CABRINI RESEARCH GOVERNANCE HANDBOOK

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This document is subject to amendment as required by the
Cabrini Research Governance Committee.
Copies of the most recent version of the document are available:
Online: www.cabrini.com.au

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1. CABRINI RESEARCH GOVERNANCE

The Cabrini Research Governance Office (CRGO) is located at the Patricia Peck Education and Research Precinct:

154 Wattletree Road
Malvern VIC 3144
Telephone: 03 9508 3412
Email: researchgovernance@cabrini.com.au

The Cabrini Research Governance Committee (CRGC) comprises an extensive, multidisciplinary membership including representative from the research executive, research operations, medical administration, legal counsel, oncology trials, pharmacy, quality systems, the CRGO and 2 consumers. CRGO, reporting to the CRGC, reviews and approves research projects that involve human participants to be conducted at Cabrini, to ensure:

- the research affirms Cabrini's mission and values and the teachings of the Catholic Church; and
- ethical standards are maintained to protect the interests of the research participants, the investigators and the institution.

Additionally, any activity that involves sending Cabrini patient data to other institutions in the name of research must be reviewed by the CRGO.

CRGO primarily conducts its business in accordance with:

- the National Statement on Ethical Conduct in Human Research, issued by the National Health and Medical Research Council (NHMRC) in March 2007 (updated 2018) and associated guidelines;
- The Australian Code for the Responsible Conduct of Research – the Cabrini Research Governance Officers are the nominated Research Integrity Advisors, responsible for promoting and upholding the principles of the Code;
- the Cabrini Research Governance Policy;
- *Chapter 6: Research*, Catholic Health Australia's Code of Ethical Standards for Catholic Health and Aged Care Services in Australia (2001);
- the Privacy Act 1988 (Commonwealth);
- the Health Records Act 2001 (Victorian);
- The National Clinical Trials Governance Framework
- The Australian Clinical Trial Handbook (2018)
- Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2)
- other relevant federal and state legislation and regulations.

2. APPLICANTS

2.1 BEFORE YOU GET STARTED

All intending investigators should familiarise themselves with Cabrini's mission statement, Cabrini's research strategy and the relevant legislation and guidelines listed in section 1.

2.2 GOOD CLINICAL PRACTICE (GCP) TRAINING REQUIREMENT

All Cabrini researchers must provide evidence of current Good Clinical Practice (GCP) training that meets the minimum criteria set out by TransCelerate Biopharma Inc. A free GCP refresher course is available to employees of any Monash Partners organisation https://monashpartners.org.au/research-facilitation/good-clinical-practice/, and the Introduction to Good Clinical Practice course is offered via various online providers (refer to Section 7: Other Resources and References).

Additionally, clinical trial researchers are encouraged to register an account with the Victorian Clinical Trials Education Centre https://vctec.myopenlms.net/ which provides a wide array of clinical trial education opportunities beyond GCP at no cost to the user. Opportunities include online courses, educational resources, 'GCP In Action' scenarios, webinars and conferences.

2.3 TYPES OF REVIEW

All projects must be approved before commencement. CRGO is unable to review projects retrospectively.

There are three types of review:

2.3.1 Full

Projects deemed to have greater than low-risk, as defined in Chapter 2.1 of the National Statement, must be approved by an NHMRC certified Human Research Ethics Committee (HREC) and will require full HREC review. Cabrini recommends using Monash Health or Alfred Health to obtain HREC approval.

2.3.2 Low or negligible risk

Expedited approval processes apply to quality assurance (QA) and low or negligible risk projects. CRGO review of these projects is commensurate with the level of risk. Final assessment of risks (see Chapter 2.1 of the National Statement) is the domain of the CRGO (not the researcher).

Refer to - *Appendix A 'Processes for Review of Human Research Applications,'* and *Appendix B 'Level of review flow chart'.*

To determine if your project is QA, complete a Level of Risk Checklist (Attachment 4). If QA review applies, send this checklist, a project protocol and any project tools and patient information to the CRGO.

If you contemplate any audits, staff surveys or any study requiring access to medical records, you must first seek approval. This ensures we have a central register of such activities. Please read the Cabrini inpatient registration form and the Cabrini privacy statement 'The privacy of your personal information' for clear guidance about how patient information may be used. If you propose using the information in any other way or for any other purpose, you must inform CRGO. A data collection project will only be considered low-risk if all data collection is done by someone involved in the patient's care. If you propose using external parties to collect the information, approval must be sought.

2.3.3 Governance

CRGO will recognise the ethical approval of HRECs constituted in accordance with the National Statement on Ethical Conduct in Human Research and appropriately certified by the NHMRC i.e. National Mutual Acceptance Scheme (NMA) HRECs. This does not mean all HREC-approved studies will be deemed suitable for Cabrini. All studies undertaken at Cabrini need to undergo a governance review to ensure they fit within Cabrini's research agenda, the Catholic Health Australia code and all Victorian requirements.

Although ***literature*** and ***systematic reviews*** do not require ethics or governance approval, it is important to inform CRGO of your intention to conduct such reviews to ensure:

- Cabrini is aware of ALL research being conducted by its representatives, regardless of risk level, and can acknowledge the work;
- There is no duplication of research;
- The reviews contribute to your department's research productivity tally; and
- The reviews are acknowledged in Cabrini Research's annual report of research activity.

For literature and systematic reviews, email researchgovernance@cabrini.com.au advising:

- Type of review

- Research question / study title
- List of investigators
- Brief summary of research method
- Intentions for publication

2.4 APPLYING

Submit a completed Low Risk & Governance Application Form (Attachment 2), following the instructions below. CRGO also accepts the Human Research Ethics Application (HREA). If submitting an HREA, you will still need to submit a completed Low Risk & Governance Application Form (Attachment 2) but may refer to the relevant section from the previously completed HREA. This applies for all types of review. The procedures for submission, attachments and wording are outlined below and apply regardless of which form/s you use.

