NHMRC
NATIONAL SCIENTIFIC COMMITTEE
FEASIBILITY REPORT

August 2018

Bellberry Limited
supporting research and ethics

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2. Introduction

As part of its work to support a nationally-consistent approach to the way human research (including clinical trials) is conducted and overseen, the National Health and Medical Research Council (NHMRC) piloted National Scientific Committees. The National Scientific Committees (NSC) were established to provide specialist advice to Human Research Ethics Committees (HRECs), sponsors and researchers on complex genetic research and clinical trials involving medical devices. Part way through the pilot, the remit of the National Scientific Committees (NSC) was extended to include Early Phase clinical trials. This change was made in response to the nature of the enquiries that were being received.

As set out in the Terms of Reference (Appendix B), the function of the NSCs was to assess studies, and provide an opinion to the applicant (HRECs, sponsors or researchers) on the scientific merit and integrity of the research protocol. The NSCs were designed to provide an expert opinion in an advisory capacity and not to undertake ethics review, or provide ethics approval for human research. HRECs were free to consider advice from a NSC meeting as equivalent to 'scientific review' (or not), but not as a review that replaced the deliberations of an HREC.

Following an open tender process, Bellberry Limited (Bellberry), a national, private not-for-profit company, was appointed host organisation for the NSC Pilot. Bellberry provided secretariat and administrative support to the NSCs. The NHMRC provided funding to Bellberry to cover the costs associated with the pilot project, including funding for the review of up to 30 unique applications.

3. Purpose of the Report

This report provides a summary of the National Scientific Committees (NSC) pilot, including the process, and analysis of the performance metrics as outlined by the NHMRC at the initiation of the pilot. The report also provides feedback on the successes and challenges of operating the pilot scheme, along with recommendations for any potential ongoing use of NSCs in Australia.

The report is prepared from the perspective of Bellberry as the manager of the NSC. Bellberry understand that the findings in this report will be used by the NHMRC to inform future policy and may be provided to the Therapeutic Goods Administration, and the states and territories to inform clinical trials initiatives.

4. The Structure of the NSC

At the commencement of the pilot, NHMRC and Bellberry developed a website (www.nationalscientificcommittees.org.au), Terms of Reference (ToRs) and Standard Operating Procedures (SOPs) for the NSC. NHMRC also developed a reviewer checklist to support the operation of the NSC. The ToRs, SOPs and Reviewer Checklist are included as appendices to this report.

Bellberry was responsible for the day-to-day management of the NSC. NHMRC provided policy oversight and advice on the scope of the pilot as required.

Members of the NSC were identified by Bellberry and, subject to NHMRC approval, engaged by Bellberry under its standard contractor engagement practices. Prior to appointment, NHMRC assessed the background and experience of each potential member, via a CV review and the conduct of an internal check. This check was to satisfy the NHMRC that a potential member had not, to NHMRC's knowledge, been the subject of recent findings of research misconduct or breaches of the *Australian Code for the Responsible Conduct of Research*, or recent formal notifications to NHMRC on research misconduct matters. Bellberry was not aware of the substantive content of the research integrity

checks and relied on timely feedback from NHMRC to complete integrity evaluations prior to the member joining the panel.

A Panel of Members was established to support the reviews for the NSC. The Panel was the pool of expert reviewers available for appointment to review relevant applications by a NSC Committee.

An initial Panel of members was identified and appointed in a proactive manner through direct approach. These members were appointed in anticipation of any specific meeting or proposal, and based on expertise expected to support the identified areas of scientific review in Genetics and Medical Devices.

However, applications received through the pilot were of such a diverse nature, that further expertise was needed. Additional members were therefore approached and added to the Panel as needed for specific applications. Panel members were very positive about the pilot and generous in their willingness to join. Most panel members who declined the offer of membership were still supportive of the concept, but time-constrained.

By the end of the Pilot, professionals in the following specialist areas had been engaged by Bellberry to serve on the NSC at one or more meetings (as needed):

- Cardiology
- Clinical Pharmacy
- Cosmetic
- Dermatology
- Endocrinology
- Epidemiology/Biostatistics
- Medical Devices
- Molecular & Cellular Immunology
- Neurology
- Oncology
- Ophthalmology
- Orthopaedics
- Paediatrics
- Pathology (specialising in Genetics & Molecular Pathology)
- Pharmacology
- Pharmacokinetics
- Pharmacotherapeutics
- Respiratory
- Toxicology

5. Overview of Applications Received

The initial scope of the pilot was to consider applications in the areas of (1) complex genetic research and (2) clinical trials involving medical devices. This was based on input that the NHMRC had received as the areas where support was needed.[1] However, during the course of the pilot, it became apparent from inquiries received that early phase clinical trials, more generally, were also a key area of need. Therefore, the scope of the pilot was expanded to include early phase clinical trials.

[1] In accordance with the findings of NHMRC's *Report to Assess the Feasibility of Establishing a Credentialing System for Ethics Review of Multi-Centre Clinical Trials in Australia*.

Summary of Applications

Over the course of the pilot, Bellberry received 65 enquiries about the NSCs. There were 21 applications submitted for review, as follows:

Applicant	Number
Sponsor/CRO	7
Independent Researcher	1
HREC	13

Type of Application	Number*
Complex genetic research	1
Clinical trials involving medical devices	3
Early phase clinical trials	19

**Some studies fit into two of the categories*

One submitted application did not proceed to Committee review. Due to the specific characteristics of the project, it was not possible to identify an individual to complete the quorum who had the appropriate expertise and also met the requirements relating to independence as defined in the Terms of Reference.

6. Operation of the Committees

Timing of Meetings

Initially, the plan was to establish set meeting dates for each committee type (Genetics, Devices, and Early Phase Clinical Trials). However, to support the applicants more effectively, it was decided to schedule meetings as needed, based on applications received. Whilst requiring more administrative support, this flexibility enabled the scheduling of meetings based on when an application was submitted, rather than fitting in to predefined dates. This resulted in a shorter timeframe for the review of each new application.

