Insights from the TGA Good Clinical Practice (GCP) Inspection Program

Dr Tahli Fenner
Director, Risk Management Section
Pharmacovigilance Branch
Department of Health and Aged Care, TGA

Anastasia Makshakova
Lead GCP inspector, Risk Management Section
Pharmacovigilance Branch Department of Health and Aged Care, TGA

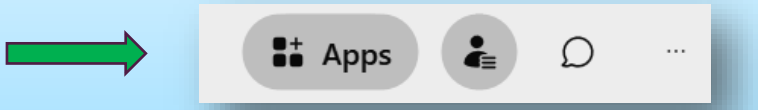
Acknowledgement of Country

I would like to acknowledge the Traditional Owners and Custodians of the lands on which we meet today and pay my respects to Elders past, present and emerging.

I would like to extend that acknowledgement and respect to any Aboriginal and Torres Strait Islander peoples here today.

How to access and use SLIDO

Slido App



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Overview

- Development of the Good Clinical Practice Inspection Program (GCPIP)
- GCPIP Guidance
- Insights from the first year of routine inspections
- Q&A session

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting clinical trials.

Legislation

Therapeutic Goods Act 1989

- Regulates access to unapproved goods for use for experimental purposes in humans

Therapeutic Goods Regulations 1990

- Sets out the conditions that therapeutic goods used in clinical trials must comply with in order for the goods to be exempted from the Act
- Specify inspection powers for trials approved under CTA scheme, and for trials notified to the TGA through the CTN scheme

The Therapeutic Goods (Clinical Trials Inspections) Specification (no.2) 2020

- Enables the Secretary to release the inspection report to approving authority for the trial site and to the Human Research Ethics Committee (HREC) and the approving authority

Development of the GCP Inspection Program (GCPIP)

01 2000: The *CPMP/ICH Note for Guidance on Good Clinical Practice* (CPMP/ICH/135/95) was recognised in Australia

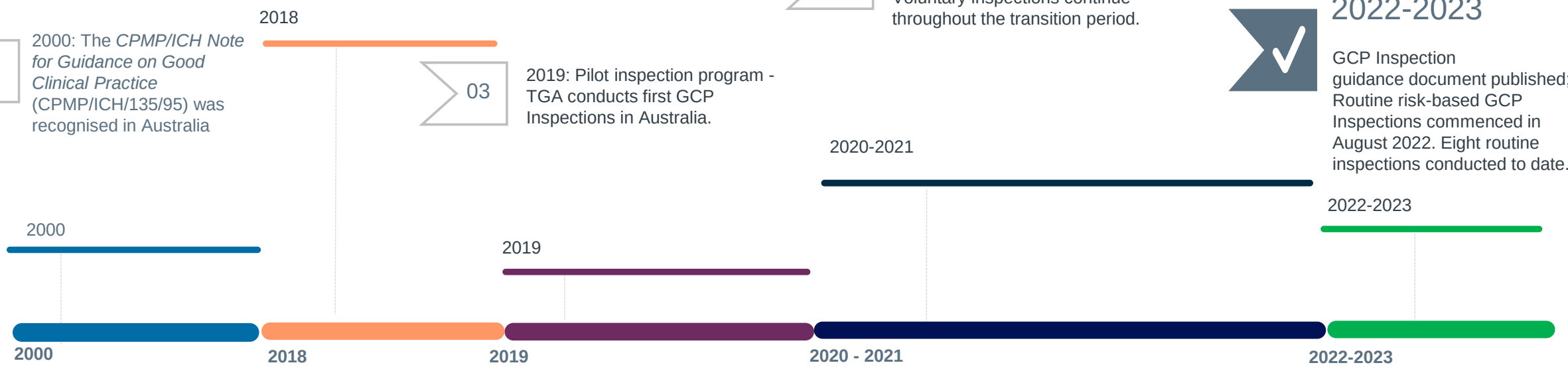
02 2018: The TGA annotated *ICH GCP E6R2* version 09 Nov 2016

03 2019: Pilot inspection program - TGA conducts first GCP Inspections in Australia.

