

## Strategy and Regulations - Preparing for Clinical Trials

Dianne Jackson-Matthews, PhD, RAC  
Director of Regulatory Affairs, ERA Consulting



Clinical Research Excellence Q&A

## Scope of this Presentation

- Clinical trial regulations in Australia
  - Pathways to approval of a clinical protocol
- Strategy for developing a trial
- Problems to avoid during development
- Benefits of building a regulatory strategy early



Clinical Research Excellence Q&A

## Strategy for Value Creation

- Earlier phase trials instrumental in design of later phase trials
- Later phase trials = most expensive undertaking in drug development
- Generation of quality clinical data is pivotal to value creation for the technology or product candidate
  - Essential for positioning the product for the targeted patients and market



Clinical Research Excellence Q&A

## Clinical Trial Regulation in Australia

- Therapeutic Goods Administration (TGA) administers programs for access to unapproved products
- Clinical trials may be conducted under
  - Clinical Trial Exemption Scheme (CTX)
  - Clinical Trial Notification Scheme (CTN)
- Special requirements for genetic therapies / GMOs
- Clinical trial conduct according to GCP
- GMP manufacture of investigational products is normally required



Clinical Research Excellence Q&A

## Clinical Trial Exemption

- CTX
  - Intended for high risk products, including innovative/biotech products
  - Also appropriate for early phase trials
  - Submission of data package to the TGA
    - Primarily focussed on safety
    - Attracts substantial fee for review
  - TGA does not evaluate protocols (but asks for them)
  - TGA evaluates the usage guidelines, pharmaceutical data, any preclinical and clinical data



Clinical Research Excellence Q&A

## Clinical Trial Exemption cont.

- CTX
  - Single CTX may cover multiple clinical trial protocols
  - Human Research Ethics Committees (HREC) approve the protocol
  - Approval is required from the HREC at each site conducting the trial
  - CTX trial can not commence until approval from both the TGA and HREC obtained
  - <5% all trials in Australia conducted under CTX



Clinical Research Excellence Q&A

## Clinical Trial Notification

- CTN
  - Notification but no submission of data to TGA
  - Information submitted to the HREC to assess the validity and ethics of trial design
    - Data package may need additional technical expertise
  - Intended for use in later stage trials, and for low risk products



Clinical Research Excellence 08


## Special Requirements

- For gene therapy and/or genetically modified organisms/cells
  - Gene therapy
    - NHMRC committee provides guidance to HRECs and TGA on clinical research proposals
  - GMOs
    - Licensure from the Office of Gene Technology Regulator (OGTR) required
    - Clinical trials generally regarded as not involving deliberate release



Clinical Research Excellence 08

## Recent Moves in Clinical Trial Regulation in Australia

- Proposed joint trans-Tasman agency (postponed) 
- Revised clinical trial scheme proposed
  - Clinical Trial Assessment (CTA), similar to CTX
  - Clinical Trial Certification (CTC), with self-certification after Ethics approval
- Implementation date?



Clinical Research Excellence 08

## Developing a Trial: Questions to Answer

- Ready to ask the question?
- What is the exact question?
- What is the primary outcome - is it direct and readily measured?
- Outcomes according to those specified by guidance documents?
  - **Essential** if trial is to be part of a marketing authorisation submission



Clinical Research Excellence 08

## Questions to Answer (cont)

- Is the trial design appropriate (patient numbers, statistics) to answer the question?
  - **Inclusion/exclusion** criteria
- Trial centres audited, capable of recruiting?
- Indemnity provisions in place?
- Correct labeling (including **expiration** dating)?
- Consent forms contain full description for participation?



Clinical Research Excellence 08

## Strategy of Developing a Trial

- Regulatory framework..... **anywhere**
  - Take account of the intended-to-treat population
  - Take account of local clinical practice and current reimbursement policies
  - Consider cost of international work vs. value
  - Build in **quality** early, according to the relevant current good practices: **GXP**s, where X = **L**aboratory, **M**anufacturing, **C**linical, **T**issue...



Clinical Research Excellence 08

## Steps in the Strategy (1)

- What if development is “not exactly” **GXP**?
- Build a strategy on a **case-by-case** basis, so it is relevant to support your program
- Be aware of inspectional policies
- Avoid the possibility you receive this **invitation**\* to sign a list of observations!!



\* Photo credit: BioMedSource Network website  
Clinical Research Excellence 08

## Steps in the Strategy (2)

- Planning a rational approach.....
- Regulatory context depends on indication and product category/type
- Review current regulations, guidances, etc
- Decide which apply / which are **relevant**
- Identify regulatory **opportunities** (rare disease?)
- Practice **risk** management and

Beware pitfalls.....



Clinical Research Excellence 08

## Steps in the Strategy (3)

- For many products, pre-submission meetings/ teleconferences with regulators are advisable
- Input on quality, non-clinical and clinical aspects
- Interact personally with potential reviewers
- Identify and discuss **hot spots**
  - Enough stability data? Suitable non-clinical package?
- Better to know **early** if there are real issues



Clinical Research Excellence 08

## Why Approach an Agency?

- Opportunity for presentation and discussion of your good science
- Strategy to **add value** for potential investment or partnering/licensing opportunities
- **Not** a mechanism for public announcements to raise the stock price, *per se*
- Agencies are well-informed, so **beware** the badly-worded press release!



Clinical Research Excellence 08

## Steps in the Strategy (4)

- **Don't** make assumptions that requirements in one jurisdiction will hold elsewhere
- Requirements may be more or less **stringent** or just **different**
- **Don't** overlook guidance, even if “**draft**”
- Obtain and use regulatory intelligence - it is a valuable tool and strong indicator of diligence in the Company



Clinical Research Excellence 08

## For a Pre-submission Meeting at TGA

- Briefing document content is critical, but **not** a thesis!
  - Reviewers have limited time
- Deliver package **by the date agreed**
- Be clear and concise, using summaries and an up-to-date Investigator's Brochure
- Give a clear **rationale** for the clinical program
  - Especially important if beyond Phase I, where the product has been studied elsewhere



Clinical Research Excellence 08

## At Pre-submission Meetings...

- Short [*or even no*] Company presentations
- Slides to contain **no new data** unless critical (and likely to be seen that way by TGA)
- Maximise interface time with reviewers
- Include Marketing/Company President with **caution**
- Agree internal strategy if difference of opinion or misunderstanding emerges
- And above all,

**LISTEN!**



Clinical Research Excellence 08



## In Summary

- Regulatory strategies supporting clinical development must be **both** relevant and up-to-date
  - Evaluate and implement **risk management**
- Regulatory Agencies are resources!
  - Interactions add value / provide **risk mitigation**
  - Leverage Agency interactions with **care**
- Consider the consequences of successful trials!
  - Long-term view: costs of further trials, regulatory submissions and reimbursement applications



Clinical Research Excellence 08  
**Get it right the first time!**

**Thank you!**

dianne.jackson-matthews@eraconsulting.com



Clinical Research Excellence 08