures (SOPs).

## Overall comments

Forty-two submitters made some overall comments about the draft SOPs. These comments covered a wide variety of substantive and procedural issues, from general queries about the SOPs to detailed aspects of their development and implementation.

**General support.** Twenty respondents expressed general support for the draft SOPs.

*“We consider this a timely and considered response to the recent review that will result in a more timely and effective service, with clearer boundaries and more transparent processes. The SOPs remain in line with stringent US federal requirements for international studies receiving US government funds.”*

*“This proposal is long overdue.”*

However, many other submitters did not support the provisions of the draft SOPs. Comments from these submitters included that the draft SOPs would undermine review quality, favour commercial research, create a false sense of expediency, and be unlikely to result in a faster overall approval process for research. One submitter thought this might actively deter the pharmaceutical industry from conducting research in New Zealand in future.

*“An appalling disaster… The SOPs are an insult to a carefully-nurtured culture of strong ethical oversight, which will be drastically undermined by the changes.*

*“There is a false sense of expedience when in actual fact the process for the researcher from seeking locality assessment to final ethics approval may take the same amount of time.*

**Length of consultation period.** Seven submitters considered that the consultation process on the new SOPs was too short, and that public debate on changes to HDECs had been insufficient.

**Consistency with international rules.** Several submitters questioned whether the draft SOPs would be consistent with national law, the Treaty of Waitangi, the findings of the Cartwright inquiry, and international guidance for the ethical conduct of health and disability research. However, apart from one submission (from the New Zealand Law Society, whose submission has since been made public), submitters did not always clearly indicate which provisions of these instruments they considered the draft SOPs would breach.

**HDEC membership.** Although not specifically mentioned in the draft SOPs or draft form, six submitters commented on aspects of HDEC membership. Comments included that chairs should continue to be lay members, that members should receive formal training in bioethics, and that the Terms of Reference for the new HDECs ought to have been included with the consultation documents.

**Ethical standards for researchers.** Some submitters thought that the SOPs should include substantive ethical guidance for researchers on a range of matters, including the need to obtain informed consent, compliance with the HDC’s Code of Rights, and consultation with Māori and Pacific peoples.

*“We are concerned about the […] omission of reference to the Treaty of Waitangi and guiding principles related to research with Māori in the draft SOPs. We also note that these standards do not make reference to Te Ara Tika Guidelines for Māori Research Ethics: a Framework for Researchers and Ethics Committee Members (HRC, 2011). We do acknowledge that consultation with Māori has been mentioned broadly, however, this provides insufficient direction for ethics committees and researchers.”*

**Framework for ethical review.** Five respondents commented on the need for a coherent framework of ethical review, and considered that the SOPs would not advance this goal. One submitter suggested that the HRCEC lead development of this framework, while others suggested that the HDECs should be hosted and administered other than by the Ministry of Health in future.

**Definitions.** Seven submitters felt that the SOPs needed to provide clearer definitions around risk, adequate peer review, and conflict of interest. Six submitters asked that the definition of “investigator” in the SOPs be amended to align with international good clinical practice guidelines.

**Implementation and monitoring.** Four submitters suggested that the SOPs be formally reviewed after their introduction, suggesting timeframes ranging from six to 24 months.

## Section 1: Purpose and application

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Sixteen submitters provided feedback on this section of the draft SOPs. This feedback tended to be brief, and included comment on the need to:

* address Treaty issues in HDEC procedure
* ensure consistency with NZ law and policy, and with international standards for ethics committee review
* ensure that the SOPs do not dilute ethical standards for health and disability research
* provide resources and training to achieve consistency in HDEC review.

Other respondents commented that the proposed purpose was clear and appropriate in the draft SOPs.

## Section 2: The role of HDECs

Thirty-four respondents commented on this section of the draft SOPs. The most frequent comments related to the separation of ethical review from review of scientific validity, the lack of specificity around what constitutes peer review, the separation of locality review from HDEC review, and the timing of consultation with Maori and other cultural groups in the application process.

**Peer review.** Nineteen submitters commented on the need for greater clarity around what would constitute “appropriate” peer review, with some noting that varying levels of thoroughness of review might be appropriate for differing levels of risk. Eight respondents noted the need for clarity around the related issue of what might constitute appropriate *evidence* of peer review in the context of HDECs applications.

