NHMRC accredited Advanced Health Research and Translation Centre

MACH
Melbourne Academic Centre for Health

Inquiry into approval processes for new drugs and novel medical technologies in Australia

Submission from the Melbourne Academic Centre for Health
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About the Melbourne Academic Centre for Health

The Melbourne Academic Centre for Health (MACH) is a National Health and Medical Research Council- (NHMRC) recognised Advanced Health Research and Translation Centre (AHRTC) and a member of the Australian Health Research Alliance (AHRA), consisting of all seven NHMRC-recognised AHRTCs and three Centres for Innovation in Regional Health (CIRH). MACH is a collaboration that includes 10 leading public health services, eight internationally excellent medical research institutes, the University of Melbourne—Australia's highest ranked University—and La Trobe University as an affiliate member. MACH brings together health services and health scientists committed to translation of interdisciplinary research that will benefit patients and strengthen the economy.

Introduction

MACH welcomes the opportunity to provide input to the Standing Committee on Health, Aged Care and Sport's *Inquiry into approval processes for new drugs and novel medical technologies in Australia* (the Inquiry).

The MACH partnership includes world-leading expertise in the development of new medicines. For example, the Walter and Eliza Hall Institute of Medical Research (WEHI) hosts the MRFF-funded National Centre for Drug Discovery; and was the leading academic partner in successful development of the Bcl-2 inhibitor Venetoclax as a new therapy for lymphomas and leukaemias.

MACH has a strong interest in ensuring our partners and Australia continue to be well positioned to access new drugs and novel medical technologies in a timely manner and respond to emerging global trends for the benefits of patients and the economy. This aligns with MACH objectives including delivering tomorrow's healthcare by ensuring that health science can be efficiently developed, often in collaboration with leading industry partners, into improvements in the prevention, diagnosis, treatment and palliation of ill health.

This submission is made by MACH on behalf of health service, medical research institute and university partners and is supported by the MACH Strategic Translational Research and Platforms Committee.

Recommendations to the Standing Committee in response to the Inquiry's Terms of Reference represent input from the following MACH partners:

- Austin Health
- The Bionics Institute
- The Centre for Eye Research Australia
- Murdoch Children's Research Institute
- Northern Health
- Peter MacCallum Cancer Centre
- The Royal Melbourne Hospital
- St Vincent's Institute of Medical Research
- The University of Melbourne
- Walter and Eliza Hall Institute
- Western Health

Recommendations

Recommendation 1
In keeping with overseas competitors, Australia should invest in providing access to the underpinning technologies needed to translate world-leading discovery science into advanced therapies, particularly biologics.

Recommendation 2
PBS listing of drugs for orphan or rare diseases and off label indications should be fast tracked.

Recommendation 3
The current Research & Development (R&D) Tax Incentive should be optimised to attract new biotech investment and further tax and non-tax incentives should be provided to companies and groups who focus on the development (or re-purposing of) medicines and technologies to treat orphan diseases and/or niche patient groups.

Recommendation 4
A funding scheme (addressing identified issues of the Biomedical Translation Bridge program) should be specifically designed to focus on strengthening collaboration between discovery scientists, drug development and medical technology experts, and clinicians.

Recommendation 5
Funding should be provided to NHMRC-accredited Translation Centres to establish and coordinate Research Hubs and New Therapies Committees with relevant expertise to advise ethics committees, and coordinate and manage clinical trials for new drugs and novel medical technologies.

Recommendation 6
To deliver international best practice in digital innovation to accelerate clinical trials, including identification, recruitment and follow-up of participants, funding should be provided to support linked data across the care continuum.

Recommendation 7
An expedited and timely marketing approval process for medicines which have already been approved in comparable international markets should be established.

Recommendation 8
The funding reimbursement model for administering new drugs and novel medical technologies should be reviewed and optimised.

