# Draft Quality Standards for Human Research Ethics Committees and their Host Institutions

April 2025

## Introduction

Formerly known as the Society of Hospital Pharmacists of Australia (SHPA), **Advanced Pharmacy Australia (AdPha)** is the progressive voice of Australian pharmacists and technicians, built on 80 years of hospital innovation that puts people and patients first. AdPha supports all practitioners across hospitals, transitions of care, aged care and general practice clinics to realise their full potential. We are the peak body committed to forging stronger connections in health care by extending advanced pharmacy expertise from hospitals to everywhere medicines are used.

AdPha welcomes the opportunity to respond to the Australian Government consultation on the *Draft Quality Standards for Human Research Ethics Committees (HRECs) and their Host Institutions*. AdPha convenes a Clinical Trials Specialty Practice stream, with over 500 members who are leaders and experts in the provision of quality and safe clinical trials pharmacy services to clinical trial participants in Australian hospitals. Many of these members are clinical trial pharmacists who sit on National Mutual Acceptance certified HRECs.

Our submission focuses on a critical safety issue identified by our members**: the current gap in oversight of investigational product quality, particularly the lack of clear requirements for Good Manufacturing Practice (GMP) assessment in non-industry sponsored clinical trials.**

While the draft Standards support key principles of risk management, governance, and training, they do not explicitly address the oversight of investigational product quality or GMP compliance. This omission is significant given the increasing complexity of clinical trial medicines and the documented safety risks in non-industry sponsored clinical trials.

In the absence of clear national guidance, HRECs are implicitly burdened with assessing GMP-related risks without the required expertise or system level support. To ensure participant safety and a consistent national approach, the standards should define



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minimum requirements for investigational product quality review, clarify the limits of HREC responsibility in GMP assessment, and establish clear HREC referral pathways to expert GMP assessment via the TGA Clinical Trial Approval (CTA) Scheme, including documentation of whether a GMP assessment has occurred, and by which subject matter expert.

AdPha provides comment on this issue in response to the following consultation topics: **quality of an ethics review, Clinical Trial Notification (CTN) and Clinical Trial Approval (CTA) Schemes, institutional conflicts of interest, incorporating external feedback into the accreditation scheme and evaluation.**

If you have any queries or would like to discuss our submission further, please contact Jerry Yik, Head of Policy and Advocacy at policy@adpha.au

# Recommendations

To enhance the safety, quality and regulatory oversight of investigational products used in clinical trials led by non-industry sponsors, and to ensure alignment with international best practice, AdPha recommends the following clarifications and supplementary measures to strengthen the draft *National Quality Standards for Human Research Ethics Committees (HRECs) and their Host Institutions:*

**Recommendation 1**

**Clarify that HRECs are not responsible for assessing GMP compliance of investigational products and introduce safeguards to prevent compliance gaps in non-industry trials under the CTN scheme.**

National Standards should state that HRECs are not responsible for conducting or interpreting GMP assessments:

- HRECs should confirm only that the Sponsor has submitted documentation showing GMP compliance was assessed via a TGA-approved process.
- This aligns with existing TGA guidance and acknowledges that many HREC members lack the technical expertise to conduct GMP assessments.

**Recommendation 2**

**Establish a standardised, nationally consistent GMP assessment framework with clear governance and documentation requirements for investigational products.**

The standards should require HRECs and host institutions to adopt a nationally consistent approach for documenting GMP compliance of investigational products under the CTN scheme:

- Establish a safety and quality threshold requirement for trials submitted to HREC with the intent to initiate via the TGA Clinical Trial Notification scheme.
- Develop a standardised GMP documentation framework, including a GMP Assessment Form or compliance declaration to be completed by the Sponsor and becomes a compulsory document for HREC submission.
- Guidance provided on which trials should be escalated for review under the CTA scheme where complexity or risk warrants deeper review.
- The standards should recommend that this framework be developed and maintained by the TGA to ensure national consistency across clinical trial sites.

The standards should recognise two acceptable governance models for GMP oversight:

- **Preferred model:** GMP assessment is undertaken and documented via a

regulatory process (e.g. by the TGA), with HRECs confirming documentation only.
- **Alternative model** (where regulatory review is not feasible): HREC oversight is supported by strict national guidance and structured documentation, developed in partnership with the TGA.

**Recommendation 3**

**Expand the CTA scheme to explicitly include GMP compliance for complex or high-risk investigational products.**

While the CTA scheme currently references 'manufacturing processes', the standards should recommend that the scope be explicitly expanded to include GMP assessment to serve as a pathway for complex or disputed cases.

