Standard Operating Procedure

6.0 Protocol Development

Version	V2.5
Author/s	V Yenson, G Prael
Approved	M Agar
Effective date	01/04/2022
Review date	01/04/2024

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Introduction / Background

All clinical studies must demonstrate that documentation meets the International Conference on Harmonisation Good Clinical Practice (ICH GCP) guidelines. These guidelines require documentation to show that the study is conducted in an ethical and appropriate manner and all legal and auditing requirements are met. This documentation comprises the study or study protocol and supporting documents. Clinical studies are conducted, monitored, and audited against the protocol.

Objective

This SOP describes what the protocol is, how it is developed, and how and under what circumstances it can be changed. All protocols are developed according to a standard procedure to ensure that the final protocol complies with all regulatory requirements and underpins a sound clinical study.

Scope

This SOP applies to all staff involved in clinical studies conducted by the IMPACCT Trials Coordination Centre (ITCC), including Palliative Care Clinical Studies Collaborative (PaCCSC) or Cancer Symptom Trials (CST), irrespective of individual organisational employment, role, or position.

Ownership and Responsibility

Responsibilities of the relevant Scientific Advisory Committees (SAC)

- To advise on study design development that contributes to a final protocol
- To meet agreed deadlines for review of and comment regarding the study design and protocol summary, including amended study designs
- To endorse the final version of the study design, which includes, but is not limited to, the appropriateness of the intervention, feasibility, eligibility criteria, and assessment and treatment schedule.This is submitted to the relevant SAC as a protocol summary for a pilot/ feasibility/ Phase III study
- To endorse any major amendments to the study design, including the review of updated protocol summary (*refer* to SOP 28 Protocol, section 2)

Responsibilities of the Coordinating Principal Investigator (CPI)

- To provide intellectual input and oversee the development of the protocol for:
  - Funding submissions
  - Study design
  - Risk analysis and mitigation strategy
  - Inclusion/exclusion criteria
  - Analysis
  - Reporting
- To provide a protocol summary to the relevant SAC for final or amendment endorsement of study design (*refer* to SOP 28 Protocol, section 2)
- To provide a completed protocol or protocol amendment for the ITCC to proofread
- To meet agreed deadlines for review and comment of the protocol summary (as reviewed by the relevant SAC) and protocol (as reviewed by ITCC)

- To notify the relevant SAC and ITCC of minor and major protocol amendments and submit the updated protocol summary for major amendments

Responsibilities of the IMPACCT Trials Coordinating Centre (ITCC)

- To provide the most recent protocol summary, including any changes to the study design to the relevant SAC for review and comments
- To coordinate the review and revision of the study design and/ or protocol within designated timeframes
- To ensure that all investigators have the latest version for comment, review, and input
- To ensure that the latest version of the protocol with the endorsed study design is distributed for ethical approval and subsequent study initiation
- To provide input and comment about the operationalisation of the protocol
- To ensure historical documentation of versions is maintained

Responsibilities of the Site Principal Investigator, and/or other designee(s), as documented in the Staff Signatures and Delegation Log (refer SOP 4.2.4 Delegation of Duties)

- To discuss implementation of the protocol at that site with the study team and during protocol training workshops
- To ensure that any site-specific plans required to implement the protocol are developed, recorded, and discussed with the ITCC

Procedure

1. Approval of new studies

- The PaCCSC / CST National Manager calls for new study proposals annually. All PaCCSC / CST members and associate members are eligible to submit new study proposals (*refer* to Templates 31a and 31b)
- A meeting of all SAC members and associate members is held twice a year after the proposal submission date closure at the PaCCSC / CST Annual Research Forum. Submitted proposals are presented at the Forum. Formal evaluation is undertaken by all members present of the relevant SAC (*refer* to Templates 32a and 32b)
- The evaluations are collated and provided to the relevant SAC
- The relevant SAC will deliberate the ideas and provide recommendations on whether to proceed to protocol development (*refer* to SOP 6.0.1 New Study Proposals)
- The relevant SAC also decides whether the proposed study will be undertaken as:
    - Pilot work as part of a program of study development that will inform but not translate into a definitive Phase III study, or
    - Pilot work that will both inform and translate into a full Phase lll study, or
    - A full Phase III study
- Pilot (or feasibility) studies are developed using Template 28 (Section 2) and Guidance 13. Pilot studies are not designed to become full studies in their own right but the results may lead to a future Phase III study
- Full Phase III studies are developed using Template 28. Full Phase III studies include pilot (or feasibility) work as part of the design of the Phase III protocol (Template 28 - Section 2). The initial pilot work of a full Phase III study may inform future funding applications, reviews of process, etc., that may enable recruitment to progress to the full study
- Template 28 contains suggested text in italics, and investigators should carefully consider the suggested text and then modify, remove, or replace as appropriate to their study

