Introduction to Good Clinical Practice

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22 February 2019

Good Clinical Practice

CONTENTS:

Government of Western Australia
Child and Adolescent Health Service

RESEARCH SKILLS SEMINAR SERIES 2019
Research Education Program

Introduction to Good Clinical Practice

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Telethon Kids Institute

Research Skills Seminar Series | Research Education Program
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GCP Overview

- Standards and why we have them
- Study Set-up – *responsibilities, approvals and essential documents*
- Informed Consent
- Case Report Form, Source Data and Data Entry
- Safety Reporting

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Standards and Why we Have Them

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Standards and why we have them

- What is the significance of standards in clinical research?
  - Safeguard and protect research subjects
  - Risk Reduction
  - Quality data/outcomes
  - Excellent research, good science

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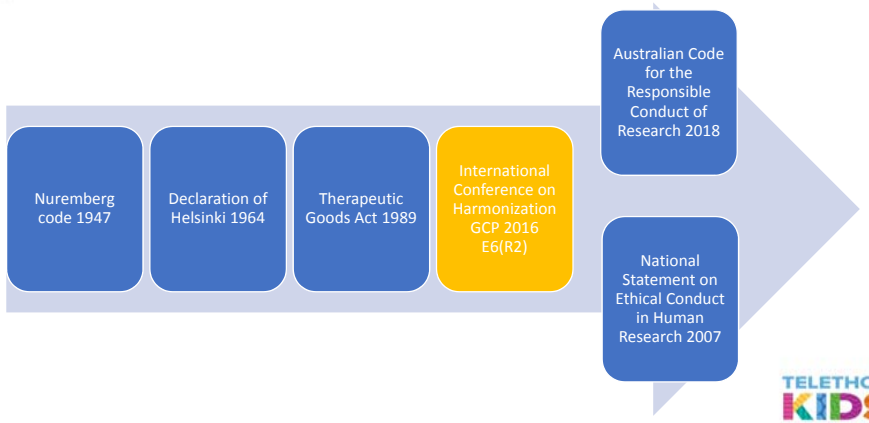
What is GCP?

International ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.

Standards and why we have them



Regulations

- **Therapeutic Goods Administration (TGA)**
  Therapeutic Goods Act 1989
  – Responsible for regulating medicines and medical devices
- **National Health and Medical Research Council (NHMRC)**
  NHMRC act 1992
  – Specifically required to issue guidelines for the conduct of medical research and ethical matters related to health.

Regulations

In Australia, all research involving humans must comply with:

- **National Statement on Ethical Conduct in Human Research** 2007 – updated 2018 NHMRC **(The Statement)**
- **Australian code for the responsible conduct of research** Developed jointly by the NHMRC, the Australian Research Council and Universities Australia **(The Code)**
- State and territory guidelines.

Regulations

- Clinical trials of **medicines and medical devices** also must comply with:

Note for guidance on good clinical practice (CMP/ICH/135/95) (Therapeutic Goods Administration)

Clinical trials of **medical devices** must also comply with **ISO 14155:2011 Medical devices** — Clinical investigation of medical devices for human subjects: Good clinical practice

WA Health Research Governance Policy

All human research and experimentation conducted within WA Health:

- **World Medical Association**
- **National Statement**
- **The Code**

And:

- National Health and Medical Research Council *"Values and Ethics: Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health Research"* 2003*;*
- TGA *"The Australian Clinical Trials Handbook"* 2006, and "Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95)" 2000; and
- Relevant Commonwealth or State legislation and guidelines including the Department of Health "Occupational Safety and Health Policy" 2005.

13 Principles of GCP

1. 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**
2. 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. The **rights, safety**, and **well-being** of the trial subjects are the **most important** considerations and should prevail over interests of science and society.
4. The available **nonclinical** and **clinical information** on an investigational product should be adequate to **support** the proposed clinical trial.

13 Principles of GCP

5. Clinical trials should be **scientifically sound**, and described in a clear, detailed **protocol**.
6. 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.
7. 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. Each **individual** involved in conducting a trial should be **qualified by education, training, and experience** to perform his or her respective task(s).
9. Freely given **informed consent** should be obtained from every subject prior to clinical trial participation.

13 Principles of GCP

10. All clinical trial **information** should be **recorded, handled, and stored** in a way that allows its **accurate** reporting, interpretation and verification.*
11. 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. **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. Systems with procedures that assure the **quality** of every aspect of the trial
should be implemented. *

Standards and why we have them

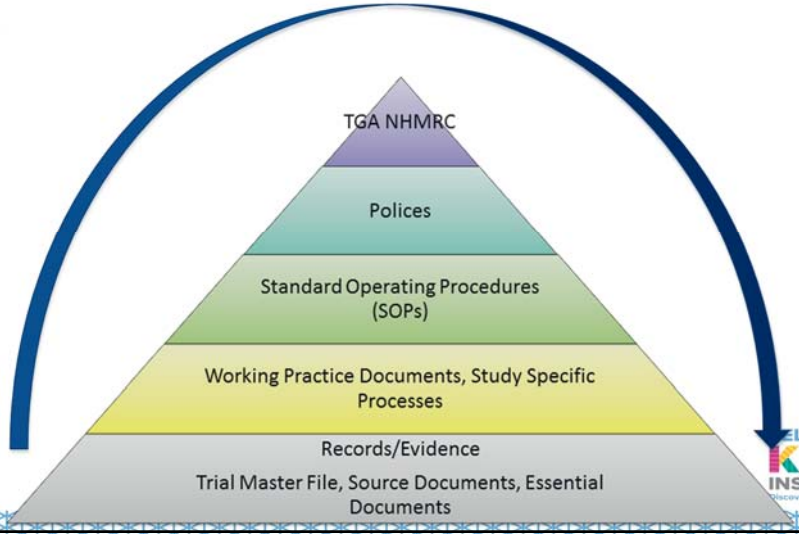
- Ever **evolving** in response to changing landscape
- **No single document** which provides the standards and laws by which you conduct clinical research.
- Ensure you are **aware of and compliant** wit relevant laws, polices and codes of conduct.
  - Additional information provided in handouts

