
GTAI GERMANY TRADE & INVEST

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# Australia's Health Innovation Pipeline

*Opportunities & Regulatory Considerations for EU-based Device Manufacturers*

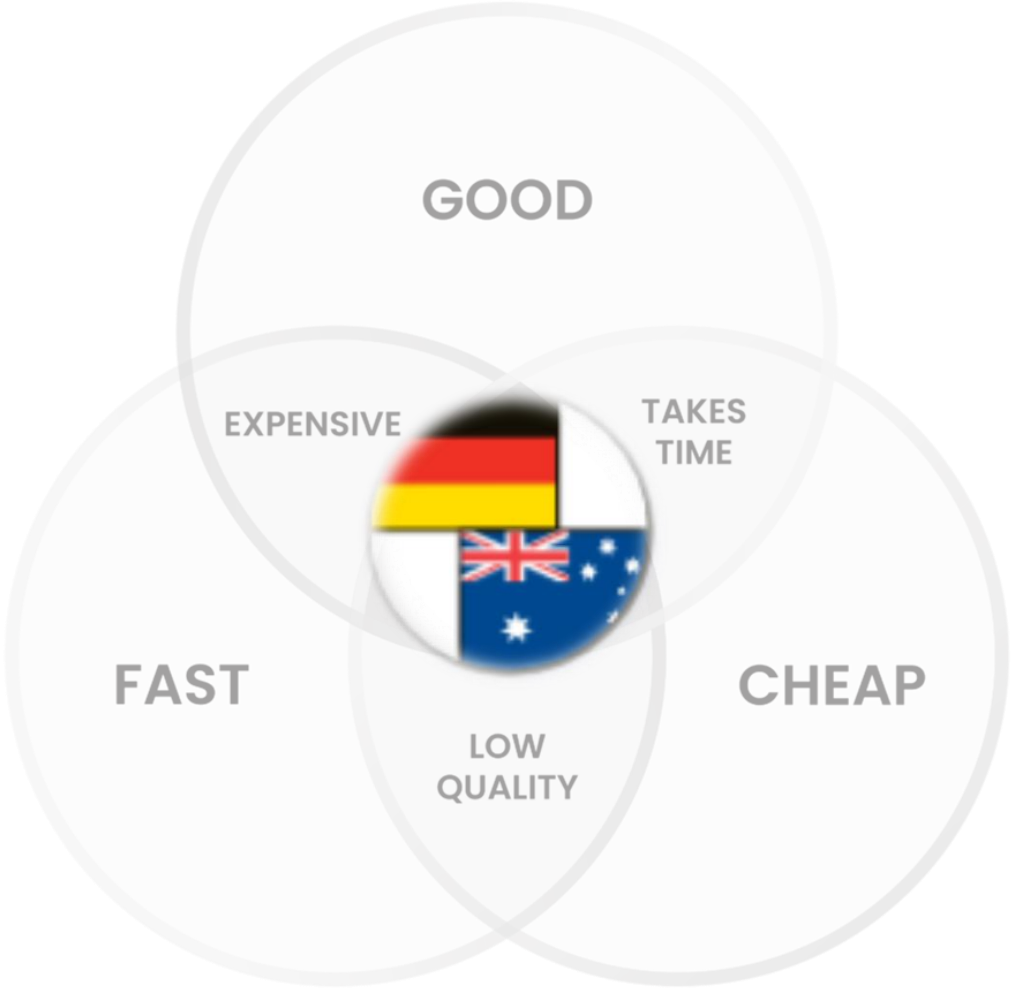
AHK Deutsch-Australische Industrie- und Handelskammer
German-Australian Chamber of Industry and Commerce

# QUALITY – SPEED – COST-EFFECTIVENESS

**GOOD – FAST – ~~CHEAP~~ VALUE**

*Can Australian clinical trials deliver all three for EU Manufacturers?*

- **Clinical Trial Stakeholders from a regulatory perspective**
  - *A familiar framework?*
- **Ethical Review Framework**
  - *Efficiencies of NMA Scheme*
  - *What do EU Manufacturers need to consider in planning*
- **Regulatory pathways for unapproved therapeutic goods**
  - *CTN / CTA Schemes*
  - *Essential Principles (EP) Checklists*
  - *Import notification requirements for EU Manufacturers*

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# Clinical Trial Regulatory Stakeholders – A Familiar Framework

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration
TGA Health Safety Regulation

## Regulator

European Commission

## Implementation

Federal Institute for Drugs and Medical Devices

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Australian Government
National Health and Medical Research Council
N H M R C