As Victorian and Commonwealth Government requirements vary, if you use the HREA, you must ensure you consider Victorian-specific issues of the Health Records Act, Ionising Radiation and Guardianship. The Victorian Specific Module is designed to address these issues and supplement the HREA in Victoria.

2.4.1 Low and negligible risk review

Complete the Low Risk & Governance Application Form (Attachment 2). Submit the signed application form and relevant attachments via email to researchgovernance@cabrini.com.au.

2.4.2 Governance review

Submit a completed Low Risk & Governance Application Form (Attachment 2) including the HREC approval and all approved documents. Ensure the application form is signed by all principal and associate investigators and submit with relevant attachments via email to researchgovernance@cabrini.com.au.

2.4.3 Low Risk & Governance Application Form

The Low Risk & Governance Application Form (Attachment 2) is available from the Cabrini website. It must be submitted via email to researchgovernance@cabrini.com.au. Applicants should use as much space as necessary to give a complete answer to each question.

The application is divided into eight sections.

Section 1: Administrative information

Complete in full and provide copies of supporting documents, including:

- letters of approval from applicable HRECs
- letters of support from clinicians expected to recruit patients
- project resourcing and costing template (Attachment 3) signed by Heads of Departments providing resources (funds, staff time, service or facilities) for the project.

External Researchers: Where one or more of the researchers is not connected with Cabrini and/or the research is being carried out in conjunction with agencies outside of Cabrini, the connection to Cabrini of all researchers and the names of all agencies participating in the project must be listed.

PI Eligibility: Eligibility to be a PI requires the applicant to be a Cabrini employee or Visiting Medical Officer (VMO). Trainee doctors can serve as co-PIs alongside their Cabrini supervisor if they have valid Cabrini accreditation and current GCP. PhD students can function as an AI only and must identify if their role in the study contributes towards their PhD, with their Cabrini supervisor listed as PI. A coordinating PI cannot serve as a site PI if they do not have immediate site responsibilities for Cabrini's involvement in the study.

Honorary Appointments: External researchers wishing to access identifiable Cabrini data (refer to 4.9 'Privacy and Confidentiality, Waiver of Consent and Data Protection') must apply for an honorary

appointment. A standard honorary appointment will permit the researcher regular site access to Cabrini clinical and corporate campuses for the duration of the project. The application process requires the review and acknowledgement of Cabrini's research and privacy policies, evidence of mandatory vaccinations, and completion of mandatory training modules. If a researcher is involved in multiple projects, only 1 honorary appointment is required. A pre-existing appointment can be extended to accommodate the expected completion date of the latest project. Honorary appointments have a 2 year duration and require renewal if an extension is needed. Contact honoraryappointment@cabrini.com.au for more information.

Mandatory training will be waived for any researcher who will not visit any Cabrini campus (clinical or corporate) for the project. Their appointments will stipulate that site access is prohibited. If this situation changes, the researcher is obliged to inform the CRGO so training can be undertaken and the honorary appointment status updated.

External researchers with honorary appointments who are accessing identifiable data can only do so under the supervision of their Cabrini clinical supervisor or Cabrini PI.

Authorship: Authorship: A guide supporting the Australian Code for the Responsible Conduct of Research (2019) states an author is an individual who has made a significant intellectual or scholarly contribution to research and its output, and agrees to be listed as an author. All listed authors are collectively accountable for the whole research output. As outlined in Section 2.1 of this guide, the criteria for attributing authorship should include a combination of 2 or more criteria listed below:

- conception and design of the project or output;
- acquisition of research data where the acquisition has required significant intellectual judgement, planning, design, or input;
- contribution of knowledge, where justified, including Indigenous knowledge;
- analysis or interpretation of research data; and
- drafting significant parts of the research output or critically revising it so as to contribute to its interpretation.

Acknowledgements: Contributions to research that do not meet the criteria for authorship should be acknowledged where appropriate; for example, contributions from individuals providing technical support. Researchers should obtain permission from named contributors before acknowledging them in research outputs, since acknowledgement may imply a contributor's endorsement of the research output.

A study's Principal Investigator and all Associate Investigators who are listed on a project that is conducted in full or in part at Cabrini, must include Cabrini in their listed author affiliations for all publications, presentations and media coverage resulting from any research conducted at Cabrini, requiring Cabrini resources or funded by Cabrini.

Section 2: Resource summary

This section should contain sufficient information to assure the Committee the resources necessary to carry out the project to completion will be made available in line with paragraph 5.2 of the National Statement. The project resourcing and costing template (Attachment 3) must be completed if Cabrini departments are required to support the project. Budgets must include all anticipated expenses and project income, and detail any internal or external funding supporting the project. Grant offer letters or funding agreements must be supplied and the assigned Cabrini Finance Reference Code stated. Ensure any variations in research project titles are aligned or appropriately communicated and justified with our office to minimise confusion i.e. the wording of project titles can vary between a grant application, protocol and ethics application.

Section 3: Project summary

The project summary (or plain language statement) should be written in simple language suitable for lay people, aimed at the reading comprehension of a 14-year-old. It should include background from literature, rationale for the project, aims, methodology and method of analysis. It should include any disease or PBS implications that would be outside the understanding of lay members of CRGO. It should be no longer than one A4 page. If the sponsor provides this document and it does not fulfil these requirements, the researcher should provide a letter summarising the project in the manner outlined above.

Section 4: Project details

Ensure any attachments provided to support the response have an appropriate footer, including the name of the document, version number, date and page number / total pages.

