ACTA

Australian Clinical Trials Alliance

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Submissions
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Response to the IHPA initiative on the development of a table of standard costs for conducting Clinical Trials in Australia

1. The Australian Clinical Trials Alliance (ACTA) welcomes the opportunity to comment on the consultation paper on the development of a table of standard costs for conducting Clinical Trials in Australia.

   ACTA, representing investigator-led clinical trials networks and coordinating centres across Australia, endorses the intention of the document. The aim of establishing a table of standard costs for conducting clinical trials to create a favourable environment for clinical research is laudable.

   However, the process will not necessarily achieve this purpose unless the proposed Table of Standard Costs clearly identifies what constitutes trial costs as compared with those costs that should rather be considered part of providing routine health care. It is important that the document therefore begins with a section outlining the principles for costing and funding clinical trials including when individual items should (or should not) be considered a trial cost.

Recommendation 1. The table of clinical trial costs should be preceded by a section outlining the principles of costing clinical trials and when these costs should be considered (or not considered) a trial cost.

2. Clinical trials are an essential part of developing and assessing the effectiveness of new and existing health care interventions. In order to provide effective and high quality care, clinical trials should be undertaken as an integral part of the health care system. Furthermore, appropriately designed and selected clinical trials can be a highly cost-effective use of the health care dollar (providing greater gains in quality adjusted life years than some currently funded health care interventions).

   Consequently clinical trial costs of appropriately chosen high priority clinical trials should be factored into health care system costs in line with the recommendation by the Mckeon review that research should be embedded in health care systems.[1-3]

Recommendation 2. The paper should recognise the importance of clinical trials research in ensuring quality health care in Australia and should recommend that there are mechanisms to factor costs of appropriate, high quality clinical trials into the health care system.

3. In particular, when considering the costs of undertaking clinical trials this should be calculated as the additional cost of the trial over and above what would have been provided as accepted standard of care for such patients. In this regard costs of care including treatment, diagnostic tests, screening tests prior to commencing particular treatments and follow-up that would be considered as an option for standard care should not be included in clinical trial costs.

   The paper currently does not recognise that there may be additional complexities in determining overall and component clinical trials costs. For example, trial costs can vary from first-in-human phase 1 trials through to larger phase 3 trials and with additional challenges in translational studies incorporating novel biomarkers. This may lead to variation in some of the trial costs as well as the costs of usual care.

   It should also be recognised that there may be cost savings in clinical trials (eg: when substituting standard care with a new treatment under evaluation) which should be considered in determining the total cost. For many investigator-initiated multi-centre controlled clinical trials there needs to be an understanding that standard of care investigations and consultations should not be costed to trials. Indeed to do so risks paralysing the very conduct of such studies. These trials subsidise the health system as much as the health system subsidises these trials.

Recommendation 3. The costs of undertaking clinical trials should be confined to the additional costs over and above what would be provided as part of a routine or standard care, or any reasonable option for such care.

4. While the draft document recognised that there are both commercial and non-commercial trials undertaken in Australia, there is currently not a distinction as to how clinical trials should be costed and how those costs should be applied in these settings. We understand that the major drive behind this initiative comes from the pharmaceutical industry, which is concerned that their studies performed across Australia experience very uneven costs depending on where they are undertaken. While standardisation of some costs will be helpful in planning clinical trial budgets, it is also critical that new charges are not added inappropriately, especially for investigator-initiated clinical trials aimed to better define optimal health care.

Recommendation 4. The application of clinical trial costs should differentiate commercial and investigator-initiated clinical trials aimed at optimising quality health care.

5. For trials evaluating alternative treatments to standard care, it is not possible to know the full costs of the trial (or cost savings) due to the additional hospitalisations, tests, and other events that may occur downstream or be avoided. For such trials, building a health economic assessment into the trial would be of value – where there may be additional costs and additional savings relevant to the final cost of the trial. These costs can't be realistically known in advance but should be considered in the overall costing and funding of future

clinical trials, for example by embedding funding for important trials in future health care expenditure. ACTA has undertaken a number of clinical trials where the trial results demonstrated a considerable saving to future health care (several millions of dollars) and which are worth considering when funding or costing future similar trials.[2,3]

Recommendation 5. Health economic assessment of the value of clinical trials (particularly investigator-initiated trials) should be factored into future costing and funding models for clinical trials in Australia.