04 2020: Endorsement of a routine risk based GCP Inspection Program. Voluntary inspections continue throughout the transition period.

2022-2023

GCP Inspection guidance document published; Routine risk-based GCP Inspections commenced in August 2022. Eight routine inspections conducted to date.



Note:
ICH stands for International Council for Harmonisation of technical requirements for pharmaceuticals in human use. The Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) is an internationally accepted standard for the designing, conducting, recording and reporting of clinical trials.
ICH GCP E6R2 stands for Integrated Addendum to ICH E6(Revision 1).

GCPIP Guidance

- Objectives and scope
- Inspection process
  - Inspection prioritisation
  - Types of inspection
  - Process of inspection
- Inspection follow-up & close-out
- Compliance and enforcement

Objectives

1. Education

- Provide guidance and work with the site to ensure there are effective systems in place in alignment with Australian legislation and the relevant GCP guideline(s).

2. Compliance check

- Verify clinical trial sites are compliant with the GCP standard and have met their clinical trial responsibilities.

Scope

1. Clinical Trials included in the CTN or CTA scheme

- Risk-based selection of a proportion of eligible clinical trials

2. Types of Investigational Products

- Medicines or biologicals
- Medical devices to be included in the scope

3. Clinical Trial Sites

- Currently limited to inspections of investigational sites for medicines or biologicals

Inspection prioritisation

1. Risk-based approach to scheduling using combination of:

- risk assessment
- internal and external intelligence

2. Risk assessment of clinical trials:

- risk assessment process as described in the *Risk-based Management and Monitoring of Clinical Trials Involving the Therapeutic Goods*, published in 2018 by National Health and Medical Research Council (NHMRC)
- risk criteria are grouped into 2 categories: the risks associated with
    - investigational medicinal product (IMP)
    - trial conduct, design and methods

GCP inspection types

- Onsite (preferred) vs remote inspections
- Routine
- ‘For cause’
- Announced and unannounced
- Reinspection

GCP process (routine announced inspections)

Pre-inspection (≈28 days)

- Notification, planning and preparation
- Agenda and logistics with trial site
- Drafting and finalisation of Inspection plan

Inspection (≈3 days)

- Opening meeting
- Facility tour
- Documents and source data review
- Closing meeting with presentation of closing summary
- Collaboration and education

Post-inspection

- Issue of the inspection report (≤30 days)
- Initial CAPA* (≤30 days from the issue of the inspection report)
- Evaluation of CAPA and close-out of the inspection
- Collaboration and education

Inspection follow-up & close-out

During inspection follow-up stage, the GCP inspector will:

- **Assess** proposed actions
- **Provide comments** if the initial response to CAPA is not acceptable
- **Monitor** completion of CAPA through review of submitted evidence
- **Close out** the inspection

