Applying GCP to Audits of Clinical Trials

NSW Regional HEALTH PARTNERS
CENTRE FOR INNOVATION IN REGIONAL HEALTH

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Working together for good health and wellbeing
Clinical Trials
Strategic Platform

Sydney HealthPartners

This presentation covers

Objectives of a clinical trial

Good Clinical Practice and its application to clinical trials

GCP clinical trial auditing

Glossary

Curriculum Vitae (CV)

Food and Drug Administration (FDA)

Good Clinical Practice (GCP)

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)

Institutional Review Board (IRB). The term Human Research Ethics Committee (HREC) is used in Australia

Therapeutic Goods Administration (TGA)

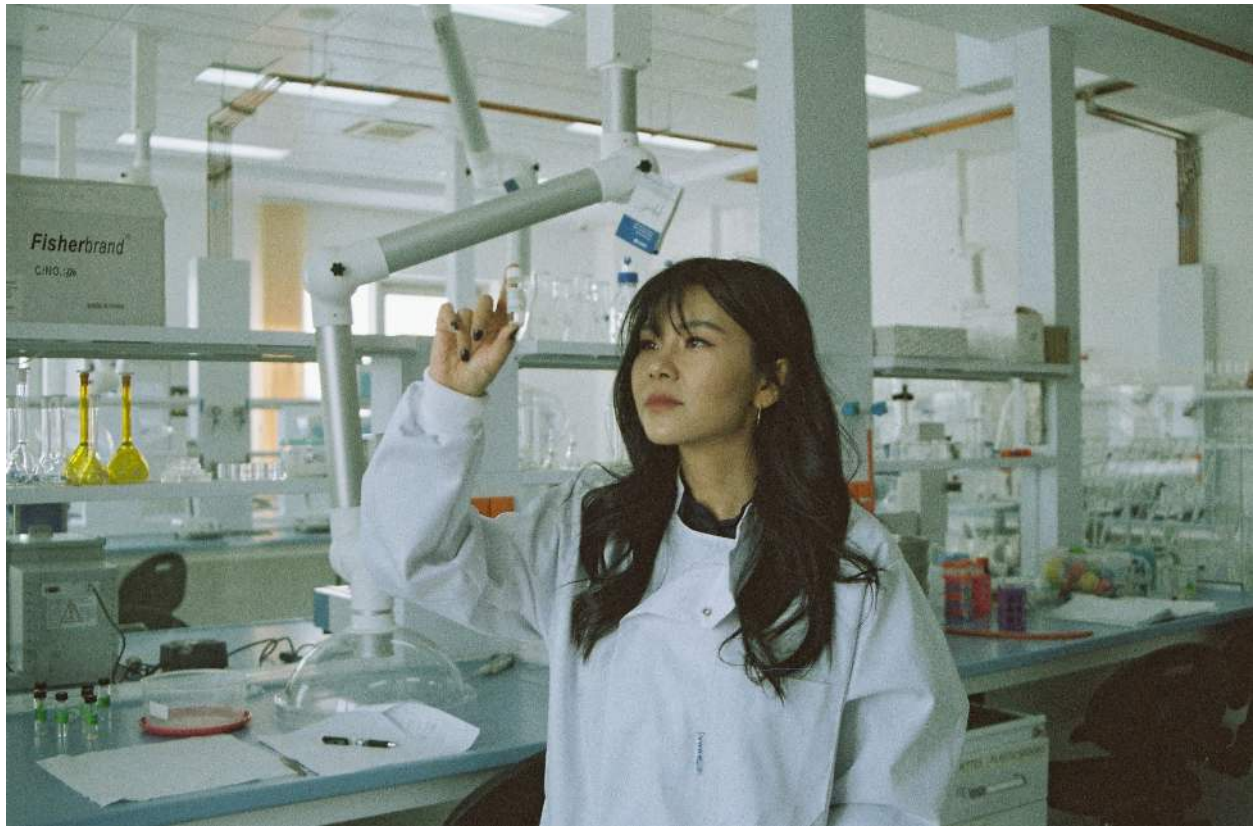

Image: Diane Serik from Unsplash

Objectives of a clinical trial

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Objectives of Conducting a Clinical Trial

Data from Clinical Trials are used to increase knowledge

The end goal is to improve health outcomes and Quality of Life (QoL) for consumers and the community

What is a clinical trial?

“Clinical trials are a type of research that studies new tests and treatments and evaluates their effects on human health outcomes.”

