CLINICAL TRIALS IN DRUG DEVELOPMENT

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RACI seminar

5 October 2022

NME drug development

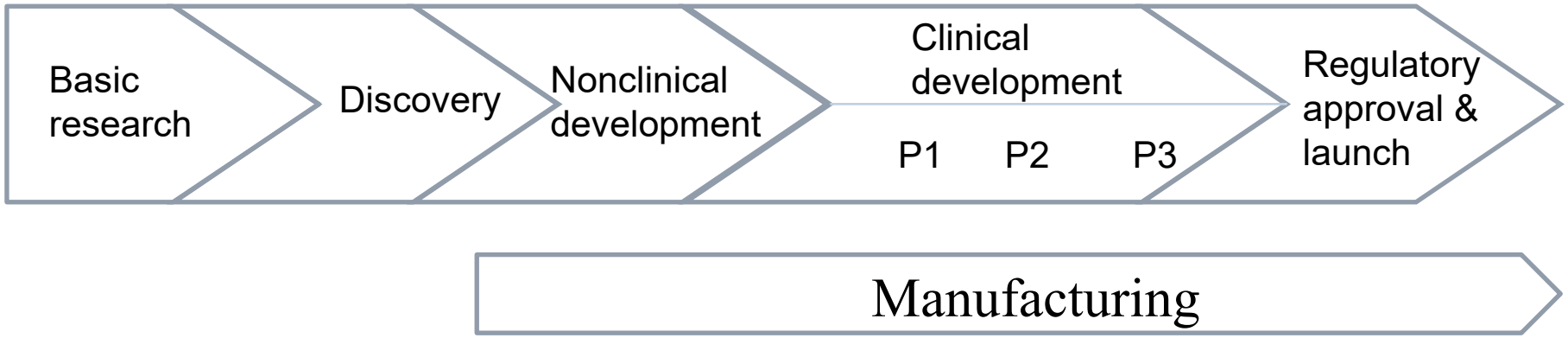
Clinical development program

CMC/Quality development program

Regulatory/industry perspective

Phases of Development for an NME

(to initial approval)



Success rate	5000 - 10000	250	5			1
Duration (yrs)	2.5	3	1	1.5	2	3.5	1.5
Cost (% total	4%	15%	10%	15%	22%	31%	3%

68%

Clinical development program

- Design Phase III confirmatory studies to deliver claims
  - Target patient population
  - Key clinical endpoints
- Design Phase II studies to give information needed for Phase III
  - Dose levels
  - Clinical endpoints
  - Instruments
- Design phase I studies
  - Support phase II design

Phase III design considerations

- Target patient population
- Objectives and endpoints based on desired claims
- Inclusion/exclusion criteria
  - Age limits
  - Women of child-bearing potential
  - Concomitant medications
  - Co-morbidities
- Dose and duration of therapy
  - Size of safety database
- Comparator
- Cost and QOL data

Data to support Phase III program: Phase II results

- Effective dose levels
  - dose response curve
  - population differences
- Clinical model, endpoints and instruments
- Safety signals
- Method of blinding
- Control group
- Comparison with competitors?

Phase I human pharmacology studies

Objective

- Assess tolerance
- Define/describe Pharmacokinetics and Pharmacodynamics
- Explore drug metabolism and drug interactions
- Estimate activity
- Preliminary efficacy, eg biomarkers

Examples

- Dose-tolerance studies
- Single and multiple dose PK and/or PD studies
- Drug interaction studies
- Human challenge studies

Drug Product to support phase I

- Quality standard
  - ICH standards designed for marketed products
  - No specific Australian guidelines for early phase products: rely on EMA *Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials (R2)*
  - GMP compliance not required in Australia for “goods prepared for the initial experimental studies in human volunteers”
    - First in human: Phase 0 and Phase 1 trials
- Early formulation
  - Intended clinical route of administration
  - Final dose preparation may be in pharmacy
  - Placebo

Drug Product to support phase II

- Suitability of Dose form
  - Patient population
  - Disease
  - Pharmacokinetic profile
  - Shelf life
  - Placebo
- Methods
  - Suitable for scale-up
  - Validated assays: active, contaminants, excipients, stability indicating