Grading of inspection findings

Critical

Major

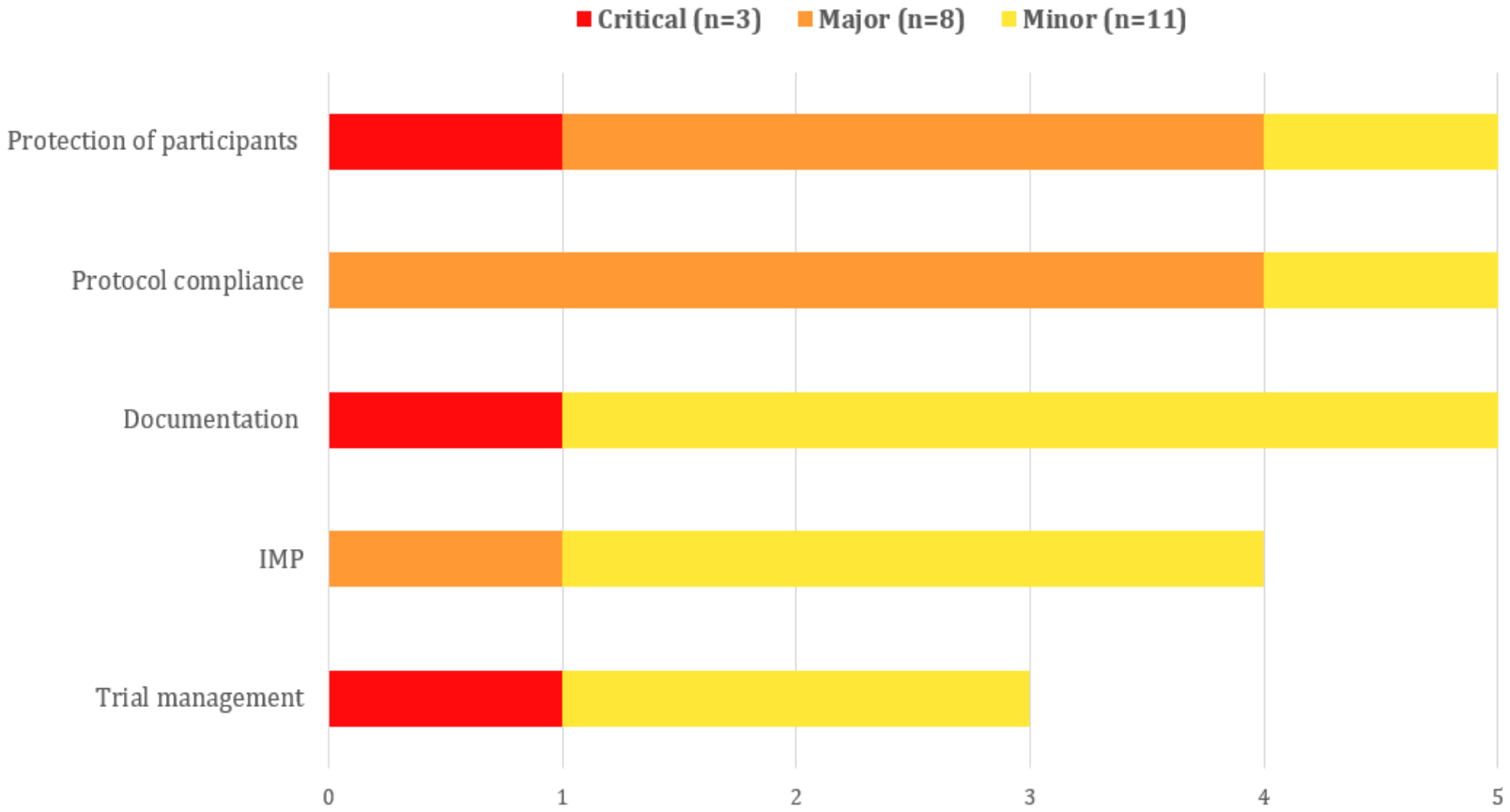
Minor

Inspection insights

Main category	No.	Sub-category
Protection of participants	1.1	Informed consent - Presence of informed consent
	1.2	Informed consent - Informed consent process
	1.3	Informed consent - Informed consent form content
	1.4	HREC/Approving authority - Favourable opinion
	1.5	HREC/Approving authority - Opinion, amendments, notifications
	1.6	HREC/Approving authority - Composition, functions, operations
	1.7	Participant protection - Personal data protection
	1.8	Participant protection - Safeguarding safety and well-being
Protocol compliance	2.1	Eligibility criteria
	2.2	Assessment of efficacy
	2.3	Safety reporting
	2.4	Non-compliance with safety reporting to HREC/RGO/TGA
	2.5	Reporting in case report form/diary as specified in the protocol
	2.6	Other protocol non-compliance not listed above
Documentation	3.1	Essential documents
	3.2	Source documentation
	3.3	Qualification and training
	3.4	Standard operating procedures
	3.5	Organisation and personnel
	3.6	Facilities and equipment
	3.7	Randomization, blinding and codes of study drug
	3.8	Direct access to data
	3.9	Contracts and agreements, including PI oversight of contractors/site-hired third-party vendors
Investigational Medicinal Product	4.1	Investigational Medicinal Product (IMP) accountability at site
	4.2	Supplying, storage, retrieving and destruction
	4.3	Prescription, administration and compliance
Trial management	5.1	Non-compliance with local regulatory requirements (other than safety reporting)
	5.2	Sponsor-investigator responsibilities