Within the patient's explanatory statement or participant information consent form (PICF), you must outline the potential risks arising from the project (Section 2.1 of the National Statement apply), the potential consequences of those risks and the measures to be taken to deal with those consequences. Explain the monitoring, reporting and other procedures to be put in place to manage serious adverse and other unforeseen events. This includes adverse events of a physical or emotional nature, as well as adverse events relating to project information, such as de-identified information becoming identified.

Section 5: Ethical issues

Ensure your responses reference the Cabrini-specific storage and data protection requirements, including local servers, desktop computers, offices etc.

Section 6: Drugs and therapeutic devices

Follow the form instructions if this section is not applicable.

Section 7: Human Biospecimens

Read chapter 3.2 of the National Statement. Respond or follow the form instructions if this section is not applicable.

Section 8: Declaration

It is the PI's responsibility to ensure the research is conducted in accordance with the guiding principles, regulatory requirements and legislation referenced in Section 1 (page 4) of this document. It is their responsibility to ensure any Associate Investigators (AI) and staff they may engage to conduct research activities are familiar with these requirements and abide by them.

In their absence, they may delegate responsibility to an appropriate AI. They must notify the Committee immediately of any intended changes to the protocol, plain language statement or project personnel after the project has been approved.

The application form - signed by all listed investigators and student researchers - and attachments can be submitted via email to researchgovernance@cabini.com.au.

2.5 SUBMISSION

Only electronic copies of research documents are required. If research agreements and indemnities are required, electronically executed contracts with approved e-signature software will be accepted. Use research agreement and indemnity templates provided by Monash Partners at https://monashpartners.org.au/research-facilitation/resources-and-forms/.

2.5.1 Low and negligible risk review

For low and negligible risk review, the following relevant documents should be sent to researchgovernance@cabrini.com.au:

- Low Risk & Governance Application Form (Attachment 2)
- Cabrini Project Resource and Costing Form (Attachment 3) if Cabrini services are required to support the research that may incur costs. Alternately, written project support is required by the relevant department head if their team is involved.
- Level of Risk Checklist (Attachment 4)
- Written project support from both the Academic Research Head and Clinical Craft Group Head
- Evidence of peer review (if applicable)
- Evidence of consumer review (if applicable)
- Database Governance Audit Tool (Attachment 11) for any low risk database / registry projects – refer to 3.6 General Information
- Budget – include all anticipated expenses and project income i.e. internal or external funding
- Grant offer letter or funding agreement – ensure the assigned Cabrini Finance Reference Code is stated
- Flow chart (or equivalent) of the study processes if available
- Protocol
- Participant information and consent form(s) – PICFS - summarising the project for participants, written in plain language (Year 8 reading level) - see chapter 2.2 and section 4 of the National Statement. Cabrini requires certain clauses and wording to be included in this information (refer to **Section 4: Informing Research Participants** of this document). PICFs should not exceed 20 pages (shorter is preferable).
- Advertisements / recruitment material
- All research tools e.g. questionnaires, surveys, data collection form, etc.
- GCP certification for all members of the research team
- CV for all members of the research team
- Relevant vaccination evidence for external researchers intending to come to Cabrini campuses and requiring honorary appointments

2.5.2 Governance reviews

Your submission to researchgovernance@cabrini.com.au must include the HREC application (HREA) with all attachments and corresponding approval(s). Ensure relevant items listed in **2.5.1 Low and negligible risk review** are included, particularly those related to **project resourcing, budgets, funding and database governance**. Include the HREC-approved master PICFs along with revised versions specific to Cabrini (both tracked and clean versions). Cabrini-specific PICFs need to list the CRGO as the complaints contact person*****, include appropriate wording regarding prevention of conception***** if applicable, compensation wording appropriate to the private hospital setting***** and include a Cabrini Research logo. The logo can be obtained from the doctors' portal or the Cabrini intranet, via Departments and Services/Marketing and Community Relations/Our Brand. You must also submit the completed and signed Low Risk & Governance Application Form (Attachment 2). Duplication can be minimised by referencing relevant parts of the prior HREC-approved application (e.g. HREA).

*****_Refer to Section 4: Informing Research Participants for specific information._

For studies involving **surgical intervention**, PI's must ensure the following is addressed in their governance application:

- Provide names of the regular surgeons involved in supporting the study, and evidence of their agreement to participate. Contingency plans - should the regular surgeons be away – must be outlined.
- Evidence the head of the anaesthetics craft group has been notified and acknowledged the intended conduct of the study.

2.6 SUBMISSION FEES

CRGO fees are available via the Cabrini website. If the project is billable, an invoice for submission fees will be sent during the review process. If a purchase order is necessitated by your institution for payment to be processed, please obtain and submit this with your application.

3. GENERAL INFORMATION

3.1 WRITING A RESEARCH PROTOCOL

A research protocol needs to clearly describe all relevant components of the research:

- **Background and literature review**
  What is already known about the research topic in relation to the wider community and the specific site(s) to be studied?

- **Rationale**
  How might new information from the study inform / improve future practice?

- **Aims and research questions**
  What gaps in knowledge do you hope to fill?

- **Inclusion / exclusion criteria**
  What are the parameters for participant selection?

- **Recruitment and consenting procedures**
  How, when, where, and by whom will these tasks be performed? Even where a retrospective review of records is proposed, patients are still considered research participants and these questions must be addressed, unless a waiver of consent can be justified – refer to National Statement 2.3.10. The PI must also familiarise themselves with National Statement 3.1.18 in relation to recruitment of participants such as patients or employees, with particular consideration to addressing a potential power imbalance and avoiding coercion.

- **Methods**
  How will the research be conducted? Does the method of data collection in the study design allow for a diversity of participants? (e.g. consider methods to address an older demographic who may not be confident with technology.) A flow chart may be helpful.