Study Set-up

"In any successful project the important factor is your belief. Without belief there can be no successful outcome"

William James

GCP Guidelines



Responsibilities : Sponsor

- For securing the arrangements to **initiate**, **manage** and **finance** a study
- They can delegate any or all of their functions to third parties but they **cannot** delegate **responsibility**
- Where delegated there **must** be arrangements in place for **oversight** of the delegated activities
- Clinical Trial responsibilities with respect to GCP are **extensive**
- Detailed in item 5 of the Note for Guidance on GCP[1]

1 http://www.tga.gov.au/industry/clinical-trials-note-ich13595.htm

Responsibilities: Sponsor

- Risk and Quality management
- Medical expertise
- Trial design analysis
- Trial management and Data Handling and Record Keeping
- Selection of appropriate investigator(s) and institution(s)
- Insurance and indemnity
- Approvals (HREC, TGA etc)
- Manufacture, packaging, labelling/coding
- Safety evaluation
- Monitoring/Audit/Inspection
- Clinical Study Report

Responsibilities: Principal Investigator

- **Coordinating Principal Investigator**
  - Overall responsibility for the research project
  - Submits the project for ethical and scientific review for multi-centre projects.
  - Ongoing communication with the Human Research Ethics Committee (HREC) and passing on any outcomes from this to the Principal Investigators. This includes annual progress reports and final report including outcomes to the HREC
  - Duties delegated by the Sponsor

Responsibilities: Principal Investigator

- Overall conduct, management, monitoring and reporting of research at a **site,** including annual progress reports, final report to RGO
- Submits the project for site authorisation(RGO approval)
- Delegation and **supervision** of duties to study team
- Sign-off to say staff are competent to work on the research
- Oversight and management of Investigational Medicinal Product
- Safety reporting signature on notifications from Sponsor if required

Responsibilities: Everyone

- **Everyone's Responsibilities**
  - Ensure the safety and wellbeing of the participant
  - Fulfil the duties delegated to you

Approvals

- Do not start until:
  - Favourable opinion from a Human Research Ethics Committee
  - Authorisation to commence a project at site
  - For Clinical Trials
    - CTN or CTX (http://www.tga.gov.au/industry/clinical-trials.htm#forms)
    - Registered on Clinical Trial Registry E.G. http://www.anzctr.org.au/

Approvals

- **Clinical Trial Notification (CTN) Scheme**
  - Notification of intent to conduct a clinical trial to TGA
  - HREC responsible for scientific validity, safety efficacy and ethical acceptability and approval
  - TGA does not review any data relating to the clinical trial

Approvals

- Once the Sponsor, PI, chairman of the HREC, and the person responsible from the Approving Authority have signed the CTN form it is submitted to the TGA along with the appropriate notification fee
- **CTN trials cannot commence until the trial has been notified to the TGA and the appropriate notification fee paid**

Approvals

- **Clinical Trial Exemption (CTX) Scheme**
  - Sponsor submits an application for evaluation and comment
  - TGA reviews summary of pre and clinical data, overseas status, proposed usage guidelines
  - **Cannot commence the trial until written advice received from the TGA AND approval obtained from an ethics committee and institution at which the trial will be conducted.**

Study Protocol

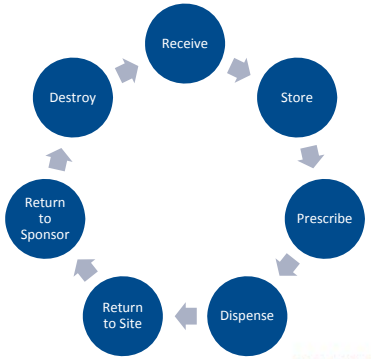
- Research approvals consider the protocol
- Sets out the specific procedures for conduct and data collection
- Must be followed to ensure consistency
- Document acceptance to follow protocol – signature page required

Feasibility

- Before agreeing to conduct the study, PI must consider;
  - Requirements of the Protocol
  - Participant population
  - Staff to conduct the study
  - Specific equipment
  - Support from other departments, e.g. pharmacy and imaging

Investigational Product

- PI must ensure appropriately trained person takes responsibility for IMP, usually Pharmacists
- **Both** responsible for ensuring systems are established, documented and people trained
- Covers all stages from receipt of IMP to return to Sponsor or destruction



Investigational Product

- Must ensure compliance with the protocol
- Records must be kept at each stage
- What been done, by whom, when
- Quantities
- Batch or Serial Numbers
- Expiration dates
- Unique codes relating to participant

And also……

- Establish Systems and processes
  - Documented, SOPs, compliance, trained
- Calibration of Equipment
- Randomisation
- Blinding
  - Everyone must know how to unblind in an emergency

Essential Documents

- "Essential documents are those documents which individually or collectively permit the evaluation of the conduct of a trial and quality of the data produced." **ICH GCP 8.1**

- Demonstrate the compliance of the Investigator, Sponsor and Monitor with the standards of Good Clinical Practice and all applicable regulatory requirements.