2. Sub-Committee (otherwise known as Individual Trial Committee)

- An individual trials committee of contributing experts is formed for protocols/studies approved by the relevant SAC. The committee includes (but is not limited to):
    - CPI
    - Biostatistician
    - Health economist
    - PaCCSC/CST National Manager or ITCC National Project Officer
    - Other individuals with the requisite skills to benefit the protocol development process (people who have attended the Association for Cooperative Operations

Research and Development [ACORD] concept development workshop are considered favourably)

- A full pilot study protocol is completed and submitted for approval to relevant Human Research Ethics Committees (HRECs)
- ITCC assists in the development of a full protocol by providing teleconference facilities and practical implementation advice as required

Note: New study ideas/proposals that fail at any stage of the above process can be re-submitted again in the future for one further attempt at gaining the support needed to take the idea/proposal forward.

Figure 1 details the new protocol development flow for PaCCSC/CST/ITCC studies.

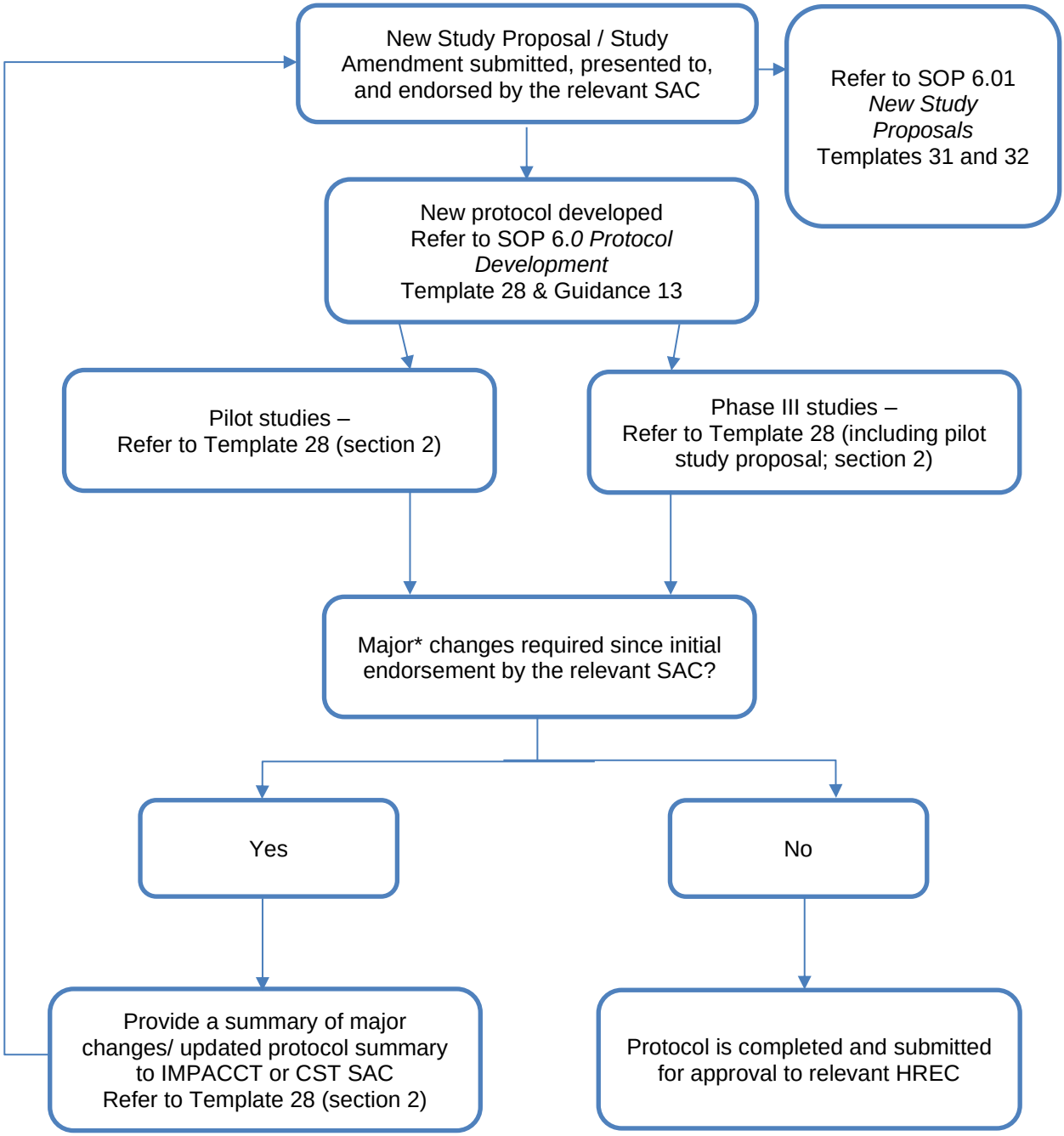

Figure 1. PaCCSC/CST/ITCC new protocol development flow

***Major changes** (can occur at any stage of study development and implementation)**:**

- Changes to study intervention, including dosing changes
- Changes to study design
- Significant safety issues bringing about change (such as eligibility criteria)
- Change in sponsor

Related SOPs

4.2.4 *Delegation of Duties*

6.0.1 *New Study Proposals*

6.12 *Ethics Approval and Reporting*

6.10 *Version Tracking*

8.0 *Essential Documents*

Related documents

Template 28:	*Protocol*
Template 31a and 31b:	*PaCCSC and CST New study Proposal*
Template 32a and 32b:	*PaCCSC and CST New Study Proposal Evaluation*
Guidance 13:	*Pilot/Feasibility Studies*

References

