



STANDARD OPERATING PROCEDURE, JUNE 2024, V10

Research Ethics
Committee



TABLE OF CONTENTS

STANDARD OPERATING PROCEDURES AND GUIDELINES FOR THE ETHICS EVALUATION OF CLINICAL TRIALS	4
DEFINITIONS AND INTERPRETATIONS	4
INTRODUCING SAMAREC	5
1. LEGISLATIVE FRAMEWORK.....	5
(IRB: 0001 1624).....	7
2. COMPOSITION OF SAMAREC.....	8
a. CONTACT DETAILS.....	8
b. PROTOCOL REVIEW FEES.....	9
3. SUBMISSION OF RESEARCH PROTOCOL REVIEWS.....	10
4. COVERING LETTER.....	11
5. DECLARATIONS	11
6. CURRICULUM VITAE.....	11
7. MALPRACTICE INSURANCE	12
8. ABBREVIATIONS	12
9. PUBLISHING OF RESULTS	12
10. LANGUAGE	13
11. SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY (SAHPRA) APPROVAL.....	13
12. MAJOR AND MINOR AMENDMENTS	13
13. PRESENTATIONS.....	14
14. REPORTING OF PROTOCOL DEVIATIONS AND VIOLATIONS	14
15. REPORTING OF ADVERSE REACTIONS AND EVENTS.....	14
16. REPORTS, POST-APPROVAL, AUDITING, SUSPENSION, NON-COMPLIANCE, PASSIVE AND ACTIVE MONITORING	15
17. ANNUAL, CONTINUING REVIEW AND RECERTIFICATION RENEWAL	17
18. REPORTING PROPOSED CHANGES IN A RESEARCH PROTOCOL.....	18
19. EXPEDITED REVIEW PROCESS	18
20. RAPID REVIEW PROCESS.....	18
21. SITE/STUDY CLOSURE PROCESS.....	19
22. REPORTING OF ALLEGATIONS OF MISCONDUCT/NON-COMPLIANT AND COMPLAINT PROCEDURES.....	19
23. WHISTLE BLOWERS	19
24. APPEALS AGAINST DECISIONS	19
25. EDUCATION.....	19
26. RECRUITMENT.....	20
27. MATERIAL TRANSFER AGREEMENT (MTAS)	20
28. BIOLOGICAL MATERIAL.....	20
29. DATA BASES, REGISTRIES AND REPOSITORIES.....	20



30.	NON-COMPLIANCE CONSEQUENCES, SUSPENDED OR TERMINATED PROJECTS	20
31.	THE SAMAREC REVIEW PROCESS.....	21
32.	REVIEW OF THE PROSPECTIVE PARTICIPANT POPULATION	21
33.	REVIEW OF METHOD(S) OF PARTICIPANT RECRUITMENT.....	21
34.	REVIEW OF EXPERIMENTAL DESIGN	22
35.	REVIEW OF THE POTENTIAL RISKS	22
36.	REVIEW OF POTENTIAL BENEFITS	23
37.	RISK-BENEFIT ANALYSIS	23
38.	REVIEW OF PARTICIPANT COMPENSATION AND ASSESSMENT OF FINANCIAL ARRANGMENTS	24
39.	REVIEW OF MEASURES TO PROTECT PERSONAL INFORMATION	24
40.	REVIEW OF THE PATIENT/PARTICIPANT INFORMATION AND INFORMED CONSENT DOCUMENT (PID) PROCESS INCLUDING MINORS AND VULNERABLE PATIENTS	24
41.	PRIVACY AND CONFIDENTIALITY REGARDING PARTICIPANTS AND THEIR HEALTH CARE INFORMATION FOR APPLICANTS	26
42.	E-CONSENT.....	27
43.	REVIEW OF INVESTIGATORS	27
44.	REVIEW OF MONITORING REQUIREMENTS.....	28
45.	REVIEW OF INJURY COMPENSATION.....	28
46.	CONFLICT OF INTEREST	28
47.	ACCESS TO AND PROTECTION OF INFORMATION/MAINTENANCE OF RECORDS	29
48.	RECIPROCAL REVIEW PROCESS.....	29
49.	SAMAREC Resolution	30
50.	DEVELOPMENT AND MANAGEMENT (REVIEW, MONITOR AND APPROVAL) OF SAMAREC SOP.....	30
51.	ANNEXURES	30



