Summary of SHPA views on the National One Stop Shop Phase III consultation, March 2024

The Society of Hospital Pharmacists of Australia (SHPA) is the national, professional organisation for the 6,100+ Hospital Pharmacists, and their Hospital Pharmacist Intern and Hospital Pharmacy Technician colleagues working across Australia's health system, advocating for their pivotal role improving the safety and quality of medicines use. SHPA convenes a Clinical Trials Specialty Practice stream, with over 470 members who are leaders and experts in the provision of quality and safe clinical trials pharmacy services to clinical trial participants in Australian hospitals.

SHPA commends the Australian Commission on Safety and Quality in Health Care (the Commission) on the progress to date in developing National One Stop Shop (OSS), a rare transformational opportunity to establish a nationally consistent and harmonised operating environment for the approval and management of clinical trials and health-related research in Australia.

In welcoming the recent face-to-face opportunity to engage with the Commission on the National OSS Phase III consultation, SHPA would like to provide further support in advocating for the integration of Pharmaceutical Inspection Co-operation Scheme (PIC/S) Good Manufacturing Practice (GMP) standards and review processes within the development of the OSS ethics application platform to improve patient safety of clinical trials in Australia.

Clinical Trial Pharmacists are imperative to the governance and success of all medicine associated clinical trials services across all settings. Given the wealth of subject matter expertise that SHPA represents for clinical trials involving Investigational Medicinal Product (IMP) management, SHPA looks forward to continuing our engagement with the Commission in the ongoing design, delivery, and implementation of national clinical trials reforms in Australia, and proposes the following recommendations:

Recommendation 1: Implement mandatory Good Manufacturing Practice (GMP) assessment of Investigational Medicinal Products (IMP) in the development of the One Stop Shop Human Research Ethics Committees (HREC) application platform to improve patient safety in clinical trials.

Recommendation 2: The Commission should engage with SHPA as a key stakeholder in the ongoing design, delivery and implementation of national clinical trials and health and medical research reforms in Australia.

If you have any queries or would like to discuss our submission further, please do not hesitate to contact Jerry Yik, Head of Policy and Advocacy on jyik@shpa.org.au.

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Background

Access and supply of clinical trial products are regulated under ethical and other clinical trials governance frameworks in addition to the therapeutic goods legislation in Australia.[1] This includes the requirement for manufactured investigational medicinal products (IMPs) to comply with the *Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) guide to Good Manufacturing Practice (GMP)*.[2]

Recognised as the international standards adopted by countries and pharmaceutical inspection authorities, the *PIC/S guide to GMP* provides a harmonised and constructive co-operation in the field of GMP. Within Australia, the *PIC/S guide to GMP* has legislative power through the operation of section 36 of the *Therapeutic Goods Act 1989*[3], enforced by the Therapeutic Goods Administration (TGA) for the manufacturing of investigational medicinal product used in clinical trials to ensure quality, safety and potency risks are minimised for the public.

The PE009-14 of the *PIC/S guide to GMP for Medicinal Products,* excluding Annexes 4, 5 and 14, emphasise quality control measures throughout the manufacturing process, including quality assurance, documentation, personnel, facilities, equipment, and validation of processes.

Through participation in the PIC/S and other agreements, including Mutual Recognition Agreements, Memorandum of Understanding, Cooperative Agreements, and other arrangements with recognised regulators, the TGA relies on shared inspection reports and assessments to validate facilities and ensure compliance with GMP standards. For IMPs manufactured overseas, where different GMP standards may be legislated, the Sponsor must ensure GMP standards equivalent to *PIC/S guide to GMP* are adhered to. Compliance with these standards is fundamental in maintaining the reliability of trial outcomes and safeguarding clinical trial patients.

Whilst these legislations and GMP processes are strictly complied with by the pharmaceutical industry for commercially sponsored clinical trials, the non-pharmaceutical sector, predominantly investigators and sponsors of collaborative research group trials, is largely unaware of these responsibilities. Human Research Ethics Committees (HRECs) are not supported through formal mechanisms to assure GMP compliance during their safety and quality reviews, i.e. the explicit requirement for GMP review in the *National Statement on Ethical Conduct in Human Research 2023*[4]; the inclusion of specialist knowledge within the HREC membership skill matrix; or inclusion of appropriate GMP documentation during the submission process.

