Policy

Directive: compliance is mandatory

Research Ethics Operational Policy Directive

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Summary The Research Ethics Operational Policy Directive outlines the processes and requirements that apply to the administration and review of research ethics applications across sites and institutions governed by SA Health.

Keywords Research ethics, human research, ethics administration, Human Research Ethics Committee, policy directive, directive

Policy history Is this a new policy? **N**
Does this policy amend or update an existing policy? **Y**
Does this policy replace an existing policy? **N**

Applies to All SA Health Portfolio

Staff impact All Staff, Management, Admin, Students, Volunteers

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Version	Date from	Date to	Amendment
1.0	01/04/2012	30/10/2013	Original version
2.0	01/11/2013	current	2013 revision

Government of South Australia
SA Health

1. INTRODUCTION

SA Health is committed to supporting the conduct of high quality health and medical research across the South Australian public health system.

It is important that research involving human participants is conducted in a manner that respects and protects all involved, including the researcher, the research participants and the Institution. Obtaining research ethics approval helps to ensure that the research is carried out professionally and takes into account relevant legal, ethical, organisational and cultural standards.

SA Health has an obligation to ensure that research being conducted within the public health sector by staff or external researchers is of a high standard and observes all ethical requirements in accordance with applicable guidelines and standards, including the *National Statement on the Ethical Conduct of Human Research* ("National Statement", NHMRC, 2007).

This document outlines the operational requirements for Human Research Ethics Committees (HRECs) under the jurisdiction of SA Health, and provides an overview of the system for researchers wishing to conduct research within the South Australian public health sector.

2. SCOPE

This policy applies to all human research being conducted within the South Australian public health system. This includes, but is not limited to:

- Clinical trials;
- Clinical research;
- Health services research;
- Population health research;
- Epidemiological research;
- Tissue banking;
- Release of data and data linkage projects; and
- Qualitative research.

It applies equally to employees of SA Health and external researchers who are undertaking approved research activity on SA Health sites and institutions.

3. GLOSSARY

AHREC: Aboriginal Health Research Ethics Committee

Clinical trial: A research study designed to test the safety and/or efficacy of a medical treatment or intervention, often involving a treatment and control arm. Trials are generally classified into phases (phases 0 to IV).

Clinical trial research agreement (CTRA): An agreement between a sponsor or third party and the institution hosting the research.

CTN: The Clinical Trial Notification scheme developed by the Therapeutic Goods Administration (TGA) to permit unregistered medicines and medical devices to be used in the context of a clinical research trial. For CTN trials, the local HREC is solely responsible for reviewing and determining the safety and appropriateness of the medicine/device in the context of the trial.

CTX: The Clinical Trial Exemption scheme developed by the Therapeutic Goods Administration (TGA) to permit unregistered medicines and medical devices to be used in the context of a clinical research trial. For CTX trials, the TGA is also involved in assessing the safety and appropriateness of the medicine/device in the context of the trial.

Coordinating Principal Investigator (CPI): The lead investigator on a research study taking overall responsibility for the conduct of the study at all of the study sites.

HREC: Human Research Ethics Committee

IBC: Institutional Biosafety Committee

ISAAC: The Integrated South Australian Activity Collection (ISAAC) is an admitted patient morbidity data collection designed to provide SA Health with the information resources necessary to effectively organise, evaluate and plan health services in South Australia.

Lead HREC: The ethics committee responsible for the single ethical and scientific review of a research ethics application.

National Mutual Acceptance: a system for single ethical and scientific review of multi-centre clinical trials across participating jurisdictions.

National Statement: The NHMRC's *National Statement on Ethical Conduct in Human Research* (2007).

NEAF: National Ethics Application Form

NHMRC: National Health and Medical Research Council

OACIS: An electronic data management system for enabling patient/client information to be shared across the SA public health system.

Principal Investigator: the lead investigator responsible for the conduct and management of a research project at a local Institution or Site.

RGO: Research Governance Officer

SA public health system: Those institutions, including incorporated hospitals, under the jurisdiction of SA Health.

SAE: Serious Adverse Event

SOP: Standard Operating Procedure

SSA: Site Specific Assessment

TGA: Therapeutic Goods Administration

4. REFERENCE DOCUMENTS

This policy should be considered in conjunction with the following documents:

- Australian Code for the Responsible Conduct of Research (2007)
- National Statement on Ethical Conduct in Human Research (NHMRC) (2007)
- Values and Ethics: Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Research (NHMRC) (2003)
- Prohibition of Human Cloning for Reproduction and Regulation of Human Embryos Research Amendment Act (2006)
- Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research (NHMRC) (2004)
- Access to Unapproved Therapeutic Goods - Clinical Trials in Australia (TGA)
- International Conference on Harmonisation / Good Clinical Practice Guidelines (ICHGCP Guidelines)
- SA Health Code of Fair Information Practice (2006)
- SA Health Research Governance Policy (2013)

5. STREAMLINED (SINGLE) ETHICAL REVIEW

SA Health promotes efficiency in the ethical and scientific review of research projects being undertaken across the South Australian public health system, providing such review is sufficiently rigorous, is in accordance with the risk level of the project, and is conducted with reference to the *National Statement* and other relevant guidelines.

