Australian Clinical Trials Alliance

Submission to Medical Research Future Fund Consultation

CONSULTATION TO INFORM THE SECOND AUSTRALIAN MEDICAL RESEARCH AND INNOVATION PRIORITIES 2018-2020

31 AUGUST 2018

Submission by Prof John Zalcberg, A/Prof Katie Groom, Ms Rebecca James, Prof Vlado Perkovic, Mr Kieran Schneemann, Prof John Simes, Prof Steve Webb, Prof Judith Trotman and Ms Margo MacGillivray. Board of Directors, Australian Clinical Trials Alliance.

Which 2016–2018 MRFF priorities do you think need further focus?

1. Clinical Trials Networks

ACTA represents Australia's clinical trial networks (CTNs), clinical quality registries (CQRs) and coordinating centres (CCs). We believe these structures are critical to informing and fostering a self-improving health care system.

In June 2017, ACTA received $5 million over four years to begin a body of work to enable existing and newly formed CTNs to reach a level of maturity and achieve their potential to drive improved health outcomes through strong evidence generation. Eight priority work areas have been established, drawing on broad collaboration across the health sector, including: 1) Efficient and effective CTNs; 2) CTN sector expansion; 3) Impact and implementation of trials; 4) Strengthening consumer engagement; 5) Embedding trials in health care; 6) Research prioritisation; 7) Innovative trial design; and 8) Innovative outcome data. These work areas are responding to key challenges such as ensuring trials are designed and conducted to maximise their implementation; meaningful involvement of consumers in the prioritisation, design and conduct of clinical trials; organisational strategies enabling CTNs to most effectively support programs of trials; collaboration with health service providers to understand what embedding research in routine care looks like; and building capacity to enable the use of novel data sources and study designs. ACTA has actively facilitated the development of new CTNs including the Australia & New Zealand Musculoskeletal CTN, the Australian and New Zealand Alliance for Cardiovascular Trials and an emerging Child and Youth Mental Health CTN, with further networks in the early stages of development, including primary care, Indigenous health, dermatology, and childhood neuromuscular disease.

Over the next three years, these work areas will present valuable opportunities to implement best practice approaches to clinical trials. To ensure this momentum is not lost, and to harness these transformative initiatives through to implementation, realising the substantial potential gains for the health system and the community more broadly, substantial investment of resources will be required from the MRFF.

CTNs provide a uniquely effective infrastructure for generating relevant new evidence. They create re-usable infrastructure owned by a community of clinicians with a deep understanding of the most pressing problems and a shared commitment to solving them. They can operate across sectors of the health system, including primary and community care settings as well as within hospital settings.

A recent economic analysis (https://www.safetyandquality.gov.au/publications/economic-evaluation-of-investigator-initiated-clinical-trials-conducted-by-networks) has demonstrated that for the 25 late-phase clinical trials conducted by three CTNs over a decade, using very conservative assumptions, the overall return on investment was $5.80 for each dollar

invested, and $50 for each dollar of NHMRC investment. A third of the $2 billion benefits identified arose from savings in direct health costs. This further demonstrates the transformative potential of trials conducted by the CTNs to improve the health of Australians and reduce healthcare expenditure via improved care and disinvestment in ineffective treatments.

2. Clinical Quality Registries

Clinical quality registries (CQRs) are a core component of a self-improving health system. By gathering evidence on current practice and risk-adjusted outcomes at a whole-of-population level, they can identify unwarranted variations in care. They are also a mechanism by which the real-world effects of interventions on health care outcomes can be identified.

By providing bench-marked, risk-adjusted measures of relative performance against quality indicators, CQRs have demonstrated both in Australia and internationally the capacity to independently improve quality of care. CQRs have demonstrated cost-effectiveness in themselves. A pilot study across five CQRs conducted by the ACSQHC demonstrated a 5-fold return on investment: (https://www.safetyandquality.gov.au/wp-content/uploads/2016/12/Economic-evaluation-of-clinical-quality-registries-Final-report-Nov-2016.pdf). CQRs represent a core component in the ACTA model of a self-improving health care system.

In addition to their inherent value, CQRs are valuable partners in clinical trials. Australia currently falls behind international standards in the linkage of CQRs to CTNs. CQRs represent core platforms for the measurement of real world outcomes (captured through routine data collection), observing current practice and providing a platform for biobanking, pharmacogenomics and precision medicine initiatives. Linking these types of data together is critical to maximizing their utility. In collaboration with CTNs, CQRs can provide a platform for registry randomised trials, providing the opportunity to study the impact of interventions in real world populations.