World Health Organisation - Clinical Trials Overview

Clinical trials (who.int)

Image: Lucas Vasques from Unsplash

Guidance and Regulatory Framework

ICH GCP Efficacy Guidelines

TGA Note for Guidance on GCP

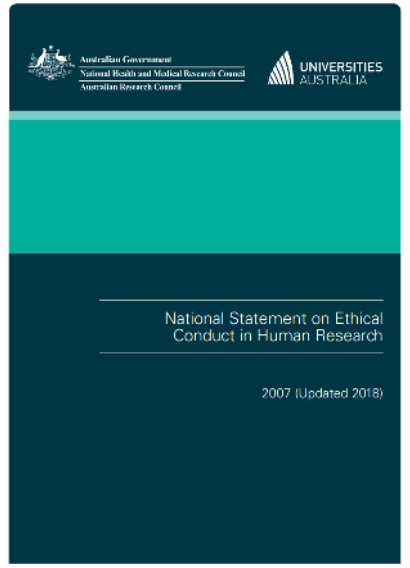
NHMRC National Statement on Ethical Conduct in Human Research

Australian Code for the Responsible Conduct of Research

TGA Australian Clinical Trial Handbook

FDA Investigator Responsibilities

Declaration of Helsinki



Images:
Presentation: TGA's Role in Clinical Trials Regulation and Administration
national-statement-2018-updated.pdf

Objectives of a clinical trial

Good Clinical Practice and its application to clinical trials

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What is GCP?

“Good Clinical Practice (GCP) is an international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials. It also serves to protect the rights, integrity and confidentiality of trial subjects.”

[The importance of Good Clinical Practice guidelines and its role in clinical trials (nih.gov)]

Who must be trained in GCP?

Compliance with the Good Clinical Practice standards is obligatory for trials involving the investigation of medicinal products for many countries, including Australia.

Training in GCP, and evidence of having successfully completed that training, is mandatory for all clinical trials site personnel.

GCP and clinical trials

Catalyst for GCP - Historical experimentation on humans.

International response - compliance with GCP and regulatory guidelines to provide **public assurance that the rights, safety and wellbeing of participants are respected and protected**, and that the data generated are credible and accurate.

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) created the set of GCP standards that are used internationally.

Image: https://www.ich.org/

ICH Guideline for GCP

ICH Guideline for Good Clinical Practice in Australia

“The Guideline for Good Clinical Practice is an internationally accepted standard for the designing, conducting, recording and reporting of clinical trials. The Guideline for Good Clinical Practice is incorporated by reference in the Therapeutic Goods Regulations 1990. Compliance with the Guideline is a condition of approval for the conduct of a clinical trial.”

Introductory comments of the TGA

The 13 Principles behind ICH-GCP

IMPORTANT NOTE

The 13 principles listed in the following slides are applicable as of April 2022.

However, the ICH Guideline for Good Clinical Practice is currently under review and is expected to be updated in 2022.

The 13 Principles behind ICH-GCP

1. Ethics: Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).

2. Trial risk vs trial benefit: Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.

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

The 13 Principles behind ICH-GCP

4. Information on the Medicinal Product: The available non-clinical and clinical information on an Investigational Product should be adequate to support the proposed clinical trial.

5. Good quality trials: Clinical trials should be scientifically sound, and described in a clear, detailed protocol.

6. Compliance with the study protocol: A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favourable opinion.

The 13 Principles behind ICH-GCP

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

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

9. Informed consent: Freely given informed consent should be obtained from every subject prior to clinical trial participation.

The 13 Principles behind ICH-GCP

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

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

12. Good Manufacturing Practice: 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.

13. Quality Assurance: Systems with procedures that assure the quality of every aspect of the trial should be implemented.

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What is a clinical trial audit?

“An Audit is a systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analysed and accurately reported according to the protocol, sponsor’s SOPs, GCP, and the applicable regulatory requirements.”

(A Comprehensive and Practical Guide to Clinical Trials, Chapter 17 Audits and Inspections, 2017).

Image: National Cancer Institute from Unsplash

Auditor reviews at site

The Investigator has overall responsibility for all aspects of trial conduct. The auditor may review:

Personnel CVs which should contain:

- Signature
- Qualifications
- Clinical research experience
- Evidence of current GCP training and certification
- Current position at site
- Current CV - Not more than 1 year old at start of study

Auditor reviews at site

- Signed and dated Confidentiality Agreement
- Signed and dated Investigator Contracts
- Signed and dated Sponsor Agreement
- Signed and dated Clinical Research Organisation Agreement
- Signed and dated Indemnity Agreement
- Signed and dated Financial Agreement
- Signed and dated Protocol Agreement
- Signed Confirmation of Case Report Form data
- Signed US Food and Drug Administration 1572 Forms (if applicable)

Auditor reviews at site

- Completed, dated and signed delegating authority logs
- HREC approval letters
- HREC correspondence i.e., annual reports
- Informed consent completeness
- CRFs are completed and accurate
- Current versions of protocol, Investigator brochure, PICF
- Approved versions of advertising
- Source data
- Documents signed as required i.e., pathology results
- Participant follow-up and outcome for safety reporting
- Storage of study drug, temperature logs, monitor review, returns
- Review of randomisation codes.