GCPIP 2022 metrics (1 July 2022 to 31 December 2022)

Summary of number of deficiencies by main category



Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

tga.gov.au

Critical finding: Informed consent process

Questions to support self-evaluation of compliance at your site

- Do you know which consent form is the currently approved version?
- How promptly is the study team notified that a new consent form has been approved?
- How do you supersede previous versions of the consent form?
- Are you familiar with the content of the consent form, including changes from the previous versions?
- Who has responsibilities in the informed consent process, and are those responsibilities outlined in an internal standard operating procedure (SOP)? Are all relevant staff adequately trained on this process?

Tip for sites

Ensure that the consenting process is documented appropriately and no study-related procedures are completed before the informed consent is signed by all relevant parties.

Example scenario: Informed consent process

Scenario

A modified consent form was electronically signed by the participants but not the investigator(s).

Questions to support self-evaluation of compliance at your site

- What is the consent process for this study?
- Has this process been tested before screening participants?
- Is the system validated for the purpose of e-signing a consent form?
- Is the signed consent exactly the same as the version that was approved by the Human Research Ethics Committee (HREC)?

Tip for sites

Ensure you understand and trial the consenting process. This includes understanding the electronic systems being used in the study, ensuring systems are validated according to the GCP requirements, and ensuring quality assurance measures and tools are in place. Have a contingency plan in case of system malfunction.

Major finding: Protocol compliance

Questions to support self-evaluation of compliance at your site

- What resources will you need to conduct the study and ensure compliance?
- Do protocol timelines facilitate compliance?
- Is there an internal process to verify protocol compliance?
- Who is responsible for protocol compliance? Are these responsibilities outlined in an internal SOP? Have all relevant staff been trained on the delegated study-related procedure(s)?

Tip for sites

Ensure your site processes allow you to comply with the ICH GCP E6(R2) section 4.5.3 '*the investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol*.' Follow the journey of a participant from screening and conduct a mock participant visit to train the delegated site staff. This is particularly useful if the protocol design is complex.

Example scenario: Protocol compliance

Scenario

Day 1 post-dose electrocardiograms (ECGs) were completed out of window for all time points.

Questions to support self-evaluation of compliance at your site

- Was the ECG performed by a fully-trained and delegated staff?
- Why were ECGs completed out of window? Was this preventable? What could be improved for next time?
- Who identified this deviation and when was it done?
- What are the consequences of not collecting the ECG data as per the protocol?

Tip for sites

Proactively assessing protocol compliance will ensure robustness of your processes. Consider if study visit checklists may help you with compliance and ensure that any additional tools used to support compliance is reviewed each time the protocol is updated.

Example scenario: Decentralised trial (DCT) management

Questions to consider on trial management

- What is the role of a primary site and the referring sites?
- Will there be any trial-related activities performed at any of the referring sites?
- How are the duties delegated? Are there any duties unique to DCT? Do you have documented processes?
- Do have the right resources? Do you need additional resources or training to run a DCT?

Tip for sites

There is no single solution that would be suitable for every DCT. A prospective risk management plan and a clear structure of the site(s) roles and responsibilities are required to support appropriate decision making about the trial management.

Example scenario: Investigational Medicinal Product (IMP) management in a DCT

Questions to consider on IMP management in a DCT

- Is there a documented process at your site for IMP delivery, temperature control during transit, return and destruction of the IMP?
- What are the IMP storage conditions? What stability data do you have about the IMP?
- Do you have an Investigator's brochure or an equivalent?
- What IMP delivery frequency would be most appropriate?
- What delivery options do you have and are there any considerations for your planned population?
- Who and how will assess participant's compliance with treatment?