With these potential benefits to the health system and the Australian community in mind, the MRFF 2018-19 priorities should retain their focus on Clinical Quality Registries and recognise their role as core infrastructure, providing a cost-effective mechanism to improve patient outcomes. To enable a productive and self-sustaining ecosystem for registry science, ACTA supports the following essential components:

- Targeted programs to support the development of and infrastructure for registry science.
- Capacity building for essential research disciplines in support of this work.
- Support for resource-intensive projects to implement data linkage between registries and national datasets such as the National Death Index, MBS and PBS and admitted-episode hospital data.
- All CQRs should be established and operated under the framework developed by the Australian Commission for Safety and Quality in Health Care (ACSQHC; see https://www.safetyandquality.gov.au/our-work/information-strategy/clinical-quality-registries), to ensure appropriate governance, sustainability and quality to deliver on their mandate and drive improvements in health care and patient outcomes.

Although included in the 2016-2018 MRFF Priorities, and named in the Lifting Clinical Trials and Registries Capacity initiative, direct investment in CQRs has not featured in MRFF funding grants to date. ACTA's funded work in this area is primarily focused on clinical trials, although we consistently aim to connect and integrate the role of registries in our work. We acknowledge that Australian Government Department of Health has been working to establishing a broad, multi-jurisdictional policy position on CQRs during this period. We now strongly support the consideration and targeting of CQRs as essential infrastructure in future rounds of MRFF funding, including consideration of support for the high priority CQRs identified by the ACSQHC.

3. Public good demonstration trials

Public good demonstration trials are a critical tool by which the sector (given sufficient funding) can address questions and challenges of national and international importance. In the real world, they establish which treatments work and which ones don't, allowing the health care system to invest appropriately, including disinvestment of ineffective or harmful treatments. As demonstrated by the Commission's report on return on investment (https://www.safetyandquality.gov.au/publications/economic-evaluation-of-investigator-initiated-clinical-trials-conducted-by-networks), public good trials pay for themselves (and more) and do so with timelines over only a few years. Public investment in these trials enables them to reach beyond the scope of existing public or commercial funding. They can tackle ambitious projects that address complex questions incorporating different health systems, public health challenges and multiple morbidities; develop and showcasing innovative research methodologies; and achieve transformative impact for our health system and the community.

We endorse support for public good demonstration trials that:

- address questions of demonstrated priority, for example through burden of disease or based on value of information which will flow through to return on investment to the health system.
- are underpinned by appropriate infrastructure for their scale, for example by CTNs, CCs or other centres with the expertise and infrastructure, given sufficient support to enable these trials.
- are designed, conducted and reported according to the highest standards and with a view to maximising implementation.

What unaddressed gaps in knowledge, capacity and effort across the healthcare system and research pipeline need to be addressed in the 2018–2020 MRFF Priorities?

1. Support for Coordinating Centres:

The generation and implementation of clinical trial evidence provide an effective and essential path to improving the quality, consistency and value of health care.

Current directions in the generation of evidence include the linkage of translational sciences to clinical trials (incorporating genomic and molecular data); the linkage of trials to electronic

health records and remote devices; opportunities for linkage and reuse of the data generated by trials; the growing use of adaptive and platform trials; embedding clinical trials into routine health care; expanding linkages between registries and trials, and the greater use of health economics in planning and applying clinical trial results.

To meet these challenges, specialised expertise will be essential to ensure that new directions are realised with sufficient validity and credibility to influence healthcare decision makers. We believe that colocation of this expertise within Coordinating Centres, which can act as incubator hubs to provide the critical mass needed to: manage and coordinate large, multicentre, often international clinical trials; manage trials with innovative new designs; provide expertise in biostatistics, health economics, bioinformatics, information technology and quality assurance; and address the changing regulatory and ethics environment. These centres will thus play a key role in ensuring Australia is well placed to maximise the benefits of clinical trials undertaken by the CTNs and CQRs.

Support mechanisms for Coordinating Centres (CCs) would create national capacity through a relatively small number of Centres of Excellence (for example, between one and three CCs per State or Territory, depending on the population base). This would contribute meaningfully to a step change in capacity to coordinate research, to provide infrastructure and develop centres of expertise. These CCs would facilitate the work and efficiency of national CTNs and CQRs. The nature of expertise required will include known areas where capacity is needed, including statistical and health economics expertise, but will also likely branch into other novel areas. An example might include the capacity to develop software solutions for data linkage and sharing between clinical information systems, registries and large datasets, clinical trials data and data repositories, use of patient-reported outcomes to drive quality of care, and the use of machine learning and artificial intelligence.

We believe this expertise is distinct from the work of the Academic Health Science Centres (AHSCs) which need to ensure linkage with and expertise across the clinical workforce, in addition to health service expertise such as data management, patient enrolment, embedding trials in health care and the translation of evidence into practice, all at the institutional/AHSC level.

2. Practitioner Fellowships

ACTA has consistently advocated for embedding clinical trials into routine health care, an aim which has the potential to expand access to clinical trials for the Australian community, enhance the applicability of trials by ensuring they evaluate interventions in routine settings and real-world populations, and reduce the risk of trial failure through poor recruitment or *ad hoc* implementation.