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9	Updated and published for implementation	October 2023
	Administrative changes	March 2024
10	Definition amendment	June 2024

STANDARD OPERATING PROCEDURES AND GUIDELINES FOR THE ETHICS EVALUATION OF CLINICAL TRIALS

DEFINITIONS AND INTERPRETATIONS

In this document, unless the contents otherwise require:

1. **Doctor** refers to a medical practitioner (or dentist, when appropriate), as defined in terms of the Health Professions Act, no. 56 of 1974 (as amended),
2. **Study doctor** refers to a doctor (or dentist, when appropriate), participating in the clinical trial / study. The words **study investigator, investigator, sub-investigator, co-investigator, trialist or researcher** may be used interchangeably, as long as the person is a clinician, where applicable. Whichever term is used, it must be used consistently throughout the documents.
3. **Principal Investigator** is a person responsible for the conduct of the clinical trial at a trial site.
4. **Co-Principal Investigator** refers to a qualified non-clinician scientist or equivalent qualified and experienced person who can provide trial oversight management, and who is jointly and severally liable for the clinical trial.
5. **Associate Investigator** refers to a member of the health care team involved for specific investigations which are required for the conduct of the clinical trial / study. This will be in accordance with their relevant field(s) of expertise and training e.g., ophthalmologist or psychologist responsible for specific aspects but not taking clinical responsibility as sub investigators for trial participants.
6. **Sub-Investigator** refers to any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions.
7. A **Clinical Trial** is a prospective biomedical or behavioral research study of human participants that is designed to answer specific questions about biomedical or behavioural interventions (vaccines, drugs, treatments, devices, or new ways of using known drugs, treatments, or devices).
8. **Study Staff** collectively refers to the investigators, study coordinators, study nurses, pharmacists, raters, and any other people rendering support to the investigator.
9. **Study site** is the location(s) where trial-related activities are actually conducted.
10. **Participant** means the person participating in the clinical trial / study and/or receiving treatment, including receiving blood or blood products, or using a health facility or establishment, as a result of participation in the clinical trial / study. The words **research participant or participant** may be used interchangeably, where applicable.
11. **Patient** is defined as a participant with a clinical condition.



12. **Research** means the creation, preservation, accumulation, and improvement of knowledge by means of scientific investigations and methods in the field of the medical and related sciences as well as those sciences the application of which is important for the promotion of health or the combating of disease, and includes the acquisition, development and transfer of expertise and technology. The word **researcher** shall have a corresponding meaning and the term experiment or clinical trial may be used interchangeably with the word **research**, when applicable.
13. **Clinical Research** is usually conducted with patients in a medical setting (e.g., hospital, clinical or private consulting rooms) to obtain information on the natural history or pathogenesis of a condition that could assist with improving strategies for diagnosis, treatment, or prevention of disease.
 - Any reference to the singular includes the plural and vice versa.
 - Any reference to natural persons includes legal persons and vice versa.
 - Any reference to a gender includes the other gender.
 - The clause headings in the Standard Operating Procedures have been inserted for convenience only and shall not be taken into account in interpreting this SOP.
14. **'Physician'** refers to a medical practitioner registered as a specialist in internal medicine, and this should not be used as an alternative term when referring to a family doctor/ general practitioner.
15. **Amendments** – changes in the PID and Protocol to be forwarded to SAMAREC in the most recently approved versions of SAMAREC . All changes must be indicated with track changes.
16. **'Witness'** is someone who witnesses the signing by the participant and not the consent procedure. However, when the participant is illiterate the meaning of 'witness' changes and it means a person who witnesses the consent procedure.