- **Risks and benefits**
  Consider all possible outcomes or repercussions for participants and the wider community (refer to Chapter 2 Section 2.1 of the National Statement)

- **Randomisation procedures**
  If comparing one intervention to another or to a placebo or no intervention, how will participants be allocated to different groups?

- **Collection, use, storage and disposal of data (including samples)**
  How, when, where, and by whom will these tasks be performed? How long will data be kept? Who will have access? (Refer to Section 4.9.3 of Informing Research Participants of this document for further information)

- **Confidentiality**
  Use the following accepted terms to describe how data / samples will be labelled at each stage of the research (refer to 4.9.3 of Informing Research Participants for further information):
  - Identifiable e.g. name, UR and date of birth
  - Re-identifiable e.g. using a unique study identification code which only specified study personnel can link back to the participant – specify how the 're-identification key' will be stored and who will have access
  - Non-identifiable / de-identified / anonymised – no possible way of linking back to the participant

- **Statistical analysis**
  How will the data be analysed to answer the research questions? CRGO strongly encourages researchers to consult a biostatistician ***during*** protocol development to ensure the data will answer the research question. This process will also assist with securing an estimated cost for statistical analysis for inclusion in project budgets and grant submissions. Cabrini employs a biostatistician, Dr Mohammad Asghari-Jafarabadi. Statistical support is available to Cabrini researchers at a rate of $100 per hour. Dr Asghari-Jafarabadi can be contacted via mjafarabadi@cabrini.com.au.

- **Results / Research Output**
  How do you plan to report, present or publish results?

To avoid delay in ethics approval, ensure the research protocol clearly addresses all of the above aspects when first submitted.

3.2 STUDENT RESEARCH

If you are a student, or the project forms part of your tertiary study, you must ask your university supervisor and the head of the relevant Cabrini Department to write a letter of endorsement to accompany the application stating that they have reviewed the scientific methodology of the study and the methodology is appropriate.

3.3 PEER REVIEW

All research applications, apart from audits of retrospectively collected data, should demonstrate that independent peer review of the study has been sought. Cabrini Research facilitates a peer review service for researchers without access to independent expertise. An independent reviewer can be sourced for you, or alternately, a panel consisting of a Cabrini biostatistician, senior researcher and research executives will be convened at regular intervals to provide peer review. Contact researchgovernance@cabrini.com.au for more information.

3.4 REGISTRATION OF CLINICAL TRIALS

All drug and device clinical trials must be registered with the Therapeutic Goods Administration. Clinical trials must also be publically registered on a WHO Registry Network platform such as ClinicalTrials.gov or Australia New Zealand Clinical Trials Registry. Attach evidence of registration notifications to your application, even if provisional or draft, and provide a copy of the trial acknowledgement once issued. The sponsor must provide evidence the trial is publically registered on a primary registry prior to enrolment of the first patient.

3.5 FIRST TIME IN PATIENT (FTIP) PHASE 1A TRIALS

Refer to the FTIP Phase 1a Cancer Trials at Cabrini standard operating procedures (SOP). An independent toxicology review may be required for any studies involving novel agents or healthy participants.

3.6 RISK MANAGEMENT—INSURANCE AND INDEMNITY

Where Cabrini projects fall within *standard of care (SOC),* they will be covered by the hospital's insurance policy.

Any treatment by professionals (doctors or therapists) which exposes them to litigation will not be covered by the hospital's insurance and is the responsibility of the professional involved. All professionals involved in treatment should provide details of their professional indemnity cover and a record kept of this information. This is a requirement for all accredited medical practitioners at Cabrini. Accredited medical practitioners undertaking clinical trials must advise their professional indemnity provider and provide correspondence within their application confirming insurance cover for their research activity.

Any queries regarding indemnification of the medical professionals involved should be addressed to the practitioner's medical defence/insurance organisation.

Any trial involving a new device, medication or biological agent must be fully indemnified by the sponsor and evidence of that indemnification will be kept on file. This indemnification needs to cover all aspects of the treatment and any potential future complications. Such cover must include the hospital and all trial personnel. Cabrini cannot allow any trials not fully indemnified to proceed.

Trials of currently approved drugs for a new indication (not currently listed) require decisions on a case-by-case basis. If a reasonable body of opinion exists among medical practitioners that this was a reasonable use of the medication, it would probably fit within *us*.

Where the placebo arm of a controlled trial involves an invasive procedure that is not part of *standard of care*, a separate insurance policy would need to be in place to cover potential litigation. The 'up front excess' requirements of hospital policies in Australia would mean it would not be financially viable to carry out such trials at Cabrini.

Placebo arms are not permitted in Phase 1 trials.

3.7 DATABASES / REGISTRIES

All new database/registry applications requesting governance approval must be presented to the Data Governance Committee to ensure that it adds value to Cabrini, the database does not duplicate data already collected and that effort required in collecting the data is minimised. Attachment 11: Cabrini Research Data Governance Audit Tool must be completed and included in the new applications submission.

3.8 OBSERVERS

Observation of a standard of care (SOC) procedure associated with a research project by a non-member of the research team for the purposes of education is permitted without the need to notify an HREC. The PI must, however, seek approval from the relevant department head and ascertain the requirements of that department to permit the presence of an observer. For example, to observe an SOC procedure in theatre, the Nurse Director Perioperative Services must authorise the presence of the observer and will advise specific training, certification and administrative requirements (if any).

Observation of and participation in a research procedure requires HREC approval.

4. INFORMING RESEARCH PARTICIPANTS

Templates for participant information and consent forms (PICF) are available from the Victorian Government's Clinical Trials and Research website.

4.1 ADVICE FOR RESEARCH PARTICIPANTS

Trials involving investigational products require a standard clause in the participant information consent form (PICF), with contact details for the study personnel saying:

We encourage you to discuss study participation with your family, friends and medical advisers. We recommend that you ask your medical advisers to contact the study investigator.