A clear theme of feedback received on this section was that HDECs should continue to be able to ensure that research is based on sound science, and to require further peer review on specific issues in applications if need be.

Other feedback on the role of HDECs in peer review included that:

* while requiring peer review prior to application will streamline the HDEC review process, it could slow down approvals for research in NZ
* some researchers may not have access to peer review or to potential reviewers without conflict of interest
* the peer review requirement will place increased burden on institutions
* the need for peer review could create a new tier of bodies to assess and approve scientific validity.

**Locality-specific governance issues.** Two respondents commented that locality-specific issues might have ethical implications, and that removing these issues from the HDEC review process as proposed could reduce protections for participants in research.

Other comments relating to locality governance included:

* that evidence of locality approval should be required before HDEC approval
* a request to clarify consequences for research carried out without locality approval
* that localities may need resources to carry out their role.

**Legal advice.** One submitter felt that HDECs should be able to withhold approval where they believe that a study may raise unresolved legal issues.

**Consultation with Māori and other population groups.** Several respondents raised concerns about the draft SOPs proposals on consultation. Nine noted that Māori consultation is currently usually done as part of locality review, and is hence carried out in parallel with HDEC submission, whereas the draft SOPs suggested that it should be carried out before HDEC review. There was concern that this could create a barrier to study approval.

Five respondents thought the determination of need for Maori consultation should not be left to researchers, and that clear guidelines would be needed for whether or not such consultation should occur. One respondent suggested that HDECs should be allowed to evaluate the ethical relevance of concerns raised during any such consultation.

## Section 3: Scope of HDEC review

Thirty-two respondents commented on this section of the draft SOPs.

The most frequent responses related to the draft SOPs’ proposals for reducing the scope of HDEC review to focus on higher-risk research. This included concern about what would happen to research that would fall outside the scope of HDECs and work displaced onto other committees, and the relationship between HDEC review and ability to publish results in peer-reviewed journals.

**Restricting the scope of review.** A number of submitters considered that the scope of HDEC review proposed in the draft SOPs was too restrictive, and too focussed on drug trials. Some submitters considered that *all* intervention and observational studies should be reviewed by HDECs, while others made a wide variety of specific suggestions as to which research should continue to be included in the scope of HDEC review. These included research involving:

* human tissue
* medical devices, regardless of class or risk
* medical professionals and other DHB staff
* linked data sets
* qualitative research
* large databases
* the establishment of tissue banks.

**Student research.** Twenty-two respondents considered that whether or not a study is being carried out for an educational qualification should have no bearing on how it is treated by the HDEC review process.

“Many studies being conducted by Masters students satisfy all the requirements for full review in terms design, source of participants and risk. It is completely artificial to put this division on what requires HDEC review and is opening up a loop hole for researchers to choose the form of ethical review that a study will receive.”

On the other hand, one respondent specifically supported removing student projects from the scope of HDEC review.

“[We are] pleased that student research (except intervention studies at or above doctoral level) has been shifted from the mainstream agendas of full ethics committees. University ethics committees can, and should, take responsibility for overseeing and approving these studies. This will also lessen the workload of HDECs.”

**Definitions.** Ten respondents thought that clearer definitions of "low-risk", "minimal risk," and "more-than-minimal risk" would be required. Four submitters thought that the definitions of observational studies and intervention studies contained in the draft SOPs were too simple, and that these needed to be checked for consistency with the NEAC guidelines. Others asked that the medical device risk classification be based on New Zealand (rather than Australian) rules.

## Section 4: Applying for HDEC review

Twenty-two respondents commented on this section of the draft SOPs, with general support for the Government’s decision to introduce an electronic application system for HDEC review from 1 July 2012.

**Study documents.** The majority of submissions on this section related to the documents that must be submitted with applications for HDEC review, with comments largely focussed on the draft SOPs’ proposal that not all study documents be required to be submitted. Submitters from the clinical research sector noted that international audit requirements would require all study documents be submitted and acknowledged. Others considered that HDECs should continue to be required to review all information to be provided to participants in studies, and questioned the usefulness of “common sense’ as a criterion in deciding what should be submitted.

Six respondents thought the SOPs should provide greater clarity as to what might constitute evidence of peer review, with one respondent asking what would happen if peer review was neutral or not entirely favourable.

Other comments included that more than one version of a document type (such as investigator’s brochure) might need to be submitted for the same study, and suggested that this be envisaged in the draft SOPs and the electronic application system.