Response to the Terms of Reference

1. The range of new drugs and emerging novel medical technologies in development in Australia and globally, including areas of innovation where there is an interface between drugs and novel therapies

The range of drugs/biologics in development needs to be responsive to the needs of evolving requirements, including for rare subtypes. As technology will continue to undergo innovation, definitions of drugs/biologics will continue to evolve.

Biologics should be a priority for drug development in Australia. Many top selling drugs are antibody based and these have a had a profound clinical impact. The clinical applications for biologics are predicted to continue expanding, with rapid recent progress in cancer treatment. Australia has great expertise in the relevant areas of immunology, and depth in target biology, but we have no national program to promote the discovery and development of new biologics.

Recommendation 1:
In keeping with overseas competitors, Australia should invest in providing access to the underpinning technologies needed to translate world-leading discovery science into advanced therapies, particularly biologics.

2. Incentives to research, develop and commercialise new drugs and novel medical technologies for conditions where there is an unmet need, in particular orphan, personalised drugs and off-patent that could be repurposed and used to treat new conditions

Reducing regulatory barriers
Ensuring access to new treatments for rare conditions and orphan indications is a major challenge in Australia where the market is significantly smaller than those overseas such as Europe, North America or Asia. Drugs already approved for common indications that can be repurposed for a rarer disease often fail to be listed on the Pharmaceutical Benefits Scheme (PBS), and as such are prohibitively expensive despite Therapeutics Goods Administration (TGA) approval.

An example of such as drug is adalimumab, which is easily accessible for rheumatoid arthritis but remains unlisted on the PBS for the orphan disease, non-infectious uveitis, despite evidence proving its efficacy (1).

Recommendation 2:
PBS listing of drugs for orphan or rare diseases and off label indications should be fast tracked.

Optimising Research & Development tax and non-tax incentives

The current Research & Development (R&D) Tax Incentive provides a mechanism to stimulate investment in Australia to research, develop and commercialise new drugs and novel medical technologies. However, optimising and enhancing this scheme would make Australia a more attractive location for overseas companies to invest in drug development, clinical trials and medical technologies. Any significant decrease in tax incentive related to this scheme would have a detrimental impact on R&D within Australia.

It is important to ensure that non-tax incentives and advantages are also provided such as:

- smaller submission requirements and reduced evaluation fees for rare indications to encourage submission by pharma (for those rare indications where otherwise they would not submit);
- more flexible rapid approval pathways, particularly for rare indications, with post-approval data collection / follow up;
- for new drug approval processes: incentives and advantages for drugs which have been developed in Australia to encourage R&D in Australia, making it all the way to successful approval; and
- for drug re-purposing: incentives and advantages for approvals initiated by non-pharma companies such as consumer groups or academic groups, with less onerous administrative requirements, for rare indications.

Recommendation 3:

The current Research & Development (R&D) Tax Incentive should be optimised to attract new biotech investment and further tax and non-tax incentives should be provided to companies and groups who focus on the development (or re-purposing of) medicines and technologies to treat orphan diseases and/or niche patient groups.

Reducing research funding barriers

It has been expressed that traditional funding bodies such as the NHMRC and the more recently established Medical Research Future Fund (MRFF) provide comparatively limited funding opportunities for early stage drug discovery and novel medical technologies, affecting the ability for local institutions to develop and commercialise new drugs and novel technologies in the treatment of rare diseases. It is recommended that funding mechanisms focused on building local drug discovery and medical technology/capabilities through culture of collaboration are explored through avenues such as the MRFF.

The MRFF Biomedical Translation Bridge program (BTB) program has been a failed attempt to bridge this gap (see **Table 1** for further detail and recommendations). This is critical, as target validation activities lay the foundation for any subsequent new medicine program. If targets are not validated in a robust manner, any subsequent investment into screening, drug discovery and development, is entirely futile.