4.2 TRIAL LANGUAGE

The PICF may refer to the investigational product as 'agent', 'drug' or 'medication' as long as it is prefaced by 'trial' or 'study' so patients do not assume therapeutic benefit. If the word 'treatment' must be used in reference to administration of a trial agent, it should be prefaced by the word 'trial' or 'study'.

4.3 STUDENTS

Studies involving students require a statement in the PICF advising participants the study is being conducted for the purpose of gaining a qualification. For example: *'This project will form part of <Name of student>'s PhD thesis.'*

4.4 RISKS

The risk of side effects from an investigational product should be stated in order of seriousness and probability. Risks of therapeutics approved for the study indication should *not* be included. Consideration should also be given to potential risks inherent with sharing information.

4.5 REQUIREMENTS FOR RESEARCH IN HUMANS OF REPRODUCTIVE AGE

CRGO has concerns about any research study involving drugs with potential side effects on the unborn child. All women participating in studies involving drugs with an unknown effect on the unborn child are required to have a pregnancy test prior to entering the study and to be informed they could potentially be excluded from the study.

As a Catholic healthcare service, Cabrini is committed to reflecting the Church's teachings regarding respect for the personal dignity of human life in all stages. It is imperative there is certainty of causing no harm to the life or integrity of a human embryo or foetus. As such, we require the following **unedited** statement, approved by Catholic Health Australia, be included in the information for participants in medical research where applicable:

'The effects of [Name of investigational product] on the unborn child and on the newborn baby are not known. Because of this, it is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the research project. If you are male, you should not father a child or donate sperm for at least [number] months after the last dose of trial agent.

Both male and female participants must avoid pregnancy during the course of the research and for a period of [number] months after completion of the research project. You should discuss effective methods of avoiding pregnancy with your doctor.

[For female participants] If you do become pregnant whilst participating in the research project, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant.

[For male participants] You should advise your study doctor if you father a child while participating in the research project. Your study doctor will advise on medical attention for your partner should this be necessary.'

Alternately, if a sponsor requires the Master PICF prevention of conception wording to be mirrored in the site specific PICF, the following pre-fix wording must be included ***in bold*** ahead of the paragraph/section not endorsed by Cabrini:

'Because of the unknown risks of this trial agent, it is important that you do not become pregnant during this trial. For legal reasons, the pharmaceutical company requires us to provide you with the following information about methods of avoiding pregnancy. Not all of this information is endorsed by Cabrini Health, nor reflects its ethical standards as a Catholic hospital. You should discuss with the study doctor and/or your own doctor and ethical advisor an effective way for you to avoid pregnancy that is in keeping with your beliefs and values.'

For studies where the impact on fertility is a concern, the following statement is acceptable for inclusion:

'You should talk to your doctor if you would like to be referred to an infertility specialist before commencing study treatment if reduced fertility or infertility is a concern for you. Infertility care is not part of this study. You should discuss this with the study doctor and/or your own doctor. Some methods of preserving fertility may not be endorsed by Cabrini Health.'

4.6 PARTICIPANTS – CHILDREN AND YOUNG PEOPLE

Chapter 4.2 of the National Statement needs to be referenced if you are recruiting participants under the age of 18. Ensure an explanation is included in 4.2.2 of the Low Risk & Governance Application Form (Attachment 2) addressing how children and young people will be appropriately consented.

4.7 STATEMENT OF ETHICS REVIEW

Participant information (plain language statements) need to include a statement about who has reviewed and approved the project. The following wording may be used:

'The ethical aspects of this study have been reviewed by the Cabrini Research Governance Office and the study complies with the NHMRC's National Statement on Ethical Conduct in Human Research 2007 (and subsequent updates).'

If the study is considered above low risk and has received ethics approval by an external HREC, ensure the following is included after the statement advising the name of organisation that has provided full HREC review:

'Cabrini Research Governance Office has approved the conduct of this study at Cabrini.'

4.8 GUIDELINES FOR INFORMING PARTICIPANTS ABOUT THE OUTCOME OF RESEARCH

CRGO notes that:

- the results of a study may not be available for many years and their relevance to participants may become remote;
- the results may not be in the public domain, that is, they may remain the property of the sponsoring agency;
- it may be that the release of results is not in the best interests of participants;
- confidentiality could be seen to be questionable if participants are contacted after studies are completed;
- researchers seldom have editorial control of publications; and
- the ability to deliver results in a secure and confidential manner is dependent on many factors, including the ability of a researcher to maintain an accurate participant database.

Notwithstanding the above and in line with paragraphs 1.3 (d) and 1.5 of the National Statement, CRGO believes that participants should have the opportunity, where possible and appropriate, to hear the

outcome of a study they have participated in and encourages researchers to consider this in their study design.

4.9 WAIVER OF CONSENT

13 Australian Privacy Principles (APPs) provide the framework for the 1988 Privacy Act. AAP6 outlines that an APP entity can only use or disclose personal information for a purpose for which it was collected (known as the '**primary purpose**'), or for a **secondary purpose** if an exception applies. The exceptions include (but are not limited to) where:

- the individual has consented to a secondary use or disclosure;
- the individual would reasonably expect the APP entity to use or disclose their personal information for the secondary purpose, and that purpose is related to the primary purpose of collection, or, in the case of sensitive information, directly related to the primary purpose; or
- the secondary use or disclosure is required or authorised by or under an Australian law.

An example of 'related secondary purpose' is quality assurance activity such as if the project involves access to identified data by clinicians or administrative staff who normally have access to that data. If the purpose goes beyond quality assurance i.e. research, or access is required by someone who would not normally have access to that data, then a *waiver of consent* must be justified, addressing 2.3.10 of the *National Statement*, and generally sought via an HREC (or alternate approved pathway).

