Research and Development Taskforce submission in response to the *Consultation on proposed regulatory changes for clinical trials of medical devices*

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Introduction

The Research and Development Taskforce (RDTF) welcomes the opportunity to submit a response to the Therapeutic Goods Administration's consultation paper on *proposed regulatory changes for clinical trials of medical devices.*

The RDTF is a multi-sector collaboration between AusBiotech, the Medical Technology Association of Australia (MTAA), and Medicines Australia. The membership consists of research and development experts, particularly in clinical trials, and offers a unique industry perspective to stakeholders across Federal and State Governments as well as the broader health and research and development sector.

Responses have been framed around the TGA's feedback questions, as requested in the consultation paper.

Question 1. Do you think the TGA should have more oversight of clinical trials involving high-risk medical devices (i.e., invasive, or implantable medical devices that have not previously been approved for use in people)?

Summary

Australia's bio-medical technology industry is supportive of the TGA's risk-based regulatory approach where regulation is commensurate with the risks posed by the therapeutic good to best protect and advance public health. While we agree with the TGA that over time, medical devices have increased in their complexity with advances in technology such as the materials used (including 3D printed materials), and the interaction with software, we contend that these developments do not infer that the risk has increased – as indicated, without evidence, in the consultation paper.

A thorough process is already in place for assessing risk, and therefore implementing the proposed changes will not better protect patients' health, as well as disadvantaging public health activities. Therefore, it is recommended that the TGA withdraws the proposal on the basis that the current provisions are sufficient regarding oversight of its delegated responsibilities for medical devices used in the context of clinical trials.

Patient safety is at the heart of the existing processes

Sound patient protection is provided through Australia's existing scientific and ethical review system in place for high-risk devices, along with the mandatory safety reporting requirements of the TGA.

The greatest value of ensuring patient safety in clinical trials lies in the provision of subject matter experts in HRECs to independently evaluate the risks and benefits of the proposed research. The NHMRC National Statement on Ethical Conduct in Human Research 2018 requires that HRECs are comprised of appropriate expertise related to the research project methods and area of practice, including:

- "At least two people with current research experience that is relevant to research proposals to be considered at the meetings they attend. These two members may be selected, according to need, from an established pool of inducted members with relevant expertise" (5.1.30a)
- "At least one third of the members should be from outside the institution for which the HREC is reviewing research" (5.1.29b), and

- "The institution should ensure that the HREC has access to the expertise necessary to enable it to address the ethical issues arising from the categories of research it is likely to consider. This may necessitate going outside the HREC membership." (5.1.33)

As such, the multi-disciplinary HREC is independent and any additional subject matter expertise also offers an independent voice, thereby delivering appropriate and high-quality consideration of the scientific and ethical impacts on patients.

Should ethics committees feel they lack the required expertise in the HREC membership, then it is taken very seriously, and they can (and do) request applications to be reviewed via the CTA scheme, thereby giving the TGA the assurance that they will have the oversight that is necessary for certain types of high-risk novel devices. In addition, the same subject matter experts can review serious adverse events and safety summary reports, as they do now.

Australia's HREC oversight practices are robust, modern, and effective which is demonstrated by the lack of examples of deficiency provided by the TGA; should such deficiencies be evident then we suggest that they be managed in accordance with HREC compliance within the national statement.

We firmly believe that in Australian clinical trials, patient safety is paramount and there are appropriate controls in place for ensuring safety prior to and during a clinical trial with the correct medical oversight and procedures.

To further support this, ethics committees already have processes in place to review First in Human (FIH) studies. To ensure the safety of the participant is protected, ACT, SA, VIC, and NSW have state-specific ethical review processes for early-phase trials and most hospitals have additional reviews for FIH studies.

Global medical device company Medtronic Australasia has reported on how Australia's current and robust clinical trial oversight framework is internationally renowned: during due diligence on a number of applications, the US FDA has specifically requested the same evidence as requested by Australian HRECs (i.e., how the medical device meets the compliance requirements) thereby reflecting the high level of oversight currently being undertaken. This experience and sentiment are echoed broadly by industry.

Given there have been no known patient-related safety issues, we question the need for these proposed changes.

Potential impact of the proposal on clinical trials conducted in Australia

As noted above, Australia has world-class regulation in place in order to best protect patients, and we suggest that implementing the proposed changes will not better protect patients' health, and equally, it will also disadvantage public health activities.

Australia's existing streamlined regulatory and ethics approval framework currently maintains essential risk management for public good, whilst simultaneously offering a key driver for global competitiveness; as outlined in MTPConnect's 2021 report on Australian clinical trials, it provides speed to start-up not provided in other jurisdictions. Another two MTPConnect reports highlight the significant growth of device trials, particularly in early phase clinical trials, in recent years attributed to the CTN scheme. The existing framework and growth in clinical trials provides robust and safe regulation, early access to

innovation for Australian patients, as well as information about products in development; economically, it offers work force skills and revenue to Australia's healthcare system.

If the proposal were to be adopted and, as anticipated, there is a reduction in FIH clinical trials, there would be a subsequent impact on follow-on clinical studies, thereby compounding the impact on patients and the Australian economy. This is because participation in FIH studies often leads to participation in follow-on studies.