Streamlined approaches to the ethical and scientific review of research are supported by the NHMRC in the *National Statement*, and more recently, have been supported through national work to promote improved efficiency in the ethical and scientific review of clinical trials[1].

The two streamlined approaches supported by SA Health are based upon the mutual recognition of ethical review by other properly constituted Human Research Ethics Committees. These approaches are complementary, and provide two pathways for researchers conducting research within the South Australian public health system to more efficiently gain ethical approval:

[1] See *Clinically competitive: boosting the business of clinical trials in Australia (2011),* Commonwealth Government.

1) The SA Health Single Ethical Review Model – for all multi-centre research taking place within the South Australian public health system only.
2) National Mutual Acceptance – for multi-centre clinical trials taking place across participating Australian jurisdictions (public health organisations only).

5.1. SA HEALTH SINGLE ETHICAL REVIEW MODEL

This section describes the Single Review Model that applies to SA Health Institutions and affiliated HRECs to permit single (once only) review of multi-centre research projects taking place across the SA public health system.

1. Every research project which is to be conducted at a site under the jurisdiction of SA Health will be ethically and scientifically reviewed once only by a SA Health HREC (single review). The reviewing committee is designated the lead HREC.

2. All sites under the jurisdiction of SA Health that are participating in the proposed research will accept the review of the lead HREC without further ethical or scientific consideration.

3. The research ethics applicant (the Coordinating Principal Investigator or CPI) will select a lead HREC to undertake single review from a register of HRECs on the SA Health ethics website. Generally, this lead committee will be located at the institution of the CPI. The applicant will assume responsibility for submitting all required documentation in accordance with SA Health and local HREC requirements.

4. Lead HRECs must be appropriately constituted in accordance with the requirements of the NHMRC, and fulfil the requirements of the *National Statement on Ethical Conduct in Human Research* (section 5.2). Additionally they must have access to the required expertise to undertake a full scientific and ethical review of the type of research which is submitted.

5. Every research application must undergo a separate research governance review at each site where the research is to be conducted to permit consideration and approval of the research governance and management requirements at that site (a site specific assessment). This is distinct from the scientific and ethical review by the lead HREC (see section 10 of this document).

6. The lead HREC will be responsible for the full scientific and ethical review of the research application. Once completed, the lead HREC will be responsible for notifying the CPI of the outcome of the review. It is the CPIs responsibility to notify the outcome of this review to each of the other sites where the project is proposed to take place, via the Research Governance Officer associated with the site/s.

7. Under this model, HRECs will have the right to refuse to consider a multi-site application only under the following circumstances:
    i. The HREC Chairperson determines there is insufficient expertise on or available to the HREC to permit an adequate scientific and ethical review of the proposal; or
    ii. The HREC is not able to review the proposal in a timely manner (e.g. the meeting agenda for the next HREC meeting has reached capacity).

8. In these circumstances (7 [i] and [ii]), the HREC should notify the applicant as soon as practicable in order that they can then submit to another suitable SA Health HREC.

9. The South Australian Aboriginal Health Research Ethics Committee (AHREC) reviews all research applications where the focus is on a topic or disease/health burden identified as being of specific concern to Aboriginal and Torres Strait Islander people (based on 4.7.6 of the *National Statement,* 2007). In addition to a research application having been submitted to and reviewed by SA Health HREC, proposals are required to be submitted to the AHREC if: :
    - The experience of Aboriginal and Torres Strait Islander people is an explicit focus of all or part of the research; or
    - Data collection is explicitly directed at Aboriginal and Torres Strait Islander people; or
    - Where it is proposed to separately identify Aboriginal and Torres Strait Islander people in the results; or
    - The information has an impact on one or more Aboriginal and Torres Strait Islander communities; or
    - The geographic location of the research is such that a significant number of the population are likely to be of Aboriginal and Torres Strait Islander origin (based on 4.7.6 of the *National Statement,* 2007); or
    - Where terms such as ‘resilience’; ‘well-being’; ‘cultural safely’; ‘cultural health’; and ‘language and culture’ are used in the description and design of the project indicating that the project has important health implications; or
    - Aboriginal and Torres Strait Islander health funds are a source of funding.

10. The ethics applicant should provide the AHREC with a copy of the research application and the lead HRECs ethical determination on the project for consideration as soon as practicable. The AHREC will then provide their evaluation of the project to the lead HREC for consideration prior to providing feedback to the applicant. The AHREC will expedite their review where possible.

11. Research involving organisations external to SA Health may require ethical approval from that organisation and/or their HREC should it be required (in addition to the review conducted by the SA Health HREC).

12. Ethics applications predominantly involving access to a database or data registry held by a site or institution should be submitted to the HREC attached to the site or institution. If there are multiple sites involved, the applicant should only apply to one HREC.