4.10 PRIVACY AND CONFIDENTIALITY

All PICFs must contain a simple and concise paragraph on how the research will comply with the *Health Records Act 2001 (Vic)*, the *Privacy Act 1988*, NHMRC Guidelines under Section 95 of the *Privacy Act 1988* and all other NHMRC privacy guidelines and regulations.

All persons who come into contact with, or have access to, confidential information, have a responsibility to maintain the privacy, confidentiality and security of that information. Any non-Cabrini employees who require access to identifiable patient records must successfully apply for an honorary appointment (refer to Section 1 2.4.3 of this document) before accessing those records. Their access to these records is only permitted under the supervision of their Cabrini clinical supervisor or Cabrini PI.

4.11 DATA PROTECTION

Where possible, data should be collected without identifiers. Any research data collected should adhere to the following:

- Hard copy data should be stored onsite (closest to the area of collection) in a locked office in a locked cabinet (or fridge for tissue samples).
- Electronic data should be stored in an encrypted file on a password protected non-portable computer, only accessible by an approved site PI or AI.
- All data should be stripped of its identifiers and assigned a unique code that prohibits re-identification of the source data other than by the approved PI or AI.
- The key-coded file that can match re-identifiable data with its original owners must also be encrypted and stored separately to the location of the source data, accessible only by an approved site PI or AI.
- All data must be stored on Australian servers that adhere to Australian privacy laws.
- Data sent off-site must be in a de-identified state (re-identifiable by the local PI only) and used for HREC approved purposes.
- Data Transfer Agreements or Research Collaboration Agreements are required for any data sharing arrangement and must outline the parameters of data use and commit the parties to lawful, HREC-approved treatment of the data.

4.12 OVERSEAS DATA / SAMPLES TRANSFER

If identifiable or re-identifiable data, including biological samples, are being transferred outside of Australia, participants must be informed that privacy laws outside of Australia may be less stringent.

The purpose of the transfer should be qualified by a statement such as *'for the sole purpose of testing and analysis related to this research project'*.

The following statement should be included:
'Participants should note that, some data derived from your participation in this study will be sent overseas << to countries such as [insert country names] >>; the regulatory regimes governing data access and use in other countries may not be the same as those that are in place in Australia. In the case of data that identifies you, or from which your identity may be ascertained, [an entity subject to Australian privacy laws that has collected your information/local Sponsor] must take reasonable steps to ensure that an overseas recipient handles the information in accordance with any relevant Australian privacy principles (unless an exemption applies). If you have any questions about this, direct them to the study doctor.'

In instances where the list of countries to which data may potentially be sent is extensive (e.g. a global entity with a centralised data repository and a large number of international corporate offices with access to this data), it is acceptable to add the following statement to the above paragraph and not list each individual country:
'A full list of countries where your de-identified data may potentially be sent is available via the study coordinator should you wish to review it.'

In the case that data/samples are potentially sent to third parties, the following statement must be included:
'The Sponsor of this trial is liable for any potential breaches to Australian privacy principles by its representatives in the handling of your data.'

Clinical Trial Research Agreements must impose privacy obligations on the Sponsor. If the Sponsor is an Australian company, they will be captured by Australian privacy laws. However, if the Sponsor is transferring data overseas, including to an international related body, affiliate or third party, the agreement must include the following clause in the Schedule 7 Special Conditions to ensure the Sponsor and their representatives understand their data protection obligations to Australian privacy law and the consequences of a breach:

Clause 10.3 'The Sponsor is required to comply with the Relevant Privacy Laws, including the Privacy Act 1988 (Cth). If the Sponsor transfers data or Personal Information to an Affiliate or third party whether in Australian or overseas, it must impose the privacy obligations in this Agreement on the relevant Affiliate or third party. The Sponsor remains liable for any failures by the Affiliate or third party to comply with the privacy obligations in this Agreement relating to Personal Information.'

If the sponsor is an international entity, legal advice should be sought on the nature of the Agreement to ensure appropriate privacy protections are in place.

4.13 DATA STORAGE FOR CABRINI RESEARCHERS

Cabrini researchers (employees and affiliates) should utilise the S drives specific to their department to store their research data as the S drives are secure and regularly backed up. Locked folders can be created within the S drive and assigned specific, unlimited membership access to enable collaboration and sharing by members of the research team. These folders should be encrypted if they contain sensitive, identifiable data – Windows encryption is preferred. ***Under no circumstances can the H:drive (personal drive) be used to store Cabrini research data.*** Submit your request to researchgovernance@cabrini.com.au for creation of a locked folder, specifying the Cabrini project title and number, membership access list and whether encryption is required.

Researchers who wish to avoid data unwittingly being sent overseas, and unknown privacy implications due to privacy laws of other countries differing from Australia, need to ensure that an Australian server is enlisted for electronic data storage.

The NHMRC's Australian Code for the Responsible Conduct of Research 2018 recommends the minimum period for retention of research data is 5 years from the date of publication. Most clinical trials will retain research data for 15 years or more if necessary. State and Federal legislation may vary this position. Researchers must ensure they have adequate storage arrangements in place and have factored any storage fees into their research budgets.

4.14 PAYMENT OF PARTICIPANTS IN RESEARCH PROJECTS

CRGO considers it appropriate to offer participants reimbursement for 'direct out of pocket' expenses (such as travel expenses). CRGO encourages researchers to consider such reimbursement when planning clinical studies, though reimbursement should be structured so as not to be considered an inducement to participants. It is also important that lack of reimbursement does not exclude patients from participation in a research study.

If payments are intended, researchers should provide CRGO with:

- A rationale for proposed payments
- The method and timing of disbursements
- Information on how prospective participants will be advised of the provision of payments

CRGO will assess whether the payments are adequate and proportionate, and will ensure the potential for undue influence is minimised.