Tip for sites

There is no single solution that would be suitable for IMP management for every DCT. This should be assessed on a case-to-case basis.

SEND YOUR QUESTIONS!

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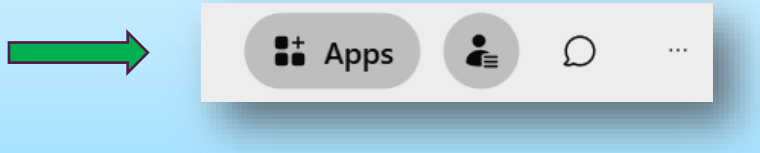

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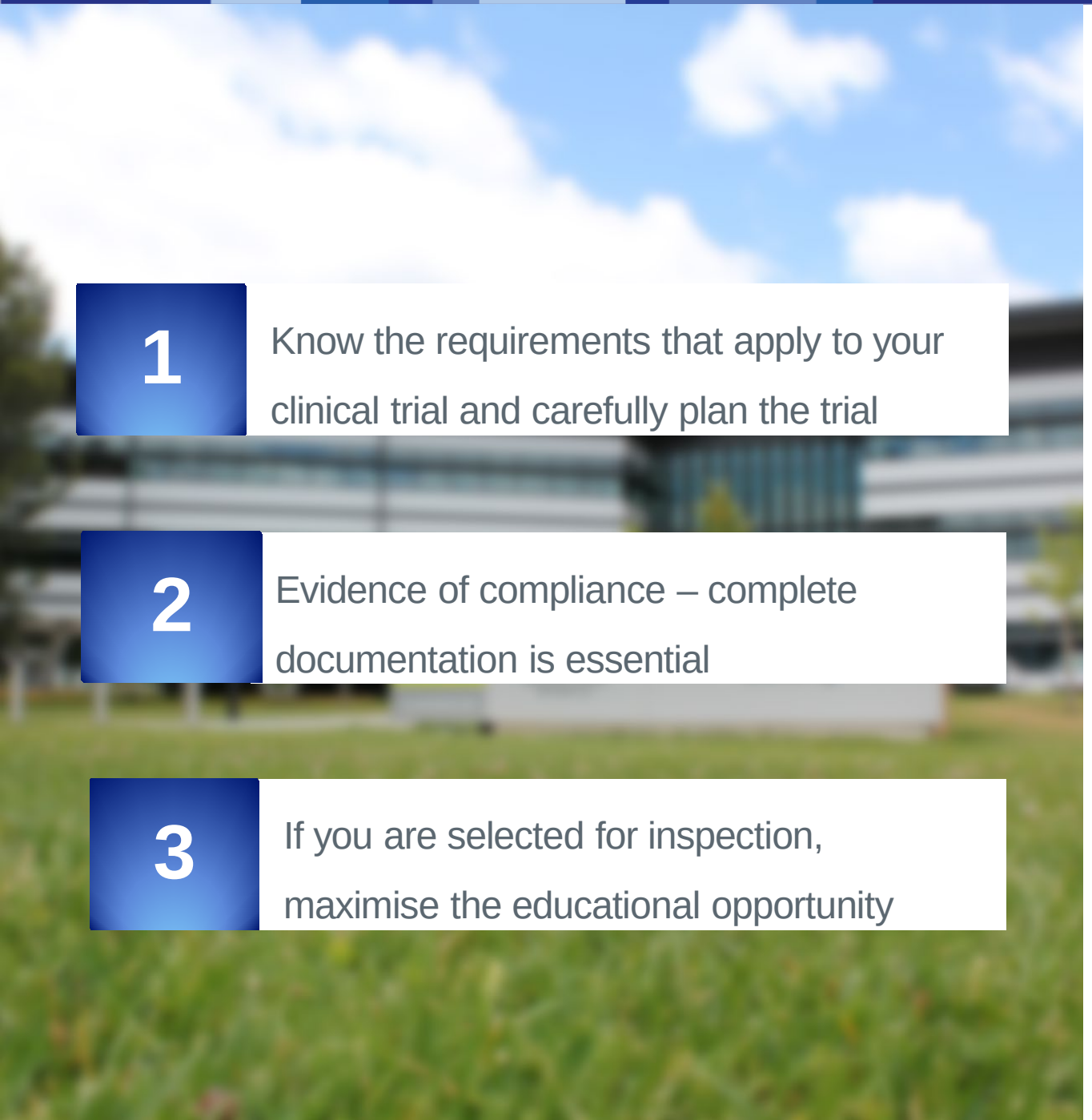