Auditor reviews at site

- Review of Quality Assurance systems used at site and levels of access
- Documentation for audit trails
- Review of Quality Control applied at every stage of data handling
- Review outcomes other internal/external audits
- Process for Quality Assurance during the trial
- Standard Operating Procedures
- Trial Master File (either electronic or hard copy)

* *Audits can also be undertaken remotely*

Common findings from audits

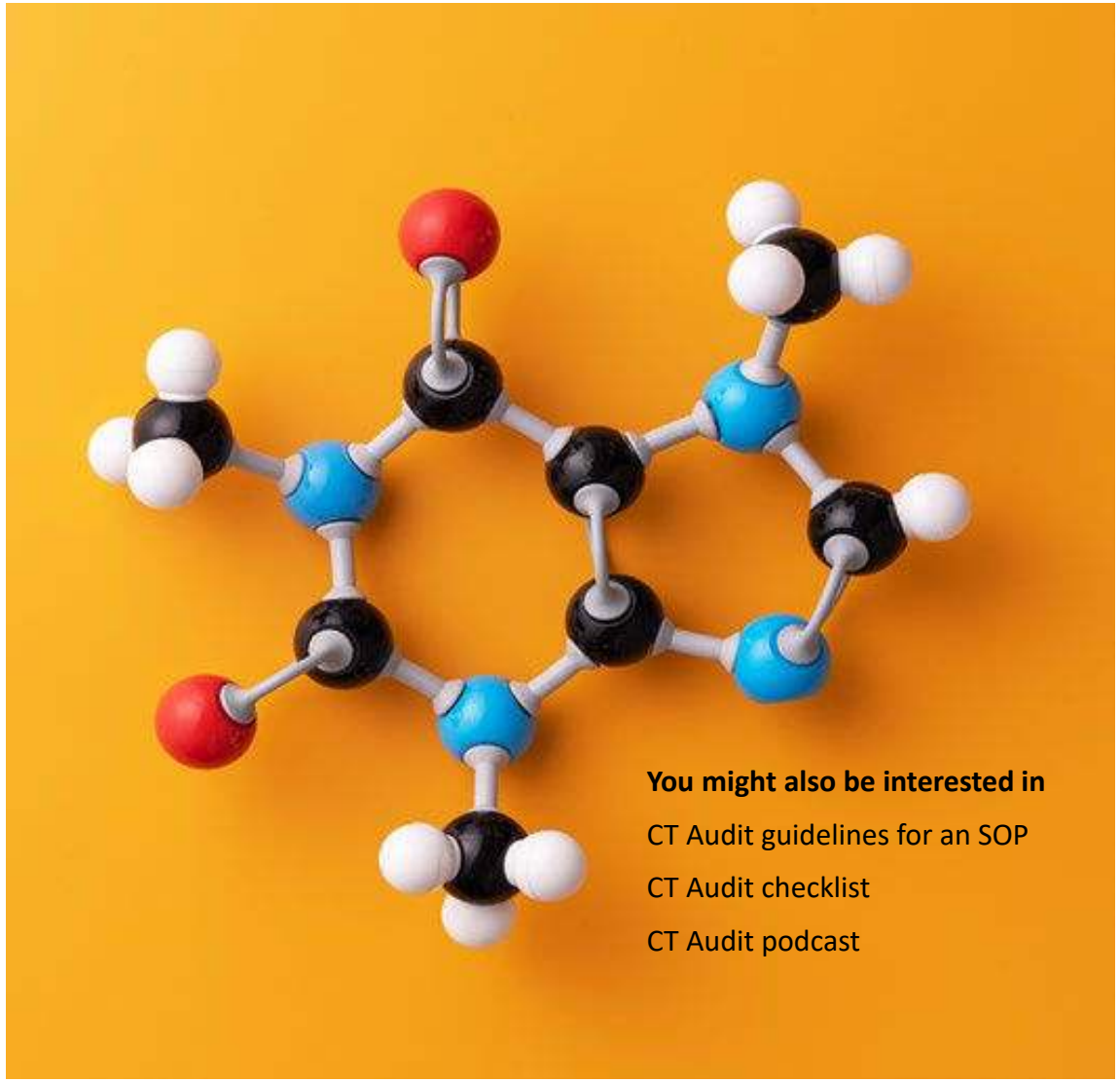
- Patient or investigator signature on Consent Form is not dated
- No version/date on consent form
- Staff CVs not on file
- Ethics Committee members composition list not current
- Ethics Committee letter did not list all documents reviewed
- Ethics Committee letter did not contain statement of GCP compliance
- Drug not temperature monitored (if required)
- Signatures not dated
- Investigator failed to report SAEs

References

- TGA ICH Guideline for Good Clinical Practice
- Australian Clinical Trial Handbook National Statement on Ethical Conduct in Human Research
- VCC Alliance. Roles involved in conducting clinical trials
- VCC Alliance. Principal Investigator
- World Health Organisation Handbook for Good Clinical Research Practice (GCP)
- Guidance for Implementation ICH Harmonised Guideline Integrated Addendum to ICH E6(R1): Guideline For Good Clinical Practice E6(R2)
- NHS Oxford University Hospitals Good Clinical Practice (GCP)
- WMA Declaration Of Helsinki – Ethical Principles For Medical Research Involving Human Subjects

Contacts for further information

- Sydney Health Partners, Clinical Trial Project Manager
- NSW Regional Health Partners Clinical Trials Network Officer
- Maridulu Budyari Gumal (SPHERE) Clinical Trials Strategic Platform



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