## Ethics Framework

*Issue guidelines for the conduct of medical research*

Deutscher Ethikrat

European Research Council
Established by the European Commission


**>200 HRECs**
*Human Research Ethics Committees*

## Ethics Committees

*Review scientific & ethical aspects, approve & monitor*


*Article 2(56)*

**RGOs**
*Site Research Governance Offices*

## Site Governance

*Authorise trial conduct at each site*

**Site Governance**
*Site Research Governance Offices*

## Trial Sponsor

*Legal responsibility for trial conduct according to ISO 14155*

*Article 2(49)*

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# Efficient Ethical Review Framework

*Reducing unnecessary duplication of ethical review*

- High quality, generalisable data & Experienced Reviewers
- Low-burden ethics submission requirements
- National Mutual Acceptance (NMA) Scheme - One submission, multiple sites

*Leveraging Australia's efficient ethical review pathways for clinical trials.*

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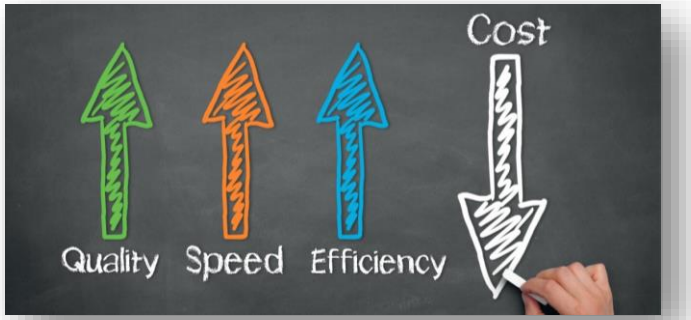
# Ethical Review in Australia – Quality, Speed & Efficiency




**Clinical trials in Australia must:**

- conform to Declaration of Helsinki
- operate in accordance with ISO 14155 / ICH GCP
- gain approval by an independent ethics committee

✓ **High quality data**

✓ **Accepted by major regulatory agencies**

*Often highly generalisable given ethnically diverse population*

**Highly-skilled clinical trials workforce:**

- Ready access to expert ethical reviewers
- Experienced across diverse therapeutic areas
- Collaboration between industry and academia

✓ **Fewer question/response rounds**

✓ **Total review cycle typically 4-8 weeks**

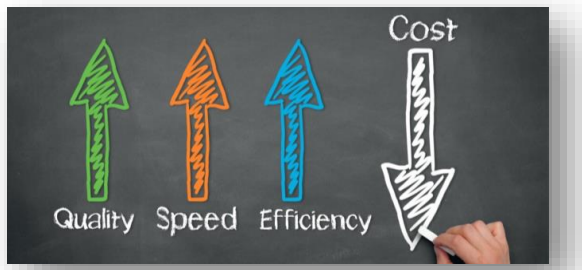


http://www.tga.gov.au/industry/clinical-trials-note-ich13595.htm
https://www.australianclinicaltrials.gov.au/why-conduct-clinical-trial-australia

# Ethical Review in Australia – Quality, Speed & Efficiency

**Low-burden ethics submission documentation**
compared to requirements under EU MDR and for US IDE studies

- ✓ Trial protocol
- ✓ Investigator's brochure
- ✓ Informed consent forms
- ✓ Patient information documents
- ✓ Subject recruitment plans
- ✓ Planned payment or compensation initiatives
- ✓ Investigator(s) qualifications
- ✓ Proof of trial insurance
- ✓ Additional information, if required




- ❑ Clinical Investigation Protocol (CIP)
- ❑ Investigator's Brochure (IB)
- ❑ Participant Information & Consent Form (PICF / PIS)
- ❑ ABR Formulier: Study design description
  - ❑ Protocol synopsis
  - ❑ Investigator's Brochure
- ❑ EU Legal Rep confirmation
- ❑ Eudamed Formulier: Eudamed Trials module replacement form
  - ❑ Actors nominated
  - ❑ GSPR conformance declaration
- ❑ Investigational Medical Device Dossier (IMDD)
  - ❑ Protocol duplication
  - ❑ Investigator's Brochure
  - ❑ Risk Management Summary
  - ❑ General Safety & Performance Requirements (GSPR) Checklist
- ❑ Declaration of Conformance to MDR Annex I (GSPRs)
- ❑ All Case Report Forms (CRFs)
- ❑ Instructions For Use
- ❑ Investigator's CV
- ❑ Proof of trials insurance
- ❑ Site contact list
- ❑ Research Agreements with sites
- ❑ Clinical Evaluation Plan
- ❑ Data Management Plan (personal health data)
- ❑ Label suite ('Exclusively for Clinical Investigation')

