Metro South Health

GCP Essentials
Good Clinical Practice
(Good Research Practice)

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Overview

- Background
- When does GCP apply?
- Definitions
- Principles of GCP
- Investigator responsibilities
- Informed consent
- Investigational Product Management
- Safety reporting
- Essential documents
- Resources

- Key learning aims
  - what does GCP actually mean?
  - Increase awareness of researchers' responsibilities
  - Meet your needs, answer your important questions

Background

- *Note for Guidance on Good Clinical Practice* is an internationally accepted standard for the design, conduct, recording and reporting of clinical trials
- TGA (Therapeutic Goods Administration)
  - Part of the Australian Government Department of Health
  - Responsible for regulating therapeutic goods including
    - prescription medicines
    - vaccines
    - medical devices
- We use the *Note for Guidance on GCP Annotated with TGA comments* *http://www.tga.gov.au/pdf/euguide/ich13595an.pdf*

  used reference numbers throughout

When does GCP apply?

In practice, GCP applies when a Clinical Trial Notification (to TGA) is required, ie for clinical investigational use of:

- any medicine, biological or device not entered in the Australian Register of Therapeutic Goods, including any new formulation of an existing product or any new route of administration; or
- a marketed medicine, biological or device beyond the conditions of its marketing approval, including new indications extending the use of the product to a new patient group and the extension of doses or duration of treatments outside the approved range.

But consider interventions that are

- dietary (ginger, pro-biotics, weight loss shakes)
- surgical
- psychological, physiotherapy, speech therapy

GCP guidelines are also be applied to other clinical investigations that may have an impact on the safety and well-being of human participants.

GCP is really just good research practice, ideally apply relevant elements to all research

Definitions

1.12 Clinical trial- Any investigation in human participants intended to

- discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s),
- and/or to identify any adverse reactions to an investigational product(s),
- and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

1.33 Investigational Product- A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled in a way different from the approved form,

or when used for an unapproved indication,

or when used to gain further information about an approved use

Principles of ICH* GCP
*International Committee for Harmonisation

2.1 Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki

2.2 Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial participant and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.

2.3 The rights, safety, and well-being of the trial participants are the most important considerations and should prevail over interests of science and society.

2.4 The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.

Principles of ICH GCP …. 2

2.5 Clinical trials should be scientifically sound, and described in a clear, detailed protocol.

2.6 A trial should be conducted in compliance with the protocol that has received prior independent ethics committee approval

2.7 The medical care given to, and medical decisions made on behalf of, participants should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.

2.8 Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).

Principles of ICH GCP … 3

2.9 Freely given informed consent should be obtained from every participant prior to clinical trial participation.

2.10 All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.

2.11 The confidentiality of records that could identify participants should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

2.12 Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol.

2.13 Systems with procedures that assure the quality of every aspect of the trial should be implemented.

4 Investigator (Principal Investigator, PI) responsibilities

4.1 Qualifications and agreements

- Appropriate qualification, training and experience
- Be thoroughly familiar with the use of the IP
- maintain a list of appropriately qualified persons to whom they have delegated significant trial related duties (Staff delegation log)

4.2 Adequate resources

- Meet recruitment targets
- Time, staff and facilities
- Ensure that all persons assisting are adequately informed about the protocol, IP, duties and functions

4.4 Communication with ethics committee

4.5 Compliance with protocol

4.8 Informed consent

4.8.1 HREC approved form (Document control)

4.8.8 Signatures personally dated

4.8.11 Copy to participant
(A copy of Patient Information and Consent document will be uploaded into ieMR with original kept at site)

4.6 Investigational Product (IP)

4.6.1 Responsibility rests with the investigator

4.6.2 May/should assign duties for accountability to pharmacist or other appropriate individual

4.6.3 Records

- Delivery to site, inventory at site, use by each participant, return to sponsor or (destruction) of unused products, ie document the chain of custody
- Dates, quantities, batch/serial numbers, expiry dates, unique codes assigned to IP and participants
- Document that participants were provided with the doses as per protocol, reconcile all IP received
- ?pill counts, returns

4.6.4 Store as specified by the sponsor & in accordance with applicable regulatory requirements

4.6.5 Investigator should ensure that the IP is used in accordance with the approved protocol

4.6.6 Investigator or designee explain the correct use of the IP to each participant and check instructions being followed

Safety reporting

1.2 Adverse Event (AE)

- any untoward medical occurrence in a patient or clinical investigation participant
- report according to protocol requirements

1.50 Serious Adverse Event (SAE)

- any untoward medical occurrence that
  - results in death
  - is life threatening
  - requires inpatient hospitalisation or prolongation of existing hospitalisation
  - results in persistent or significant disability or incapacity

  Or is a congenital anomaly/birth defect
- includes events unrelated to research

4.11.1 Report SAEs immediately to the sponsor, comply with regulatory requirements (report to HREC)

Consider specifying reporting in protocol

Essential documents

- Staff delegation log
- Trial master file
- Participant logs (screening, identification, enrolment)
- Document control
  - Consent form, protocol etc.
  - Keep just one copy of superseded versions and clearly mark (hard copies and electronic copies)
- GCP specifies requirements for PICFs and protocols (section 6)

Trial master file index

1. Protocol- current, superseded
2. Patient information
3. Case report form (data collection forms)
4. Ethics- approvals, correspondence
5. Governance
6. Funding and finance
7. Investigational product
8. Randomisation/unblinding
9. Quality assurance
10. Data management procedures
11. Adverse events
12. Statistical analysis- plan, analysis
13. Correspondence
14. Miscellaneous (specify)

Principal Investigator Signature: Date:

SIGNATURE LOG AND DELEGATION OF DUTIES

Protocol No:

Investigator Name: | Site Name and Number

Sponsor:

Print Name	Signature	Sample Initials	Sample numbers if required.	Function (e.g. P.I.)	Task Delegated	Authorised By P.I. (initial+ date)	Start Date Of Involvement	End date of Involvement

Project Staff Function Codes:

Coordinating Investigator
CI

Principal Investigator
PI

Associate/sub Investigator
AI / SI

Study coordinator
SC

Research Assistant
RA

Other (please nominate)

Delegated Tasks Codes

a. Informed discussion

b. Informed consent sign off

c. CRF / DCF Completion and Correction

d. CRF / DCF Sign-Off

e. Subject examination / evaluation

f. Investigational product dispensing

g. Investigational product accountability

h. Randomisation of subjects (eg IVRS)

i. Essential / regulatory documents handling

j. Study specific procedures

k. Other (eg vital signs measurement, collation and faxing of SAE's and other study documentation etc)

Resources

GCP Training

- Quintiles web based training
- ARCS- Web based
- 2 day courses- ARCS, Datapharm

Research framework

- NHMRC National Statement on Ethical Conduct in Human Research (2007)
- The Australian Clinical Trial Handbook http://www.tga.gov.au/pdf/clinical-trials-handbook.pdf
- National Mutual Acceptance of Ethical Review of Multi-centre Clinical Trial Research http://www.health.qld.gov.au/ohmr/html/regu/mutual_accept.asp
- Research Governance Handbook: Guidance for the national approach to single ethical review http://www.health.qld.gov.au/ohmr/documents/regu/nhmrc_gov_hbk.pdf

Conclusions

- GCP is essentially good practice
  - Research design, conduct, record keeping
- Any Questions?
- Comments
- Thanks to all for your time and interest
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