Review NHMRC's 2019 publication 'Payment of participants in research: information for researchers, HRECS and other ethics review bodies' for further guidance.

4.15 COMPENSATION FOR INJURY ATTRIBUTABLE TO THE STUDY

If your study is commercially-sponsored, your PICF should include this paragraph:

'In the event that you suffer any injury attributable to the administration of a medicinal product within the study or any clinical intervention or procedure required under the study that would not have occurred but for your inclusion in the study, you will be compensated in accordance with the Medicines Australia Guidelines for compensation for injury resulting from participating in a company-sponsored research project. A copy of the Medicines Australia Guidelines is available to you from the research staff on request.'

If your study is not sponsored, please substitute an appropriate paragraph. Participants who suffer any injury as a result of participation in research conducted at Cabrini are expected to have access to treatment for that injury at Cabrini, at no cost to them.

4.16 OUT OF POCKET COSTS

If your study is commercially-sponsored, your PICF should include this paragraph:

'All medication, tests and medical care required as part of the research project will be provided to you free of charge. Regular medical care in circumstances unrelated to the research project will be provided as per your insurance arrangements or through Medicare. If you do not have private insurance, you may incur additional costs if you choose to receive medical care at a private hospital where the medical care is unrelated to the research project.'

If your study is not commercially-sponsored, the following paragraph can be used instead:
'You will not receive payment for participating in this study. All routine standard examinations will be handled as if you were receiving standard treatment and not participating in a clinical study. You will be responsible for the cost of the tests or treatments that are considered standard care in the usual way

(health insurance, Medicare and your personal contribution depending on your circumstances). You should ask the study doctor to explain any payments for which you may be responsible.'

4.17 DISCLOSURE REGARDING POTENTIAL REWARDS FOR RESEARCHERS

Researchers are asked to describe the arrangements, costs and potential rewards and benefits of the study. This includes, but is not limited to:

- study budget, grants, sources of funding and additional study costs and payments incurred by investigators;
- organisational structure of the study, any beneficial interests, duality and/or conflict of interest for the investigators; and
- intellectual property ownership, impact on career and reputation, requirements for course work or higher education, travel grants and publications.

The PICF should include a statement advising who is paying for the study, who gets something out of it and what are the financial and organisational arrangements underpinning the study.

4.18 COMPLAINTS

Please read chapter 5.6 of the National Statement regarding handling complaints. All PICFs need to include the CRGO as the contact for a complaint relating to the ethical conduct of the project. Contact details are in the table below, which you may copy and paste into your PICF:

Position	Cabrini Research Governance Officer
Telephone	03 9508 3412
Email	researchgovernance@cabrini.com.au

4.19 GENETICS AND PHARMACOGENETIC STUDIES

4.19.1 Impact of genetic research

Useful references, particularly regarding the insurance, employment and other implications for participants, include:

- Chapter 3.3: Genomic Research from the National Statement on Ethical Conduct in Human Research (2007) – updated 2018
- Life insurance products and genetic testing in Australia

4.19.2 Genetic research involving human embryos

As outlined in Chapter 6 of Catholic Health Australia's Code of Ethical Standards for Catholic Health and Aged Care Services in Australia, any genetic research that involves techniques that are contrary to respect for human life or human dignity are prohibited.

The CRGO may request a signed statement from the PI affirming an understanding of Cabrini's ethical position on the treatment of human tissue in research and compliance with the treatment of human tissue only as outlined in the HREC-approved study protocol. CRGO can provide a sample template if required.

4.20 ADVERTISING

All advertising on noticeboards within the hospital environment and the media requires the approval of the CRGO.

The advertisement may include a statement that this study complies with the NHMRC's National Statement on Ethical Conduct in Human Research but need not state that this study was approved by the Cabrini Research Governance Office.

4.21 WITNESSES

Cabrini generally does not require witnesses to be included in the consent process as this cannot be audited, however Cabrini is comfortable that interpreters can serve as impartial witnesses.

5. POST-APPROVAL RESEARCH

Report notable events and submit revised documents for review via email to researchgovernance@cabrini.com.au.

- PI must confirm events or documents to be presented either via email or signed CRGO submission form (see below).
- Forward email confirmation from PI (or signed coversheet) to researchgovernance@cabrini.com.au .
- CRGO will acknowledge, via return email, once documents have been reviewed and noted.

5.1 POST-APPROVAL DOCUMENTS REQUIRING REVIEW

Researchers should immediately report anything which might warrant ethical review, that might impact participant safety, the ongoing conduct of the study or data integrity, including:

- serious or unexpected adverse effects on participants;
- proposed changes in the protocol and participant consent;
- unforeseen events that might affect continued ethical acceptability of the project;
- breaches – serious or non-serious;
- protocol deviations; and/or
- protocol violations.

All post approval documents should first be submitted to the reviewing HREC for approval, then sent to the CRGO for site-specific review and noting. These post-approval documents may include, but are not limited to, amended ***study protocols***, updated ***investigator brochures***, revised ***participant information consent forms****** (PICFs – both master and site-specific), any patient-facing content such ***surveys***, ***questionnaires***, ***audio*** / ***video tools***, as well as ***recruitment material*** such as ***advertisements*** and ***letters of invitation***.

CRGO does not require submission of extra documents with no ethical content, such as patient diaries and patient cards.

To facilitate review, all changes to previously submitted documents must be shown using '***tracked changes***' i.e. underlining for additions and ~~strikethrough~~ for deletions. Revised documents must include an updated version number and date (preferably in the footer). Both 'tracked' and 'clean' copies must be submitted for review.