6. Whilst the CTAG report was focused on clinical trials in the public sector (restated in section 2.1), many patients around Australia are treated in the private sector. These patients should also have access to clinical trials but the issues and drivers are different from the public sector and this also needs to be addressed in this document. In particular, there is no comment about private health insurers and the role they play in paying for services related to clinical trials. We believe this is a significant omission.

Recommendation 6. Acknowledgement of the important role of the private sector and of private insurance to the clinical trials effort in Australia should be added

Finally, we wish to re-iterate our concern that any table of standardised costings will inevitably lead to greater scrutiny of clinical trial activity in both the public and private sector with an emphasis on making trials pay their way in every aspect. We have all experienced ever-increasing "governance" bureaucracies within hospitals and the trials run by members of ACTA may find themselves unable to afford to undertake trials any longer. Such an outcome may perversely achieve the exact opposite of the intended outcome by decreasing competitiveness in Australia for increasing clinical trial activity - adversely impacting both investigator-initiated and pharmaceutical-industry-run trials.

We appreciate that some of our comments may be seen as beyond the scope of this document. However, unless these issues are addressed and embedded within the document our concerns may well be realised.

With kind regards,

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NHMRC Clinical Trials Centre

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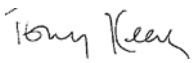

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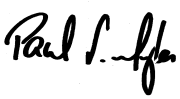

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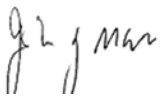

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References

1. McKeon Review. Strategic Review of Health and Medical Research in Australia – Better Health Through Research. ISBN: 978-0-9872039-6-0 Commonwealth of Australia. 2013
2. Simes RJ, Steven A R Webb SAR [Editorial]. Sustaining Australian research through clinical trials and investigator networks. Med J Aust 2013; 198: 127-128.
3. Winship IM, John McNeil J, Simes RJ, A funding model for public-good clinical trials. Med J Aust 2013 (in press).

Attachment – The Australian Clinical Trials Alliance, 2013.

Australian Clinical Trials Alliance

The mission of ACTA is to promote effective and cost-effective healthcare in Australia, best done by investigator-led clinical trials that generate evidence to support decision making by health practitioners, policy-makers, and consumers.

The investigator-initiated trial sector in Australia

Australia is a world-leader in the conduct of clinical trials. Each year, Australian researchers, often supported by funding from the National Health and Medical Research Council, complete clinical trials that provide vital evidence that leads to better outcomes for patients. Frequently, these trials achieve both better outcomes and save money. Most of this research is undertaken by clinical research networks that involve collaborations, sometimes involving up to hundreds of clinicians and researchers. The strength and effectiveness of these Australian networks arises from them being led by clinicians who understand the gaps in the evidence/knowledge base and collaborate with colleagues such that the results of these clinical trials are subsequently translated into routine clinical practice in a timely manner.

Much clinical research in Australia is conducted by the pharmaceutical and to a lessor extent the device industry (although this investment is said to be falling rapidly with the development of Asian hubs close to much larger potential markets). Such trials are generally of a very high quality, but industry research focuses on establishing the effectiveness of products that they wish to market. As such, while industry research often leads to improved outcomes, it is less common for it to lead to direct cost-savings due to the actual intervention. In contrast, investigator-initiated trials tend more to test inexpensive interventions or identify treatments (inexpensive or otherwise) that are already in current practice and are ineffective or even harmful (see Appendix).

Why is ACTA needed?

If Australia is already conducting world-leading clinical research (either as part of industry collaborations or within academic networks), why is ACTA needed? The answer is simple - although much is already being achieved, so much more is needed, is possible and could be conducted if we could create sustainable infrastructure for these virtual networks of academic clinical trials groups as well as clinical registries.

> It is often assumed that the vast majority of clinical decision making is supported by high quality evidence derived from clinical trials. Unfortunately, this is not the case. The majority of clinical decisions in medicine, are based either on low quality evidence or no relevant evidence. Some of the best research conducted in Australia has demonstrated that therapies in widespread use, sometimes quite expensive, were either ineffective or harmful. For example, based on limited evidence, bone marrow transplantation became the standard of care for women with high risk breast cancer around the world. This practice required no approvals from the PBAC or MSAC and was widely utilized despite being associated with considerable toxicity and required multiple hospitalizations.