13. Ethics applications involving multiple sites, including Women's and Children's Health Network (WCHN), and where the primary research participants are children and young people, or where the project involves access to paediatric data primarily held by WCHN, must be submitted to the WCHN HREC for review as the lead HREC.

14. Any multi-site or whole of state project where the primary data being used for the project is held centrally by SA Health (e.g. OACIS, ISAAC, SAMSS or Cancer Registry Data) must be submitted to the SA Health HREC for review as the lead HREC.

15. Projects that have been reviewed by a HREC outside the jurisdiction of SA Health may be reviewed again at the discretion of a SA Health HREC. However, if the research is being undertaken at multiple SA Health sites, these projects should only be reviewed once by an additional SA Health HREC to minimise further duplication of review.

16. If a research site is added to an existing project with lead HREC approval, SA Health requires that the CPI completes a Site Specific Assessment (SSA) form and submits this to the Research Governance Officer (RGO) responsible for that site along with a copy of the lead HREC's approval letter.

17. Each site shall have a person/s nominated to undertake the RGO role as required under this model on behalf of their site.

18. For quality assurance purposes, HRECs that have jurisdiction over the sites where the research is being undertaken (but who have not performed the lead ethical review) may choose to conduct a full ethical and scientific review of up to two submissions which have been previously reviewed by a lead SA Health HREC. These reviews will be provided to the lead HREC. This quality assurance review may happen concurrently with the initial review or subsequently. When it happens subsequent to the initial review, the original review outcome will still apply. This process will be reviewed 12 months after the implementation of this model.

<u>Project Commencement</u>

- A multi-site research project must not commence at a SA Health research site until the following has been completed:
    - The research protocol has received ethical approval from a lead SA Health HREC;
    - A satisfactory Site Specific Assessment has been submitted to the site where the research is to be conducted and;

- The project has been authorised to commence at the site (see Section 11).

Please see Appendix 1 for a diagrammatic overview of this model.

5.2. NATIONAL MUTUAL ACCEPTANCE

SA Health has signed a Memorandum of Understanding to support a national system of streamlined ethical review of clinical trials across participating public health organisations (National Mutual Acceptance).

Under this system, a NHMRC certified HREC provides the single ethical and scientific review of a multi-centre clinical trial application. Once a decision to approve the ethics protocol is made, this decision is then accepted by all participating jurisdictions without the requirement for further ethical and scientific review.

The single ethical and scientific review exists separately from any local jurisdictional research governance requirements that may exist, including site specific assessments.

In South Australia, Phase 0 and Phase I clinical trials (exploratory and first time in human studies) are currently exempt from single ethical review within the South Australian public health system, and will require ethical and scientific review by each participating SA public health organisation through their associated HREC.

Clinical trials involving South Australian Aboriginal and Torres Strait Islander participants will also need to be reviewed by the Aboriginal Human Research Ethics Committee (AHREC) in addition to a Certified HREC.

For the South Australian public health system, each of the following public health system HRECs has been certified to undertake the single review of clinical trials under the national system:

- Womens and Childrens Health Network Human Research Ethics Committee: Phases I – IV Clinical Trials
- Southern Adelaide Clinical Human Research Ethics Committee: Phase II, III and IV Clinical Trials
- Royal Adelaide Hospital Human Research Ethics Committee: Phase I – IV Clinical Trials
- Human Research Ethics Committee (TQEH/LMH/MH): Phases I – IV Clinical Trials

Procedures for SA Health HRECs acting as the 'lead' HREC

1. South Australian clinical trial researchers who wish to undertake new clinical trials within the South Australian public health system, and where no prior ethical and scientific review has been undertaken, should identify an appropriate HREC to apply to for review in South Australia (the 'lead' HREC).

2. It is a requirement that the Coordinating Principal Investigator submits their ethics protocol to the HREC affiliated with their employing public health organisation, where possible.

3. The Coordinating Principal Investigator must complete the ethics application using the National Ethics Application Form (NEAF), via the Online Forms portal.

4. The lead HREC should consider the ethics protocol in accordance with their standard operating procedures, and usual committee processes.

5. A timeframe of 60 calendar days (the 60 day clock) will apply to the ethical and scientific review of clinical trial protocols.

6. Once the review of the protocol is complete, the lead HREC will notify the Coordinating Principal Investigator of the outcome of the ethical and scientific review.

7. The Coordinating Principal Investigator will be responsible for communicating the outcomes of the ethical and scientific review to all participating research sites.

8. Where a protocol is not approved, the Coordinating Principal Investigator may resubmit the protocol to the lead HREC, providing the grounds for non-approval are resolved satisfactorily.

9. The lead HREC will be responsible for reviewing any amendments to the protocol that are submitted during the life of the trial. In all cases, the Coordinating Principal Investigator is responsible for notifying all participating sites of the outcomes of the review of such amendments.