Constitution of the Committees

Each Committee meeting was constituted according to the expertise each application required. Where possible, a number of studies were reviewed at one meeting. However, in those multiple study meetings, the committee members changed for each study across the meeting, in order that the quorum reflected the expertise required for each review. Again, this flexibility gave the most effective support for the applicants in providing efficient timeframes for review based on when the applicants submitted their application. It also allowed consolidation of the reviewer's time where they could provide review across more than one study. Whilst this did not affect the cost per review paid to the reviewing member, it was time efficient for reviewers to review more than one study at a single meeting rather than separate meetings. It was also helpful administratively to maximise the number of studies being reviewed at the same meeting, thereby minimising the number meetings to be arranged.

The quorum of the Committee was generally the Chair and three expert members, in line with the Terms of Reference. For two studies, an additional fourth member was included to complement the expertise required. Whilst the Chairs also had scientific expertise, it was considered important that the Chair role remain separate from a reviewer role in conducting the meeting and ensuring a robust and comprehensive review process. The provision of an independent Chair was enshrined in the terms of reference.

Activity of the Committee

There were a total of 11 meetings held to review the 20 applications:

- 2 meetings where 3 applications were reviewed
- 5 meetings where 2 applications were reviewed
- 4 meetings where 1 application was reviewed

The average time from submission of a complete application to meeting was 22.3 calendar days. 70% (14/20) of applications were reviewed in under 22 days from submission.

The additional timeframe for five of these studies was due to their submission in mid to late December 2017. It proved to be a challenge to identify members with the appropriate expertise and establish their availability over the Christmas to January holiday period. It is noted that many HRECs shutdown during December and/or January for similar reasons. For the other study, additional time was required to include an available reviewer with the appropriate expertise.

For every application, each Committee member provided comment against the review criteria provided in the NHMRC review checklist. The NHMRC review checklist concludes with an overall assessment of the application as being of "High Quality", "Satisfactory" or "Deficient". Three applications were considered to be of overall High Quality, and six applications were considered to be Deficient and needing significant revision and further supportive work. The remaining applications were considered to be Satisfactory. These terms were used to provide an overall categorisation of the quality of the applications against the review criteria. High Quality indicated the criteria were generally well met. Satisfactory indicated criteria were met, however further information was generally required. Deficient indicated that the NSC recommended that significant further information or protocol revision was required.

The Committee opinion was presented using a template prepared by the NHMRC.[2] Each committee reviewer provided an independent assessment prior to or at the meeting. All comments were then discussed at the meeting to form a consolidated opinion of the NSC that was subsequently sent to the Applicant.

7. Perspectives about the NSC

An important outcome measure of the pilot was to capture the perspectives of relevant stakeholders – applicants, panel members and HRECS using the review. In addition to general feedback received, surveys of Applicants, Reviewers and HRECs were conducted at the end of the pilot to formally seek feedback. Across the groups there was strong support for the concept of the NSCs.

[2] See appendix F.

The ambit of the pilot was that the review and opinions of the NSC were a scientific opinion only, and were completely separate to any HREC review (including a Bellberry HREC review).

One issue identified was the lack of awareness of the NSC pilot across sectors and with potential users. It was a challenge in the initial stages, and throughout the pilot, to establish the best avenues to build awareness of the NSC. Early and repeated efforts by NHMRC to promote the NSC pilot through its HREC and industry contacts did not lead to a significant improvement in uptake. This trend turned around somewhat with the expansion of the pilot to include early phase clinical trials in mid-2017. Once the NSC met the need of the sector, interest increased.

Applicants

Over 90% of the applicants surveyed thought the review and opinions provided by the NSC were helpful. The following feedback was provided:

> *"Very good quality opinion. We had hoped for it to be a substitute for independent toxicology review but that was beyond the scope of the pilot. Helpful nonetheless"*
>
> *"The NSC seemed to understand the request we were making for a straight to phase 2 trial given the established safety profile of the active ingredient, albeit a different formulation. Our concern over this was the reason we engaged the NSC, for their opinion on this. We have just received HREC cycle 1 comments back on the application. It is a little frustrating that the NSC supported the straight to Phase 2 nature of the trial, whereas the HREC responses suggest this is not fully supported as additional, logistically difficult assessments are being requested, more in keeping with a phase 1 trial. More harmonization between the NSC recommendations and the HREC decisions would make this process more worthwhile."*
>
> *"The review was delayed, as the panel was unable to meet in January, so it took longer than we expected."*
>
> *"Would like inclusion of more therapeutic areas as Sponsors are keen to review their protocol and study design."*
>
> *"The (Application) form is fairly straightforward but I'd suggest some improvements. It would be nice if it is an actual form with fields (e.g. instead of highlighting the options using Word highlighting function, you may want to have check boxes). Also, in section 1, it was a bit unclear who should be the "Nominated Contact". It would be nice to have instructions that go with the form."*
>
> *"It was a difficult time of the year to submit (around Christmas) and I understand there was some delay and difficulty in finding committee members due to the time of year. However once the committee met, I had a response very quickly."*
>
> *"The process is good. It would be helpful if we can have online submission/review. Also, if sponsor representative is allowed to present during the NSC discussions, it will be more productive than following with questions/responses."*
>
> *"Found the process very easy and concise. Communication was excellent and within expected timeframes."*
>
> *"I liked the transparency of the whole process and the quick response we received from NSC."*

"Very easy and straightforward, great admin help, timely responses, I was impressed with the service."

"The quick turnaround allowed client to consider alterations to the clinical development of their IP."

"The turnaround time was as promised."

"Very impressed with the process"

"It's a great programme. The fee for the review will determine how successful the programme will be."

"This service is invaluable for clinical development programs of IPs that are truly innovative and we are require some external advice. In our submission we highlighted the aspects of the trial that were of concern to us. The feedback was considered and concise."

"Very useful service. Access to national specialists is a very valuable service. This NSC approach appears to support HRECs to make difficult decisions and facilitates high quality research across the country."

"I would like to see the program extend beyond this pilot stage. It is a very useful path to seek advice early and will definitely streamline our HREC application in the future"

"The application form was simple and quick to complete, which was appreciated"

Feedback from applicants appeared to show good engagement with the concept of the NSC. Applicants were open with their views, and provided constructive suggestions for development and improvement of the NSC service. In general, feedback for the quality and content of the NSC review was good and found to be useful.

It was recognised that there were some delays over the Christmas – New Year period, however even with the longer review over that period, the average review time was 22.3 days, indicating that reviews were generally within the proposed 21 day timeframe.

The feedback also showed support for the pilot across all of the applicant sectors (sponsor, investigator and HREC). Some sponsors likened the review to having an Australian version of a pre-IND meeting. HRECs found being able to reach out to an independent expert panel a useful resource to have available. Applicants were supportive of the change in scope of the NSC to review early phase clinical trials. This flexibility represented understanding of applicant needs and the survey results showed this was valued.

Reviewing Members

The Committee reviewers understood that the pilot program was the NHMRC's program, and Bellberry was responsible for the day-to-day management of the Committees. The reviewers understood that all of the policies, study documentation and review requirements were created based on what the NHMRC thought the applicants needed from a review. Several of the Panel Members suggested that changes could be made to the checklist if there was any future for the NSC model. These suggestions were generally around flexibility in reviewing against each question, as not all questions were relevant to all submissions. The members also suggested changes to the format of the form fields in order for ease of information entry and to minimise the amount of reformatting required.

It was clear to the reviewers that the remit of the NSC was the scientific (and not ethics) evaluation of the study. Where any discussions started to lead toward more ethical considerations, the Chair and Committee brought the conversation back to the appropriate focus.

The reviewers were in general supportive of the pilot, however did also raise some differing perspectives:

> *"I believe that it fulfils a very necessary function in particular for HRECs that are unable, for whatever reason, to provide the expertise required to evaluate a scientific study. It is also very useful for companies who are seeking guidance of how to fill out an HREC application that will be treated appropriately by an HREC, as all of the requirements would have been covered before the formal application."*
>
> *"Specific information about completion of HREC applications was not provided with the NSC, however general application requirements in the discussions of the NSC applications may have proved to be useful."*
>
> *"Many of the applications were from commercial Sponsors that appeared to be taking advantage of a 'free' process to get feedback from quality reviewers. Thus, I did not 'enjoy' providing that service."*
>
> *"I felt that in several cases the process was making up for the applicant not doing their own due diligence. This is inappropriate use of the system."*
>
> *"I think it is valuable as a referral for HRECs which consider they do not have the expertise for a certain submission. I am not convinced of the merits of the NSC for sponsor submissions. In general, the NSC was providing information that could have been provided by a CRO or someone engaged by the sponsor who is experienced in regulatory matters. Further, there is a danger that the NSC's response to a sponsor will be considered to 'trump' the considerations of an HREC."*
>
> *"Mixed feelings. Can be of assistance but appeared to be open to abuse. In one case it was clearly an example of a sponsor seeking a tacit "pre-approval approval" of their fully formed protocol."*
>
> *"This should be restricted to Investigator-driven trials based on the remuneration for expert reviewers. If applications are from commercial interests, then the remuneration is not sufficient."*
>
> *"Great service for investigators with access to expert opinion"*
>
> *"I think it is worthwhile to continue this service"*
>
> *"I think it is important that Committees have access to this expertise and Bellberry are very good at finding it, and administering the process"*
>
> *"The NSC pilot was an excellent learning exercise and a step in the right direction. There is a definite need to educate and guide Sponsors who are new to the preparation of the HREC submissions. In general, there is a lack of understanding of the type and detail of data that is needed to support clinical trials, and the NSC makes an attempt to 'educate' Sponsors on data requirements. I fully support continuation to the NSC as it will potentially improve the quality of HREC submissions as Sponsors gain an understanding of the information required for a successful clinical trial application."*

"A fantastic idea and I would hope it continues."

"I think it should continue, we just need to consider that not all studies fit the single template"

"Bellberry were able to get experts specific to the topic of the applicant, which a local hospital ethics committee cannot always provide."

The reviewers agreed that the scientific review was an appropriate scope for the NSCs to provide an opinion. The reviewers were also supportive of the process in providing a one-off opinion, rather than necessarily working through cycles of responses with the applicant on an ongoing basis. The differing types of advice sought indicated that there is demand for two distinct services: (1) review of protocols for HREC review to provide independent, expert advice and (2) advice to researchers and sponsors in the development of their protocol processes and documentation.

The area of most differing opinion was in the scope of applicants that should use the NSC. Whilst the reviewers were supportive of providing an expert opinion to HRECs and researchers, there were questions about whether applications from sponsors should be reviewed under this system. Some made it clear that if the NSC was to continue they did not think it should include applications submitted by a Sponsor company.

Applicants did not pay a fee for the review of applications under the pilot. Members were remunerated a nominal amount. These members were very generous in providing reviews to support the pilot. It is however clear that for any ongoing program a fee structure for applications would need to be established to support an appropriate remuneration for reviewing members.

Of the 18 Panel Members that completed the survey, 13 have said they would be happy to continue to review future applications, while the remaining 5 would commit subject to changes to Terms of Reference and process.

HRECs

Feedback received from HRECs that utilised the NSCs was supportive of the concept and process. The main reason for using an NSC was to provide additional expertise for the HREC review.

"We found the opinions of the NSC very useful, but by default the application was also reviewed by our scientific subcommittee."

"Provides an outstanding service to HREC's where they are considering trials which require specific expertise to review."

"Would be great if this service continued!"

"Very useful pilot project. Multiple members of our committee and within our researcher's office were disappointed to learn that the pilot had concluded."

"I think it is a really valuable resource to support the HREC committee review process. We have a scientific advisory committee that makes recommendations to our HREC but our internal committee were very impressed with the opportunity to seek additional scientific input and also to have their own position supported. This was for an early phase project that is not in keeping with the majority of the projects our committee reviews. The option of external scientific input ensures the quality of research being approved is of an acceptable standard and that the scientific integrity and safety of the participants is appropriately managed. It would be wonderful to continue this service if at all possible."

The HRECs that referred proposals to the NSC indicated that they used the NSC reviews as part of their HREC review. Two of the HRECs said that, although they used the NSC, they were still required to send the application to be reviewed by their institution's scientific subcommittee. In any future program, it would be useful to engage with the HREC and institutions to determine whether there could be pathways implemented to reduce this duplication.

Bellberry views

Bellberry provided a dedicated administrator to the NSC. In addition, management support was provided in the business process development, triage of applications, identification of expertise required, recruitment of members, and oversight of the pilot. The NSCs were managed and run independently of Bellberry's HREC process.