Resource impact of the proposal on clinical trials conducted in Australia

The TGA states in the proposal that the "*level of oversight is in contrast with comparable regulators overseas (Europe, UK, USA, Canada, and Japan) where the medical device regulator is typically involved in the approval process for medical devices clinical trials, particularly for higher risk implantable products".*

While this is correct, we contend it is unnecessary. The same level of risk oversight is already in place, with responsibility delegated to the HRECs. Other countries are working to minimise their regulatory burden while maintaining risk-based regulation, and the proposed timeline is moving away from what other jurisdictions are aiming for.

For example, the UK is seeking to pass legislation on clinical trials regulation which would mean the regulator and ethics committees have a maximum of 30 days to approve the trial, with an option to issue a request for further information. After the MHRA and REC have 10 days to respond to the questions in the RFI. The US FDA's process is similar to the UK's proposed legislative process.

The TGA also states in the proposal that "*The anticipated change that the regulatory burden is minimal. This is because information required to be submitted to the TGA as part of a CTA is already held by the manufacturer, no additional effort is required to gather data"*. This statement is incorrect because the additional effort required of sponsors would include global regulatory affairs involvement, and additional time and resources to prepare submissions and respond to questions. This will result in significant delay and financial burden on sponsors.

The proposed timeline of 90-day minimum pre-trial regulatory approval process and CTA fee of $19,699 in addition to ethics, governance, and high site costs (compared to many countries in the world) would be prohibitive for many sponsors. It adds an additional barrier to home-grown SMEs and is incongruent with the whole-of-government's policy objectives to set up and stimulate entrepreneurs – including in the priority area of medical health.

The additional cost barrier to a pre-revenue generating start-up risks stifling Australian innovation and would result in a reduction in FIH trials conducted in Australia and that manufacturers/sponsors would most likely go elsewhere to conduct the clinical trial. This impacts both clinical trials activities, but also Australian's early access to innovative technology.

The fee structure is also not in line with the US, Canada, Japan, and the UK as they do not charge for their review of trials, which means the approximated cost proposed by the TGA alone will put Australia at a disadvantage.

The responsibility for determining which types of high-risk novel devices will be reviewed under the CTA scheme has not been clearly defined in the proposal. The TGA states in the proposal that "*if agreed, it is estimated that less than 10 per cent of device clinical trials (i.e., 20 or less per year) would be affected by the proposal".* Who will have the responsibility for determining which devices are assessed under the CTA scheme?

Alternative routes

Industry appreciates the opportunity to thoroughly review the current design of clinical trials oversight.

The proposal asks for ideas for alternative routes to achieve the goal of more oversight by the TGA for early phase trials. As the current regulatory process is commensurate with risk and has led to many positive clinical trials being conducted in Australia allowing patients very early access to novel devices, it is contended that the status quo is retained.

Should the TGA still seek greater overview of the existing processes, spot audits by the TGA on existing HRECs would be accepted. This would enable a scalable solution to government without adding additional barriers to innovators in Australia.

Conclusion

The evidence demonstrates that the current process is safe and efficient for participants in FIH studies and eliminating the CTN pathway for FIH studies would be detrimental to Australia and the healthcare sector.

The RDTF recommends that the proposal is withdrawn, and we encourage engagement with the medical technology and clinical research sectors to discuss concerns held by the TGA so that consensus on a suitable path forward can be reached.

Question 2. Do you think clinical trials of medical devices should be included in the existing GCP Inspection Program?

There is overall support from industry for the proposed inclusion of clinical trials of medical devices in the existing GCP inspection program.

Moreover, including medical device trials in the existing GCP Inspection Program could serve the purpose of increasing TGA's oversight of those trials. Contrary to the above discussed proposal to mandate the CTA scheme for some of those trials, this proposal would not eliminate Australia's competitive advantage and affect Australia's ability to attract clinical trials.

If this change were to be implemented, the TGA would need to recruit or train appropriately skilled personnel able to audit according to ISO 14155.

Industry would like to point out that all medical device trials conducted under ISO14155 are under obligation to be audited. Consequently, many industry-sponsored clinical trials are subject to internal and external audits already. In addition, trial sites strive to be always 'audit ready'. Hence, this proposal would not add additional burden.

About AusBiotech

AusBiotech is the Australian representative body for one of Australia's most innovative industries with a well-connected network of over 3,000 members in the life sciences industry, which includes biotherapeutics, medical technology (devices and diagnostics), food technology and agricultural biotechnology sectors.

This response has also been developed together with the AusBiotech's Clinical Trials Advisory Group, AusMedtech Advisory Group, and AusMedtech Regulatory Affairs Advisory Group, which each provide guidance and advice on operational and policy-

related regulatory matters. The submission represents AusBiotech members actively engaged in delivering social and economic benefits to Australia through the commercialisation of biotechnologies and medical technologies, and member companies working toward a more effective environment for clinical trials in Australia.

About the Medical Technology Association of Australia

The Medical Technology Association of Australia (MTAA) is the national association representing companies in the medical technology industry. MTAA aims to ensure the benefits of modern, innovative and reliable medical technology are delivered effectively to provide better health outcomes to the Australian community

About Medicines Australia

Medicines Australia is the peak body representing the innovative, research-based, medicines industry in Australia. Our members develop, manufacture and supply critical medicines and vaccines available on the Pharmaceutical Benefits Scheme (PBS) and the National Immunisation Program (NIP). Our membership comprises small, medium and large Australian and multinational companies.