- Where trials are submitted under the CTA scheme, a formal desktop review of GMP compliance by the TGA should be required.
- Guidance should be made clear when a trial is more appropriately reviewed under the CTA scheme (rather than CTN), due to the complexity or risk associated with investigational product manufacturing, handling, and storage processes.

**Recommendation 4**

**Develop and implement accessible, nationally standardised GMP training for HRECs, Sponsors, and clinical trial sites.**

The standards should require accessible, practical GMP training for Sponsors, HREC members and host institutions.

- A national GMP training module should be developed, in partnership with the TGA, to build capacity across HRECs, Sponsors and the clinical trial workforce.
- Training should provide a consistent understanding of GMP obligations across trial stakeholders aligned to roles and responsibilities.

## Quality of an Ethics Review

### Context and Issue

Australia's current regulatory framework poses safety risks due to inadequate oversight of GMP compliance for clinical trial investigational products. While GMP adherence is a legal requirement under Good Clinical Practice (GCP) and Therapeutic Goods Administration (TGA) guidelines, the CTN scheme does not provide for robust assessment of medicine quality before trial commencement. This is particularly a risk in non-industry sponsored trials.

Unlike industry sponsored trials, which are typically well resourced and GMP compliant, non-industry institutions acting as the Sponsor rarely have the resources or technical capability to ensure procured clinical trial medication is fully compliant with GMP, especially when procured or blinded from international facilities. The TGA, as the regulator, does not currently assess GMP for clinical trial medications under the CTN model.

Responsibility for GMP oversight is frequently placed on HRECs, which are not mandated or technically capable to assess GMP. The lack of standardised GMP training for the ethics and clinical trial workforce further compounds this issue, resulting in inconsistent identification of non-compliance and limited authority to rectify quality concerns. This often shifts the burden to clinical trial pharmacists, often post-ethics approval, limiting their ability to intervene or address risks to participants effectively.

Adding further complexity, assessing GMP compliance for overseas investigational products - especially unregistered medicines or those sourced from non-Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) member countries - is not straightforward. In many cases, the quality assurance of manufacturing practices from these jurisdictions cannot be reliably verified.

There have been documented cases where substandard investigational products manufactured in facilities that do not adhere to GMP standards have entered Australian trials, posing serious public health risks. Historic issues with products from such facilities have included counterfeiting, variations in potency, and microorganism or other contamination. Large and well published clusters of injury and death have resulted from products produced at such facilities. These risks undermine the safety of trial participants and the integrity of Australia's clinical trial environment.

AdPha has recently advocated for the national approach to establish a consistent and harmonised operating environment for the approval and management of clinical trials and health-related research in Australia, through supporting the National One Stop Shop platform across Australia.[1] Recommendations, as outlined in the identified priorities above, include implementing mandatory GMP assessment of investigational product in the development of the One Stop Shop HREC application platform to improve patient safety in clinical trials.



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### Commentary

This results in inconsistent safety standards, particularly an appropriate, standardised GMP assessment process for investigational products, particularly in non-commercial trials, is urgently needed. Such reform would elevate safety standards without diminishing Australia's research competitiveness and improve the reputation of Australian research. A standardised, minimum GMP assessment process should be established, such that Sponsors have clear guidance on the expected standardised portfolio of evidence required to submit to HREC for trials under the TGA's CTN scheme. This process should include safety and quality assessment triggers under which positive assessment via the TGA's CTA pathway would be required for HREC approval.

## Clinical Trial Notification (CTN) and Clinical Trial Approval (CTA) Schemes

### Context and Issue

In Australia, the TGA regulates the importation into and/or supply of 'unapproved' therapeutic goods for use in a clinical trial through two schemes: Clinical Trial Notification (CTN) and Clinical Trial Approval (CTA).

Under both schemes, the HREC is responsible for considering the scientific and ethical issues of the proposed trial protocol. The CTN scheme is a notification process while the CTA scheme involves quality and safety evaluation by the TGA. The CTA scheme is generally for higher-risk or novel treatments, where there is no or limited knowledge of safety.

In contrast to the TGA's CTN and CTA Schemes, regulators in other jurisdictions take on a much more involved role in the review of new clinical trials. For instance, clinical trials involving medications in the USA must be submitted to the Food and Drug Administration (FDA) under an Investigational New Drug (IND) Application. In the UK and EU, a Clinical Trial Authorisation application is submitted to the Medicines & Healthcare products Regulatory Agency (MHRA) and European Medicines Agency (EMA), respectively.

AdPha has previously advocated for stronger regulatory oversight of clinical trials in Australia, noting that unlike comparable jurisdictions such as the US, UK and EU, where regulators conduct scientific and manufacturing quality assessments alongside ethics review, Australia places full responsibility on HRECs, often without the technical expertise required. Recommendations from previous submissions include expanding the TGA's role in reviewing investigational product quality, ensuring alignment with international best practice, and establishing clear minimum requirements for GMP compliance assessment to support trial integrity and participant safety[2].

### Commentary

The CTN scheme lacks a robust quality gate for investigational products, relying entirely on Sponsor self-assessment. Non-industry Sponsors may not have the resources or knowledge to ensure GMP compliance, and HRECs are left without a standardised process for identifying high-risk cases that should be escalated under the CTA scheme.

The current approach exposes patients to risk and leads to inconsistent practice across institutions. A standardised national framework is needed to determine when a trial must be escalated to the CTA scheme for expert review of investigational product quality.

## Institutional conflicts of interest

### Context and Issue

Non-industry Sponsors, such as universities or collaborative research groups, often operate under tight grant funding and may lack the specialist expertise required to ensure investigational products meet GMP standards. In some cases, investigational products may be procured without adequate GMP assurances due to limited resources and awareness, inadvertently introducing risks to participant safety. These situations may give rise to institutional conflicts of interest, where operational or financial pressures intersect with an institution's ethical responsibility to protect research participants.

### Commentary

While the National Statement includes safeguards around HREC decision-making, it does not address institutional-level risks related to investigational product procurement or oversight of product quality. In the absence of clear guidance and national support mechanisms, institutions may unknowingly approve or sponsor trials using products that do not meet acceptable GMP standards. This highlights the need for national processes that support institutions in managing product quality risks and preventing unintended compromises to participant safety.

## Incorporating external feedback into the accreditation scheme

### Context and Issue

Participants expect that products used in clinical trials meet the same safety and quality standards as those in general clinical use. However, current processes allow substandard investigational products to enter trials without appropriate oversight. This creates a risk that substandard or unsafe products are administered to participants without proper review of manufacturing quality or regulatory compliance.

### Case examples: Safety Risks from Inadequate GMP Oversight

AdPha members have reported several cases where investigational products used in trials posed significant safety risks due to poor manufacturing quality. In two separate

cases, investigational products sourced from overseas were found to lack sufficient GMP documentation, with one batch ultimately confirmed to be contaminated with *Pseudomonas aeruginosa*. In both cases, GMP non-compliance was only identified after HREC and Research Governance Office (RGO) approvals, when trial pharmacists intervened at the site level. These incidents demonstrate systemic gaps in current GMP assessment processes and underscore the urgent need for national standards that clarify HREC responsibilities and establish structured mechanisms for GMP review. **These case studies are provided in detail in Appendix A.**

AdPha has previously advocated for strengthened regulatory oversight of investigational product quality in clinical trials, particularly where trials are not industry sponsored. Clinical trial pharmacists report ongoing risks linked to poor GMP compliance in unregistered medicines, with Sponsors and HRECs often lacking the capacity to properly assess product quality. AdPha's recommendations included requiring the TGA to assess GMP adherence as part of trial approval, improving regulatory guidance and enforcement, and introducing standardised GMP training for the pharmacy and trial workforce to support safe handling of investigational products and reduce public safety risks.[3]

Commentary

These real-world case examples reported by AdPha members show the consequences of GMP oversight gaps, and highlight the need to incorporate practical, frontline feedback into the design of the accreditation scheme. Trial pharmacists and clinical trial staff working within the system are well positioned to identify gaps in oversight that may not be visible at the policy level. Embedding these insights into the Standards will help ensure that future accreditation processes are grounded in operational realities, and that systems are strengthened to prevent risks before they reach trial participants.

## Evaluation

AdPha **disagrees** that the proposed Quality Standards address the issues of quality ethics and HREC or lead to improvements in the conduct of human research in Australia.

Key Gaps Identified:

- **No mention of GMP or investigational product quality oversight:**
  The draft Standards do not reference investigational product quality or the requirement for GMP compliance, despite this being a fundamental component of participant safety and regulatory compliance.
- **HRECs remain implicitly responsible for broad risk assessment:**
  In the absence of explicit direction, HRECs are left to determine the safety and quality of investigational products – often without technical expertise, resources or authority to do so effectively.
- **Limitations of the CTN scheme are not addressed:**

As a notification-only system, the CTN scheme provides limited opportunity for oversight of trials before they commence, where safety and quality risks can be proactively managed.

- **No system level or centralised product quality assessment pathway or escalation guidance.**
- The TGA has not established minimum criteria for HRECs to identify and refer trials requiring expert GMP assessment under the CTA pathway, leading to a critical gap in oversight
- **Training standards do not specify content related to GMP or investigational product oversight.**
  While workforce training is referenced in the Standards, there is no requirement for content on investigational product quality, GMP obligations, or the roles and responsibilities of different stakeholders in maintaining medicine quality in trials.

### Commentary

The absence of clear oversight for investigational product quality places participants at unnecessary risk and undermines confidence in the integrity of Australia's clinical trials sector. Without defined roles and system level support mechanisms, responsibility for GMP compliance is unfairly shifted onto HRECs, which may not have the expertise or authority to manage such risks. and embed GMP specific capability development. Strengthening the Standards to clearly delineate responsibilities, embed GMP-specific capability, and introduce appropriate regulatory and institutional support is essential to protect participants and uphold Australia's reputation as a safe and trusted location for clinical research.

### Relevant Standards to Expand

**Standard 2 (Scientific and Ethical review)**

This Standard acknowledges the need for appropriate expertise on HRECs or mechanisms to access additional expert advice where needed. However, it does not explicitly address the current lack of GMP-related expertise within most HRECs.

- To support safe and effective ethics review, the Standard **should acknowledge investigational product quality as a specific area requiring expert advice or structured support within ethics review processes.**

**Standard 4 (Governance and accountability)**

This standard highlights the need for institutions to have appropriate systems for identifying, managing and escalating risks. However, it does not currently address governance of investigational product quality or GMP oversight.

- To ensure accountability, the Standard should **define clear institutional roles and responsibilities for investigational product quality to GMP standards.**



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**Standard 5 (Capability and Training)**

This standard outlines the importance of training and professional development for HREC members but does not specify core content areas.

- To ensure training reflects emerging needs in clinical trials, including understanding GMP principles, identifying product quality risks, and knowing when and how to seek expert advice, the Standard **should mandate standardised GMP training for the clinical trials sector, with content aligned to the role and responsibility of HREC members, Sponsors and clinical trial staff. Ideally this would be developed and delivered by the regulating body.**

## Summary

AdPha's submission highlights a critical oversight in the draft Standards: the lack of national guidance on GMP compliance and investigational product quality in non-industry clinical trials. Our response focuses on addressing systemic risks to participant safety, the undue burden placed on HRECs, and the need for consistent, regulator-supported processes. Strengthening these areas is essential to ensure safe, high-quality clinical trials and maintain confidence in Australia's research environment.



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# Appendix A: Good Manufacturing Practice (GMP) non-compliance case examples

## Case 1: Infant vaccine

An ongoing multicentre grant funded double-blind randomized controlled trial was comparing outcomes of two vaccines given at 2 months of age in up to 3000 participants. The trial Sponsor was an Australian university.

One vaccine was a TGA registered product, and the second vaccine was an overseas registered product imported under the CTN scheme. Due to global shortages in the overseas vaccine, the Sponsor submitted a HREC amendment that included changing the overseas vaccine to the only available product, a vaccine registered in and sourced from India.

Concerns were raised at HREC by a volunteer clinical trial pharmacist member around patient safety in the context of the GMP of the proposed product. No GMP documents or evidence were provided by the Sponsor to support their application. Upon further requests for evidence the Sponsor provided a locally issued GMP certificate and a letter of recommendation from the DSMB stating they considered the vaccine to be appropriate for use.

On advice from the pharmacist the amendment was not approved, and recruitment was paused.

The key concerns around the GMP evidence for the product used to justify the rejection of the amendment included:

- GMP non-compliance has the potential to cause injury and death, as evidenced by a range of well published cases.
- India (nor any of its state medicines regulators) is not a country with whom Australia has an international agreement or arrangement for mutual GMP clearance. Therefore, locally issued Indian GMP certificates would not be accepted by the TGA as sufficient evidence for GMP clearance and so should not be considered sufficient evidence by the HREC.
- India (nor any of its state medicines regulators) is not a member of PIC/S and may not enforce PIC/S equivalent GMP standards for this facility as legally required for clinical trial products used in Australia.
- A current passing inspection of the facility for that product type was not published on the FDA Inspections or Eudra GMP databases.
- No further evidence for GMP compliance could be provided by the Sponsor to justify the quality of the product.

