AusBiotech’s response to the TGA’s proposal to pilot a ‘Good Clinical Practice Inspections Program’ that will inform a routine program

To:
Inspections Section
Manufacturing Quality Branch
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606
https://www.tga.gov.au/node/873295

22 February 2019

From: AusBiotech Ltd
ABN 87 006 509 726
Level 4, 627 Chapel St
South Yarra VIC 3141
Telephone: +61 3 9828 1400
Website: www.ausbiotech.org
Context

AusBiotech is pleased to provide comments to the Therapeutic Goods Administration (TGA) in response to its draft paper entitled ‘Good Clinical Practice (GCP) Inspections Program.’

AusBiotech is a well-connected network of over 3,000 members in the life sciences industry, which includes bio-therapeutics, medical technology (devices and diagnostics), food technology, industrial and agricultural biotechnology sectors. Within AusBiotech, the AusBiotech Clinical Trials Advisory Group provides expert advice on operational and policy-related clinical trial matters. Our response has been led by this group.

Response to proposal

AusBiotech is supportive of measures that seek to enhance the safety, quality and efficacy of clinical trials, and other measures that seek Australia’s desirability as a destination for clinical trials.

Clinical trials make a critical contribution to the health and wellbeing of Australians, and bring significant economic benefits to this country. All Australians have a vested interest in attracting more trials to Australia and in ensuring that all trials continue to be undertaken to high ethical, safety and quality standards.

This submission provides AusBiotech’s view of the TGA’s proposed pilot of a Good Clinical Practice Inspections Program.

Purpose of the pilot and a permanent inspections program

The rationale and evidence-base presented by the TGA do not support that an inspections program would further enhance the safety and quality of the overall clinical trials system in Australia.

In proposing that a domestic GCP inspections program would strengthen the clinical trials environment, the document states that ‘a domestic GCP inspections program will address a gap in the current regulatory oversight of the conduct of Australian clinical trials.’ It is AusBiotech’s position that no gap is articulated. Australia already has a strong regulatory and ethical/governance framework for clinical trials and a pre-existing reputation as a safe and desirable place to conduct trials. It is also stated that ‘It will support the TGA’s ability to identify and manage risk under the CTN and CTX schemes.’ What is the TGA’s current role in identifying and managing risk under the CTN scheme? Is this not this delegated to HRECs, unless further information requested under the Section 31A scheme?

The evidence cited which underpins the proposed pilot appears to be based on the UK program of auditing Investigator Initiated Trials (IITs):

“A domestic GCP inspections program in the United Kingdom raised the standard of conduct and quality of clinical trials - particularly those sponsored by non-commercial organisations - and reduced the risk of GCP non-compliance.”

There is no discussion as to how this experience may relate to commercially sponsored clinical trials, or how a domestic audit program may enhance Australia’s clinical trial infrastructure, quality or reputation in this sector.
The document also states that inspections will ‘address the potential risk of a decline in international recognition of Australian clinical trial data quality and integrity,’ however there is no evidence nor hypothesis proposed as to why there may be a potential decline.

Further, the FDA, EMA and other regulatory bodies can and do already audit commercially sponsored clinical trials in Australia. Australia already has a reputation for high quality clinical trials and any potential benefit of the new program has not been articulated in the proposal. In the absence of cogent articulation of a potential benefit in this already highly governed and managed sector, we propose that, given a resource-constrained environment, the TGA’s resources may be more efficiently and effectively used for other activities, for example greater early consultation in the licensure process.

Alignment with other ongoing clinical trial initiatives is crucial, and this is not articulated in the document. For example, how does this program align with the Australian Commission on Safety and Quality in Health’s standards and the Clinical Trials Governance Framework it is developing? This alignment is important, to ensure that duplication and confusion are avoided, and to maximise the efficacy of these new initiatives. It also needs to complement healthcare initiatives generally.