Essential Documents

- **ICH GCP 8.2 – 8.4**

Table of Essential Documents that are required before, during and after completion of the study

Essential Documents

- So how do we organise this mass of documents?

Site File

- The Sponsor and Principal Investigator **must** keep a **Trial Master File** (TMF) for **each study**
  - ICH GCP refers to a TMF for all studies, not only clinical trials
  - PI copy sometimes known as a Site File
  - TMF normally held at CI office or study coordinating centre

Site File

- A collection of documents **which 'tell the story' of the study which has a beginning, middle and end**
- Not a single file, but a **filing system**
- Contains **every** piece of information you receive at site relating to a specific study (including emails/letters/conversations between Investigators and team)

Examples of Essential Documents

- An easy way to remember all essential documents is to put them into two simple categories
  - **Non-participant specific**
  - **Participant Specific**

Non-participant Specific

- Protocol including amendments
- Letters of invitation to send to potential participants
- Participant Information Sheet
- Consent/Assent Form (unused)
- Regulatory applications and responses/approvals
- Delegation log/CVs/GCP certificates
- Correspondence/newsletters
- Safety reports

Participant Specific

- Case Report Form (data collection tool)
- Signed consent forms/assent forms
- Data queries
- Patient notes
- Search lists identifying potentially eligible participants

Essential Documents should be

- Filed in a designated file(s)
- Kept in a designated place
- Maintained by a designated person(s)
- Archived for recommended time

Storage of Essential Documents

- Safe secure storage is vital
- The physical integrity of the Site File must be maintained
- The Site File must have protection from the environment (damp, mould, fire, pests etc.)
- Space to store essential documents is often underestimated

Storage of Essential Documents

- Although the Sponsor will hold almost identical TMF, only the local Site File (Principal Investigator's) will contain the subject identification list.

No participant identifiable data should be provided to the Sponsor
(unless agreed by Research Ethics Committee)

Delegation of Duties Logs

Probably the most important 'essential' document as it is the only one which identifies the individuals to whom the PI has delegated study specific tasks.

Delegation of Duties Logs

- The PI must review and sign the Delegation of Duties Log for each study and
  - Must be satisfied as to the **competence** of the individuals to whom they are delegating
  - Ensure that all individuals are **informed** of their involvement and the duties required of them
- CVs, GCP certificates (and job descriptions) must be available for everyone on the Delegation of Duties Log

Remember

If it is not documented it did not happen!

Informed Consent

Informed Consent

"A **process** by which a subject **voluntarily** confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is **documented** by means of a written signed and dated Informed Consent Forms."

ICH GCP 1.28

Informed Consent Children and Young People

- The Statement Chapter 4.2 Children and Young People addresses principles that apply specifically in research
- WA Health Research Governance Procedures section 3.6.1 Recruitment of Minor (aged less than 18 years of age) in Research

Consent Process

Process is not a single act

- Introduce study idea, give verbal/written information to the participant
  - Participant Information Sheets, consent and assent forms as approved by the HREC
  - Refer to 4.8.10 of Note for Guidance on Good Clinical Practice for comprehensive breakdown of what to discuss regarding consent (a-t)

Consent Process

- Time to think
- Ask/answer questions
- Agreement to proceed from parent/guardian (and child)
- Initial each box
- Sign and date Consent form
  - Parent/guardian must sign and date the forms themselves, the date should not be added by any member of the team
- Completed assent forms, where appropriate
- Re-confirm willingness to continue at **every visit**

Case Report Form, Source Data and Data Entry

Case Report Form, Source Data and Data Entry

Case Report Form (CRF)

"A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial"

ICH GCP 1.11

Case Report Form, Source Data and Data Entry

Source Data/Documents

"Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial)"

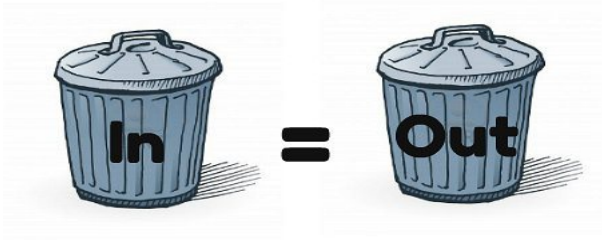
ICH GCP 1.52

Case Report Form, Source Data and Data Entry

- The investigator/institution should maintain adequate and accurate **source documents** and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be **attributable, legible, contemporaneous, original, accurate, and complete**. **Changes** to source data should be **traceable**, should **not obscure** the **original entry**, and should be explained if necessary (e.g., *via* an audit trail).