**Transition to electronic applications.** Some submitters raised concerns about the process of transitioning to a new electronic application process, noting the need to ensure that the new system was secure and that all parties were adequately trained in its use.

**Sub-studies.** Three respondents considered that the requirement to include all sub-studies on the initial study application might be too restrictive, and could stymie research in some cases.

## Section 5: The full review pathway

Thirty-one respondents provided feedback on this section of the draft SOPs.

**Scope of full review pathway.** A number of submitters suggested that the scope of the full review pathway proposed in the draft SOPs was too restrictive, and made specific suggestions were made as to which studies should remain within this scope, including:

* all intervention studies / clinical trials
* studies involving medical devices other than class III and active implantable medical devices, particularly class IIb devices
* studies involving new surgical procedures
* trials of probiotic use in serious illness
* qualitative research
* studies involving large databases.

“The category for the full review pathway is restrictive. It appears that all observational studies will be considered under [the] expedited review pathway regardless of risk, while intervention studies without the use of medicines or medical devices will be excluded from full review (e.g. dietary or physical intervention).

Three submitters specifically questioned the definition of “vulnerable”, taken from NEAC’s *Ethical Guidelines for Intervention Studies.*

“In my view, the categories of vulnerable people are much wider than those stated in the ethical guidelines for intervention studies. For example, in the list of vulnerable people set out in the ethical guidelines for intervention studies there is no recognition that people who have formerly suffered a mental illness may remain vulnerable in some circumstances. People involved in research may be vulnerable because of the nature of the research and their lack of understanding of what is occurring.”

Other respondents felt that the proposed scope of the full review pathway was not clearly based on risk, or was unclear. Specific suggestions for areas requiring clarification included the definitions of “new medicine” and “standard treatment”.

**Who decides?** Two submitters suggested that the draft SOPs could be clearer as to who decides whether an application meets the criteria for full review, and whether the HDEC chairs could override such decisions. Other submitters made a variety of suggestions as to who should decide whether a given study requires full or expedited review, such as the HRCEC or an independent body. Two submitters considered that it would be inappropriate for such decisions to be made by the HDEC secretariat.

Three submitters requested that the SOPs clarify how amendments to previously approved studies would be reviewed, and whether this would necessarily be done by the HDEC that had approved the original application.

**Review clock.** Three submitters suggested that the SOPs should provide greater clarity on when the 35-day review clock should start, that the review clock should not include weekends and holidays, and that the SOPs should more clearly emphasise that 35 days is the upper limit rather than the norm.

**Agendas and minutes.** Seven respondents thought that the discussion timeframes for meetings were unrealistically short and restrictive, and could compromise decision quality. Two respondents considered that electronic notification of information in the “noting” section of the agenda should go to all signatories, including localities and DHBs. Other submitters were concerned that study protocols would be excluded from the documentation circulated to HDEC members with the agenda papers, and argued that all documents should be included.

Five respondents requested a timeline for publication of minutes, and notification of where and when meetings would be held. One respondent pointed out that references to "minutes" in this section should read "draft minutes" until they are confirmed by the committee.

**Quorum.** Six respondents commented on the draft SOPs’ requirements for quorum, suggesting that members should be able to teleconference or videoconference rather than being required to attend in person, quorum should be *six* members (rather than five) including one Māori member, and co-opted members be from the same membership category as those they replace.

**Attendance of investigators and sponsors.** Three submitters thought that study sponsors ought to be allowed to attend meetings alongside investigators, in part because they may be best-placed to answer the committee's questions.

“[Investigators] and sponsors often find that questions asked in the response letter from ethics are difficult to decipher. This often results in the PI and sponsor not being about to answer the question adequately, as they never really understood what was being asked. This issue could be rectified significantly if the sponsor’s representative was able to attend the meeting and listen to the discussion.”

**Other.** Other submitters suggested that HDECs ought to be able to require researchers to leave the meeting room during their discussions, that researchers be able to attend meetings by videoconference (as well as by teleconference), and that further guidance was required around observer attendance to ensure respect for intellectual property.

## Section 6: The expedited review pathway

Twenty-one respondents commented on this section of the draft SOPs. Many comments were similar to those received on the previous section (“The full review pathway”), including the need to clarify:

* the scope of the expedited review pathway, and base it clearly on risk
* who would decide the review pathway appropriate to a given study
* that holidays and weekends did not count for the purposes of the 15-day timeline for expedited review.