Table 1: MRFF Biomedical Translation Bridge program (BTB) current issues and recommendations

Current Process	**Issue resulting from current process**	**Recommendation**
Rushed mentoring process at EOI stage	No value brought by mentoring process	Allow more time for EOI review and mentoring process
Requirement for matched funding	This means the BTB program is not bringing any funding gap, it is only increasing (doubling) budget for projects with existing funding	Eliminate requirement for matching funding to truly bridge funding gap
Matching funding cannot come from federal funding source	This means most of academic projects were not eligible in the first place. Most eligible projects were coming from companies with private funds available, making the BTB a corporate welfare exercise and not benefitting the academic sector	Eliminate requirement for matching funding to truly bridge funding gap and be able to support innovations from medical research institutes who cannot provide proprietary funds for matched funding
Review and award criteria skewed the awards towards less risky and more advanced projects	Earlier stage more innovative projects (for example still at target validation stage) were not funded	Built award criteria to have a balanced portfolio across all of the early stages of development and translational research as opposed to only the most advanced ones: target validation, hit generation, hit-to-lead development, lead optimisation and preclinical development
Very limited size of funding (maximum A$1M per project)	A$1M is not sufficient to bridge any funding gap given the spent required for drug discovery programs. This is not an issue at present as the strategy should be to first find the winning BTB formula then expand the program in term of funding size.	Implement the next round of program based on all above recommendations with similar amounts, then increase awards amounts as appropriate in future rounds.

Additionally, an opportunity exists for providing incentives to enhance university collaboration with drug discovery focused industry partners and encouraging commercialisation skills in higher education STEM training. This would establish and strengthen both collaborative and translational pathways, and business savvy researchers.

Recommendation 4:

A funding scheme (addressing identified issues of the Biomedical Translation Bridge program) should be specifically designed to focus on strengthening collaboration between discovery scientists, drug development and medical technology experts, and clinicians.

3. Measures that could make Australia a more attractive location for clinical trials for new drugs and novel medical technologies

Experience overseas shows that trials for novel therapies are not fully cost recovered from industry and new capacity must be funded by either government or philanthropy. This is not just about recruitment, this is not just about streamlining governance, which are important too, it is primarily about incentives and support for large scale efficient business models. Without these Australia will not be a preferred destination for new therapies and we shall have no hope of ever translating our own discoveries.

Establishment of Research Hubs coordinated by Translation Centres

Australia requires incentives to centralise clinical trial management and government investment to achieve this as there is currently minimal, if any, co-ordination of research activities between hospitals, which are often run in separate departments within hospitals. This leads to inefficient business models as well as difficult and massively duplicated interaction with industry. These current business models have no capacity to invest in the infrastructure of facilities, and the people and skills needed to run novel therapies.

The establishment of Research Hubs, coordinated by NHMRC-accredited AHTRCs and CIRHs (Translation Centres), would streamline the approval process and management of clinical trials which would undoubtedly make Australia a more attractive location for clinical trials for new drugs and novel medical technologies resulting in benefits to both health and the economy.

These Translation Centres, which form the Australian Health Research Alliance (AHRA), collectively account for 95% of Australia's academic and research teams, and 78% of its acute health services (2). These Centres are ideally configured to foster bidirectional translation of research evidence from across the research continuum, driving not only improvements in health, but also in wealth by stimulating the economy; and they have the expertise to move discovery research into clinical and commercial implementation.

MACH proposes that with financial support, Translation Centres provide an excellent mechanism to coordinate Research Hubs across Australia providing scientific and cost-benefit assessment of new drugs and novel medical technologies in addition to: **Leadership** in outstanding research- and evidence-based clinical care, including for the most difficult clinical conditions; and **Excellence** in innovative biomedical and clinical research (3).

Coordinated and streamlined ethics and governance, and clinical trials processes

Measures to streamline and harmonise ethics and governance reviews across jurisdictions supported by New Therapies Committees which provide the scientific expertise to support ethics review are an additional measure that would enhance Australia's appeal as a location for clinical trials.