10. The lead HREC will be responsible for considering safety information that is submitted during the life of the trial, and making an ethical and scientific determination of the significance of this information for the conduct of the trial. This may include serious adverse event (SAE) reports, data and safety monitoring board reports, and other sponsor initiated documents.

11. The lead HREC will provide advice to the Coordinating Principal Investigator as to whether this safety information impacts the ethical acceptability of the trial. The Coordinating Principal Investigator is responsible for notifying all participating sites and other relevant parties

of any decisions made by the lead HREC concerning safety related issues.

Clinical Trial Commencement

A multi-site clinical trial submitted through National Mutual Acceptance must not commence at a SA Health research site until the following has been completed:

1. The research protocol has received ethical approval from a NHMRC certified lead HREC;
2. A satisfactory Site Specific Assessment has been submitted at the site where the research is to be conducted; and
3. The project has been authorised to commence at the site (see Section 11).

6. NEAF REQUIREMENTS

The National Ethics Application Form (NEAF) has been developed by the National Health and Medical Research Council as a standardised human research ethics application form that may be accepted by Australian research ethics committees. The NEAF is available on Online Forms or from the NEAF website.

SA Health supports the use of the NEAF where possible, and the following guidelines should be followed.

SA Single Review Model and NEAF

For multi-centre research proposals taking place within the SA public health system only, SA Health encourages HRECs to accept the NEAF. Ethics applicants may discuss alternative application forms with the reviewing HREC.

National Mutual Acceptance

The NEAF is a requirement for all research ethics proposals submitted through the National Mutual Acceptance system.

Single Site Research

For single-site research only, the HREC may choose to accept proposals using a locally developed ethics application form or the NEAF.

7. ETHICS APPLICATION SUBMISSION

The use of Online Forms is required for ethics applications that will be submitted to a SA public health system HREC using the NEAF. Online Forms uses a licensed version of the NEAF, and enables ethics applicants to create both ethics and site specific applications for submission to SA public health system HRECs and institutions. The use of Online Forms for the submission

of NEAF applications should be clearly communicated by SA public health system HRECs to prospective ethics applicants.

For institutions hosting a HREC, they are responsible for ensuring submission requirements are readily available and accessible, e.g. on a local HREC web page, and maintained as required.

Generally, electronic submission of ethics applications is preferable as it provides flexibility in document management and storage; however, each public health system HREC is responsible for developing submission guidelines that meet their individual needs.

The ethics applicant is responsible for submitting all required documents to the HREC in accordance with the submission requirements.

7.1 Low and Negligible Risk Research

The *National Statement* enables HRECs to adopt processes for expediting the review of low risk projects. Low risk projects are those where the 'only foreseeable risk is one of discomfort', while negligible risk projects include those which may only involve 'inconvenience' to research participants[2]. Projects that are deemed to be of negligible risk may be exempt from ethical review.

It is a requirement that HRECs under the jurisdiction of SA Health have clear and documented processes for expediting the review of low risk project applications.

To facilitate the efficient review of research applications deemed to be low risk, SA Health has developed a Low and Negligible Risk (LNR) Ethics Application Form and Site Specific Assessment Form that may be used by South Australian public health system HRECs to support the submission and review of these applications. These forms are available for researchers on the Online Forms site.

The determination as to whether a project qualifies as low or negligible risk must be made by the reviewing HREC. Interventional studies including clinical trials generally should *not* be considered for expedited review as they are not typically 'low risk', and nor should projects involving research on sensitive personal or cultural issues or involving 'at risk' individuals or groups.

Ethics applicants should contact their local HREC office to discuss the proposed research and identify whether the project may be submitted for ethical review through the LNR submission process.

[2] See *National Statement*, p16 and section 5.1.18 to 5.1.23.

8. BENCHMARKS FOR REVIEW: THE 60 DAY CLOCK

SA Health adopts a benchmark of 60 calendar days (60 day clock) for full scientific and ethical review of research proposals. This clock commences upon receipt of a valid (complete) research ethics application. While Site Specific Assessments should be reviewed efficiently, the 60 day clock does not apply to these applications.

Should the ethics application be incomplete, the CPI will be requested to resubmit the application and supply any additional information required by the HREC. The clock is effectively stopped if the HREC requests further information to make a decision about the research ethics application.

It should be noted that the 60 day clock is a measure of performance only. Should the review period exceed 60 days, the CPI is not entitled to any remedies, such as the return of any ethics review fees that may be charged by the HREC.

9. STANDARD OPERATING PROCEDURES

SA public health system HRECs are expected to develop and publish their own standard operating procedures (SOPs) that describe how their HREC will function.

The SOPs must be made available to all committee members and ethics applicants, and should be published on the local research ethics website. These procedures should encompass all facets of the operation of the ethics committee, and be maintained and updated as necessary. All SOPs developed must be consistent with the broader policy framework of SA Health.