The MRFF funds a number of Practitioner Fellowships through the existing NHMRC funding scheme. While the state aim of the Practitioner Fellowships scheme has been to target active clinicians rather that academics with clinical responsibilities, in practice these fellowships have largely been awarded to very senior researchers with academic appointments (at the Professor or Associate Professor level). A large proportion of clinicians/health professionals who work at the clinical coalface have been unable to access these Fellowships in the current model, including those whose primary role remains clinical practice rather than research and who have not yet had the opportunity to establish an academic track record likely to be

competitive at the professorial level. In addition, health professionals in the best position to be competitive for existing Fellowships may not be those working in fields aligned with priority research questions. The existing Practitioner Fellowships will be replaced in 2019 with the new NHRMC Investigator Grants, and so it is uncertain as yet how these new grants will be awarded in practice.

While the existing support frameworks for clinicians are highly valuable and should continue to be supported, there is an opportunity to more effectively harness this highly talented, skilled workforce, and to focus on facilitating active clinicians to engage in clinical research, as distinct from drawing more clinicians into academic or research-focused roles. This shift would facilitate the embedding of research into daily clinical practice, as well as help create a culture of innovation and continuous evaluation and improvement, with all the associated benefits to the success of the research, the implementability of the results, and the quality of care delivered to the community.

The MRFF should continue to support the NHMRC framework for providing funding to practising clinicians. However, we believe alternative models should be considered to address two areas that have not been addressed successfully within the current scheme.
Firstly, these new models should consider the alignment of practitioner fellowships to areas of priority of research, across appropriate areas of the health system.
Secondly, they should enable access for health professionals unable to access (or historically unsuccessful in) Practitioner Fellowships. For example, funding frameworks should:

- ensure that applications for part-time funding at lower FTE for active clinicians are both eligible and competitive.
- enable funding for blocks of time rather than steady FTE over five years
- enable flexible funding models including payment of salary to other staff back-filling for clinicians during research periods.
- enable funding of new and early career clinical researchers to build capacity in association with organisations able to provide a research platform and mentoring support (such as CTNs, CCs, AHRTCs, etc.).

We would also support active monitoring of the outcomes of future funding rounds to transparently review whether these goals are achieved.

3. Linking research with health service funding agencies

We believe there is an opportunity for greater direct collaboration between health service funding agencies and investigator-led research groups such as the CTNs and CQRs to maximise the extent to which research can align with questions relevant to policy and regulatory decision making. Effective knowledge translation and research implementation require two-way communication, allowing policy decision makers to influence the research agenda, as well as research contributing to policy decisions.

For example, the Pharmaceutical Benefits Scheme and Medicare Benefits Schedule (MBS) currently fund a large segment of the health care system, and yet the evidence base on which these decisions is made is often limited by small patient numbers, commercial drivers, short-term outcome measures and limited real-world data. This presents an opportunity for novel

treatments and interventions to be funded with the provision that they are linked to ongoing research and evaluation efforts managed by the CTNs or CQRs.

Currently, the Pharmaceutical Benefits Advisory Committee maintains a framework for managed entry of drugs with a high clinical need, subject to establishing an MOU with the sponsor (usually the manufacturer) for ongoing research to reduce the identified uncertainty in the evidence (http://www.pbs.gov.au/info/publication/factsheets/shared/framework-for-introduction-of-managed-entry-scheme-for-PBAC-submissions). Similarly, the Medical Services Advisory Committee maintains a framework for approval of services with a planned formal review of actual usage: (http://www.msac.gov.au/internet/msac/publishing.nsf/Content/Predicted-versus-Actual), although this is not a review of the clinical evidence to support the service.

We believe there is an opportunity to expand this kind of approach using broader collaboration with the CTNs and CQRs, expanding the range of interventions that could be considered and the transparency and independence of the resulting evidence. For example, a new device used in cardiology could be supported through the MBS for a limited period provided there is additional supportive data generated by the cardiac CTN or national cardiac CQR on the real world activity/utility of this device, in order to substantiate ongoing funding.

High level policy discussions are required at the Federal Government level to determine how to maximise the opportunities of linking research and evaluation to large Government health funding agencies. Because of the complexity of linking the PBS and MBS to the clinical trials sector and CTNs/CQRs in particular, we believe this planning and development stage should be approached as a project in itself, and may require a number of collaborating participants with knowledge and detailed understanding of the Australian health care system, health policy and research contexts.

How can current research capacity, production and use within the health system be further strengthened through the MRFF?

ACTA supports an approach to MRFF funding that prioritises:

1. Significance / impact of the proposal on practice, policy, outcomes and research
2. Scientific quality appropriate to deliver the stated aims of the proposal
3. Feasibility and team capability (either existing or through a capacity-building approach)
4. Return on investment / value of information

ACTA believes that the proposals outlined above would collectively strengthen the infrastructure needed to support high-quality and coordinated clinical, public health and health services research.