A range of gaps around GMP in Australian clinical trials were highlighted from this incident:

- The TGA does not provide any formal guidance on assessment of GMP for overseas sourced products for use in clinical trials. Nor do they have the opportunity to assess GMP under the CTN scheme.
- As this was a clinical trial with Australian sites only, comparable regulators such as the FDA, EMA, or MHRA had not assessed GMP evidence under their equivalent clinical trial schemes as commonly occurs with international multicentre clinical trials.
- As the Sponsor was an Australian university, they lacked expertise in GMP for clinical trial products, and GMP was not initially a consideration in their planned procurement of the product.
- The volunteer HREC lacked expertise in GMP. The pharmacist that raised the issue had recently joined the committee and had they not, the issue would not have been raised.
- The Sponsor countered to the HREC that since the Australian Clinical Trial Handbook detailed that GMP compliance is a Sponsor responsibility, it should be solely within their scope to consider the products GMP quality. This was complicated by the fact that GMP is not explicitly mentioned as a consideration for HRECs in the National Statement.

## Case 2: Pseudomonas contamination

An ongoing multicentre NHMRC funded double-blind randomized controlled trial was comparing outcomes of an IV intervention or matched placebo administered during surgery in 3300 participants.

The clinical trial Sponsor was an Australian university, and it had received HREC approval by an NMA accredited committee, opened at dozens of sites within Australia, and hundreds of participants had been treated under the protocol.

Upon planned site initiation at a new site, and after RGO approval, the trial was sent to the site pharmacy, at which point a clinical trial pharmacist identified potential quality issues with the provenance of the product, and an inappropriately formulated placebo (water for injection, which is contraindicated for IV administration).

All manufacturing steps for the product were performed on contract for the trial Sponsor by a facility located in India. Upon request for evidence of GMP compliance the Sponsor provided a locally issued GMP certificate which did not detail approved product types. A Certificate of Analysis was also provided that did not contain the correct batch details matching to the batch received by the site pharmacy. No other documents or evidence

of GMP compliance could be provided by the Sponsor. Despite being outside the scope of the FDA and Eudra GMP Inspections databases as a custom manufactured clinical trial product, these databases were reviewed by the pharmacist for further evidence of inspections at the facility, but none had occurred.

Despite the concerns raised, having received HREC and RGO approval, the Principal Investigator (PI) tried to pressure the pharmacy to initiate the trial and dispense the investigational product. A small sample of vials were sent by the pharmacy to a TGA licenced pathology facility for testing. Returned results indicated Pseudomonas aeruginosa contamination in multiple samples.

Upon being notified of the pathology results, the response of the Sponsor was to suspend recruitment and provide a mandatory notification the TGA. The Sponsor stated that they had met with the drug supplier who 'reaffirmed their GMP certification', and that safety data indicated that Pseudomonas infection rate was within expected incidence. Communication with the site pharmacy was ceased by the Sponsor.

This incident highlighted many of the same concerns that arose in Case 1. In particular, this case reinforced that a gap exists in assessment of GMP for overseas sourced clinical trial products for non-commercial Australian Sponsors. Namely, that insufficient GMP review or expertise occurs at the level of TGA, Sponsor, NHMRC, and HREC, resulting in the burden being shifted to site pharmacists.

Additional concerns raised by this case include:

- A concerning pattern within Australian non-commercial Sponsors and investigators of not only lacking GMP expertise and consideration but actively dismissing GMP risks once presented.
- A lack of support and feedback for Sponsors at the grant application stage for GMP compliance. Once issues are uncovered by site pharmacists, significant disruption to the conduct of the clinical trial will be caused.
- Power dynamics between Sponsor, PI, and pharmacists in Australia do not empower pharmacists to make or report such interventions. In this case, the clinical trial should not have proceeded further when the Sponsor could not provide adequate GMP evidence. Additionally, the quantity of samples that were able to be supplied for batch testing did not conform to established guidelines for batch test sampling, and contamination may have only been detected by chance in such a small sample.
- Despite GMP compliance being a Sponsor obligation, there is a blurring of professional liability and responsibility when pharmacists become expected to make judgements on GMP compliance as part of their role as advocates of patient safety.

# References

[1] Advanced Pharmacy Australia. (2024). National One Stop Shop Phase III Consultation. Available at: Summary-of-SHPA-views-on-National-One-Stop-Shop-Phase-III-consultation--March-2024.pdf

[2] Advanced Pharmacy Australia. (2024). TGA consultation on Clinical Trial Approval (CTA) scheme. Available at: SHPA-response-to-TGA-consultation-on-Clinical-Trial-Approvals-Scheme.pdf (adpha.au)

[3] Advanced Pharmacy Australia. (2025). National Health and Medical Research Strategy Survey. Available at: https://adpha.au/publicassets/7119de1b-8bf8-ef11-9146-00505696223b/National-Health-Medical-Research-Strategy-Survey--Department-of-Health-and-Aged-Care.pdf



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