ICH GCP 4.9.0

Case Report Form, Source Data and Data Entry



Case Report Form, Source Data and Data Entry

Responsibilities

- Investigator responsibilities refer to section 4.9 of ICH GCP
- Sponsor responsibilities refer to section 5.5 of ICH GCP

Case Report Form, Source Data and Data Entry

Source Data Verification =SDV

- Monitors verify the data collected in the CRF is correct and transcribed accurately from the source
- **Every** piece of information entered into a CRF or eCRF must be documented in the source data
- **Every** piece of information should be recorded twice
  - Source is the original entry
  - Transcribed onto the Sponsor's data collection tool

Golden rules of data entry

• All fields must be complete	• Put a single line through any mistake
• Not Known (NK) only when all avenues are exhausted	• Make the amendment clear
• If Not Done (ND) why?	• Never occlude the original entry
• It is not enough simply to write NK or ND – need to give an explanation why in the Site File/CRF	• Initial and date any alteration even if completing blank fields retrospectively
• Make sure your writing is legible	• **Never, ever use White-out or POST-IT notes**
• Always write in black	

Protocol Deviations

- **Minor** or Administrative departures from protocol
- **Do not affect** the scientific soundness of the research or the rights, safety, or welfare of research participants
- Examples:
  - Follow-up visits outside of protocolled time frame due to participants schedule
  - Blood samples obtained close to but not precisely at the time points specified in the protocol
- Only to be reported if they occur to a significant proportion of the participants

Protocol Violations

- **Major** departures from the approved protocol and/or regulatory guidelines
- **Compromise** the ethical acceptability of the project and potentially affect the scientific soundness of the research and/or the rights, safety or welfare of research participants.
- Examples:
  - Failure to obtain participant consent
  - Participant inclusion/exclusion violations
  - Compromises to data integrity
- Must be reported to HREC where the event occurred

Ensuring the Quality of the Data

Monitoring

- Ongoing process
- Oversee progress of the trial
- Ensure trial is conducted, recorded and reported properly
- To the protocol, Sponsor's SOPs, GCP and applicable regulatory requirements

Ensuring the Quality of the Data

Audit

- Asses at any given moment
- Systematic and independent
- Ensure trial is conducted, recorded and reported properly
- To the protocol, Sponsor's SOPs, GCP and applicable regulatory requirements

Ensuring the Quality of the Data

Inspection

- By Regulatory authority – TGA
- Official review of documents, facilities, records and any other resources related to the trial
- Ensure correct conduct and compliant to appropriate regulatory requirements

What is monitored?

Everything that has been covered today

Regulatory Approvals
CTX CTN HREC | Institute

Essential Documents
Site File | Delegation of Duties | CRF/Source | Pharmacovigilance

Recruitment Process
Eligibility Criteria | Consent

Training and Education
Everyone involved in the research process

What is monitored?

Everything that has been covered today

Monitoring Plan
A document that describes the strategy, methods, responsibilities, and requirements for monitoring the trial

Safety Reporting

Safety Reporting

What is safety reporting?

- In all types of study, data are gathered in order to monitor the effects of the study and any interventions on the participants to ensure their safety
- Safety reporting is important in order to protect participant during the study and once a practice or treatment becomes standard care

Safety Reporting

- Safety reports are analysed along with the other study data collected to ensure that the benefits of any potential side effects with every treatment or practice but the likelihood of them occurring and the potential risks associated with them are carefully considered before being approved as standard care.

How do we assess safety?

- By asking the participant a series of questions at every visit
- By collecting base line information on the health status of trial participants
- Being aware of concomitant medications
- Asking about health and concomitant medications at every visit
- By recording all untoward medical occurrences as required in the protocol
- By collecting accurate data as appropriate
- By reporting within specified timelines

Adverse Event/Reaction

An **Adverse Event (AE)** is any untoward medical occurrence – there does not need to be a causal relationship between the occurrence and the study or any treatments administered

An **Adverse Reaction (AR):** an untoward or unintended response to a new medicinal product or its new usages

- Record the details in the source data and check the protocol for reporting requirements

Serious Adverse Event

Serious Adverse Event (SAE) is any adverse event that:

- Results in death
- Is life threatening
- Requires hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability or incapacity
- Consists of a congenital anomaly or birth defect

Check the definition of Serious in each Protocol

- Other events are sometimes added by Sponsors as appropriate to each study

Serious Adverse Reaction

Causality is the difference between an **Event** and a **Related** event or **Reaction**

Definition of Serious is always the same i.e.:

- Results in death
- Is life threatening
- Requires hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability or incapacity
- Consists of a congenital anomaly or birth defect

Was the event expected?

- There are potential adverse effects to any procedure or medicine. The Sponsor will provide you with details of **known adverse effects** associated with any of the research procedures and interventions.
  - Clinical and non-clinical data relating to the investigation product will also be provided in the **Investigator Brochure**
- Any event which is **not consistent** with the known adverse effects is **Unexpected**

SUSARs

- The most closely monitored events are those where there is **a combination** of being
  - **Serious, Related/Reaction** and **Unexpected**
- In a Clinical Trial of an Investigation Product these are known as SUSARs:

Suspected Unexpected Serious Adverse Reactions

A Serious Adverse Reaction which is unexpected, the nature or severity of which is not consistent with the applicable product information.