Other submitters asked that the SOPs specifically note that studies involving medical devices other than class III and active implantable medical devices would come within the scope of the expedited review pathway.

Four respondents suggested that applications for expedited review ought to be able to be reassigned to the full review pathway in certain circumstances, such as when sub-committee members could not come to a unanimous decision on them.

**Role of the Chair.** Ten respondents expressed concern with the draft SOPs’ proposal that the chair act as the final decision-maker in the expedited review pathway, with other sub-committee members (if any) taking an advisory role. These respondents considered that this process could provide insufficient safeguards for research participants, undermine robust ethical review process, overburden the Chair, and be inconsistent with consensus decision-making expectations. Two respondents thought that sub-committee review of some or all items of business should require the involvement and agreement of at least one member besides the chair.

*“We consider that the Chair is overly empowered in his/her decision making under these provisions and urge stronger rules around the requirement to consult with and be guided by a subcommittee of ethics committee members.”*

*“Review by a single person should not be considered an adequate safeguard for the public, and gives the appearance of considering speed of processing to be more important than participant safety. We recommend that the guidelines be revised to require review of all applications by at least two people.”*

One respondent thought that the ability of the chair to replace him or herself with any other member of the HDEC would violate the principles of natural justice.

**Process and documentation.** Five respondents requested that the SOPs clarify what documentation occurs around sub-committee meetings and decisions, including recording of outcomes in minutes, and issuance of decision letters, noting that applicants will need notification in writing of the review outcome. Two respondents considered that decisions taken in the expedited review pathway should be required to be ratified by the full committee.

## Section 7: Decisions open to HDECs

Nineteen respondents provided a variety of comments on this section of the draft SOPs.

**Approval conditions and letters.** Submitters suggested a range of changes to the draft SOPs, including:

* a five-year limit for HDEC approval, with a new application required after that time
* greater clarity around how much time can elapse between approval and commencement
* requiring that intervention studies have *applied for* registration before they commences, rather that requiring them to be so registered before they commence
* replacing “locality approval” with “local research governance processes” in approval letters, to ensure that localities do not give approval prima facie
* ensuring that localities be informed of any extension in a study’s duration
* giving HDECs four *working* days to notify applicants of decisions
* requiring HDECs to check that all conditions of approval (including registration and locality approval) have been satisfied before allowing the study to proceed.

**Declined letters.** One respondent queried whether applications that had been declined would go back to the same committee if they were submitted a second time, and whether they would retain the same ethics reference number.

**Provisional approval.** Two respondents thought that HDECs should not use the "provisionally approved" category at all, as this category was seen to be confusing and changes required in provisionally approved cases are not monitored or checked by the HDEC.

*“[Provisional approval] is very confusing. The researcher either has ethical approval or not. Principal investigators often think that once they have provisional approval they can commence their study.*

Other respondents considered that:

* the task of checking a response to a request for further information and making a final decision should not be delegated to the HDEC secretariat by the HDEC
* researchers should be able to contact the HDEC itself (rather than the secretariat) with questions regarding unclear approval conditions
* HDECs should provisionally approve studies for which SCOTT approval and Māori consultation was pending
* clarification was required on the timeframe within which HDECs should notify applicants that a response has been deemed incomplete.

## Section 8: HDECs and the ACC Act

Fourteen respondents commented on this section of the draft SOPs.

**Informed consent.** Five submitters emphasised that participants in clinical trials must continue to be adequately informed of whether or not they will be able to access compensation for injury through ACC as part of the informed consent process. It was suggested that an independent third party (such as the Office of the Health and Disability Commissioner) could check that this was the case.

Other respondents considered that:

* HDECs should not rely on sponsors, localities or investigators to ensure that appropriate arrangements are in place
* the SOPs should contain a clearer definition of what might constitute “credible assurances from the sponsor and the PI”
* the standard compensation offered by some sponsors might be in excess of that available under ACC
* protection would be required for participants in the event of the bankruptcy of parties to clinical trials.

## Section 9: Challenging HDEC decisions

Nine respondents commented on this section of the draft SOPs.

**Challenge by third parties.** Four respondents considered that third parties, such as members of the public and prospective participants, should have the same rights as applicants to formally challenge HDEC decisions.