Non-pharmaceutical sector risks in non-GMP compliant production of IMPs

Manufacturing IMPs in facilities that do not adhere to *PIC/S guide to GMP* standards poses inherent risks to patients and clinical trial data integrity. Such facilities may lack stringent quality controls, potentially resulting in IMP of unacceptable quality. Historic issues with products from such facilities have included counterfeiting, variations in potency, and microorganism or other contamination. Large and well publicised clusters of injury and death have resulted from products produced at such facilities.

The TGA expects Sponsors to take responsibility for the quality assessment of applicable GMP for imported products in a clinical trial and recommends that the trial sponsor ensures that the GMP licensing for other countries adheres to the principles of GMP as set out in the *PIC/S guide to GMP*. An adequate assessment of

such a product must be based on sound Quality Risk Management processes and a thorough understanding of the principles of GMP.

Non-pharmaceutical sector sponsors are generally less knowledgeable regarding their GMP obligations as required by the TGA and are often unaware of the legally enforceable requirements. It is not uncommon for non-pharma sponsors to include non-compliant IMP within their clinical trials. The legislation governing GMP is difficult to understand, highly complex, includes all stages of manufacture, and there is minimal structural support for this sector to comply with their legislative obligations unlike the pharmaceutical sector, which generally employs regulatory specialists.

Opportunity for risk mitigation through mandatory GMP review within the National One Stop Shop framework

Recommendation 1: Implement mandatory Good Manufacturing Practice (GMP) assessment of Investigational Medicinal Products (IMP) in the development of the One Stop Shop Human Research Ethics Committees (HREC) application platform to improve patient safety in clinical trials.

Incorporating PIC/S GMP standards review at a system level can mitigate serious risks to patient safety in alignment with global standards and support the reliability of clinical trials data. SHPA suggests that PIC/S GMP review is mandated and integrated within the OSS HREC application platform for clinical trials of IMPs, to ensure risks associated with GMP non-compliance is minimised. This would allow HREC to pre-emptively address concerns related to IMP quality and patient safety, introducing a systems-level, patient safety guardrail earlier on in the clinical trials approval process. A list of details suggested for mandatory reporting by Sponsor during the HREC application is summarised in Table 1.

Table 1: List of details recommended as mandatory reporting by Sponsors during HREC application

Domestic manufactured products	**Overseas manufactured products**
▪ Australian Register/List of Therapeutics Goods number, or, ▪ The TGA License to Manufacture Therapeutic Goods for the manufacturing facility, which must detail approval for the manufacturing steps and type of products under the product category of 'Therapeutic Goods for Clinical Trials' ▪ Details of the formulation	Uploading of a Quality Risk Management assessment of the GMP product, which many include: ▪ GMP certificate(s) from any facility involved in any step of IMP manufacture. This should include details on the restrictions of the types of products and manufacturing steps covered by the certificate, and should ideally be issued by a TGA recognised regulator ▪ Details of the formulation ▪ Certificate of GMP Conformance ▪ Certificate of Analysis ▪ The contract between the Sponsor and manufacturer detailing a full breakdown of responsibilities of both parties with respect to the IMP ▪ Any other documents and data to support the Sponsors risk assessment of the product

Recommendation 2: The Commission should engage with SHPA as a key stakeholder in the ongoing design, delivery and implementation of national clinical trials and health and medical research reforms in Australia.

According to the Australian New Zealand Clinical Trials Registry, medicines were the most researched intervention in Australian clinical trials, accounting for 45% of all clinical trials registered between 2006 to 2020.[5] Clinical Trial Pharmacists are imperative to the governance and success of all medicine associated clinical trials services in hospitals. Given the wealth of subject matter expertise that SHPA represents for clinical trials involving IMP management, SHPA recommends that the Commission continues to engage with SHPA as a key stakeholder in the ongoing design, delivery and implementation of national clinical trials and health and medical research reforms in Australia.

References

[1] Therapeutic Goods Administration. (2023). Legislation and legislative instruments. Available at: https://www.tga.gov.au/about-tga/legislation/legislation-and-legislative-instruments
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[4] National Health and Medical Research Council. (2023). National statement on ethical conduct in human research. Canberra: National Health and Medical Research Council.
[5] Willson ML, Seidler AL, Aberoumand M, Williams JG, Hunter KE, Barba A, et al. (2022). Latest update of the clinical trials landscape in Australia 2006 – 2020. ANZCTR. https://doi.org/10.25910/t9n1-bm45