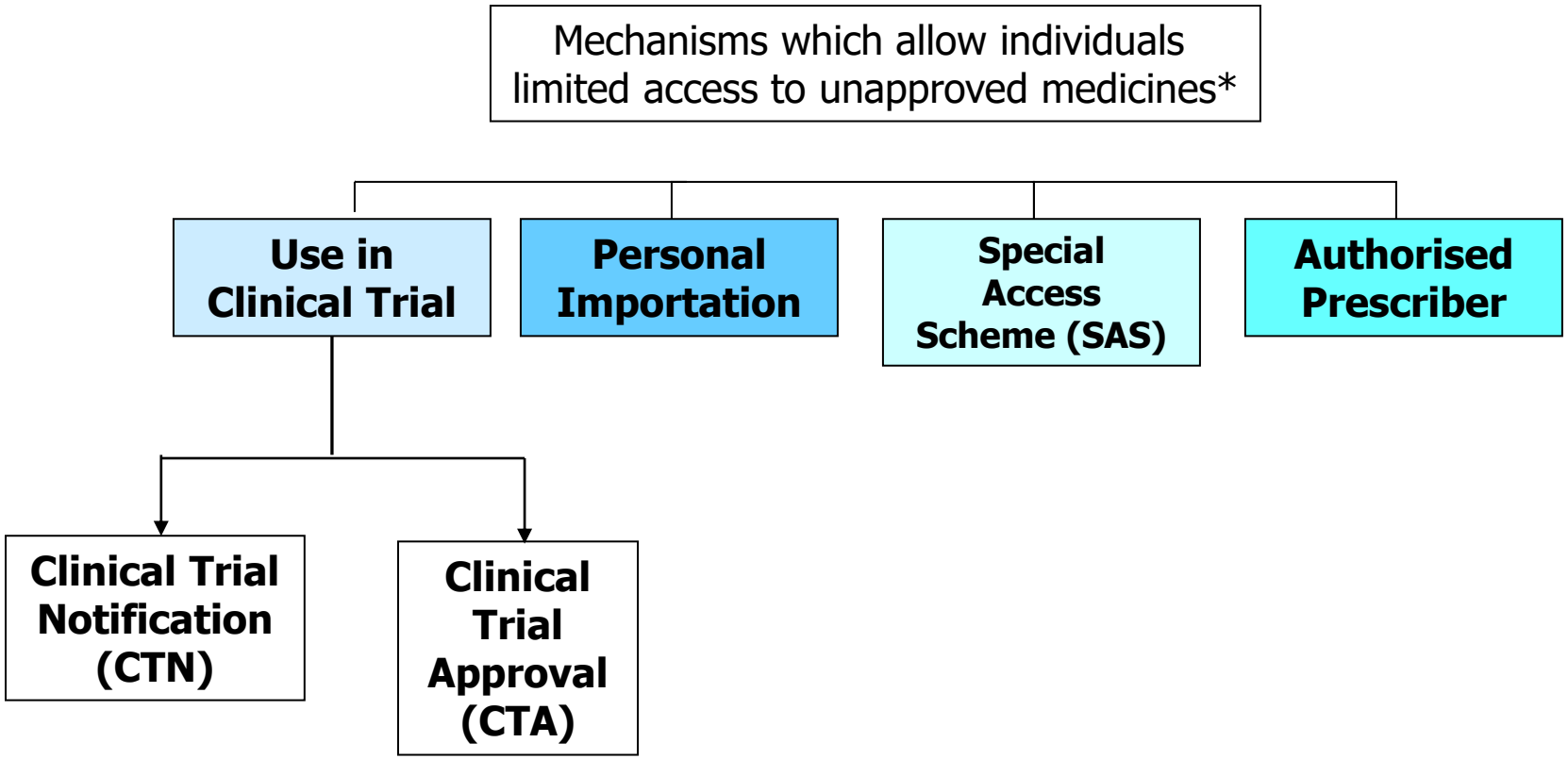
Drug Product support Phase III program

- Manufacturing process established and well controlled
- Formulation and presentation proposed for marketing
- Manufacturer for commercial product
- Sufficient quantity and stability data for planned size and duration of phase III trial
- Documentation
- Quality Risk assessment