1. Know the requirements that apply to your clinical trial and carefully plan the trial
2. Evidence of compliance – complete documentation is essential
3. If you are selected for inspection, maximise the educational opportunity

Do not wait until an inspection to be inspection-ready.

- Take time to **proactively understand** the TGA requirements and guidance on clinical trial conduct.
- Compliance with GCP should be **integrated** into the site's processes – it is not a standalone function.
- TGA GCP inspectors aim to work with clinical trial sites and provide education to improve compliance and protect clinical trial participants.

GCPIP focus for 2023/24

Education and collaboration

GCPIP metrics report
Webinars
Guidelines and resources
Collaboration with external stakeholders

Compliance

Ongoing GCP inspections
Seeking feedback from inspectees
Expanding the GCPIP scope to include devices

Questions and Answers

Dr Tahli Fenner
Director, Risk Management Section
Pharmacovigilance Branch
Department of Health and Aged Care, TGA

Amanda Chan
GCP and PV inspector, Risk Management Section
Pharmacovigilance Branch
Department of Health and Aged Care, TGA

Anastasia Makshakova
Lead GCP inspector, Risk Management Section
Pharmacovigilance Branch
Department of Health and Aged Care, TGA

Survey - Poll

How did we go?

We'll be back with you in **1 minute.**

1. Please open SLIDO *(located from your APPS icon)*
2. Open the POLL tab
3. Complete short survey

Website and link references

Clinical trials | TGA	https://www.tga.gov.au/clinical-trials
Good Clinical Practice (GCP) inspection program | TGA: guidance and metrics report	https://www.tga.gov.au/resource/good-clinical-practice-gcp-inspection-program
Clinical Trials Toolkit | Australian Clinical Trials	https://www.australianclinicaltrials.gov.au/clinical-trials-toolkit
Consultation on proposed regulatory changes for clinical trials of medical devices I TGA	https://www.tga.gov.au/sites/default/files/2022-08/consultation-proposed-regulatory-changes-clinical-trials-medical-devices.pdf
Learning Modules | Australian Clinical Trials	https://www.australianclinicaltrials.gov.au/_files/elearn/index.html
Resources for Clinical Trials in Australia | Australian Clinical Trials	https://www.australianclinicaltrials.gov.au/resources-clinical-trials-australia
ICH Guideline for Good Clinical Practice | TGA	https://www.tga.gov.au/publication/note-guidance-good-clinical-practice
About health and medical research in Australia | Department of Health and Aged Care	https://www.health.gov.au/topics/health-data-and-medical-research/about-health-and-medical-research
National Standard Operating Procedures for Clinical Trials | Australian Government Department of Health and Aged Care	https://www.health.gov.au/resources/publications/national-standard-operating-procedures-for-clinical-trials
The National Statement 2018 | National Health and Medical Research Council (NHMRC)	https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018
Safety monitoring and reporting in clinical trials involving therapeutic goods | NHMRC	https://www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods

Contact Us

Clinical trials enquiries
clinical.trials@health.gov.au

GCP enquiries
GCP.Inspection@health.gov.au

More information

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TGA YouTube	https://www.youtube.com/channel/UCem9INJbMSOeW1Ry9cNbucw
TGA topics blog	https://www.tga.gov.au/blogs/tga-topics
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Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration