Consultation Paper on clinical trial research governance

A Good Practice Process for the Governance Authorisation of Clinical Trials

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Purpose of the Consultation

NHMRC is seeking feedback on a Good Practice Process for the Governance Authorisation of Clinical Trials (the Process), and has developed a set of questions to elicit information around the proposed process.

The desired outcome of the consultation is an understanding of the views of researchers, jurisdictional representatives, institutions, sponsors and Contract Research Organisations (CROs) from both the public and private health sectors who conduct or are otherwise involved in the conduct or governance of clinical trials in Australia, particularly with respect to the design, feasibility and implementation of the proposed assessment and authorisation processes for clinical trials.

The focus of the consultation is on processes used to assess and authorise clinical trials that have a commercial sponsor. NHMRC anticipates that these processes are also broadly applicable to academic and non-commercial trials and specifically encourages feedback on this aspect of the Process.

In conducting this consultation on the Process, NHMRC is seeking input on 2 specific phases:

1. A planning and preparation phase; and
2. The site assessment and authorisation phase.

The desired input includes comments on the allocation of activities to individuals and entities involved in the above phases.

NHMRC is aware of other initiatives currently underway to improve the clinical trials and research environment, including state and territory- or institution-specific reviews of HRECs, site assessment processes and the adoption of common forms. This consultation will also consider how this proposed approach interacts with other initiatives that are underway with a view to developing a nationally consistent process for clinical trial site assessment and authorisation.

1. Background

Clinical trials are an important element of health and medical research and are required for the evaluation of the safety and effectiveness of interventions or treatments. To ensure the safety of research participants, the integrity of each research project, the effective use of research funds and the responsible conduct of research, all clinical trials are subject to a process of institutional assessment prior to their commencement. The framework, systems and processes leading to the
authorisation and commencement of a clinical trial at a research site are commonly referred to as ‘research governance’.  

The pharmaceutical industry and clinical trial practitioners have raised concerns about aspects of research governance in Australia and that the time taken to complete research governance activities can lead to delays in the commencement of clinical trials. Variations in the processes used by institutions to assess whether the proposed clinical trial fulfils all necessary institutional and legislative requirements prior to commencing at that site may contribute to unnecessary delays to the approval process for the conduct of a clinical trial. Reducing delays will help to ensure that Australia remains an attractive destination for clinical trials, in particular commercially sponsored drug and device clinical trials.

In an effort to address delays in clinical trial start up time, the Australian Government provided funding for NHMRC to work with:

• States and Territories to improve institutional governance and ethics review arrangements for clinical trials in the public hospital sector; and
• Public and private sector organisations to establish arrangements to streamline approval processes for CTs involving multiple levels of jurisdiction.

In mid to late-2013, NHMRC held a National Forum and follow on workshop to gauge stakeholder interest in, and thoughts on, possible changes to the institutional process for the assessment and authorisation of research. A report from this forum, including a summary of stakeholder input is available on the NHMRC website at http://www.nhmrc.gov.au/research/clinical-trials.

The expertise of key stakeholders from public and private hospitals, jurisdictions, industry, academia and medical research institutes, and organisations involved in conducting clinical trials in Australia was then utilised to consider and develop a ‘Good Practice’ process to enable efficient and effective assessment and authorisation of clinical trials. NHMRC is now seeking feedback on the Process. The Process describes the activities that are considered to be essential for the site assessment and site authorisation processes for clinical trials to be conducted in an efficient manner. It is believed that if this Process is adopted, it will lead to a decrease in the time taken for clinical trials commencement and thereby ensure that Australia has a competitive edge to attract clinical trials.

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1 See further: Research Governance Handbook: Guidance for the national approach to single ethical review. NHMRC. December 2011. Note that, as a formal matter, the term ‘research governance’ applies to components of institutional research-related activity beyond the assessment and authorisation of individual research projects. Some jurisdictions also use the term Site Specific Assessment (SSA) to refer to both a process and specific form used by researchers and institutional staff.
2. Terminology and definitions used in this document

**Research governance:** a *framework* or system used by an organisation for the oversight, assessment, authorisation and monitoring of research conducted at one or more of its sites or under its auspices. A research governance framework includes good research culture and practice, organisational strategy, role definition and accountabilities, risk, resource and financial assessment and management, compliance with legal, regulatory and contractual requirements, competencies and training of personnel, site assessment, scientific review, ethical review and approval, site authorisation, monitoring of research, and management of conflicts of interest, complaints and allegations of research misconduct.

**Site assessment:** a *process* that assesses research against institutional requirements.

**Ethical review:** a *process* to explore the ethical issues presented by, and implications of, a research project.

**Ethical approval:** a *determination* by an ethics review body that a research project satisfies ethical standards and requirements, including, but not limited to, the NHMRC/ARC/AVCC National Statement on Ethical Conduct in Human Research.