Australian clinical research environment

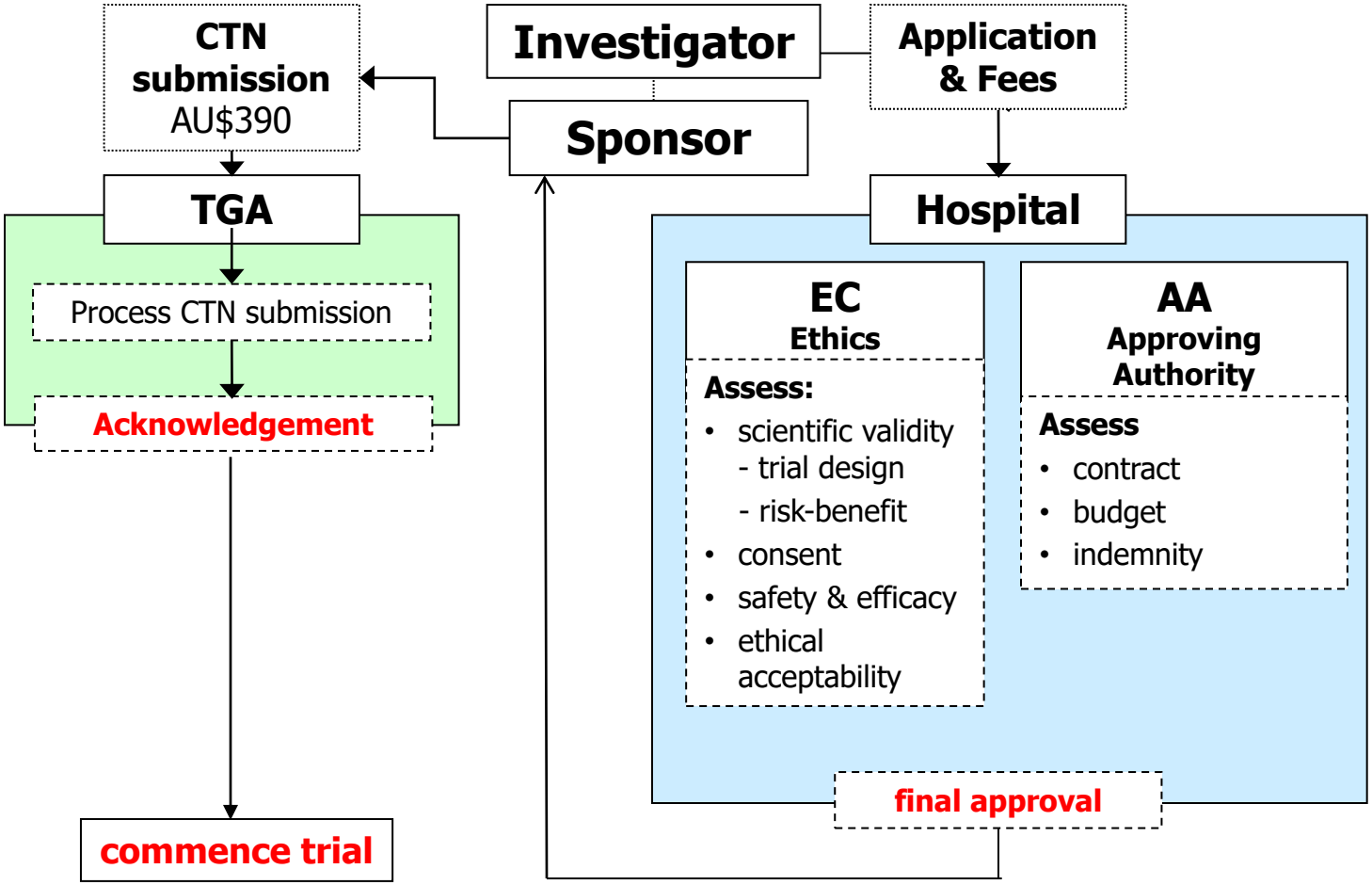
- Regulatory
  - CTN (Clinical Trial Notification)
  - CTA (Clinical Trial Approval)
- Human Research Ethics Committees
- Industry
  - Why Australia
  - The industry in Australia
  - Limitations

Access to Unapproved Medicines



*Therapeutic Goods Regulations 1990

Clinical Trials Notification (CTN)