“We are of the view that [not allowing third parties to challenge HDEC decisions] unnecessarily restricts the right of public scrutiny of public decisions and may conflict with the right to seek judicial review. Given past history of ethical decisions in New Zealand, we view this with concern.”

Other submitters considered that:

* the SOPs should more clearly highlight that only investigators can challenge HDEC decisions
* the HDEC secretariat should not have any role in advising HDECs as to whether their decision-making process accords with the SOPs
* complaints should be heard by an independent third party, such as the HRCEC
* the HRCEC should not have the power to “undermine” HDECs through an appeal process
* the rules on challenging HDEC decisions set down in the draft SOPs were clear and appropriate.

## Section 10: Locality review

Twenty-four respondents commented on this section of the draft SOPs.

The most frequent responses related to concern about risk associated with distancing the HDEC from the locality review process, and to the assertion in the SOPs that as observational studies do not have localities they do not need locality review.

**Definition of “locality”.** Five submitters suggested that the definition of “locality” be extended to include observational studies, where appropriate. Two respondents considered that the directive that observational studies need to obtain management approval from organisations involved in their studies is confusing, as “management approval” and “locality approval” are the same thing in most research institutions.

Three respondents noted that the SOPs relating to localities may not work well for research involving general practices.

*“In general, the Locality Assessment section doesn’t appear to work well for research involving general practice. What constitutes a “locality” is unclear in these circumstances. The document states it should be the organisation responsible for a hospital, surgery etc, but it is unclear what degree of “responsibility” is meant with respect to ownership and/or governance particularly for organisations like general practice and those with overlapping governance.*

One respondent noted that the draft SOP would work well where there is a research office in place, but might pose risk where this was not the case.

**Who is responsible?** Two respondents noted that investigators and sponsors may not necessarily be able to ensure that an appropriate person has completed locality review, and suggested that the SOPs clarify that the "local study team" be responsible for ensuring this. One submitter considered that the requirement for locality approval to be completed by a manager should be tightened further to require delegation from the CEO in all circumstances.

**Issues relevant to locality review.** Five respondents noted that this section (as with sections above) should be applicable to all studies, not just intervention studies. Other comments included:

* provisions relating to local cultural issues, other local staff, and information for those who may not adequately understand English need to be more clearly defined, including, for example, clear guidelines on what constitutes “reasonable steps”
* HDECs should continue to check the suitability of each locality’s investigator, local cultural issues, provision of information to those for whom English is not their first language, and local participant information sheet and consent forms.

**Oversight of locality approvals.** Five respondents disagreed with the draft SOPs’ proposal that HDECs not need to be notified when locality review approval had been granted, and considered that locality approvals ought to be monitored in some way by HDECs (or notified to all parties to a study).

Other submitters raised issues around:

* cancelation of locality approval, suggesting that all locality cancelations ought to be notified to the HDEC, and questioning who should be responsible for deciding whether further action needed to be taken by the HDEC and other parties in such circumstances
* changes in lead investigators at localities, noting that immediate cancelation of locality approval could lead to serious interruption or termination of research, and suggesting that the rules allow for an interim lead investigator to be appointed.

**Other.** Other comments included the need to ensure that training and resources for locality review are appropriate, the possible introduction of “research passports” to ensure competence, and the standardisation of locality review forms and processes.

## Section 11: Amendments to approved studies

Eighteen respondents provided feedback on this section of the draft SOPs.

**Definition of “substantial amendment”.** Most feedback on this section related to the need to distinguish clearly between “substantial” and “non-substantial” (or minor) amendments. Ten submitters considered that the draft SOPs were not sufficiently clear on this point, or that some of the examples of “non-substantial” amendments were inappropriate.

“[We] would like some clarification on what constitutes a ‘significant change’ or ‘significant degree’? We consider the wording here to be overly subjective and reliant on the researchers discretion. We urge the development of much clearer guidelines about what amendments require approval. It is our perspective that anything other than extremely minor administrative changes should be notified to HDECs and the committees themselves ascertain whether approval is required.”

Eight submitters thought that researchers should not have the power to decide whether or not a given amendment to a study was substantial, and suggested that all proposed amendments go to a third party (possibly the HDEC chair, who might consult with others) to determine whether review was required.