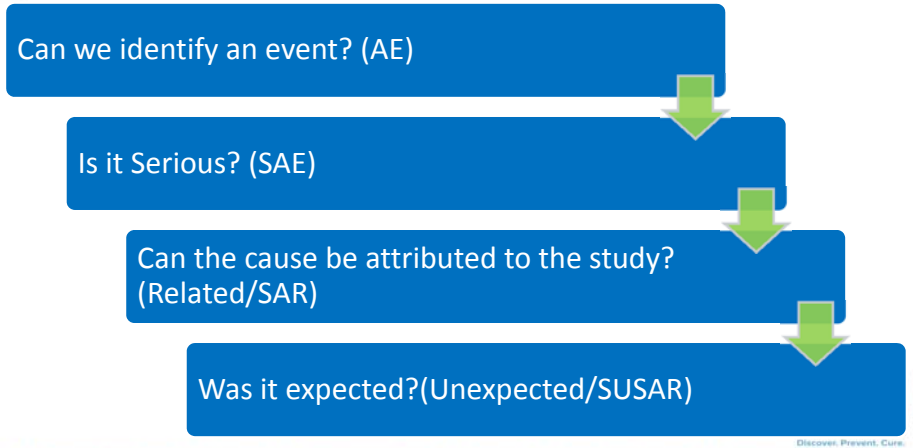
NHMRC Guidance

- NHMRC Guidance – Safety Monitoring and reporting in clinical trials involving therapeutic goods
- Addresses the collection, verification and reporting of AEs and ARs of IMPs and IMDs under CTX or CTN schemes
- Includes a number of **new definitions**

NHMRC Guidance

- Significant Safety Issue (SSI)
  - A safety issue that could adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial
- Urgent Safety Measure (USM)
  - A measure required to be taken in order to eliminate hazard to a participant's health or safety

Adverse Event Decision Tree



Reporting: Investigator/Researcher

- Investigator/researcher
  - Must capture and report AEs, including SAEs, which occur at their site to the Sponsor in accordance with the study protocol
  - Must report all SAEs to the **Sponsor** and **HREC** immediately (within 24 hours) in accordance with the protocol and GCP guidelines as adopted by the TGA

Reporting: Sponsor

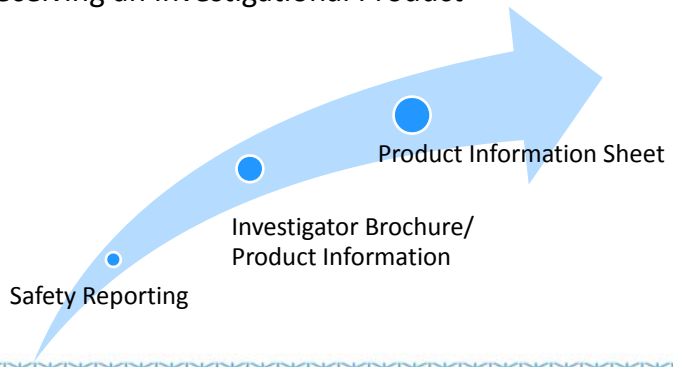
Sponsor

All adverse reactions that are both serious and unexpected are subject to expedited reporting to the **TGA**

- Fatal or Life-Threatening Unexpected AR
  - As soon as possible but no later than 7 calendar days after first knowledge by the sponsor
  - Follow-up, complete report as possible within 8 additional calendar days
- For all other serious and unexpected ARs
  - Full report no later than 15 calendar days of first knowledge by the sponsor

Pharmacovigilance

- The process of evaluating the safety of trial subjects receiving an Investigational Product



Investigator Brochure

- **Brief description** of the drug substance and the formulation including the structural formula
- **Summary** of pharmacological and toxicological effects of the drug in animals and, if known, in humans
- Summary of information relating to **safety and effectiveness** in humans obtained from prior clinical trials
- A description of **possible risks and side effects** to be anticipated on the basis of prior experiences with the drug under investigation or with related drugs, and of precautions or special monitoring to be done as part of the investigational use of the drug.

Investigator Brochure (cont.)

- Sponsor will update the Investigator Brochure (IB) every 12 months or sooner if any significant new information becomes available
- Principal Investigator must provide a record (usually a receipt), signed and dated upon receipt of the IB.
- If a drug is licensed and used within licensing indications, a Product Information Sheet may be provided by a Sponsor as an alternative to the IB.

Session Wrap-up

Covered:

- Standards and why we have them
- Study Set-up – responsibilities, approvals and essential documents
- Informed Consent
- Case Report Form, Source Data and Data Entry
- Safety Reporting

Questions?

Upcoming Research Skills Seminars:

8 Mar 12:30-13:30 Knowledge Translation
Dr Fenella Gull

22 Mar 12:30-13:30 Research Governance
A/Prof Sunalene Devadason

**Full 2019 Research Skills Seminar schedule in back of handouts*

Please give us your feedback!
A survey is included in the back of your handout or complete it online via:
www.surveymonkey.com/r/introgcp19

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Child and Adolescent Health Service

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2 GOOD CLINICAL PRACTICE – ADDITIONAL NOTES AND RESOURCES

2.1 GOOD CLINCAL PRACTICE – 13 PRINCIPLES

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

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

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

6. 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.

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

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

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

    This principle applies to all records referenced in this guideline, irrespective of the type of media used.

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

    Aspects of the trial that are essential to ensure human subject protection and reliability of trial results should be the focus of such systems.