A major upheaval of clinical trial review by centralising ethics reviews within each state coordinated by Translation Centres following standardised review and approval processes would significantly increase the efficiency of running clinical trials across Australia. An additional step of a single governance application covering relevant trial sites across Translation Centres would harmonise review of clinical trials and assist clinicians by a streamlined submission.

In addition, a national, coordinated clinical trials network (consisting of subspecialty groups) with a fast, streamlined, efficient and centralised human ethics and governance framework and a single ethics submission and review system (portal) would alleviate jurisdictional differences and reduce time and resources required to obtain ethics approval for multisite studies, which is often the case for commercially sponsored clinical trials.

See: AHRA Research Translators paper (4) for a proposed funding model to support this recommendation.

Recommendation 5:

Funding should be provided to NHMRC-accredited Translation Centres to establish and coordinate Research Hubs and New Therapies Committees with relevant expertise to advise ethics committees, and coordinate and manage clinical trials for new drugs and novel medical technologies.

Guaranteeing patient recruitment

Patient accrual is an equally important aspect to make Australia a more attractive location for clinical trials for new drugs and novel medical technologies. TeleTrials will assist which has been funded in the last budget and has the capacity to improve accrual across a wide range of trials (A$75M). While Australia is considered a global leader in this respect by our pharma partners, additional innovative strategies based on data integration must be explored to better be able to identify appropriate patients in real time. Exploring new innovative methods of data integration such as BioGrid Australia and others such as TRICEPS (Treat Rare Collect Data and Share – rare cancer data integration via the International Rare Cancer Initiative (IRCI)) is critical.

Recommendation 6:

To deliver international best practice in digital innovation to accelerate clinical trials, including identification, recruitment and follow-up of participants, funding should be provided to support linked data across the care continuum.

4. Without compromising the assessment of safety, quality, efficacy or cost-effectiveness, whether the approval process for new drugs and novel medical technologies, could be made more efficient, including through greater use of international approval processes, greater alignment of registration and reimbursement processes or post market assessment

Increased regulatory support for approvals

Efficiency of the approval processes for new drugs and novel medical technologies could be achieved by an expedited marketing approval path for medicines which have already been approved in the EU and the US. In cases where this is suitable, it would be necessary for there not to be a long delay. For example, if it takes two years from the FDA approval to the PBAC approval, then other data may well have changed, necessitating a whole new set of data to be reviewed, negating the concept of tight alignment. *'Greater use of international approval processes'* would require timeliness of process. This would be greatly welcomed, not least by our patients who currently have to wait 2-3 years or longer to access life-prolonging or life-saving drugs. For many, that simply means dying while waiting.

Recommendation 7:

An expedited and timely marketing approval process for medicines which have already been approved in comparable international markets should be established.

Optimised financial reimbursement model

Another opportunity is parallel regulatory evaluation and reimbursement assessment for new medicines to streamline a new medicine's market entry in line with listing on the PBS. This would expedite availability to all potential patients.

In addition, it is recommended that due to the expense associated with administering new drugs and novel medical technologies the funding model is reviewed and optimised to enable institutions to access GST reimbursement in a more timely manner.

Recommendation 8:

The funding reimbursement model for administering new drugs and novel medical technologies should be reviewed and optimised

References:

1) Glenn J. Jaffe et al. (2016). The New England Journal of Medicine. Adalimumab in Patients with Active Noninfectious Uveitis. N Engl J Med 2016; 375:932-94: https://www.nejm.org/doi/full/10.1056/NEJMoa1509852

2) Australian Health Research Alliance: https://ahra.org.au/

3) National Health and Medical Research Council Accreditation Criteria: https://www.nhmrc.gov.au/research-policy/research-translation/recognised-health-research-and-translation-centres

4) Research Translators to Improve Healthcare and Boost the Economy: Addressing the Workforce Gap in Health Research Translation: https://ahra.org.au/wp-content/uploads/Research-Translators-to-Improve-Healthcare-Outcomes-and-Boost-the-Economy_06Oct20.pdf

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