Five respondents asked that the SOPs be amended to confirm that HDECs would continue to acknowledge the submission of "non-substantial" amendments, as might be required by sponsors and auditors to demonstrate compliance with international good clinical practice guidelines.

Three respondents suggested that all substantial amendments should be approved by at least two people in addition to the Chair, or that a delegated authority be used to approve non-substantial amendments.

**Other.** Other comments on this section included the need for HDEC process to recognise that multiple minor amendments could constitute a substantial amendment, and the suggestion that all amendments be attached to the application in the electronic applications database.

## Section 12: Post-approval processes

Nineteen submitters commented on this section of the draft SOPs.

**Annual progress reports**. A variety of comment was received on the draft SOPs’ description of annual reporting processes.

* Three submitters suggested that the SOPs require acknowledgement letters for annual progress reports to include start and end dates for re-approval, as required by some study sponsors and auditors.
* Three submitters noted the difficulty of producing local safety information specifically for the proposed “annual safety report”, which would be required for studies involving a new medicine. These submitters suggested that the SOPs allow researchers and sponsors to align the timing of reports with other jurisdictions, and specify that international safety documents (such as the executive summary to safety reports required by European regulator) be able to be used, with extra commentary from the New Zealand researcher if required. One submitter considered that annual safety reports be required for studies other than those involving new medicines.
* Two submitters suggested that a standard form be used for annual progress reports, and that these be recorded electronically in the online application system, and that other parties to a study be informed of when an annual progress report was due.

**Individual reporting of SAEs and SUSARs.** Eleven respondents did not support the draft SOPs’ proposal to remove the requirement for serious adverse events (SAEs) and suspected unexpected serious adverse reactions (SUSARs) to be individually reported to HDECs. Some of these submitters considered that this change would be inconsistent with the HDECs’ role in protecting participants, and could create an undue burden of risk on communities.

“Researchers must be required to report adverse effects of clinical trials, so that decisions about continuing or terminating research are open to scrutiny and review of the risks and health and safety concerns of participants.”

Submitters suggested that an independent body could be empowered to review SAEs on behalf of the HDECs, and that studies should be able to be halted on the basis of SAE information.

**Protocol deviations and violations.** Six submitters commented on the draft SOPs’ requirements for reporting deviations and violations, suggesting:

* that the draft SOPs would not be consistent with international rules on the reporting of deviations and violations
* greater clarification of what constitutes a "substantial" deviation or violation
* the insertion of the word "prior" before "knowledge" in par 206
* greater clarity in the SOPs that deviations and violations should not occur, and that all fraud or misconduct should be reported to the HDEC.

**Final reports.** Four submitters commented on the draft SOPs’ provisions on final reports. Two submitters considered that final reports ought to be required for all studies, and that HDECs should not simply close studies where they had not been received. Others noted that final reports for global studies would not be available until the conclusion of study worldwide, which may not be within the proposed timelines for HDEC final reporting.

## Section 13: HDEC review of tissue banks

Seven respondents commented on this section of the draft SOPs.

**Cultural issues.** Three respondents were concerned that the draft SOPs did not clearly require HDECs to give adequate consideration to cultural issues around tissue collection and storage, particularly in relation to Maori tikanga.

“The Board is concerned that no consideration has been given to Māori cultural issues in regard to tissue banking in the review of HDEC. Tissue management, storage and retention have important cultural significance for Māori. How will the mana of Māori be safeguarded to ensure cultural safety is actively addressed?” (22, Maori Review Office)

**Other.** Two submitters felt that the SOPs should be amended to require HDEC review for the establishment and management of *all* new tissue banks. Other comments suggested a need for:

* clarification of what might constitute appropriate peer review for studies using banked tissue
* standard policies for all tissue banks, including a requirement that tissue not be used without consent
* specific retention timeframes for tissue and associated information
* a national registry of tissue banks in New Zealand.

# Feedback on draft HDEC application form

Thirty four respondents commented on the draft application form.

## Overall comments

Twenty-five respondents provided overall comments on the draft form. Six of these respondents expressed explicit support for the draft form, and considered that it would be likely to improve the process by making it simpler and more focussed on ethical issues.

*“This appears to be a far clearer, fairer process which is more in line with overseas systems particularly the Australian submission process.”*

However, three respondents thought that the draft form would be unlikely to significantly improve the HDEC review process, while others considered that it would not be appropriate for all types of research (including qualitative research or research on health services providers).