*CRGO does not support the ***unnecessary re-consenting*** of participants, particularly if they have completed treatment and are only in survival follow-up. Re-consenting can be a stressful and even traumatising experience for vulnerable, unwell participants, particularly given the large volume of information that can be delivered through a PICF. Re-consenting will only be considered in the event there is a ***significant practice change*** for a participant on active treatment, or a ***new or increased risk*** has been identified, resulting in a protocol amendment. Administrative changes or minor practice changes that do not have the potential to negatively or adversely affect a participant may be noted in a PICF update, however re-consenting must be deferred until a future amendment warrants re-consenting as per CRGO guidelines. Ethics submission specialists are advised to first check with the PI if they support re-consenting of proposed changes prior to CRGO submission.

CRGO Submission Forms

The following CRGO submission forms are for use when submitting any documents relating to your project:

- Documents to be presented (Attachment 7) – for all document submissions, including protocols, PICFs, investigator brochures, letters, memos etc.
- Administrative Amendments (Attachment 8) – for changes to the research project team, dates, contact details, logistics and other issues which raise no ethical concerns.
- Events to be noted (Attachment 9) – for all events such as breaches, protocol deviations and violations, excluding SAEs. These must be reported as soon as the study team becomes aware that the event has deviated from or violated the approved protocol. As well as an explanation of the event, some comment as to what action has been taken to avoid a repeat occurrence needs to be provided. Comment on any impact on participant safety, ongoing conduct of the study or data integrity must also be included. A root cause analysis and correct action and prevention plan (CAPA) may be required.

When completing these forms, please include:

- Cabrini project number and title;
- rationale and brief summary of what has changed since the previous edition; and
- comments from the PI about how this may impact on the study.

Submit the form and relevant document(s) via email to researchgovernance@cabrini.com.au. The submission should be made by the PI. If the submission is made by someone other than the PI, the form detailing all changes must be authorised by the PI and included in the submission.

5.2 SAFETY MONITORING AND REPORTING

A detailed safety monitoring and reporting policy is available upon request from researchgovernance@cabrini.com.au or via the Cabrini website. The Victorian government template, CIOMS and most sponsor templates will be accepted for clinical trials adverse event reporting. Attachment 10 can be used as an alternate.

5.3 POST APPROVAL MONITORING – INTERNAL

Under Chapter 5.5. of the National Statement, the CRGO is responsible for ensuring that all approved research is monitored, and the PI is responsible for notifying the reviewing HREC that appropriate monitoring mechanisms are in place. Such monitoring includes:

- Audits/site visits/interviews to ensure compliance with conditions of approval;
- Review of completed annual progress reports, final reports and publications which can be emailed to researchgovernance@cabrini.com.au. For a single site (Cabrini-specific) study, the reviewing HREC progress and final report templates will be accepted. For multisite studies, either the reviewing HREC or government progress / final report templates will be accepted as long as Cabrini-specific data is highlighted against the aggregated data, otherwise the CRGO progress report (Attachment 6) is required.
- Review of serious adverse event reporting.

5.4 POST-APPROVAL MONITORING – EXTERNAL

Commercially-sponsored clinical trial monitoring involves stringent, regulated processes largely dictated by the trial sponsor. However, monitors are required to adhere to specific local site requirements including presentation of vaccination evidence and mandatory mask requirements as well as use of mutually approved data sharing platforms. Sponsored trials are still subject to internal monitoring.

For collaborative research group studies and trials, the monitoring protocol, processes and data sharing platforms proposed by the coordinating site must receive HREC and site governance approval.

Refer to the Cabrini website for the full post-approval monitoring policy.

Cabrini must be acknowledged in all publications, presentations and media coverage resulting from any research conducted at Cabrini, requiring Cabrini resources or funded by Cabrini. CRGO will review a project's research output to ensure Cabrini's involvement is appropriately referenced. Failure to do so may have implications on a project's approval status, funding, and future research applications.

Approval granted by the CRGO is ongoing for the life of the project, subject to satisfactory compliance and reporting. Progress reports and their respective acknowledgments can be shared with relevant parties if evidence of active approval and monitoring is required, however updated approval letters will not be issued.

6. OTHER RESOURCES AND REFERENCES

Alfred Health HREC
Australian Clinical Trials Education Centre
Australian Code for the Responsible Conduct of Research (2018)
Australian National Data Service guide
Australia New Zealand Clinical Trials Registry
Australian Privacy Principles (Office of the Australian Information Commissioner)
Authorship: A guide supporting the Australian Code for the Responsible Conduct of Research (2019)
Cabrini Privacy Policy
Cabrini Research Data Governance Audit Tool
Cabrini Research Governance Policy
Catholic Health Australia - Code of Ethical Standards
Catholic Health Australia - PICF statement where pregnancy must be avoided
ClinicalTrials.gov
First Time In Patient (FTIP) Phase 1a SOP
Health Records Act 2001
How to make an HREC application
ICH GCP
ICH GCP Provider – Monash Partners
ICH GCP Provider – Western Australian Health Translation Network
ICH GCP Provider – Genesis Research Services
ICH GCP Provider – The Global Health Network
Medicines Australia Clinical Trials Research Agreement
Medicines Australia Standard Indemnity Agreement
Monash Health HREC
Monash Partners
National Clinical Trials Governance Framework
National Clinical Trials Governance Framework Fact Sheets
Nationals Principles for Teletrials in Australia
National Standard Operating Procedures for Clinical Trials, including Teletrials, in Australia
National Statement on Ethical Conduct in Human research (2007) – Updated 2018
Privacy Act 1988
Victorian Specific Module
Therapeutic Goods Administration
Therapeutic Goods Administration Guidance on clinical safety data management: definitions and standards for expedited reporting
Victorian Clinical Trials Education Centre
World Health Organisation's Recommended Format For a Research Protocol