The meetings were attended by the administrator who prepared the summary opinion report, along with the Operations Manager for oversight. Bellberry support staff were not however involved in any decisions made by the Committee.

The activity that required the greatest amount of administration time was the identification and recruitment of relevant members to ensure expertise on each application received. While there is considerable expertise available in Australia across a vast array of therapeutic areas, challenges in finding reviewers included, identifying the experts required for each study who; complemented each other's skills, fulfilled the expertise required, did not have conflicts of interest, had availability at a common suitable time, and under the pilot would accept doing the review for a minimal fee. Because of the cross section of studies submitted, it was generally the case that at least one new Panel Member was required to be recruited for most studies.

All experts identified as potential panel members were independently approved by the NHMRC. This was very relevant to the process of being NHMRC committees. It was recognised that having to not only find individuals, but to get them approved by a second body added time to the process. This may be a challenge during the establishment of a similar body to the NSC. Utilising or establishing internal systems for the review and acceptance of new members would streamline that aspect of the process for any future NSC format.

8. Costs of review

As the pilot was funded by the NHMRC, there was no fee to the applicants for the review of their submissions. Bellberry provided administrative support and management of the committees. Members were remunerated a nominal fee, as independent contractors on a per review basis

The cost considerations for any future NSC format would need to include;

- Administrative support - This is likely to be part time, however would need to be flexible and dependent upon when applications were received, and the number submitted.
- Management support - A part time role, but flexibility is required for the oversight of the Committees, triage of studies and identification and recruitment of relevant expertise.
- Resources – support of the documentation, policies, procedures and forms
- Facilities – to support staff and run the meetings.
- Committee member remuneration.

The ongoing viability of the Committees would be dependent upon establishing an appropriate application fee structure to support the resources and facilities required to run the NSC. The setting of an application fee would be based upon the cost of review, taking into account each of the above noted cost considerations.

In recognition of differences in the complexity of applications which can vary from the details of a HREC submission, it is proposed that there be a two tiered fee structure for any ongoing NSC applications. HRECs may also need to consider how they would manage those costs, whether they are covered by the institution or passed on to the applicant.

9. Summary Findings – Usefulness, Viability, Improvements

The following summarises the findings of the pilot:

- Overall, there was strong support for the NSC concept from applicants, HREC and panel members.
- While the NSC did not reach the expected number of applications over the pilot period, it is clear from the stakeholder feedback that the NSCs fill a gap in the research governance process and when independent review is required, there are limited options outside the NSC.
- Early phase studies were recognised as the key support area of need. A number of enquiries were also received on other study phases that required review by multiple HRECs.
- The viability of the NSC will be dependent upon the establishment of, and support for, an Application fee. It is proposed that this be a tiered approach on which further consultation is required.
- The concept of the Committee Panel should continue in order to build the expertise required to support the diversity of applications.
- The expertise pool in Australia is limited and international assistance is likely to be required in the future.
- In future iterations of the scheme, consideration will need to be given to how integrity checks can take place on researchers and experts outside of Australia.
- The quorum of the NSCs was considered appropriate and should remain as a Chair and 3-4 expert reviewers.
- There was strong support from those who were aware of the NSC; however, there appeared to be limited knowledge of its existence. There would therefore need to be further promotion of the NSCs through successful channels such as conferences.
- It is suggested that an NSC recruitment advertisement be published to create a larger initial Committee Panel, this should be widely advertised in publications such as the MJA.
- It is suggested that the scope for applications from HRECs be expanded to be available for any therapeutic area, and any phase in which they request additional expertise.
- Committee reviewers should be remunerated.
- The proposed 21 day review time from complete application to submission is viable. Building in flexibility, may allow timeframes to be further managed to support key dates, such as being able to provide NSC reports for the relevant upcoming HREC meetings.
- While the turnaround times are important and demonstrate an efficient and effective service, KPIs around turnaround times are unlikely to deliver the desired outputs of the NSC – high quality scientific review that is of use to applicants and reviewing HRECS. Therefore success factors of the NSC should be reconsidered in measures of timeliness of HREC approval, reduced duplication of scientific review and stakeholder feedback on the value of the NSC opinion.

- Review of all documentation related to the NSC, including Policies, SOPs, application forms, the reviewer report and the opinion report format provided to the applicant will be required. This will reflect the change from the pilot to an established service, and incorporate format changes recommended by users.
- It is recommended that the National Scientific Committees continue with consideration to these suggestions.
- If the NHMRC decision is to discontinue the NSCs, Bellberry will consider establishing these committees to continue this support for research and clinical trials in Australia.

Appendices:

Appendix A	Summary of Study Submissions **- REMOVED FROM PUBLISHED DOCUMENT**
Appendix B	Terms of Reference
Appendix C	Standard Operating Procedures
Appendix D	01 Standard Operating Procedure 02 Research of Proposals
Appendix E	Standard Operating Procedure 03 Conduct of Meetings
Appendix F	Members Review Checklist

NHMRC National Scientific Committees

hosted by Bellberry Limited

National Scientific Committees

Terms of Reference

October 2017

All enquiries and for further information about NHRMC National Scientific Committees, contact Bellberry Limited:

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Australian Government
National Health and Medical Research Council

Bellberry Limited
supporting research and ethics

BACKGROUND

The National Health and Medical Research Council (NHMRC) is Australia's peak body for supporting health and medical research; for developing health advice for the Australian community, health professionals and governments; and for providing advice on ethical behaviour in health care and in the conduct of health and medical research. As part of its work to support a nationally consistent approach to the way human research (including clinical trials) is conducted and overseen, NHMRC is piloting National Scientific Committees to provide advice to Human Research Ethics Committees (HRECs), sponsors and researchers on complex genetic research, clinical trials involving medical devices and early phase clinical trials and first-in-human studies.

The National Scientific Committees will provide advice to HRECs, sponsors and researchers on the scientific merit and integrity of a research protocol. The committees will not provide ethics approval for human research and positive advice from a committee does not constitute an approval to commence a research project.

Under this pilot, Bellberry Limited (Bellberry), a private not-for-profit company based in South Australia, will provide secretariat and administrative support to the committees established to conduct scientific reviews of applications for complex genetic research and clinical trials involving medical devices including handling applications for review. NHMRC has provided funding to Bellberry to cover the costs associated with the pilot committees.