*“We […] are broadly content with the new application form, though we are unconvinced that this is a matter where all that much positive change will be affected.”*

Several submitters suggested ways in which the form could be improved, including: making better use of colour and tone to make the form more user-friendly for people with visual impairments; using a simpler numbering system for the form’s sections; and replacing the “four principles” with those in the current *Operational Standard* and NEAC guidelines, plus the three Treaty principles. Other submitters suggested that terminology in the form be amended for consistency with international good clinical practice guidelines.

Other overall comments on the draft form included: detailed suggestions around training and support for the online application process, including online tutorials, 0800 phone numbers, tool tips, hyperlinks, and an appropriate lead-in time; concern at the brief word limits proposed for some questions; the need to ensure the form and application process were accessible to localities; and a need to strengthen Treaty provisions of the form.

## X – Administrative section

Sixteen submitters commented on this section, with most suggesting minor changes to the wording or order of questions.

Two respondents thought requiring researchers to describe the object, phase and design of the study (as per question x.2) could result in studies being “pigeon holed”, and suggested that asking researchers to give a brief summary of the design might give ethics committees more meaningful information. One respondent suggested

Two respondents considered that some of the compulsory questions might not be appropriate for all studies. For example, some studies may not have a sponsor (question x.5), while others would not use their own, separate reference number (question x.1.3).

## B – Research should produce benefits

Nineteen respondents commented on this section. Many of these comments were around proposed word limits and specific wording changes to questions.

Four respondents noted the need for clarity around what constitutes suitable evidence of peer review, with one highlighting that clarity is particularly needed in regard to reviews that are conducted by experts within the research team or senior colleagues in the field. (This point was also made in submissions on the draft SOPs.) One respondent considered that the “mere promise” of a future peer review is not appropriate, and suggested that a short report summarising the findings of the peer review and names the peer referee or organisation be submitted when an application is made.

Three respondents commented on the requirement to provide a Universal Trial Number (UTN), which they considered may not be applicable to some studies. One respondent submitted that the requirement for a UTN would add “unnecessary complexity” to the HDEC submission process, and submitted that registration was not necessary for early-phase trials.

Two respondents thought that this section of the document needed to make clearer reference to the benefits of research for Māori. One respondent suggested that researchers should be required to demonstrate a consultative process regarding how any cultural risks to Maori have been identified and how they will be managed.

## R – Research should minimise and manage risk

Fourteen respondents commented on this section of the draft form, with most comments offering suggestions for minor changes to questions.

A range of feedback was received on the draft form’s questions on monitoring of safety data. Two respondents asked for clarification on how this will be done, while one expressed concern that the form did not require external data monitoring for all studies. Others suggested that an independent New Zealand data safety monitoring committee should be in place to ensure New Zealand participants are protected.

Five respondents commented on this section of the form in relation to tissue banks, with one suggesting that HDECs should be informed of whether tissue sent overseas for diagnostic purposes could be identified.

## P – Research should respect persons and populations

Sixteen respondents commented on this section of the draft form, suggesting a number of changes to question wording.

Eight submitters commented on section p.4 of the draft form, which dealt with consultation with Māori and other populations. Comments included that:

* researchers should be required to address culturally appropriate ways to recruit Maori into research, collect and store tissue samples and disseminate findings
* question p4.1 could make it easy for researchers not to carry out Maori consultation
* more clarity is required as to whether a letter from Māori review committees should be mandatory prior to submission, approval or commencement of a study
* an explanation of “kaupapa Māori methodologies” should be provided.

Seven respondents commented on the use of the ‘FOG index’ at question p2.5 as a proxy for readability. Five respondents requested clearer guidance on what FOG requirements will be acceptable to HDECs, or an explanation of why the data is being collected. Two respondents considered that the FOG index would not be a suitable tool for determining readability.

## F – Research should be fair

Thirteen respondents commented on this section of the draft form. As with other sections, many of the comments focused on minor changes to the questions contained within the section.

Other comments raised the need to:

* ascertain whether on-going treatment would be available to study participants, and to develop clear guidance for this for clinical trials in New Zealand
* consider whether questions about placebo would more properly be considered elsewhere in the form’s structure
* provide a clearer definition of “best proven intervention”
* clarify why researchers are to be asked about the potential for adverse impact on services for non-participants
* ensure that research adequately addressed issues of fairness for Māori.