INTRODUCING SAMAREC

1. LEGISLATIVE FRAMEWORK

National Health Act

The South African Medical Association Research Ethics Committee (SAMAREC) was established by the South African Medical Association (SAMA) in 1992 to evaluate the ethics of research protocols developed for clinical trials to be conducted in the private healthcare sector. In terms of national and international regulatory requirements, all health research involving human participants must undergo an independent ethics review. The National Health Act (NHA), 61 of 2003, as amended, provides for the establishment of a National Health Research Ethics Council (NHREC) with which all research ethics committees are required to be registered. SAMAREC is registered on the Department of Health (DOH) National Research Ethics Council database.

The main responsibility of SAMAREC is to ensure the protection and respect of the rights, safety and well-being of participants involved in clinical trials and to provide assurance to the public of that protection, *inter alia*, by reviewing, approving, and providing comment on clinical trial protocols, the suitability of investigator(s), facilities, methods, and procedures used to obtain informed consent. The Bill of Rights which is entrenched in the Constitution of South Africa provides that everyone has the right not to be subjected to medical or scientific experiments/research without their informed consent.

In terms of the NHA "clinical trials" means a systematic study, involving human participants that aims to answer



specific questions about the safety or efficacy of a medicine or method of treatment.

Research can be broadly classified as therapeutic and non-therapeutic. Therapeutic research is a clinical investigation designed to determine the efficacy and safety of a therapeutic or diagnostic method. The interventions are not applied solely to enhance the well-being of the individual participant.

The objective of therapeutic research is to increase general knowledge (i.e., test a hypothesis and draw conclusions) and at the same time provide the patient with a needed health benefit. Accordingly, the duties of the study doctors are to take into consideration the fact that the patient is also a research participant.

In contrast to therapeutic research, non-therapeutic research is an investigation that has no intent of producing a diagnostic, preventive, or therapeutic benefit to the research participant, who is usually healthy and is not seeking nor expecting a health benefit from the research.

In the execution of its responsibilities in evaluating the ethics of research protocols, SAMAREC is guided by the relevant South African law, research and ethics guidelines, professional standards, international standards and guidelines and codes of practice.

The NHA provides that health research ethics committees (RECs) must be established by every institution, health agency and health establishment at which health research is conducted, or they must have access to a health research ethics committee, which is registered with the NHREC.

“The NHA further provides that a health research ethics committee must-

- (a) review research proposals and protocols in order to ensure that research conducted by the relevant institution, agency or establishment will promote health, contribute to the prevention of communicable or non-communicable diseases or disability, or result in cures for communicable or non-communicable; and*
- (b) grant approval for research by the relevant institution, agency, or establishment in instances where research proposals and protocol meet the ethical standards of that health research ethics committee.”*

*The **NHREC** was established by the Minister of Health after consultation with the National Health Council. The Minister appoints as members of the NHREC not more than 15 persons nominated by interested parties at the invitation of the Minister by notice in the Government Gazette.*

In terms of the NHA the NHREC must: -

- (a) determine guidelines for the functioning of health RECs.*
- (b) register and audit health RECs.*
- (c) set norms and standards for conducting research on humans and animals, including norms and standards for conducting clinical trials.*
- (d) adjudicate complaints about the functioning of health RECs and hear any complaint by a researcher who believes that he or she has been discriminated against by a health REC.*
- (e) refer to the relevant statutory health professional council matters involving the violation or potential violation of an ethical or professional rule by a healthcare provider.*
- (f) institute such disciplinary action as may be prescribed against any person found to be in violation of any norms and standards, or guidelines, set for the conducting of research in terms of this Act.*
- (g) advise the national department and provincial departments on any ethical issues concerning research.”*

According to the Guidelines for Ethics in Health Research, published by the Department of Health, ethics review provides an objective appraisal of the research proposal as it affects the prospective participants and the general day to day functioning of the health system.

SAMAREC has been registered and audited in accordance with the NHA (61 of 2003). Registration number:



280808-016. Valid until 30 November 2023.

In March 2002, SAMAREC became a registered REC at the Department of Health and Human Services (DHHS) of the USA.

(IRB: 0001 1624)

In May 2002, Federal Wide Assurance was also obtained from the Office of Human Research Protection (Office of Human Research Protection-Group) of the USA.