While the Terms of Reference, Standard Operating Procedures and the membership of the committees have been approved by NHMRC, Bellberry will be responsible for the day-to-day management of the committees.

For further information about the National Scientific Committees please see:
http://www.nationalscientificcommittees.org.au/

PURPOSE

This document describes the Terms of Reference for the National Scientific Committee (the Committee).

1 OBJECTIVES

1.1 The Committee will provide independent, robust and timely expert review of the scientific merit and integrity of the following types of research proposals:

(a) complex genetic research

(b) clinical trials involving medical devices

(c) early phase clinical trials or first-in-human studies

1.2 Based on the review conducted, the Committee will provide advice to the applicant to assist them identify any specific ethical issues arising from the research proposal. The NSC will provide an opinion on the scientific and technical merit of the application, to be used to support HREC review.

2 FUNCTION

2.1 The Committee will assess studies submitted to it and provide advice to the applicant on the research merit and integrity of the research proposal, including the scientific rationale of the proposal, the appropriateness of the research protocol and representations regarding risk and benefit.

2.2 The NSC will review the sufficiency of the experimental plan and identify shortcomings. It is the responsibility of the Investigator to resolve any issues identified.

3 SCOPE OFRESPONSIBILITY

3.1 The Committee will provide advice to HRECs, sponsors and researchers on the scientific merit and integrity of a research proposal.

3.2 The Committee will not undertake ethics review or provide ethics approval for research proposals.

3.3 The Committee will review research proposals determined by Bellberry to be eligible for review by the Committee, in accordance with these Terms of Reference.

3.4 Through Bellberry, the Committee will accept applications and referrals from sponsors, researchers and HRECs.

4 ACCOUNTABILITY

4.1 The Committee will be under the day-to-day management of Bellberry, and will be accountable to the Chief Executive Officer (CEO) of Bellberry or their delegate.

4.2 The Committee will adhere to the requirements of relevant written policies and procedures as developed by Bellberry.

4.3 The Chair of the Committee may bring issues of concern to the CEO of Bellberry or their delegate.

4.4 In its capacity as host organisation, Bellberry will:

(a) Provide NHMRC with reports on the meetings of the Committee (including attendance records) and other progress reports as required;

(b) make available to NHMRC for audit purposes, Minutes of Committee meetings and records of attendance;

(c) Publish the Terms of Reference, Standard Operating Procedures and Committee membership at www.nationalscientificcommittees.org.au (the website);

(d) Provide information on matters relating to the day to day operation of the committee via the website and an appointed contact, including:

i. the lodgement and review process;

ii. the review status of a proposal;

iii. how to respond to questions from the Committee;

iv. the day-to-day management of the Committee;

v. the expertise of the Committee members; and

vi. Bellberry generally.

4.5 NHMRC will provide information on matters relating to the National Scientific Committee pilot generally, including:

(a) questions regarding the relationship between the reviews and advice provided by the Committee and review by HRECs; and

(b) questions and comments regarding NHMRC's relationship with Bellberry.

5 COMPOSITION AND SELECTION OF THE COMMITTEE

5.1 A Committee will be drawn from a Panel of eligible members. The Panel will comprise a minimum of eight members with experience in:

(a) Human genetic research;

(b) Medical Devices

(c) Clinical research;

(d) Early Phase Clinical Trials and First-In-Human studies

(e) Good Clinical Practice and TGA Requirements for biologicals and medical devices; and

(f) the review and assessment of human research protocols.

5.2 In consultation with NHMRC, the Bellberry CEO will ensure that a Chairperson is appointed to the Committee with suitable experience in one of the above areas identified in 5.1, and whose other responsibilities will not impair their ability to oversee the operations of Committee meetings.

5.3 The Chairperson should not be the Chair of a HREC to which the advice from the Committee will be provided, if known.

5.4 Potential Panel members will be identified and nominated by the Bellberry CEO for consideration by NHMRC.

5.5 NHMRC will assess all potential Panel members for outstanding or proven allegations of research misconduct. Individuals with a proven allegation of research misconduct will be ineligible to be appointed to the Panel.

5.6 Members must hold appropriate qualifications and be recognised in their field as possessing expertise in the areas outlined in 5.1, for example a Fellowship in a relevant professional college, or a senior academic position (Level D or E).

5.7 NHMRC will approve or decline to approve nominated Panel members, based on their expertise in the areas of 5.1.

5.8 NHMRC-approved Panel members will be officially appointed by the Bellberry CEO.

5.9 Subject to NHMRC approval, members may be added to the Panel at any time.

5.10 Bellberry will select a Chairperson and at least three Panel members to make up a Committee for each meeting. Members will be selected based on:

(a) ensuring that appropriate expertise is available for the review of each proposal;

(b) enabling the timely review of all studies;

(c) the availability of individual members of the Panel;

(d) assessment of any disclosed interests; and

(e) any relevant advice provided by the Chairperson.

6 MEETINGS

6.1 A quorum for a meeting will be a Chairperson and three members of the Committee.

6.2 At the meeting, the Chairperson will seek any further disclosures of interests not previously advised from Committee members and advise on how those interests will be managed.

6.3 The Committee may review one or more research proposals at any meeting.

6.4 NHMRC or Bellberry representatives may attend a Committee meeting in an ex officio capacity, subject to confidentiality agreements being in place.

6.5 Meetings may be held physically, or in alternative format such as by video or teleconferences. Where possible, all members should be present at the meeting. However, where absence is unavoidable, the Chairperson should be satisfied, before a decision is reached, that the written opinion of the absent member has been received and considered.

7 MEMBER REMUNERATION

7.1 Committee members are remunerated in accordance with a schedule developed by Bellberry, in consultation with NHMRC, and this schedule will be published online.

8 OTHER MATTERS

8.1 Committee members who review a research proposal may be able to take part in a subsequent HREC review of the same proposal, provided they disclose their involvement in the prior review of the proposal and the HREC Chairperson agrees.

NHMRC National Scientific Committees

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01

Standard Operating Procedure: Committee Chairperson and Members

All enquiries and for further information about NHMRC National Scientific Committees, contact Bellberry Limited:

129 Glen Osmond Road, Eastwood, SA 5063

P 08 83613222 **E** nsc@bellberry.com.au

Australian Government
National Health and Medical Research Council

PURPOSE

To outline the procedures for the appointment, orientation and responsibilities of Committee members in the National Scientific Committee Pilot (the Pilot).