It was only when academic groups in Australia in conjunction with similar groups internationally conducted randomized clinical trials comparing such therapy to standard care, that it was realized the benefits were generally non-existent and the treatment was indeed harmful (including occasionally fatal side-effects).

Australia conducts world-leading research in many medical specialties but there are some sectors of clinical care for which there is no infrastructure to conduct high quality clinical trials that can address clinically important questions. Such trials need to not only include the major sub-specialties in medicine, but also in primary care, especially in rural and remote Australia as well as indigenous health.

Some networks, including those networks already involved in world-class research, aren't sustainable. This means that the infrastructure they create for each trial degrades and must be (expensively) reconstructed, for each new trial.

Some networks have not had the opportunity to work together, so questions that are multi-disciplinary cannot be answered and expertise, skills, and infrastructure are not shared among the networks.

The research conducted by the networks is much less efficient than it could be when these need to be rebuilt for each trial. Cheap reforms would allow the research dollar to go much further.

Who are ACTA?

ACTA has been established by individuals who have played key roles in the successful clinical trials networks and clinical registries in Australia. ACTA will represent the investigator-initiated trial networks and the centres, that conduct and manage trials. ACTA will also have strong representation from health consumers as well as industry sponsors who also conduct clinical trials.

ACTA's vision

To:

Achieve a healthcare system that delivers high quality and cost-effective care through the systematic generation and application of evidence derived from clinical research.

Ensure that clinical research, through both clinical trials and registries, occurs as a routine, integral, and universal component of healthcare delivery.

Promote that the best evidence to inform optimal heath care is based on well conducted controlled trials of the effect of interventions on clinically relevant outcomes

Achieve widespread appreciation and support by consumers, health practitioners, and policy-makers for the critical importance of clinical research in Australia to improve practice and policy.

Ensure all patients who require treatment for which there is uncertainty about the most effective treatment have the opportunity to participate in high quality clinical trials.

How will ACTA implement their vision?

ACTA will not conduct clinical trials. This is best done by existing or new networks. The activities of ACTA will allow these networks to conduct more and better research and realize the opportunity that sustainable infrastructure will create. ACTA will advocate to help these networks achieve their vision by promoting the creation of sustainable capacity in investigator-initiated clinical trials including networks, trial management centres, and trial professionals. We will undertake an advisory and advocacy role in shaping future health care and health care research in Australia including streamlining and simplifying clinical trial processes, and promoting sustainable funding pathways that create maximum value from each health research dollar. We will provide a forum to share ideas, develop more standardized and streamlined systems for clinical trials, and promote common education and training opportunities.

The activities of ACTA will help develop an important area of public policy - the best use of healthcare resources. ACTA will develop solutions- some that can be implemented with no new resources and others, that will require investment, but will pay for themselves through improved health and cost savings.

Membership

Current ACTA Committee membership:

(Interim Chair) **Professor John Zalcberg OAM** MB BS, PhD, FRACP, FRACMA, FAICD Chief Med Officer & Exec Director Cancer Medicine, Peter MacCallum Cancer Centre Chair, Australasian Gastro-Intestinal Trials Group	**Professor Fran Boyle AM** MBBS FRACP PhD Med Oncologist, Nth Sydney's Mater Hospital Director Patricia Ritchie Ctr for Cancer Care & Res Prof of Med Oncology, U of Sydney
Professor Alan Cass BA MBBS FRACP PhD Director, Menzies School of Health Res, Darwin Prof Res Fellow, Renal & Metabolic Division, The George Institute for Global Health	**Professor Derek P. Chew** MBBS MPH FRACP Edwards Heart Foundation Senior Res Fellow Prof of Cardiology, Flinders University Dept of Cardiovascular Medicine
Professor Geoff Donnan AO MBBS MD FRACP FRCP Director, Florey Institute of Neuroscience & Mental Health Co-Chair, Neuroscience Trials Australia	**Professor Mark Harris** MB BS MD Syd, DRACOG, FRACGP Foundation Prof of Gen Practice & Exec Director, Ctr for Primary Health Care & Equity, UNSW

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