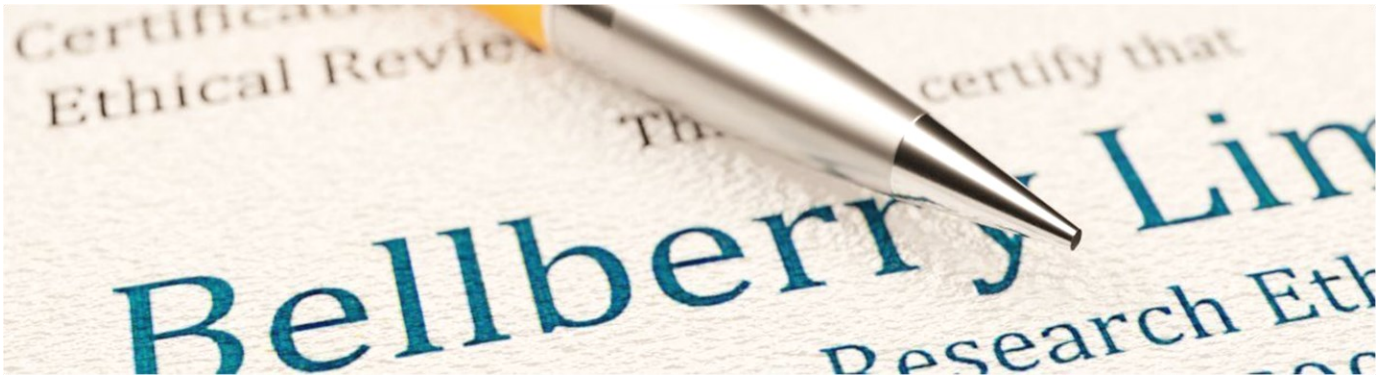


(95% of trials in Australia)