10. HREC COMPLAINTS AND APPEALS PROCESS

10.1 Background

Section 5.1(4) of the *National Statement* states that Institutions need to establish processes to handle complaints concerning research. This process specifically outlines a process for managing complaints made by ethics applicants for decisions made by a SA public health system Human Research Ethics Committee (HREC).

10.2 Appeals regarding HREC decisions

Where a SA public health system HREC rejects a research proposal outright on ethical grounds, makes an unfavourable decision about a component of the research proposal, or fails to reach a decision about the ethics of a research proposal, the investigator has the following rights:

a) Where a proposal has been rejected, the investigator may submit a new application to the HREC, taking due account of the HREC's concerns. The revised application will be processed and reviewed in accordance with the HREC's usual processes; or

b) Where (a) does not apply, the investigator may lodge a written appeal with the HREC Chairperson specifying the grounds of the appeal. The Chairperson will investigate the appeal, and recommend to the HREC the appropriate course of action within 4 weeks from the date of the appeal being lodged. The HREC will notify the appellant of the course of action and determination in a timely manner.

10.3 Appeal to the Chief Executive Officer / delegate

Following an appeal under section 1b, if the appellant considers that the HREC has not followed due process or remains unsatisfied with the decision, they may choose to lodge an appeal with the Chief Executive Officer / delegate responsible for the HREC.

The following process will be followed:

a) The Chairperson will provide the Chief Executive Officer / delegate with all relevant material, including:
    - Details of the appeal;
    - Material reviewed by the HREC; and
    - The outcome/decision of the ethical review process.

b) The Chief Executive Officer / delegate will determine if further investigation of the appeal is necessary. If so, a panel will be established to consider the appeal.
   The panel will include the following members:
    a. The Chief Executive Officer / delegate;
    b. Two nominees of the Chief Executive Officer / delegate (not members of the HREC);
    c. At least one nominee with relevant expertise in human research ethics; and
    d. Expert(s) in a discipline of research related to the project under consideration.

c) The panel will allow the HREC and the appellant the opportunity to make submissions.

d) The Chief Executive Officer / delegate will notify the HREC and the appellant of the outcome of the investigation. The possible outcomes include:
    a. The appeal is dismissed; or
    b. The appeal is upheld and the panel makes recommendation to resolve the issues based on the findings of the panel. The panel does not have the authority to approve an ethics application, but may choose to refer an ethics application to an independent ethics committee for re-review.

If the panel or Chief Executive Officer / delegate requests that a second ethical review is required as a recommendation of the investigation, an

alternative SA public health system HREC (where possible) with suitable expertise and no prior involvement in the matter will be invited to undertake this review.

The panel or Chief Executive Officer / delegate cannot reverse the final determination of any HREC.

10. SITE SPECIFIC ASSESSMENT

To support the effective management of research governance across public health system institutions, and the streamlined approaches to ethical review outlined in section 5, a Site Specific Assessment (SSA) process is now required as a standardised research governance requirement across the SA public health system.

The SSA process is designed to enable an Institution to consider whether there are sufficient resources to undertake the project at their Institution, and whether all insurance, legal, financial and risk management requirements are met. A SSA form must be submitted for both single and multi-site research being undertaken at a SA public health system Institution.

The RGO associated with the Institution will have responsibility for assessing the completed SSA form. Following endorsement of the SSA form by the RGO, the project should be submitted for authorisation (see section 11).

Further details about SSA requirements can be found in the *SA Health Research Governance Policy*.

11. PROJECT AUTHORISATION

Authorisation of a research project is the final approval granted by the site or Institution to permit the CPI to commence the research. A decision to authorise a project may occur once the research protocol has been approved by the reviewing HREC, and once the RGO has assessed and endorsed the SSA. The responsibility for authorising the project to commence falls to the Chief Executive Officer / Executive Director / General Manager (or delegate) of the Institution.

To enable a decision to be made concerning authorisation, the responsible RGO should supply copies of the HREC approval letter, endorsed SSA form, and any other relevant documentation to the Chief Executive Officer / Executive Director / General Manager (or delegate) of the site or institution, for consideration.

Once the decision concerning authorisation has been made, the RGO is responsible for notifying the Principal Investigator of the outcomes of the SSA review process, including whether project authorisation has been granted.

12. CLINICAL TRIAL RESEARCH AGREEMENTS

SA Health endorses the use of the following standard clinical trial research agreements developed by Medicines Australia:

1) Standard Clinical Trial Research Agreement for Commercially Sponsored Clinical Trials
2) Standard Clinical Trial Research Agreement for Contract Research Organisations
3) Standard Clinical Trial Research Agreement for Collaborative Research Group (CRG) Studies
4) Standard Clinical Trial Research Agreement for Phase IV Clinical Trials.

Please refer to the associated Guideline for further information regarding the use of these agreements, available on the SA Health website.

13. USE OF APPROVED AND UNAPPROVED MEDICINES AND MEDICAL DEVICES

Research that involves the use of approved or unapproved medicines, medical devices, blood, tissues and chemicals must be compliant with the legislation, regulations and guidelines of the Therapeutic Goods Administration (TGA).