2.2 GENERAL WEBSITE LINKS

- NHMRC: http://www.nhmrc.gov.au/
- Therapeutic Goods Administration (TGA): http://www.tga.gov.au/
- Department of Health WA: http://www.health.wa.gov.au/home/
- Australian Clinical Trials: https://australianclinicaltrials.com/clinical-trials/
- Medicines Australia: http://medicinesaustralia.com.au/
- Australia New Zealand Clinical Trials Registry: http://www.anzctr.org.au/Default.aspx
- Australian Clinical Trials Alliance: http://www.clinicaltrialsalliance.org.au/

2.3 GUIDANCE DOCUMENT LINKS

WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects (October 2013 version).
https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

National Statement on Ethical Conduct in Human Research (Updated 2018)
https://nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018

Australian Code for the Responsible Conduct of Research,2018 (the 2018 Code)
https://nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018

Integrated Addendum to ICH E6(R1): Guidance for Good Clinical Practice E6(R2)
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4_2016_1109.pdf

Clinical investigation of medical devices for human subjects -- Good clinical practice ISO 14155:2011
http://www.iso.org/iso/catalogue_detail?csnumber=45557

The Australian Clinical Trial Handbook (October 2018)
https://www.tga.gov.au/publication/australian-clinical-trial-handbook

WA Health Research Policies & Procedures
http://www.health.wa.gov.au/CircularsNew/circular.cfm?Circ_ID=12923

Safety Monitoring and reporting in clinical trials involving therapeutic goods
https://nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods

Guidance on clinical safety data management: definitions and standards for expedient reporting
http://www.tga.gov.au/industry/clinical-trials-note-ich37795.htm#.U31zpE0U-Uk

Values and Ethics - Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health Research
https://nhmrc.gov.au/about-us/publications/values-and-ethics-guidelines-ethical-conduct-aboriginal-and-torres-strait-islander-health-research

Human Research Ethics Application (HREA)

https://hrea.gov.au/

Health Research Privacy Framework
http://www.nhmrc.gov.au/health-ethics/human-research-ethics-committees-hrecs/health-research-privacy-framework

Privacy Act
http://www.oaic.gov.au/privacy/applying-privacy-law/app-guidelines/

Ethical Considerations in Quality Assurance and Evaluation Activities (NH MRC)
https://www.nhmrc.gov.au/guidelines-publications/e111

Guide to good manufacturing practice for medicinal products annexes
http://www.tga.gov.au/sites/default/files/manuf-pics-gmp-medicines-annexes.pdf

2.4 FORMS

CTN Form
https://www.tga.gov.au/form/ctn-scheme-forms

CTX Form
https://www.tga.gov.au/form/ctx-scheme-forms

Ethics Application Forms
https://rgs.health.wa.gov.au/Pages/Home.aspx

Amendments and monitoring forms
https://rgs.health.wa.gov.au/Pages/Home.aspx

2.5 TEMPLATES

Trial Master File
http://www.diahome.org/en/News-and-Publications/Publications-and-Research/EDM-Corner.aspx
http://tmfrefmodel.com/2015/06/16/version-3-released/

Protocol
https://rgs.health.wa.gov.au/pages/Document-Templates.aspx
http://www.spirit-statement.org/

Participant Information and Consent Forms
https://rgs.health.wa.gov.au/pages/Document-Templates.aspx

Contracts and Agreements
http://medicinesaustralia.com.au/issues-information/clinical-trials/clinical-trials-research-agreements/
http://www.health.wa.gov.au/researchdevelopment/home/research_gov.cfm#clinical

2.6 WA Health Guidance and Principle Origins

- World Medical Association "Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects" 2008;
- National Health and Medical Research Council, Australian Research Council and Australian Vice-Chancellors' Committee "National Statement on Ethical Conduct in Human Research" 2007 – Updated 2018 (National Statement);
- National Health and Medical Research Council, Australian Research Council and Universities Australia "Australian Code for the Responsible Conduct of Research" 2018 (The Code);
- National Health and Medical Research Council "Values and Ethics: Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health Research" 2003*;*
- Therapeutics Goods Administration "The Australian Clinical Trials Handbook" 2018, and "Integrated Addendum to ICH E6(R1): Guidance for Good Clinical Practice E6(R2)" 2016
- Relevant Commonwealth or State legislation and guidelines including the Department of Health "Occupational Safety and Health Policy" 2005.

2.7 Sponsor Responsibilities

- Ensuring **QA and QC systems** are in place to ensure trials are conducted, data is gathered, and subsequently reported, in **compliance with GCP**, the trial **protocol**, and any **TGA** requirements.
- Ensuring **medical expertise** is on hand for trial-related medical queries or patient care
- **Trial design** and appropriate **analysis**
- **Data** Handling, record keeping, and **overall trial management**
- **Selection** of appropriate **investigator(s)** and **institution(s)**
- Definitive, unambiguous allocation of trial related duties and responsibilities
- Securing agreement in writing from all involved parties
- Provision of **appropriate insurance** and **indemnity** for the trial and trial-related staff, as well as measures for **subject compensation** for trial-related injury
- Ensuring the confirmation of **endorsement** from the relevant **HREC(s)** and notifications of the **approval** etc. to the **TGA**
- Ensuring appropriate **manufacture, packaging, labelling/coding** and distribution to trial sites of all investigational medicinal products
- Ongoing **safety evaluation** and Suspected Unexpected Serious Adverse Reaction (**SUSAR**)/Unanticipated Serious Adverse Device Effect (**USADE**) reporting
- Compliance with **Monitoring/Audit/Inspection** requirements
- Notification of any premature termination of the trial in question
- Completion of **Clinical Study Report**

http://www.tga.gov.au/industry/clinical-trials-note-ich13595.htm

2.8 Principal Investigator Responsibilities

- Ensuring that informed consent is properly obtained from research participants
- Overall conduct, management, monitoring and reporting of research at a **site,** including annual progress reports, final report to RGO
- Submits the project for site authorisation (RGO approval)
- Delegation and **supervision** of duties to study team
- Sign-off to say staff are competent to work on the research
- Oversight and management of Investigational Medicinal Product
- Safety reporting signature on notifications from Sponsor if required