**Site authorisation:** a *determination* by an organisation that a research project to be conducted at one or more of its sites or under its auspices satisfies organisational requirements and may commence at the site/s over which it exercises its authority. Site authorisation is the *outcome* of the site assessment process.

3. Introduction

Clinical trials are essential for evaluating the effectiveness and safety of medications, services and interventions to help prevent, detect or treat health and medical conditions. Trials also have the potential to bring hundreds of millions of dollars each year into the Australian economy.

The Australian Government is committed to ensuring Australia maintains a competitive clinical trials sector that encourages innovation and protects the safety and wellbeing of clinical trial participants. To that end, the Government, through NHMRC, is working to move towards a nationally consistent approach to the way that clinical trials are overseen and conducted and to improve the opportunity for patients to enrol in clinical trials.

The 2011 Clinical Trial Action Group Report, “Clinically Competitive: Boosting the Business of Clinical Trials in Australia” made 11 recommendations that it was believed if implemented would lead to better coordination of the clinical research system and a more efficient interaction between health agencies, researchers, hospitals, sponsors and health consumers. The Australian Government accepted all of the CTAG Recommendations and has implemented most key Recommendations, including: launching a consumer-friendly clinical trials website; conducting a feasibility study for the development of a comprehensive, interactive clinical trials web portal; developing and costing a list

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2 www.australianclinicaltrials.gov.au
of standard items associated with clinical trials; and finalising the development of a series of tools and guidance material supporting the National Approach to Single Ethical Review of multi-centre human research.

In 2013, NHMRC was tasked with working with States, Territories and other stakeholders to:

- Improve clinical trials governance mechanisms in public and private sector health organisations, while continuing to protect participant safety;
- Assist the Department of Industry with a pilot project to develop a fully interactive web portal which, it is hoped, will help to increase patient recruitment into clinical trials; and
- Develop education, guidance and support material for the clinical trials sector which will lead to a clearer understanding or the roles and work required for clinical trial approvals.

4. Development of the Process

In considering the views and input of stakeholders, NHMRC proposes two key improvements that would reduce the time taken to commence clinical trials:

1. An increased commitment to planning, preparation and ongoing support for clinical trials within those institutions where clinical trials are conducted; and
2. A change to the order in which the activities within the assessment and authorisation process are conducted, whereby key assessment activities occur much earlier.

This latter proposed improvement represents a significant paradigm shift from the way in which the site assessment and authorisation process is usually conducted in 2 ways:

i. The majority of site assessment activities can be conducted not just in parallel with, but prior to, ethical review being undertaken; and
ii. Some key site assessment activities can be substantively completed in the feasibility assessment stage and then formalised in documentation rather than be delayed until all documentation is submitted.

Activities within the site assessment and authorisation processes for clinical trials can be described in terms of six phases, shown below. These activities are usually conducted sequentially to lead to the authorisation of a clinical trial to commence at an individual site. The phases are presented in more detail in the process diagram at Attachment A. In this diagram the roles of individuals or entities, and the activities for which they are responsible, are presented in a ‘swim lane’ process diagram, referred to as a Process Diagram. It is important to note that the planning and preparation phase comprises activities that apply to all clinical trials, whereas the remaining phases are completed on a trial by trial basis and are dependent on the characteristics of the clinical trial proposal.
4.1 Planning and preparation for clinical trials readiness

Upfront planning and preparation for readiness to conduct clinical trials is critical to efficient approval of individual trials and ensures that sites and all personnel involved in the process are ready and available to conduct clinical trials.

The following table (Table 1) summarises the tasks that are thought to be appropriate during the planning and preparation phase and identifies the individuals and entities to which these tasks can be allocated.

Table 1- Roles and activities for individuals and entities involved in the clinical trial planning and preparation phase