1 APPOINTMENT OF COMMITTEE MEMBERS

1.1 The Chief Executive Officer (CEO) of Bellberry will identify and nominate potential Panel members from which Committee members will be drawn. Recruitment will be conducted via advertisement, referral or direct approach.

1.2 NHMRC will review potential Panel members to ensure that:

(a) Panel members have suitable expertise, and

(b) the Panel does not include any member against whom an allegation of research misconduct has been proven or who is otherwise excluded from receiving funds from NHMRC on conduct grounds.

1.3 NHMRC will notify the CEO of the outcomes of its review of potential members within five working days.

1.4 Once a potential member is approved by NHMRC, the CEO will appoint the member directly.

1.5 Appointment to the Panel will be on the basis of engagement as a consultant; the legal relationship between the Panel member and Bellberry is that of independent contractor. There is no legal relationship between the Panel member and NHMRC.

1.6 The appointment process will include training, induction and administrative requirements.

1.7 Subject to NHMRC approval, members may be added to the Panel at any time.

1.8 A prospective Panel member may be invited to attend a Committee meeting as an observer subject to a confidentiality agreement being signed.

1.9 The CEO will, in consultation with NHMRC, appoint a Chairperson of each Committee having regards to:

(a) the member's expertise

(b) the member's responsibilities outside of the work of the Committee

(c) the member not being the Chairperson of an Human Research Ethics Committee (HREC) to which the Committee's advice will be provided, if known.

2 TERM OF APPOINTMENT

2.1 Members will initially be appointed to the Panel for a period of 12 months or the duration of the Pilot (whichever ends first). Members will be advised when their term has expired.

2.2 Members will be provided with a written notice outlining their duration of appointment, their responsibilities and duties as a Committee member and meeting attendance requirements.

3 CONDITIONS OF APPOINTMENT

3.1 Panel members must undertake to become familiar with and be willing to fulfil the duties and responsibilities of a Committee member.

3.2 Members must sign a Confidentiality Agreement and a Disclosure of Interests form related to Committee deliberations, applications submitted for review and related matters and disclose any interests that may constitute an actual, potential or perceived conflict of interest.

3.3 Indemnity for members is provided by Bellberry for any liabilities that may arise as a result of the members exercising their duties as a member of the Committee.

3.4 Members must be willing to be trained in and utilise a web-based system, eProtocol, to undertake the review of research projects and submit comments.

3.5 Members will be remunerated for review activities. Remuneration recognises the requirement to provide both quality and timeliness of review. Remuneration is not dependent on review outcome. Members will be held accountable to both quality and timeliness of review.

3.6 Approval from the CEO and NHMRC must be obtained before a member may represent, act on behalf of or make public representations regarding the Committee or the Pilot.

3.7 Members must agree to their name being placed on the National Scientific Committees website and made available to NHMRC and relevant regulatory authorities such as the Therapeutic Goods Administration (TGA) and the United States' Office for Human Research Protections (OHRP).

4 ORIENTATION, INDUCTION AND EDUCATION

4.1 Panel members will be given orientation information that outlines their rights and obligations.

4.2 The orientation documents that will be provided to new members include:

(a) National Statement on Ethical Conduct in Human Research (2007), incorporating all updates

(b) Terms of Reference and Standard Operating Procedures of the National Scientific Committee and any relevant Bellberry documents

(c) Bellberry contact details and directions to Bellberry offices

(d) a list of Panel members with contact details

4.3 Induction may involve some or all of the following:

(a) one or more informal meetings with the CEO/Deputy Chief Executive/Operations Manager and/or Committee Manager to explain Committee member responsibilities, and relevant policies and procedures

(b) training on eProtocol

(c) introduction to other Panel members

(d) an opportunity to sit in on a Committee meeting before the appointment takes effect.

4.4 Members will be given the opportunity to attend relevant training and education sessions to assist with development.

5 RIGHTS AND OBLIGATIONS OF COMMITTEE MEMBERS

5.1 Committee members have the right to:

(a) bring any matter within the scope of the National Scientific Committee's Terms of Reference to the attention of the Chairperson or CEO

(b) review and comment on checklists written in the NSC meeting, and any changes made following meetings

(c) request an amendment of any meeting minutes or a draft report on the grounds that they are inaccurate

(d) any difference of opinion will be recorded

(e) have their personal information handled according to Bellberry privacy policy and, to the extent that information is handled by NHMRC, according to the Privacy Act 1988 (Cth).

5.2 Committee members are obliged to advise the Chairperson or Bellberry Operations Manager of:

(a) any inability to attend a scheduled meeting for unexpected reasons

(b) any planned absence

(c) their resignation from the Committee.

6 CONFIDENTIALITY

6.1 Committee members will sign a confidentiality agreement confirming that they will not:

(a) discuss any matters relating to Committee discussions and deliberations, with the exception that questions of a general nature that do not divulge commercially sensitive or confidential information may be discussed with other relevant experts for the purposes of gaining further knowledge to assist with Committee deliberations. Where the view of a non-Committee member (i.e. another Panel member or other relevant expert) has been sought this must be disclosed in the meeting minutes and recorded in the final report

(b) compromise intellectual property, commercial-in-confidence information or participant confidentiality (e.g. in dealing with complaints).

6.2 Members will ensure the security of any documents that they receive at all times.

6.3 Members will securely destroy, shred or return to Bellberry any confidential printed material and securely delete any confidential electronic documents that are no longer required.

6.4 Members will adhere to the following protocol to ensure that confidential information is kept secure:

(a) avoid downloading any documents from eProtocol to a USB/memory stick or hard drive

(b) avoid using public computers to access eProtocol

(c) set a secure password for eProtocol (i.e. combination of upper and lower case letters, numbers and symbols) and change as instructed

(d) limit disclosure of the password to Bellberry staff

(e) where operating systems and internet browsers automatically create a download of documents upon opening and save these to the desktop or a download folder, ensure that automatically saved documents are securely deleted and the trash emptied at the close of each user session

(f) sign out of eProtocol when a session has been finished

(g) keep any relevant computer software, personal firewall and antivirus protection up to date

(h) comply with any other IT security policy as determined by Bellberry.

6.5 Members will only use an email address that is not shared with work

associates, friends or family members and will maintain access to a computer with an internet connection that permits use of the eProtocol online system.

7 CONFLICTS OF INTEREST

7.1 Upon appointment and with respect to the review of any individual research project, Committee members will disclose any interests that may constitute an actual or potential conflict of interest, including any:

(a) personal involvement or participation in the research

(b) financial or other interest or affiliation associated with the research, or

(c) involvement in competing research.

7.2 Members will review the agenda for each meeting and disclose any relevant interests to the Chairperson as soon as possible and no later than the commencement of a Committee meeting in which the member is participating.

7.3 The Chairperson will determine how the interest is to be managed. Where a conflict is determined to exist, the relevant member may be able to participate in discussions at the meeting, but not in any deliberative decisions of the Committee.

7.4 The Chairperson will notify the CEO or Operations Manager of any disclosed interests and any determination of a conflict of interest. If a conflict of interest has been determined to exist and the decision is made that the relevant member must withdraw from participation in the meeting.

7.5 All assessments and decisions involving potential conflicts of interest will be recorded in the meeting minutes and the final report.

8 ROLE AND RESPONSIBILITIES OF THE CHAIRPERSON

8.1 The Chairperson is accountable to Bellberry and reports to the CEO or delegate.

8.2 The Chairperson will ensure that all research is reviewed appropriately and in accordance with NHMRC guidelines (e.g. the National Statement on Ethical Conduct in Human Research, 2007), and that Committee has the capacity to conduct its business by:

(a) providing leadership to the Committee in relevant deliberative processes

(b) conducting meetings in an effective, timely and efficient manner in accordance with the Committee Terms of Reference and Standard Operating Procedures

(c) reaching an agreed outcome for each research proposal review

(d) in accordance with mechanisms to be developed by Bellberry, undertaking a review and acceptance function for minor clarifications or submissions of requested additional information as relevant to a research proposal reviewed by the Committee

(e) upon request, contributing to any assessment of the National Scientific Committee pilot.

9 ROLE AND RESPONSIBILITIES OF MEMBERS

9.1 Committee members are accountable to Bellberry and report to the Committee Manager.

9.2 Members will ensure that all research is reviewed appropriately and in accordance with NHMRC guidelines (e.g. the National Statement on Ethical Conduct in Human Research, 2007).

9.3 Members will submit their comments on projects listed on the agenda to eProtocol by 8:00am on the day prior to the meeting and actively participate in Committee meetings.

9.4 In their comments and in Committee deliberations, members will confine their discussion to the scientific merit and integrity of the project, including:

(a) the rigour of the project design

(b) the sufficiency and appropriateness of any statistical analysis

(c) the value of referenced research and relevance of associated findings

(d) the wording of any participant information as it relates to an explanation of the scientific rationale, risks or benefits of the proposed research.

NHMRC National Scientific Committees

hosted by Bellberry Limited

02

Standard Operating Procedure: Review of Research Proposals

All enquiries and for further information about NHMRC National Scientific Committees, contact Bellberry Limited:

129 Glen Osmond Road, Eastwood, SA 5063

P 08 83613222 **E** nsc@bellberry.com.au

Australian Government
National Health and Medical Research Council

PURPOSE

To outline the procedure for review of research proposals in the National Scientific Committee Pilot (the Pilot).

PROCEDURES

1.1 The Operations Manager, Bellberry, or their delegate will review all submitted research proposals to determine:

(a) whether a submitted proposal is eligible for review by a Committee established under the Pilot

(b) whether the project submission is complete or, alternatively, whether further information is required prior to scheduling the review of the proposal

(c) how many research proposals will be included on the agenda for the next scheduled meeting.

1.2 Proposals scheduled for review will be provided to Committee members for review and comment on eProtocol in accordance with Bellberry processes and forms.

1.3 Bellberry may assign a member the responsibility to introduce a proposal at a Committee meeting.

1.4 Committee members will discuss proposals on the agenda and determine whether:

(a) the proposal has established sufficient scientific merit and integrity

(b) the proposal requires modification or additional information in order to establish its scientific merit and integrity.

1.5 For each proposal reviewed, a checklist will be completed which captures the opinion of the Committeee on the scientific merit and integrity of the application.

1.6 Any additional information required by members in order to comment on, assess or provide advice regarding a submitted proposal will be sought from the applicant by Bellberry and provided to Committeee members so as to enable the finalisation of the checklist.

1.7 The checklist will provide the framework for capturing the opinion of the Committeee on the scientific merit of the application. It will include:

(a) an assessment of the scientific merit and integrity of the proposal

(b) a description of any outstanding questions or issues that the Committee believes the researcher and/or research sponsor should address or pursue further

(c) an indication as to whether the Committee relied on the opinion of a non-Committee member (i.e. another Panel member or other relevant expert) in forming its opinion and advice

(d) a description of any issues that the Committee believes a Human Research Ethics Committee (HREC) should address or pursue further.

1.8 The final checklist will be notified to the applicant via eProtocol.

1.9 Any report on proposals submitted for review constitutes expertscientific advice and does not constitute ethical approval for the project.

1.10 Post-review questions and concerns submitted by applicants or reviewing HRECs will be managed by Bellberry staff in accordance with Bellberry policies and procedures.

NHMRC National Scientific Committees

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03

Standard Operating Procedure: Conduct of Meetings

All enquiries and for further information about NH M RC National Scientific Committ ees, contact Bellberry Limited:

129 Glen Osmond Road , Eastwood, SA 5063

P 08 83613222 **E** nsc@bellberry.com.au

Australian Government
National Health and Medical Research Council

PURPOSE

To describe matters related to the conduct of Committee meetings in the National Scientific Committee Pilot (the Pilot).

1 MEETING FREQUENCY AND SCHEDULING

The National Scientific Committee Panel

1.1 The Panel is the pool of expert reviewers available for appointment to Committee reviews.

1.2 The National Scientific Committee Panel Members will meet with the Bellberry secretariat at least once during the Pilot to discuss the concept and operation of the Pilot and how the Committees will function.