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International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2). November 2016 November 2016 (accessed 06/01/2022)

https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf

ISRCTN International Standard Randomised Controlled Trial Number Register (accessed 27/03/2020) https://www.isrctn.com/

Liu MB, Davis K. Lessons from a horse named Jim. Duke Clinical Research Institute. 2001.

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Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95). Annotated with TGA comments 2000 (accessed 06/01/2022)

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Thabane L, Ma J, Chu R, Cheng J, Ismaila A, Rios LP, Robson R, Thabane M, Giangregorio L, Goldsmith CH. A tutorial on pilot studies: the what, why and how. BMC Medical Research Methodology 2010; 10: 1-10.

Acknowledgments

Trans-Tasman Radiation Oncology Group (TROG), for generous access to the Policy and Procedure Manual – the Red Book.

History			
Version	Date	Author	Reason
1.1	10/01/2006	Contributing authors	New procedure
1.2	25/02/2007	S Whicker	Administrative update
1.3	11/07/2007	B Fazekas	Update prior to MAB review
1.4	13/08/2007	B Fazekas	Changes ratified by MAB
1.5	16/10/2007	B Fazekas	Update after David Currow review
1.6	21/07/2008	B Fazekas	Inclusion of updated proposal template
1.7	2/09/2010	B Fazekas, T Shelby-James	Periodic review
2.0	3/02/2011	B Fazekas	Changes ratified by MAB
2.1	7/03/2014	B Fazekas	Changed to include pilot/feasibility study conduct following meeting of the Scientific Committee
2.2	3/06/2015	C Hope	Periodic review
2.3	28/02/2018	B Fazekas, S Kochovska	Periodic review Publication of the ICH GCP E6 (R2)
2.4	27/03/2020	V Yenson	Periodic review and update for CST
2.5	18/01/2022 2/2/2022	V Yenson G Prael	Periodic review and update for PaCCSC/CST, including change to process for SAC review Periodic review

Approval		
Version	Approval Name	Approval Signature
2.5	Meera Agar