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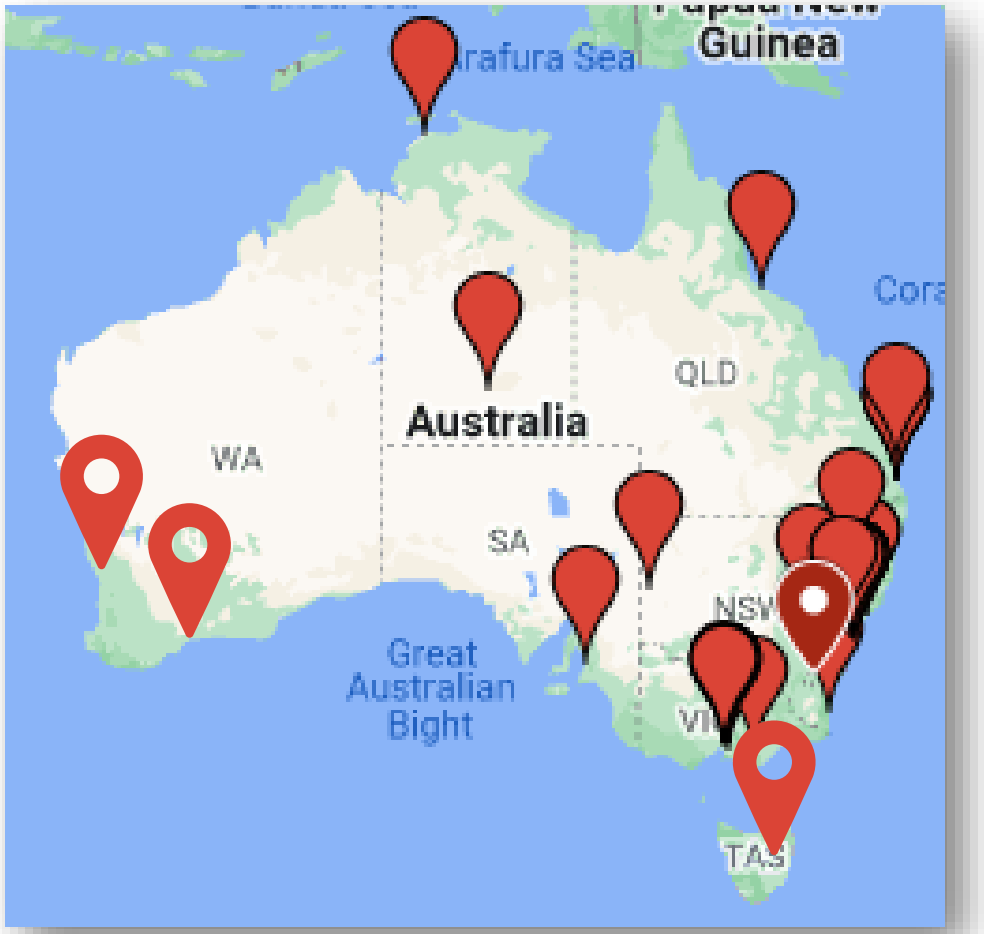
# Efficient Ethics Framework – National Mutual Acceptance (NMA) Scheme

National Mutual Acceptance (NMA) is a national system for mutual acceptance of scientific and ethical review for multi-centre clinical trials conducted in publicly funded health services.

- **ALL** states and territories now participate!
- **SINGLE** ethical and scientific review for multi-centre trials
- Access to **EVERY** established clinical trials site across Australia, in **ONE** submission, **<$3,000 AUD**

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https://www.nhmrc.gov.au/research-policy/ethics/national-certification-scheme-ethics-review-multi-centre-research

## Research Governance Office (RGO)

- provide a governance review
- site specific assessment (SSA) prior to authorisation of a research project
- suitability of site & investigators to conduct the research

## Australian Local Sponsor

- An Australian entity
- Individual, company, institution or org
- responsible for trial initiation, management, insurance indemnity, and/or financing

# Public Trial Registry Listing

Compliance with ISO 14155 & conformance with Declaration of Helsinki means Public Trials Registry listing is mandatory:

- **ANZCTR (pulls data from CT.gov)**
- Any WHO-recognised registry is acceptable for Australian clinical trials
- Start before or during ethics review – but start early!

ANZCTR
Australian New Zealand Clinical Trials Registry
The ANZCTR is an online registry of clinical trials being undertaken in Australia, New Zealand and elsewhere.

https://www.anzctr.org.au/

# Efficient Regulatory Framework

*Supplying unapproved therapeutic goods for clinical trials*

- Regulatory pathways for clinical trials – CTN & CTA Schemes
- Conformance with the Essential Principles
- Import notification requirements for EU manufacturers

*Australia's fast and pragmatic regulatory pathways for clinical trials.*

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# Regulatory pathways for clinical trials

Two regulatory pathways provide for importation and supply of unapproved therapeutic goods for use in clinical trials:

## Clinical Trial Notification (CTN) Scheme

- Sponsor notifies TGA of trial using online form
- No scientific or product review by TGA (5-7 days)
- Ethics Committee responsible for ethical & scientific review

- Used when **adequate** pre-clinical data is available to support reasonable expectation of safety

- $390 AUD

## Clinical Trial Approval (CTA) Scheme

- Sponsor makes 2-step application to TGA for trial approval
- TGA reviews application (30-50 days)
- TGA approves or rejects application

- Used when **limited** pre-clinical data is available and for high risk or novel treatments

Key regulatory difference is extent of TGA's oversight of investigational products being studied...

*Under CTN Scheme, research proposals are submitted directly to **human research ethics committees (HRECs)** which assume primary review responsibility for **ethical and scientific review**. This effective and efficient process avoids costly preparation of extensive regulatory applications and means that research can start much sooner.*

*- The Australian Clinical Trials website*

# Regulatory pathways for clinical trials

Two regulatory pathways provide for importation and supply of unapproved therapeutic goods for use in clinical trials:

## Clinical Trial Notification (CTN) Scheme

- Sponsor notifies TGA of trial using online form
- No scientific or product review by TGA (5-7 days)
- Trial supply can commence upon TGA acknowledgement

- Used when **adequate** pre-clinical data is available to support reasonable expectation of safety

- $390 AUD

## Clinical Trial Approval (CTA) Scheme

- Sponsor makes 2-step application to TGA for trial approval
- TGA reviews application (30-50 days)
- TGA approves or rejects application

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- $19,699 AUD for devices / $1,857 - $22,085 AUD for drugs

Key regulatory difference is extent of TGA's oversight of investigational products being studied...

Between 2018 – 2022, TGA received ZERO medical device trial CTA applications.

## How to choose between CTN & CTA Schemes?

If investigational product is a Class 4 Biological (live animal organs, cells or tissues) -> CTA Scheme is mandatory.

Otherwise, it's your choice… provided the Human Research Ethics Committee also agrees with you!



https://www.tga.gov.au/sites/default/files/2022-09/fees-and-charges-summary-1-october-2022.pdf#page=44

# CTN Scheme Online Form - Declaration

CTN Declaration is an acknowledgement of three key items by the Trial Sponsor:

- Device is **acceptable** for deployment into the clinical trial
- Trial will be run according to **ISO 14155**
- Sponsor has **"information and documents"** about the exempt device available to them at the time of the declaration

*What exactly does "Information and documents" mean?*

- Documentation relevant to the supply of a device under CTN/CTA exemptions; and
- Evidence that the exempt device was manufactured in such a way that it conforms to the **Essential Principles**.

## The Essential Principles:

*Australia's equivalent of EU MDR General Safety & Performance Requirements*

**TGA can request anytime…**

***10 days to comply.***

# Essential Principles – An important CTN requirement

## Essential Principles Checklist

1. **Use of medical devices not to compromise health and safety**
2. **Design and construction of medical devices to conform to safety principles**
3. **Medical devices to be suitable for intended purpose**
4. **Long-term safety**
5. **Medical devices not to be adversely affected by transport or storage**
6. **Benefits of medical devices to outweigh any side effects**

7. Chemical, physical and biological properties
8. Infection and microbial contamination
9. Construction and environmental properties
10. Medical devices with a measuring function
11. Protection against radiation
12. Medical devices connected to or equipped with an energy source

13. Information to be provided with medical devices

14. Clinical evidence

https://www.tga.gov.au/resources/resource/forms/essential-principles-checklist-medical-devices

## GSPR Checklist

1. Performance and Safety
2. Reduction of risk
3. Risk Management System
4. Risk control measures and residual risks
5. Risks related to use error
6. Performance and lifetime of the device
7. Characteristics & performance not adversely affected by transport and storage
8. Acceptable Risk Benefit Ratio
9. Devices without medical purpose

General

Design & MU

EU MDR Annex I, Chapter II, Clause 10 to 22

Label & IFU

EU MDR Annex I, Chapter III, Clause 23

Nothing new for EU device manufacturers!