(FWA: 0002 7240) Valid until **06 July 2028**.

American Food & Drug Administration (FDA) and International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), Guidelines for Good Clinical Practice
SAMAREC follows the standards adopted by the latest version of the FDA and ICH Guidelines for Good Clinical Practice; and conforms to the guidelines laid down by the World Medical Association, in particular, the latest version of the Declaration of Helsinki, the Belmont Report, the National Department of Health, the South African Health Products Regulatory Authority (SAHPRA) and other relevant statutory bodies involved in the healthcare sector.

A REC should consider the following issues when reviewing a proposal for a clinical study:

- the scientific relevance of the clinical study;
- the suitability of the investigator(s) for the proposed study in terms of his/her availability, qualifications, experience, supporting staff, and available facilities;
- the relevance of the study rationale and the appropriateness of the inclusion / exclusion criteria to the South African context;
- the suitability of the study application in relation to the objectives of the study, i.e., the potential for reaching sound conclusions with the smallest possible exposure to risk of participants, and the justification of predictable risks and **inconveniences** weighed against the anticipated benefits for the participants and/or others;
- the suitability of the study population, whether they constitute a vulnerable group, if so whether justified and whether sufficient measures to protect their interest are in place;
- that the number of participants to be recruited is adequate to demonstrate the predicted effect;
- the risk-benefit analysis takes full cognisance of benefits and harms beyond the life of the study itself, particularly in relation to chronic life-threatening conditions;
- if placebos are to be used, whether their use can be justified;
- that by their participation in a clinical study the participants are not denied timely access to medical personnel, investigations, equipment, or procedures;
- the means by which initial recruitment is to be conducted and by which full information is to be given and how informed consent is to be obtained;
- the adequacy and completeness of the written information to be given to the participants, their relatives, guardians and, if necessary, legal representatives. All written information for the participant and/or legal representative must be submitted in its final form;
- that the application allows the participants and/or their representatives adequate time to consider the patient information document before informed consent is sought;
- the content of any advertisements or public notices which will be used to recruit participants to a study;
- the study protects participants' rights to privacy and confidentiality according to the provisions of the Protection of Personal Information (POPI) Act, Act 4 of 2013;
- the provision of compensation/treatment in the case of injury or death of a participant if attributable to a clinical study, and the insurance or indemnity to cover the liability of the investigator and sponsor;
- the extent to which investigator(s) and participants are to be compensated for participation in the study;



- making specific recommendations regarding the continuation of treatments beyond the duration of the study, or mechanisms to ensure that participants' access to treatment are fairly protected and not unduly compromised;
- the demographic information available to assess whether the patient population is adequate to support the study;
- whether there is no cost to the participant, medical schemes, or insurance for trial specific procedures;
- whether the product will be made available to participants after the trial ends, and if so whether there is any cost to the participant to continue treatment post-trial;
- whether any restrictions will be placed on the publication of results by the investigators after completion of the trial;
- the adequacy of the statistical methods proposed to evaluate the data generated; and whether the study is advancing knowledge in the research field.

SAMAREC reviews health research involving human participants, prior to initiation of such research and focuses on the ethical implications relating to the clinical research. Ensuring protection of the rights and welfare of the participants is the Committee's primary concern. Based on the above-mentioned standards and guidelines, SAMAREC will advise and make suggestions to study doctors and applicants, when requested.

2. COMPOSITION OF SAMAREC

Research ethics committees must consist of members who collectively have the qualifications and experience to review and evaluate the science, health and legal aspects, and ethics of proposed research. Committees must be independent, multi-disciplinary, multi-sectorial and pluralistic. When a specific portfolio on the committee is required (e.g., legal member) a new member will be recruited by means of advertisements in the applicable field. Prospective members are then requested to present their credentials and then attend a formal meeting (while signing a confidentiality agreement). Should the specific member have the required expertise and have a definite interest in the committee they are requested to join the committee. The composition of SAMAREC complies with the prescriptions of the Department of Health Guidelines for Ethics in Health Research and consists of members as approved by the SAMA Board of Directors. Once elected, members will receive formal appointment letters signed by the current General Manager of SAMA (On behalf of the Board of Directors of SAMA). The Chairperson and Vice (Deputy)-Chairperson are elected by the current committee members based on their expertise and experience levels. The Vice (Deputy) Chairperson will assist the Chairperson and will act as Chairperson as necessary and also assist the Chairperson with responsibilities as required.