Use of medicines or medical devices within the context of a research project does not guarantee their use beyond the scope of the project.

14. CLINICAL RESEARCH TRIALS CONDUCTED UNDER THE CTN OR CTX SCHEMES

The TGA permits the use of unregistered or unapproved medicines or medical devices for the purposes of examining their safety and efficacy within the context of a monitored clinical research trial under Sections 18 and 19 of the *Therapeutic Goods Act* (1989). This is done through either the Clinical Trial Notification (CTN) or Clinical Trial Exemption (CTX) schemes.

For the CTN scheme, the reviewing HREC has sole responsibility for reviewing all the data relating to the trial, such as safety data pertaining to the investigative medicine or device. It also has responsibility for making a determination about the scientific and ethical merit of the trial.

For the CTX scheme, the TGA has responsibility for reviewing relevant data including preclinical data pertaining to the investigative medicine or device. The TGA's review of this data is taken into account by the reviewing HREC, who will then make a determination about the scientific and ethical merit of the trial as a whole.

Under both schemes, the reviewing HREC has the authority to approve (or reject) the trial based on the scientific and ethical merit of the trial.

Ethics applications for clinical trials being conducted under the CTN or CTX schemes must be accompanied by the appropriate signed notification forms. Applicants are responsible for ensuring the forms are completed in full prior to submission.

Once the application has been reviewed and approved by the lead HREC, the CTN/CTX form should be signed by the HREC Chairperson and then forwarded to the RGO with a copy of the HREC approval letter. Once the SSA has been reviewed and approved by the RGO, the CTN/CTX form should be forwarded for signature by the Chief Executive Officer / Executive Director / General Manger (or delegate) of the Institution once the project has been authorised.

15. REGULATION OF GENE TECHNOLOGIES AND RELATED THERAPIES

Health and medical researchers in South Australia are legally required to comply with *the Gene Technology Act* (2001) and the *Gene Technology Regulations* (2002) for research involving Genetically Modified Organisms.

SA Health facilities in which researchers are using gene technology must be accredited and maintain, or have an established link with, a properly constituted Institutional Biosafety Committee (IBC) within a collaborating organisation.

Any formal review provided by an IBC should be given to the lead HREC by the applicant upon submission of a new application for review.

All research protocols involving gene therapy and related gene technologies including xenotransplantation must be submitted to a HREC for review.

Research involving embryos must comply with the *Prohibition of Human Cloning for Reproduction* and the *Regulation of Human Embryos Research Amendment Act* (2006), and the *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research* (NHMRC, 2007).

16. IONISING RADIATION

All research involving any form of radiation must comply with relevant National and State legislation, organisational policies and procedures, and codes and standards of practice provided by the NHMRC and the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA).

SA Health HRECs assessing research proposals involving exposure of participants to ionising radiation must be provided with a written report from an accredited medical physicist.

In South Australia, the Environment Protection Authority (EPA) has responsibility for administering the *Environmental Protection Act* (1993) and *Radiation Protection and Control Act* (1982). The Radiation Protection

Branch of the EPA must be notified of all research involving exposure of research participants to ionising radiation. This form should be used for notification purposes.

17. SA HEALTH DATA

For research ethics applications that require access to data or confidential information held by SA Health, it is a requirement that access be granted on the basis of ethical approval from an appropriate SA Health HREC and project authorisation by the appropriate Institution/s, following submission of a complete and satisfactory SSA.

The CPI should contact their local HREC first to determine whether it is an appropriate committee to review their application. As a general rule, if an ethics application seeks access to a database or data registry, the application should be submitted to the HREC associated with the Institution where the data is being held.

Any multi-site or whole of state project where the primary data being used for the project is held centrally by SA Health (e.g. OACIS, ISAAC, Cancer Registry Data) must be submitted to the SA Health HREC for ethical review as the lead HREC.

The data custodian reserves the right to refuse access to the data if the SSA is unsatisfactory or the application otherwise does not meet the requirements of SA Health including information privacy and data security requirements.

18. ADVERSE EVENTS REPORTING

Upon ethical approval of a research application, the lead HREC shall require notification of anything which might warrant review of the ethical approval of the project, including serious and unexpected adverse events (SAEs). If the adverse event applies to participants at a specific site, the HREC associated with this site should be notified. If it applies to all sites equally, then reports should be provided to each of the associated HRECs. The Coordinating Principal Investigator is responsible for reporting adverse events.

For multi-centre clinical trials, the reporting of serious adverse events or serious adverse reactions should follow the requirements of the NHMRC AHEC Position Statement, *"Monitoring and reporting of safety for clinical trials involving therapeutic products" (May 2009).*

This document sets out the monitoring and reporting requirements, including reporting of adverse events, for clinical trials. A HREC may impose additional reporting requirements reflecting the degree of risk of the research to participants.

The HREC SOP's should outline the specific adverse event reporting requirements of the local HREC.

