



Australian Government

Clinical Trials Action Group

Discussion Paper Three

Ensuring the Rapid Uptake of Streamlined Ethics, Scientific and Governance Review Process

(Harmonisation of Multi-centre Ethical Review (HoMER) and Research Governance)

November 2009

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The Government is seeking feedback and comments on options outlined in this paper. The options have not received Government approval and are not law. Feedback and comments received will help to inform the Government's proposed approach on the way forward.

Making a submission:

Submissions on this paper are requested by: Friday, 12 February 2010

Submissions can be sent to:

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Ensuring the rapid uptake of streamlined ethics, scientific and governance review processes

Purpose - an investigation of how to ensure the rapid uptake of the National Health and Medical Research Council (NHMRC) HoMER multicentre human research ethics approval process and adoption of best practice institutional processes for research governance approval.

Background

In 1991, the introduction of the Clinical Trials Notification (CTN) scheme had a tremendous impact on the number of clinical trials conducted in Australia by providing a major competitive advantage through, at the time, rapid trial start-up. The number of new trials jumped from approximately 70 per year to the current 600-700 trials per year in a relatively short number of years. In recent years, global timelines for trial approval have been falling around the world. The EU directive mandated a 60 day approval timeline from submission of the trial application. South Korea is about to introduce its version of the CTN scheme in 2010.

Timelines for multicentre trial approval in Australia on average are now behind many countries based on individual pharmaceutical company metrics. A key issue is the large variability in times for research governance and ethics approval across sites and trials. On occasion we can be the fastest in the world but more often we are not.

In addition to the reducing timelines for trial approval in many countries, there is some data to show that times taken for regulatory approval to commence clinical trials in Australia may have been increasing. Hicks *et al* showed approval times have increased from a median time of 100 days in 2005-2007 to 137 days in 2008 for multicentre clinical trials in New South Wales¹. An Australian pharmaceuticals industry (Pharma) survey showed that in 2008 start up times in Australia were slower for 44% and 36% of European and North American headquartered companies respectively². Pharma believes that one of the most significant barriers to clinical trial investment in Australia is the increasing comparatively lengthy time taken to gain regulatory approval for multicentre clinical trials. Reforms in both of the following areas are most likely to reduce approvals times: (1) ethics and scientific review and (2) research governance review. Strategies to reduce approval times may also include concurrent reviews of ethics and science, and research governance.

Ethics and scientific review

Multicentre trials have traditionally required the approval of the Human Research Ethics Committee (HREC) at each site, leading to process duplication and often delays in trial start times. This inefficiency has led to efforts both nationally and at state and territory level to develop single ethical review processes so that only one HREC approval is required for a multicentre trial.

¹ *Medical Journal of Australia* Volume 191 Number 5, 7 September 2009

² <http://www.pharmacouncil.com.au/resources.php>, Forum Report March 2009, *Clinical Research in Crisis, Preparing Ourselves for Survival* p37

In 2007, the NSW government commenced a centralised ethics approval process that enabled single review to cover all public health sites in the state, which has resulted in shorter approval times for ethics reviews and significantly less process duplication. Other jurisdictions have made arrangements in streamlining their ethical reviews.

Presently, the National Health and Medical Research Council (NHMRC) is developing a national approach to the ethical and scientific approval of multicentre health and medical research, which includes clinical trials, through their Harmonisation of Multicentre Ethical Review project (HoMER) (see **Attachment 3A** for more information on HoMER). The aim of HoMER is to develop a national system where a multicentre clinical trial will require one ethics approval for the entire study.

NHMRC has no statutory or directive role to impose change on institutions and relies on the collaboration between jurisdictions and institutions to implement the national approach. HoMER relies on linking existing jurisdictional processes and, where appropriate, developing additional elements that would enable the national system. Its uptake will depend to a large degree on the support of state and territory governments. Accordingly, throughout HoMER, the NHMRC has undertaken extensive consultation to gain consensus, trust and support.

HoMER has made progress in the area of information sharing principles and tools, including a web portal and standardised forms for applications. NMHRC will shortly commence small scale ‘pilots’ to investigate the best approach to reviewing research projects across jurisdictions. Also, the development of an Human Research and Ethics Committee (HREC) certification system has commenced which is seen an essential component in HoMER and its implementation next year.

What strategies can be used to encourage the rapid adoption by institutions across Australia as the various elements of HoMER become ready for use?

Do these strategies vary depending on whether the institution is a public hospital, university or research institute?

Do private funders of clinical research, such as pharmaceuticals and biotechnology sectors, have a role to play in streamlining ethics, scientific and governance review processes?

What role do State and Federal governments have to play in rapid adoption of a national streamlined approach?

Ethical review may also determine, depending on jurisdictional or institutional requirements, whether a trials indemnity and insurance (I&I) arrangements are adequate. There is significant uncertainty around appropriate I&I arrangements for the conduct of multicentre clinical trials across Australia. The NHMRC has led efforts to clarify how I&I arrangements are affected under HoMER. State and Territory governments have also been working towards addressing I&I, for example the Victorian Managed Insurance Association.

Research governance review

Research governance review, also known as single site assessment, is a determination of whether a site has the capacity and expertise to conduct the clinical trial and may consider I&I arrangements. The time taken to complete a research governance review is increasingly lengthy and highly variable across Australia. Hicks *et al* showed that research governance review added a median time of 60 days after ethics and scientific approval in NSW.³

Anecdotally, lengthy times taken for approval may be due to the uncertainty and variability of review procedures and/or a lack of dedicated staff. HoMER is currently developing a research governance handbook that will provide national guidance on best practice policy and the roles and responsibilities of stakeholders.