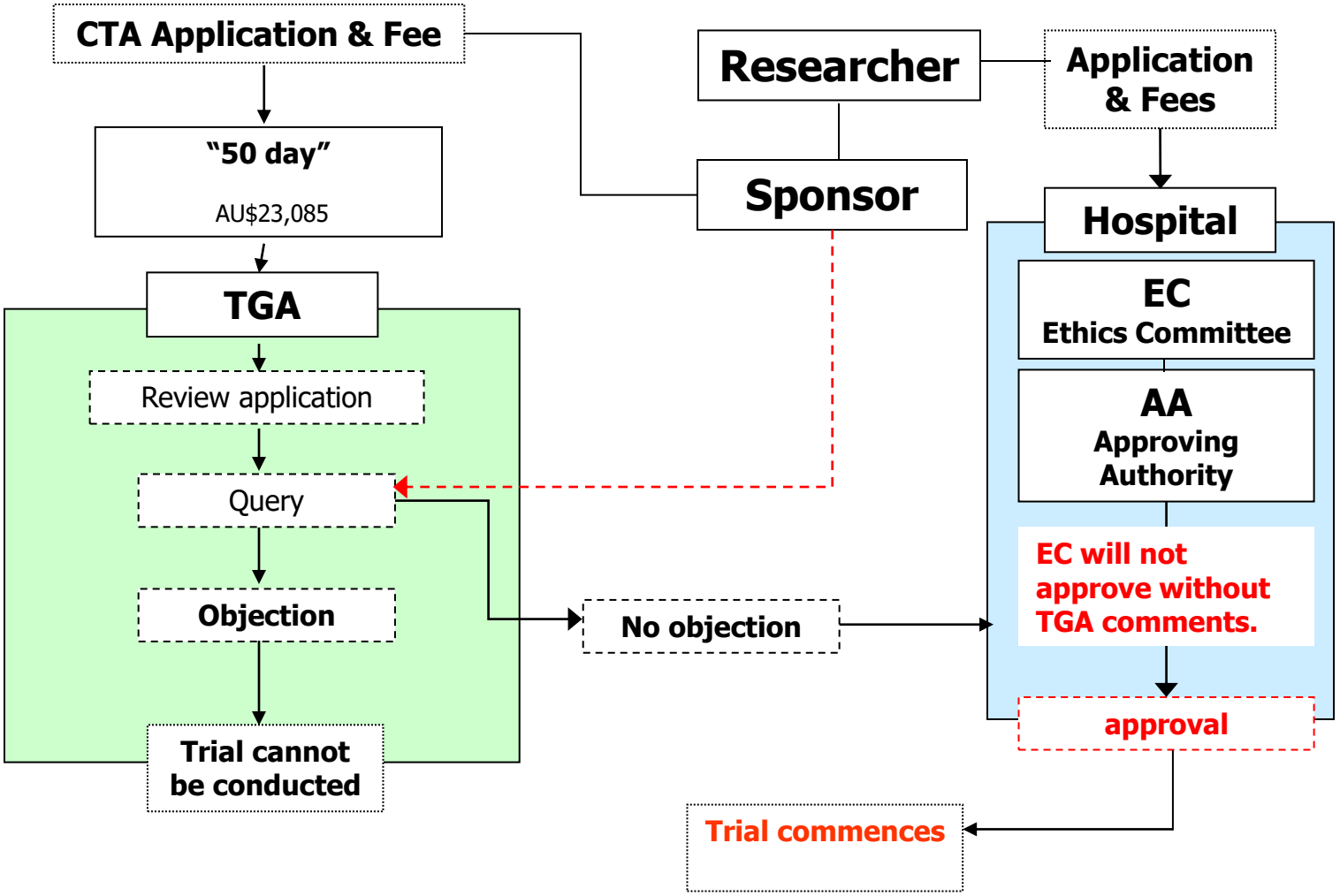
Human Research Ethics Committee

- NHMRC Guidelines
- Membership
  - Independent lay person (2)
  - Healthcare professional
  - Pastoral care
  - Lawyer
  - Research expertise (2)
- Public and private sector committees

- Documents
  - Protocol
  - Investigator brochure
  - Consent forms
- May request review under CTA Scheme



Clinical Trial Approval (CTA)



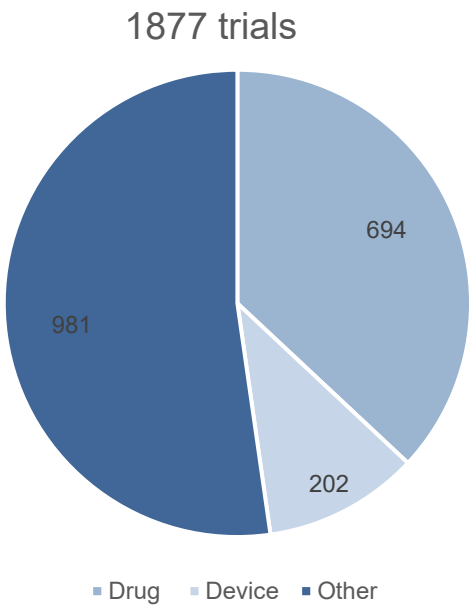
CTA Scheme

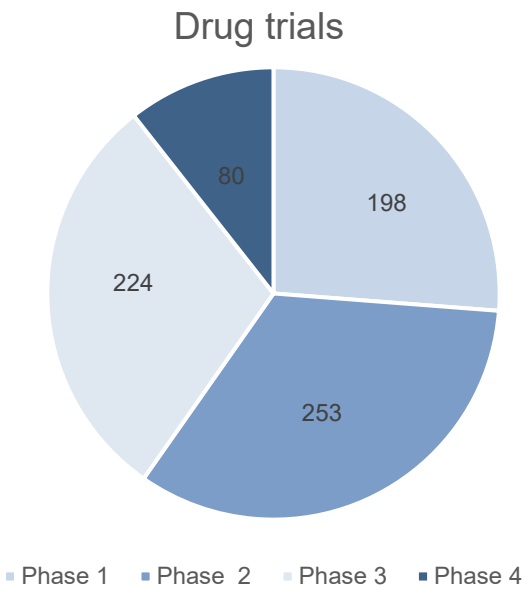
- Mandatory only for Class 4 biologicals:
  - except if supported by evidence from previous clinical use
  - except if trial has been approved by another comparable Regulatory authority
- TGA evaluates summary information
- Presubmission meeting recommended
- HREC evaluates scientific and ethical aspects of protocol

Australian advantage

- Rapid start-up
  - Single review process
  - Standard Medicine Australia contract
- Investigators
  - World class
  - Experienced in GCP trials
  - Interested in clinical research
- Infrastructure
  - World class healthcare system
- Patients
  - Early access to new medicines/devices
  - Ethnically diverse
- Costs
  - Significantly lower than in US or UK
  - R&D Tax rebate

Clinical trials commenced in Australia 2019





*MTP Connect Clinical Trials in Australia 2019

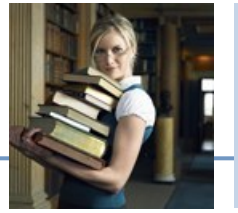
Australian limitations

- Patient recruitment may be slow in some indications
- Some expertise not available
  - eg biosafety
- Access to scale up manufacture
- Limited choices for nonclinical pharmacology and toxicology
- Australian companies seek advice from US FDA and EMA as these agencies have broad experience in assisting startup companies

"I think everyone in the industry would tell you that your lot are the best people to have on set"

US actor to an Australian reporter (The Age 4 Oct 22)




Thankyou

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