2.9 Protocol Deviations/Serious Breaches

https://nhmrc.gov.au/sites/default/files/images/reporting-of-serious-breaches-of-good-clinical-practice.pdf

2.9.1 Protocol Deviations

Must be reported to the trial sponsor

- **Minor** or **Administrative** departures from protocol
- **Do not affect** the scientific soundness of the research or the rights, safety, or welfare of research participants
- Examples:
    - Follow-up visits outside of protocolled time frame due to participants schedule
    - Blood samples obtained close to but not precisely at the time points specified in the protocol

2.9.2 Serious Breaches

Must be reported to the reviewing HREC. Must notify the site's principal investigator where the serious breach occurred.

- **Major** departures from the approved protocol and/or regulatory guidelines
- **Breach** that is likely to affect to a **significant degree**
    a) The safety or rights of a research participant, or
    b) The reliability and robustness of the data generated in the research project
- Examples:
    - A participant was dosed with IMP from the incorrect treatment arm. In addition, some months later, the participants in an entire cohort were incorrectly dosed with IMP three times daily when they should have been dosed once daily.
    - Participant safety was compromised because repeat ECGs were not performed, as required by the protocol.

2.10 Protocol Deviations/Violations

http://www.health.wa.gov.au/researchdevelopment/home/hrec.cfm#monitoring

2.10.1 Protocol Deviations

- **Minor** or Administrative departures from protocol
- **Do not affect** the scientific soundness of the research or the rights, safety, or welfare of research participants
- Examples:
    - Follow-up visits outside of protocolled time frame due to participants schedule
    - Blood samples obtained close to but not precisely at the time points specified in the protocol
- Only to be reported if they occur to a significant proportion of the participants

2.10.2 Protocol Violations

- **Major** departures from the approved protocol and/or regulatory guidelines
- **Compromise** the ethical acceptability of the project and potentially affect the scientific soundness of the research and/or the rights, safety or welfare of research participants.
- Examples:
    - Failure to obtain participant consent
    - Participant inclusion/exclusion violations
    - Compromises to data integrity
- Must be reported to HREC where the event occurred

2.11 Ensuring the Quality of the Data

2.11.1 Monitoring

- Ongoing process
- Oversee progress of the trial
- Ensure trial is conducted, recorded and reported properly
- To the protocol, Sponsor's SOPs, GCP and applicable regulatory requirements

2.11.2 Auditing

- Asses at any given moment
- Systematic and independent
- Ensure trial is conducted, recorded and reported properly
- To the protocol, Sponsor's SOPs, GCP and applicable regulatory requirements

2.11.3 Inspection

- By Regulatory authority – TGA
- Official review of documents, facilities, records and any other resources related to the trial
- Ensure correct conduct and compliant to appropriate regulatory requirements

2.12 Investigator Brochure

- **Brief description** of the drug substance and the formulation including the structural formula
- **Summary** of pharmacological and toxicological effects of the drug in animals and, if known, in humans
- Summary of information relating to **safety and effectiveness** in humans obtained from prior clinical trials
- A description of **possible risks and side effects** to be anticipated on the basis of prior experiences with the drug under investigation or with related drugs, and of precautions or special monitoring to be done as part of the investigational use of the drug.
- Sponsor will update the Investigator Brochure (IB) every 12 months or sooner if any significant new information becomes available
- Principal Investigator must provide a record (usually a receipt), signed and dated upon receipt of the IB.
- If a drug is licensed and used within licensing indications, a Product Information Sheet may be provided by a Sponsor as an alternative to the IB.

Recommended GCP Courses

- Research Education & Trainnig Program (RETP) - WA Health Translation Network (WAHTN)
  https://www.retp.org/portfolio-item/good-clinical-practice-v-3/
  (Transcelerate accreditated training)

- Global Health Trials
  https://globalhealthtrials.tghn.org/elearning/

- ARCS Australia
  https://www.arcs.com.au/events/category/online-learning

Government of Western Australia
Child and Adolescent Health Service

Research Skills Seminar Series 2019
Research Education Program

Knowledge Translation

Planning for impact and implementation of research outcomes

Friday, 8 March 12:30 – 1:30PM

Knowledge Translation is a vital consideration for all research and having a plan from the outset is increasingly important for research projects.

KT refers to how we exchange, disseminate and apply our research results to improve the community's health. This seminar outlines what it is, why it is so important, and how to get started. It will provide an overview of KT considerations for research project design, implementation, dissemination, and measuring impact.

Fenella Gill

Associate Professor Acute Paediatric Nursing at Perth Children's Hospital and Curtin University.