GSPR Checklist evidence should easily address all EP Checklist items, albeit in a slightly different layout.

# Importing Investigational Products to Australia

**Who**
*Who's involved*

Sponsor of therapeutic goods (the Importer) -> NOT the Sponsor of the clinical trial.
TGA's Exports Team -> but **ONLY** if investigational product is being imported (to AUS) for subsequent export (overseas)

**What**
*What needs to be done*

Importer (AUS Sponsor Agent) **does not** require approval from TGA to import the investigational product.
Investigational product must be held under direct control of importer (Sponsor Agent) until CTN is acknowledged.

**When**
*When does it need to be done*

CTN must be in place prior to supply of the unapproved goods to trial sites.
No 6 monthly reporting required for EU-based manufacturers, only for AUS manufacturers!

**Where**
*Where can I find more information*

https://www.tga.gov.au/resources/resource/forms/importexport-unapproved-therapeutic-goods-experimental-purposes

**How**
*How do we submit this*

Unapproved therapeutic goods enquiries: eps@tga.gov.au

# What you need to start a trial in AU:

## Product Documentation:

- Essential Principles Checklist
- Evidence of EP conformance (per GSPR)

## Trial Documentation & Stakeholders:

- ISO 14155 Essential Documents (Annex E)
- Local Sponsor appointed
- Insurance

## Ethics & Governance:

- HREC approval under NMA Scheme
- RGO Site Authorisation
- Public Trials Registry listing

## TGA Regulatory Notifications:

- CTN acknowledgement or
- CTA approval

# What you get:

## GOOD:

- ✓ GCP / ISO 14155-compliant clinical evidence that supports conformity in major markets
- ✓ Generalisable, high quality data from a diverse population

## FAST:

- ✓ No Regulatory review of IMD dossier
- ✓ SINGLE Ethics approval in <8 weeks
- ✓ Access all AUS states
- ✓ Streamlined site-specific authorisation

## ~~CHEAP~~ VALUE:

- ✓ CTN/CTA $390 AUD
- ✓ HREC <$3,000 AUD
- ✓ Experienced researchers & established trials infrastructure

# Useful Links for EU Manufacturers

**Regulatory Framework for Clinical Trials in Australia**

*Therapeutic Goods Act 1989(link is external)* (Cth)(TG Act)
*Therapeutic Goods Regulations 1990*(link is external) (Cth)
*Privacy Act 1988* (Cth)
NHMRC:
Clinical Trials Notification (CTN) scheme, and
Clinical Trials Approval (CTA) scheme

TGA's Clinical Trial website (includes contact details for further information)
The Australian Clinical Trial Handbook
Australian Clinical Trials - Useful Links for Industry and Sponsors

**Ethics & Governance:**

NHMRC's Human Research Ethics Application
ICH Guideline for Good Clinical Practice (ICH-GCP) (Annotated by the TGA)
*National Statement on Ethical Conduct in Human Research 2007 (updated 2018)*
*The Australian Code for the Responsible Conduct of Research, 2018*
Site Specific Assessment
NHMRC's eLearning module: Research Governance related to Clinical Trials

**Clinical Trial Agreements, Insurance and Templates**

Medical Technology Association of Australia: https://www.mtaa.org.au/clinical-investigation-research-agreements
Medicines Australia Clinical Trials Research Agreements
Medicines Australia: Medicines Australia indemnity forms
Indemnity and Insurance Arrangements for Clinical Trials in the Public and Private Sectors in Australia 2014(link is external) (NHMRC)
FAQs: Indemnity and insurance arrangements for clinical trials in Australia

Essential Principles Checklist: https://www.tga.gov.au/resources/resource/forms/essential-principles-checklist-medical-devices


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## Thank You!

*We welcome any questions you might have…*

We support you in bringing your medical products to market in a timely manner and in compliance with the law.

SaMD-specific expertise:

- Regulatory & Clinical Evaluation Strategy integration
- Product Design & Development technical documentation, incl. QMS build under ISO 13485 & 21 CFR 820
- Verification & Validation
- Regulatory Agency engagement & pre-market submissions
- Seminars & workshops on development and approval for SaMD products

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