<table>
<thead>
<tr>
<th>Contract Research Organisation / Sponsor</th>
<th>All Principal Investigators (including coordinating principal investigator)</th>
<th>Human Research Ethics Committee (HREC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Agree, having regard to the Independent Hospital Pricing Authority (IHPA) process [LINK: <a href="http://www.ihma.gov.au/internet/ihpa/publishing.nsf/Content/home-1">http://www.ihma.gov.au/internet/ihpa/publishing.nsf/Content/home-1</a>], to the costs of and cost-sharing approach to standard clinical trial items with participating institutions</td>
<td>• Complete Good Clinical Practice (GCP) training</td>
<td>• Document and promote process to efficiently manage clinical trial applications</td>
</tr>
<tr>
<td>• Agree to use standard research agreements (contracts)</td>
<td>• Agree to comply with nationally consistent insurance and indemnity requirements</td>
<td>• Use certified ethical review processes for multi-centre clinical trials and single site trials as appropriate</td>
</tr>
<tr>
<td>• Agree to comply with nationally consistent insurance and indemnity requirements</td>
<td>• Develop guidelines and processes to ensure trial protocols are compatible with the Australian context before providing to investigators</td>
<td>• Utilise the current national ethics application form</td>
</tr>
<tr>
<td>• Develop guidelines and processes to ensure trial protocols are compatible with the Australian context before providing to investigators</td>
<td>• Agree to use a suite of nationally agreed standard patient information and consent forms (PICF) templates</td>
<td>• Adopt standardised/harmonised ethical review forms, templates and processes</td>
</tr>
<tr>
<td>• Conduct regular audits of institutions, researchers, facilities and patient profiles</td>
<td>• Conduct regular audits of institutions, researchers, facilities and patient profiles</td>
<td>• Advertise HREC meeting dates and deadlines</td>
</tr>
<tr>
<td>• Conduct regular audits of institutions, researchers, facilities and patient profiles</td>
<td></td>
<td>• Require use of a suite of nationally agreed standard PICF templates</td>
</tr>
<tr>
<td>Institution management and administrative personnel (eg. Research Director, Research Governance Officer, Delegate for authorisation)</td>
<td></td>
<td></td>
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<tr>
<td>---------------------------------------------------------------</td>
<td></td>
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<tr>
<td>• Maintain certification for ethical review processes related to multi-centre clinical trials and single site trials as appropriate.</td>
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<td>• Make templates documents available on websites</td>
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<tr>
<td>• Complete relevant learning modules</td>
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<tr>
<td>• Accept single ethical review without further site-specific ethical review</td>
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<tr>
<td>• Establish and communicate research priorities</td>
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<tr>
<td>• Promote capacity to conduct clinical trials on web site and via other mechanisms</td>
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<tr>
<td>• Comply with national standards and processes for implementing a research governance framework</td>
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<tr>
<td>• Ensure all staff participating in clinical trials are appropriately trained</td>
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<tr>
<td>• Use nationally agreed electronic site assessment document templates</td>
<td></td>
<td></td>
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<tr>
<td>• Use nationally agreed standard contracts</td>
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<tr>
<td>• Agree, with reference to IHPA advice, to the costs of and cost-sharing approach to clinical trial items with sponsors</td>
<td></td>
<td></td>
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<tr>
<td>• Utilise national standard operating procedures for site assessment</td>
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<tr>
<td>• Maintain IT system that enables electronic submission of documents and compliance with national requirements</td>
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</tbody>
</table>

4.1.1 Consultation Questions: Proposed roles and activities allocated during the Planning and preparation Phase for clinical trials readiness

1. Does the above table describe the correct set of tasks?

2. Are the tasks allocated to the correct individual(s) or entity?

3. Is there more that could be done in planning and preparation and, if so, what and by whom?

4. Are you aware of any institutional, state, territory or national law or binding rule that would prevent you or your institution from implementing the tasks in this phase as proposed?

5. Generally, are the identified tasks, roles and responsibilities suitable for non-commercially sponsored and academic clinical trials? If not, which tasks/roles/responsibilities are not and why not?
4.2 Key activities for assessment and authorisation of each clinical trial

The process diagram (Attachment A) includes the activities and roles of groups or personnel involved in the process (rows) across the five phases (columns) considered necessary for the assessment and authorisation of each clinical trial.

The five individuals or entities that are allocated roles are:

- Contract Research Organisation / Sponsor
- All Principal Investigators (PI)
- Coordinating Principal Investigator (CPI)
- Human Research Ethics Committee (HREC)
- Institutional Delegate/s.

4.2.1 Consultation Questions: Key activities for assessment and authorisation of clinical trials

6. Does the process diagram identify the appropriate **high level** process steps?

7. Are the high level activities matched to the correct responsible person/s, or entities?

8. Does the process diagram reflect ‘good practice’ throughout the phases?

9. Are there any points at which the process could be made more efficient?

10. Does the proposed process compromise or nullify any important governance principles that should be maintained?

11. Are you aware of any institutional, State, Territory or National law or binding rule that would prevent you or your institution from implementing the proposed approach?

12. Are you aware of any national or international initiatives that are relevant to any of these phases and that should be considered?

13. Generally, are the identified tasks, roles and responsibilities suitable for non-commercially sponsored and academic clinical trials? If not, which tasks/roles/responsibilities are not and why not?

14. Could the process be further modified to support the expedited assessment of ‘low risk’ clinical trials? If so, how?