Dr Gill is a 2019 WAHTN Early Career Fellow in Research Translation. She was awarded a NHMRC (TRIP) Translating Research into Practice Fellowship in 2015 which involved training in knowledge translation and implementation science methodologies and undertaking knowledge translation research. She leads a program of research focusing on paediatric patient and family experience and patient safety in hospitals.

Perth Children's Hospital
PCH Auditorium, Level 5
(Pink or Yellow lifts)
15 Hospital Ave, Nedlands

Register Online

ResearchEducationProgram
.eventbrite.com

Further information:
ResearchEducationProgram@health.wa.gov.au

ResearchEducationProgram.org

***Hosted VC Sites Include:**

Bunbury Hospital
Child and Adolescent Community Health
DonateLife WA
Fiona Stanley Hospital
Joondalup Health Campus
Lions Eye Institute
Midland Community Health Centre
Royal Perth Hospital

For more locations, visit:
ResearchEducationProgram.org

***Online VC via Scopia App**

The Research Skills Seminar Series is part of the Research Education Program, Department of Child Health Research, Child and Adolescent Health Service, WA Department of Health. Seminars are hosted by WA Department of Health.

Government of Western Australia
Child and Adolescent Health Service

Research Education Program

Research Skills Seminar Series 2019

All sessions held Fridays 12.30-1.30pm

Perth Children's Hospital Auditorium

	Date	Topic *(abbreviated)*	Presenter
1	Feb 15	Research Fundamentals: Question and Protocol Development	Sue Skull
2	Feb 22	Introduction to Good Clinical Practice	Natalie Barber
3	Mar 8	Knowledge Translation	Fenella Gill
4	Mar 22	Research Governance	Sunalene Devadason
5	Apr 5	Practical Ethical Considerations	Nik Zeps
6	Apr 12	Survey Design and Techniques	Sue Skull
7	May 3	Consumer and Community Involvement in Research	Anne McKenzie AM
8	May 10	Scientific Writing	Sue Skull
9	May 24	Getting the most out of Research Supervision – Tips for supervisors and students	Jonathan Carapetis AM
10	Jun 7	Introductory Biostatistics – Understanding and reporting research results including P-values and Confidence intervals	Julie Marsh
11	Jun 21	Data Collection and Management	Sue Skull
12	Jun 28	Media and Communications – How to refine and pitch your message for maximum impact	Liz Chester
13	Aug 2	Involving Aboriginal People in Research	Michael Wright / Sue Skull
14	Aug 16	Sample Size Calculations – Using PS Software	Julie Marsh
15	Aug 30	Oral Presentation of Research Methods	Sue Skull
16	Sep 6	Conducting Systematic Reviews	Sonya Girdler
17	Sep 20	Rapid Critical Appraisal of Scientific Literature	Sue Skull
18	Oct 18	Statistical Tips for Interpreting Scientific Claims	Julie Marsh
19	Nov 1	Grant Applications and Finding Funding	Sue Skull
20	Nov 8	Qualitative Research Methods	Dianne Wynaden
21	Nov 22	Ethics Processes within WA Health Research	Sue Skull

*Topics may occasionally need to be moved/changed; email notice will be provided.
*All seminars and corresponding handouts are regularly revised and updated.
*Attendance Certificates are available upon request.

Contact: ResearchEducationProgram@health.wa.gov.au | http://ResearchEducationProgram.org/

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RESEARCH SKILLS SEMINAR SERIES 2019

SEMINAR FEEDBACK FORM

SEMINAR: Introduction to Good Clinical Practice

DATE: 22 February 2019

LECTURERS NAME: Natalie Barber

INSTRUCTIONS:
- *Please rate the following statements*
- *Use a pen to mark circles*
- *One response per item*
- *Please return to coordinator*

1. How did you attend the seminar?

O Live Seminar at Perth Children's Hospital

O Hosted Site Video-Conference

Bunbury, CACH, DonateLife, Fiona Stanley Hospital, JHC, Lions Eye, Midland, OPH, Royal Perth Hospital

O Online via Scopia

	Not Applicable	Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
2. The aim and learning objectives were clear. (I felt well informed about scope and content)	O	O	O	O	O	O
3. The learning materials were helpful. (handouts, slides, lecture notes supported learning)	O	O	O	O	O	O
4. The session content was well structured.	O	O	O	O	O	O
5. The material was presented in a way which maintained my interest.	O	O	O	O	O	O
6. The material challenged me to think more critically about the subject. (covered at the right level)	O	O	O	O	O	O
7. The lecturer/s communicated clearly. (lecture presentation, clear instructions)	O	O	O	O	O	O
8. The material presented extended my knowledge in this area.	O	O	O	O	O	O

9. What were the best aspects?

10. What changes would you suggest?

11. How did you hear about the seminar?
You may select multiple responses

O Email Invitation from Research Education Program

O "Health Happenings" E-News O CAHS Newsletters e.g. "The Headlines"

O Healthpoint Intranet

O Displayed Poster/Flyer

O Other (please specify): _____

e.g. Curtin email, CACH, colleague, supervisor etc.

THANK YOU - your comments will be provided to the presenter and inform other education activities.

The Research Skills Seminar Series is part of the Research Education Program, Dept. of Child Health Research,
Child and Adolescent Health Service, WA Department of Health.
Seminars are hosted by WA Department of Health.