19. COMPLAINTS PROCESS

Each SA Health HREC is responsible for maintaining an appropriate complaints process for health and medical research projects that undergo ethics review and/or ethics approval that should consider:

- Complaints made by research participants and/or research (or other) staff concerning the conduct of approved research being undertaken at an Institution;
- Complaints made by ethics applicants regarding the ethical review process and/or outcome.

The process for dealing with such complaints should be documented in the HREC SOPs, and be published on the local HREC website.

Sites must also have policies and/or procedures for managing complaints related to health and medical research projects in the event the complaint cannot be resolved by the HREC, or falls outside the scope of the HREC responsibilities.

20. SUSPENSION OR WITHDRAWAL OF ETHICS APPROVAL OR SITE SPECIFIC (RESEARCH GOVERNANCE) APPROVAL

The Institution reserves the right to suspend activity on an approved research project at any time should the CPI fail to observe the HRECs conditions of approval, or any conditions of research governance (site specific assessment) approval. The Institution is responsible for initiating this process. Grounds for suspending the activity on a project may include:

- Failure to provide regular (at least annual) reports of progress;
- The reporting of a serious adverse event that poses a risk to other participants involved in the research at the local Institution;
- A complaint issued by a research participant and/or staff member that has implications for the ethical conduct of the project.

It is recommended that each SA public health system HREC has documented processes that outline how breaches of ethical approval will be managed. These processes should be included in the HREC Standard Operating Procedures, and provide a consistent and transparent approach to these issues.

Where there is a failure to comply with any conditions that concern SSA approval and project authorisation, the RGO associated with the Institution should establish clear processes to manage these breaches.

All matters concerning possible breaches of research ethics or governance approval should be dealt with in a timely manner, and any decision to either review of suspend / withdraw approval should be communicated clearly to all key parties involved with the conduct of the project (e.g. the Principal Investigator, research staff, and associated institutions and HRECs).

21. DATA STORAGE, RETENTION AND DISPOSAL REQUIREMENTS

The information privacy provisions outlined in SA Health's *Code of Fair Information Practice* (2006) must be observed by all researchers undertaking approved research on sites and facilities governed by SA Health. This document outlines the requirements and standards pertaining to the collection, use, storage and disclosure of personal information.

Access to data and information collected during the conduct of research should be limited to those who are directly involved in the conduct of the project, e.g. the CPI, PI and the research team. Appropriate storage of research data must also be considered, and mechanisms such as use of locked filing cabinets or password protected computers may be warranted.

Provisions should be also made for the storage and disposal of records and data in the event that a researcher leaves the institution.

SA Health requires all institutions under its jurisdiction to dispose of research materials in accordance with the requirements outlined in the Australian Code[3]. These requirements are as follows:

> In general, the minimum recommended period for retention of research data is 5 years from the date of publication. However, in any particular case, the period for which data should be retained should be determined by the specific type of research. For example:
> - For short term research projects, that are for assessment purposes only (e.g. research projects completed by students), retention of research data for 12 months after completion of the project may be sufficient.
> - For clinical trials, data should be retained for a minimum of 15 years for adult studies or 25 years for paediatric studies after formal notification is received that all study procedures are completed and the study is closed.
> - For areas such as gene therapy, research data must be retained permanently (e.g. patient records).
> - If the work has community or heritage value, research data should be kept permanently, preferably within a national collection.

Some agencies may also need to consider specific organisational requirements around data disposal, e.g. the requirements outlined in the *SA Public Hospitals Retention Disposal Schedule (2000).*

Those involved in the conduct of sponsored clinical trials should also be aware of the TGA requirements around data retention[4].

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[3] Please refer to Section 2.1 of the Code.

[4] Please refer to *Note for Guidance on Good Clinical Practice (Annotated with TGA Comments),* page 25, http://www.tga.gov.au/pdf/euguide/ich13595.pdf.

For legal reasons, SA public health system institutions may wish to consider indefinite archiving periods for some types of research, and legal advice should be sought if further clarity is required

22. RESEARCH MONITORING

Monitoring of approved research is an important component of effective research governance. Under the *National Statement* (chapter 5.5*)*, it is a responsibility of the Institution hosting the research to monitor the conduct of the research.

Across the SA public health system, this function should be undertaken by the HREC and/or RGO that has provided the ethical and/or research governance approval for the project. Institutions must establish processes whereby approved research is effectively monitored.

Research monitoring can capture a range of activities, including the following:

- Review of annual reports from researchers;
- Review of reports from independent agencies (e.g. data and safety monitoring boards);
- Review of adverse event reports;
- Audits of research records, e.g. consent documentation;
- Interviews or review of written feedback from research participants[5].

The level of monitoring that is undertaken should correspond to the risk associated with the project. The CPI has a significant responsibility to monitor the research over the course of the project, and advise the Institution, via the HREC or RGO, of matters which may impact the ethical and scientific acceptability of the project, or site (research governance) acceptance of the project.