1.3 Bellberry, on the recommendation of the members and in consultation with NHMRC, may call an extraordinary meeting of the Panel to discuss any urgent matter that concerns the conduct or viability of the Pilot.

The Committees

1.4 Bellberry will convene a Committee within three weeks of the submission of one or more applications for scientific review of an eligible research proposal.

1.5 A NSC Committee will comprise a Chair and a quorum of reviewers appointed from the Panel. Reviewers will be appointed according to the skills needed for the review, availability, and consideration.

1.6 Committee consideration of a research proposal will constitute a 'meeting of the Committee,' whatever the format of the meeting.

1.7 Projects may be added to a meeting agenda up until the closing date for the agenda (i.e. two week prior to the scheduled meeting).

1.8 In the event that a large number of submissions are received within a three week period, Bellberry may schedule a second meeting to take place within the same month.

2 QUORUM

2.1 A quorum of a Committee will be four, including the Chairperson.

2.2 Bellberry or NHMRC representatives may attend a Committee meeting as observers, and neither will be counted for the purposes of determining a quorum.

3 VIDEO AND TELECONFERENCING

3.1 Meetings of the Panel or Committee may take place via video or

teleconference or face to face.

3.2 Where a meeting takes place by video or teleconferencing, quorum will be determined as if the members were physically present.

3.3 Where the Chairperson has determined that a member has a conflict of interest related to an item on the agenda, and that they must be absent from discussion of that item, the member must fully disconnect from the video or teleconference for the duration of the discussion of that item. Being placed on hold or mute is insufficient.

3.4 Where a meeting takes place by video or teleconference, members will take steps to ensure that confidential information is not overheard by non-members.

4 AGENDAS

The National Scientific Committee Panel

4.1 The agenda for a meeting of the Panel will not include the consideration of individual applications for scientific review. Agenda items for the Panel should relate to:

(a) the operation of the Panel or Committees and related issues

(b) generic issues related to research proposals or applications for Committee review

(c) presentations of an educational or informative nature for the benefit of members

(d) the operation of the Pilot and the preparation of advice to NHMRC.

4.2 The agenda for a meeting of the Panel will be circulated to members by email not less than one week before the meeting.

4.3 Agendas should include a standing item for disclosures of interests.

The Committees

4.4 The agenda for a meeting of a Committee will be capped at a level to be determined by Bellberry. In this instance, Bellberry, may schedule additional Committee meetings to take place on the same or a different day, so long as no application that has been accepted for review remains unreviewed for more than three weeks.

4.5 The meeting agenda will be made available to individual members a minimum of one week prior to the meeting to enable members to be fully informed.

5 MINUTES AND REPORTS

The National Scientific Committee Panel

For any extra-ordinary Panel meetings:

5.1 All decisions and actions taken by the Panel will be recorded.

5.2 Minutes of each meeting of the Panel will be circulated to members for approval.

5.3 The approved minutes of each meeting will be circulated to members for information.

5.4 Approved minutes will be confirmed at any subsequent meeting of the Panel.

5.5 A summary of the minutes of a Panel meeting may be used by NHMRC in any internal and external reporting on the Pilot.

The Committees

5.6 All decisions and actions taken by the Committee will be recorded, including information related to disclosures and management of interests.

5.7 Minutes of each meeting of the Committee will be agreed by the members live during the meeting.

5.8 The Checklist will be completed during the meeting. Any post-meeting changes will be agreed by the Chair, and circulated to the Committee Members if needed.

5.9 Minutes and reports are to be considered confidential to the members of the relevant Committee, Bellberry staff and the applicant.

6 DECISION MAKING

The Committees

6.1 Determinations regarding the scientific merit and integrity of a research proposal will be recorded in the minutes and in the Checklist.

6.2 To the extent possible, decisions should be reached by consensus.

6.3 When a consensus cannot be reached, this will be reported in the checklist. Where there is a difference of opinion between Committee members regarding the scientific merit and integrity of the application, this will be articulated to the applicant. Explanation of the different views will be provided.

6.4 Dissenting opinions will be recorded in the minutes, but the identity of the member dissenting will be kept confidential.

6.5 Decisions may be made out-of-session, subject to the rules of quorum that apply at a meeting.

7 COMMUNICATING DECISIONS

7.1 Minutes of a Panel or Committee meeting are confidential and will not be published or distributed except as required by law except with reference to 5.5 above.

7.2 The final checklist on a research project submitted for review by the Committee will be provided by Bellberry to the applicant no later than two days post-meeting.

NHMRC National Scientific Committees

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04

Members Review Checklist

All enquiries and for further information about NHM RC National Scientific Committees, contact Bellberry Limited:

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P 08 83613222 **E** nsc@bellberry.com.au

Australian Government
National Health and Medical Research Council

(To be filled in by NSC Secretariat, except for reviewer and date fields)

RESEARCH TYPE ☐ Complex Genetic Research ☐ Medical Device

PROJECT TITLE

PRINCIPAL INVESTIGATOR

REVIEWER DATE

The documents listed below are attached for your review

1. X
2. X
3. X

Project Team	Comment
☐ Appropriate	
☐ Sufficient	
☐ Deficient	

Hypotheses/Objectives	Comment
☐ Appropriate	
☐ Sufficient	
☐ Deficient	

Project Design	Comment
☐ Appropriate	
☐ Sufficient	
☐ Deficient	

Procedures/Implementation	Comment
☐ Appropriate	
☐ Sufficient	
☐ Deficient	

Eligibility criteria ☐ Appropriate ☐ Sufficient ☐ Deficient	Comment
Sample size ☐ Appropriate ☐ Sufficient ☐ Deficient	Comment
Statistical analysis plan ☐ Appropriate ☐ Sufficient ☐ Deficient	Comment
Data management plan ☐ Appropriate ☐ Sufficient ☐ Deficient	Comment
Risk profile (protocol) ☐ Appropriate	Comment

☐ Sufficient

☐ Deficient

Communication of risks (PICF Comment

☐ Appropriate

☐ Sufficient

☐ Deficient

Safety monitoring and reporting Comment

☐ Appropriate

☐ Sufficient

☐ Deficient

OVERALL QUALITY Comment

☐ High

☐ Satisfactory

☐ Deficient

Additional Comments/Concerns/Questions:

Additional Expert Opinion Required: Yes No