**Characterisation of commercially-sponsored clinical trials**

The language in the report should be refined to improve its accuracy and better reflect the positive impacts of commercially-sponsored clinical trials in Australia. The report states, in comparison to trials sponsored by industry, which the document identifies as companies ‘with a commercial agenda focused on the regulatory requirements for the marketing of the therapeutic goods investigated’:

“By contrast, non-industry sponsored clinical trials are conducted for the public good (emphasis added) by investigating clinically relevant questions to identify the best treatment irrespective of its commercial value” (p. 9).

The language used in this way inherently implies that commercially sponsored clinical trials are not conducted ‘for the public good’, a notion with which we strongly disagree.

One of the strengths of Australia as a place to conduct clinical trials is the clinical trials eco-system that currently exists here. We have a strong regulatory regime, an active medical research and development sector, a variety of trial sites, a skilled workforce, and a diverse population. Commercial trials play an important role in this system, alongside IITs, and produce diagnostics and medical products that save lives as well as potential, cutting-edge alternative treatment pathways.

**Establishment and remit of the pilot program**

We suggest that the current audit program of commercially-sponsored clinical trials from other regulatory agencies and clinical trial sponsors adequately addresses this sector of the market. The TGA audit of same would not serve the purpose of improving Australia’s commercially-sponsored clinical trial capability or quality, nor would it improve Australia’s desirability as a destination for clinical trials.

The pilot program seeks to inform the progress of a proposal to implement a routine GCP inspection program in Australia across all parts of the sector, however the evidence in support of the cited objectives of the program only support a potential benefit to investigator-initiated sites, and only in relation to pharmaceutical trials. Importantly, the proposal excludes complementary medicine trials and medical devices where there may be a possible benefit (though none have been articulated).
Information pertaining to the ultimate disposition of the results should be articulated prior to decision as to whether to pilot an audit program. The document states that sites will receive an inspection report inclusive of any issues identified, but does not identify what constitutes an ‘issue’ and who else will have access to the report. It also states that:

“If an inspection of a clinical trial identifies serious issues with the conduct of the trial or data integrity then information of the observed issues would be released to the HREC and/or Authorising Institution. Where an inspection identifies issues that might be seen to have a public safety risk for participants then various compliance powers may be considered.”

More information and consultation is needed on whether this will be published (and if so, when), what constitutes a ‘serious issue,’ and which ‘compliance powers’ would be used. Rationale in support of the ultimate disposition of audit results needs to be provided.

Cost

There is discussion in the document as to who should ultimately bear the cost of conducting clinical trial audits. We propose that, were clinical trial sites or sponsors be obliged to bear the costs, the cost of Australian clinical trials would increase, having a detrimental effect on Australia’s attractiveness as a destination for clinical trials.

It is stated ‘The cost of the TGA’s regulatory services are recovered by the fees and charges levied on Australian Manufacturers and Sponsors.’ How will the system ensure that local, Australian companies are not compensating and taking the brunt of the cost when the majority of inspections are for internationally-sponsored clinical trials?

Risks and unintended consequences

The TGA should more thoughtfully consider the potential negative consequences of undertaking the pilot.

As mentioned above, cost may be one unintended negative consequence.

There may also be unintended consequences in creating a permanent clinical trials inspection program for the whole sector that is based on a small number of pharmaceutical, investigator-initiated trials, since commercially sponsored trials are conducted and governed significantly differently from IITs. We suggest that the results from one sector (e.g. IITs) are not transferrable to the other (i.e. commercially-sponsored trials). AusBiotech encourages the TGA to consider an alternative, more efficient use of resources, or a better-articulated rationale for conducting a pilot of auditing commercially-sponsored clinical trials.

There is a risk of generating poorer performance metrics than the FDA or EMA due to selection of high-risk clinical trials and IITs which are not generally subject to as stringent Sponsor audits as industry-funded clinical trials.

Further consideration is required by the TGA on whether the results and data from the pilot program as currently envisaged will allow for the development of a permanent programme that meets its stated objectives across the entire clinical trials eco-system.