What strategies can be used to ensure the adoption of best practice processes for streamlined research governance across Australia?

What are the opportunities for appropriate standardisation of processes?

Is it feasible to gather benchmarking data across Australia to encourage improvements in research governance review?

It seems that many research governance reviews are conducted after ethics and scientific approval for a trial. *Prima facie* trial start up times would be quicker if there were concurrent reviews of ethics and scientific and research governance.

What are the practical barriers to having concurrent reviews? Can these barriers be overcome and if so, how?

What strategies or measures are there to encourage concurrent review?

What other strategies are there to expedite approvals for clinical trials e.g. adequate resourcing and training of research governance officers?

Who will drive improvements and coordinate the efforts of stakeholders in this system?

International activities to improve approval systems for clinical trials

The UK National Institute of Health Research Clinical Research Network (NIHR CRN) aims to support clinical research and facilities throughout the UK in order to improve the research environment. This initiative is working to improve the whole clinical trials environment in the UK including reducing approval times and providing support and guidance for regulatory issues.

Presently, the EU has requested public input into how the application of their clinical trials directive, which includes ethics and scientific approval systems across member

³ *Medical Journal of Australia* Volume 191 Number 5, 7 September 2009

states, can be harmonised. The multiple and divergent assessments of clinical trials has led to reduced competitiveness in attracting clinical trials to the EU.

The US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have embarked on a pilot program to collaborate and share information on good clinical practice (GCP) inspections⁴. The initiative is aimed at ensuring that clinical trials submitted in marketing applications in the US and the EU are conducted uniformly, appropriately and ethically. The partners outlined three objectives for the initiative: to conduct periodic information exchanges; to conduct collaborative inspections; and to share information on interpretation of GCPs.

What other examples are there of streamlined review processes? What are the lessons and/or implications for Australia?

Can Australia achieve best practice of streamlined review processes?

⁴ *Scrip: World Pharmaceutical News*, 'FDA and EMA to co-operate on clinical trial inspections', 5th August 2009

ATTACHMENT 3A

Background information on HoMER

Taken from http://www.nhmrc.gov.au/health_ethics/homer/index.htm

Overview

In 2006, the Australian Health Ministers Advisory Council (AHMAC) directed the NHMRC to facilitate the development and implementation of a national system where the single ethical review of a HREC would be recognised by all institutions participating in a collaborative research project. By having a single ethical review outcome accepted by collaborating institutions, protection of human participants would be maintained while delays due to the current practice of seeking multiple ethical reviews would be mitigated and timelines for research start-up and results could be shortened.

The 2007 joint NHMRC/Australian Research Council/Australian Vice-Chancellors Committee National Statement on Ethical Conduct in Human Research (the National Statement) guides institutions to eliminate unnecessary duplication of ethical review processes (Chapter 5.3).

Several States have formal systems for streamlining ethical review processes in public health organisations. Other jurisdictions have more informal arrangements operating as agreements of acceptance between institutions in the private and public sector and between public health organisations and universities.

AHMAC's initiative directed that the existing and planned State and Territory systems should be 'harmonised' such that collaborative research across jurisdictional borders would be subject only to a single ethical review.

The benefits of adopting a national and formal approach to single ethical review are many:

- The amount of time from ethical review application to research start-up is shortened with the resultant savings in human and monetary resources;
- Australia's attractiveness as a place for international investment in commercial sponsored clinical trials is enhanced;
- Public confidence in the rigour of Australia's system of ethical review of human research is increased due to the standardisation of ethical review processes; and
- The roles and responsibilities of the researcher, the institution, the HREC and other key stakeholders in the conduct of multicentre research are transparent and consistent.

The uptake of the national approach for single ethical review will respect institutional autonomy to determine whether research should be conducted at a given site. Advice received from a HREC undertaking the single ethical review will not replace the need for local institutional decision making on matters of research governance.

The HoMER Model

The model for implementing single ethical review is not complex. The national approach for single ethical review is based on five simple principles:

- Efficiency – agreed timeframes for processes and procedures are adopted in all jurisdictional systems;
- Authority – the single ethical review of a multicentre research proposal is accepted by institutions without re-review by their institutional HREC;
- Respect – the national approach accommodates the differences in jurisdictional statutory and administrative frameworks and institutional arrangements;
- Verifiable – the capacity of the HREC carrying out the single ethical review is subject to independent verification; and
- Compliance – multicentre single ethical review meets the requirements of the National Statement to protect human research participants as well as relevant jurisdictional statutory and administrative frameworks.

The HoMER model is designed to deliver three key outcomes:

- Trust building between institutions and their HRECs;
- Information sharing to enable single ethical review across jurisdictions; and
- A better understanding of the ethical review of multicentre research.

HoMER tools

Single ethical review is supported by a suite of tools which will enable delivery of the key outcomes. Under the HoMER model, existing State and Territory systems of streamlined ethical review use in-common policies, processes, forms and guidance.

The ‘tools’ that enable institutions to utilise a single ethical review for their collaborative research are:

- In-common policies;
- In-common processes;
- Standardised forms; and
- Guidance.