23. ELECTRONIC MANAGEMENT OF APPLICATIONS

SA Health mandates the use of Infonetica's AU RED (Australian Research Ethics Database) for the management of all research ethics and research governance applications to HRECs and institutions across SA Health.

Each of the SA public health system HRECs and RGO's have a licence to access AU RED as the recommended research ethics and governance management system. Training and maintenance of the AU RED platform will be coordinated centrally by the Office for Research Development. In the event of staffing changes in the ethics offices or Institutions, the Office for Research Development should be informed to arrange for suitable training to occur.

A record of each research application and associated site specific assessment application received by a South Australian public health system

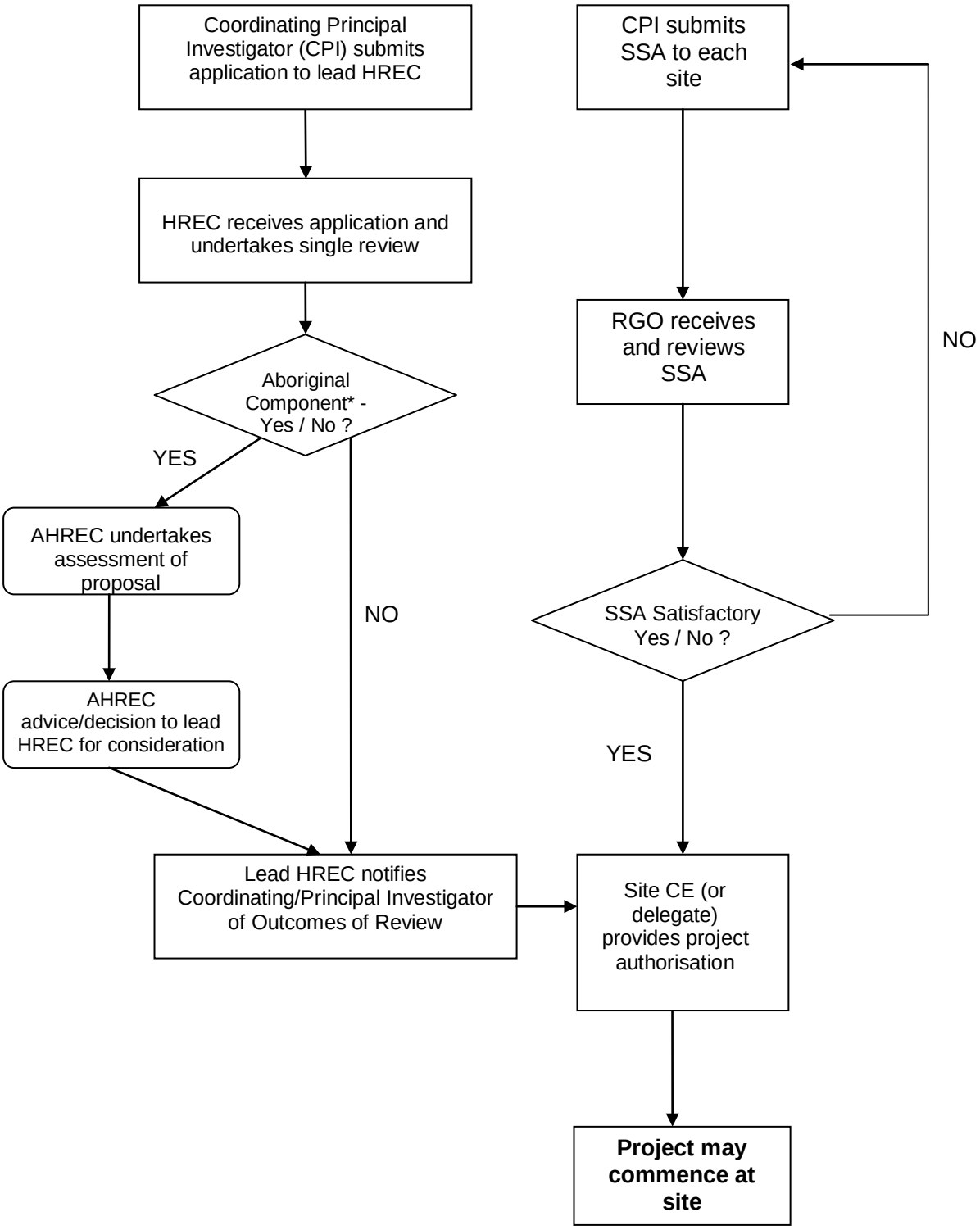
[5] See *National Statement*, p91.

HREC and Institution should be maintained within the AU RED database, including decisions relating to these applications.

23.1 Use of the AU RED clock

AU RED has an in-built clock function that will enable each HREC to monitor the time taken to review research ethics applications. The clock should only commence upon receipt of a valid research ethics application. The clock is effectively stopped when the HREC is awaiting a response or clarification from the CPI regarding the ethics application.

Appendix 1: Flowchart of SA Model for Single Ethical Review



* Please refer to section 5 (9) of this policy for specific considerations.