The current composition of SAMAREC is as per Annexure 5

- 2.1. The SAMAREC Composition will be updated as and when changes occur.
- 2.2. The Committee may request other individuals to assist in the review of complex issues outside the expertise of the members, but such individuals may not vote on matters requiring a decision to be taken. These individuals will also only be approached should they not have a conflict of interest in the study in question and will also be required to sign a confidentiality agreement. These individuals will be approached based on a referral basis.
- 2.3. *Curricula vitae* of the Committee members and external experts (if applicable) are available on request. These are kept by the Officer.

a. CONTACT DETAILS

The SAMAREC Officer (Lisa Reid) or SAMAREC Administrator (Michelle Snijder) may be contacted at:



Telephone : (012) 481 2082
Postal Address : P O Box 74789
Lynwood Ridge
0040
Physical Address : Castle Walk Office Park, Block F,
Nossob Street
Erasmuskloof
Ext.3 Pretoria
0183
E-mail : samarec@samedical.org

b. PROTOCOL REVIEW FEES

SAMAREC Submission and other relevant Fees for evaluation of protocols appears on Annexure 6 (hereto attached). All submissions must be submitted with the SAMAREC Application form. Once applications are received SAMA will send through an invoice for payment.

No refunds will be given should the protocol, once evaluated, not be approved. Administrative changes, report-back and adverse event reports will not be charged for.

SAMA reserves the right to retain approval letters until payment is received in full.

PROCEDURES AND ADMINISTRATIVE GUIDELINES

MEETINGS

- SAMAREC meets on the second Wednesday of each month unless circumstances require otherwise E.g., loadshedding, no quorum indicated prior to the meeting.
- Applications for consideration must be submitted via e-mail to the SAMAREC Officer via email samarec@samedical.org, Please request the latest Meeting Dates and Submission details – available in SOP Annexure 1. Kindly contact the SAMAREC Officer if you are unable to meet a submission deadline for alternative arrangements.

DECISIONAL ANALYSIS, PROTOCOL, AND INFORMED CONSENT REVIEW PROCESS

- A written response regarding decisions is usually forwarded to applicants within ten working days after the meeting.
- Sixty percent of the Committee constitutes a quorum.
- Confidentiality of the content of applications, the protocols, and the procedures of SAMAREC, is maintained as far as is reasonably possible.
- SAMAREC Officer will prepare the meeting packs as per the submission dates and submit to the Committee at least 10 days prior to meeting dates.
- Final Decisions are discussed during the SAMAREC Meetings via voting, discussion and noted accordingly in the meeting minutes.
- SAMAREC will always ensure the privacy and confidentiality of patients and participants is the priority of the study.
- Decisions will be finalized by with the approval of the entire Committee and feedback will be provided to applicants within ten working days of the SAMAREC Meeting.

(A list of the scheduled meetings for the current year is available in the SAMAREC SOP Annexures)



3. SUBMISSION OF RESEARCH PROTOCOL REVIEWS

All submissions to SAMAREC should be done electronically (via e-mail) to samarec@samedical.org

3.1. New applications

For new applications, the following documents - with dates and version numbers - relevant to the proposed study need to be submitted: -

- SAMAREC Application Form (Refer to Annexure 2)
- Covering letter (for rapid and expedited reviews, covering letter must detail the request. Motivation for rapid review must also clearly indicate the need for urgency). Please provide a numbered list of all documents submitted with the application.
- Protocol summary/synopsis
- Protocol
- Patient Information and Informed Consent Document (PID) (*pro forma* attached as Annexure 4). This document must be submitted in Word format.
- Investigator's Brochure
- Material Transfer Agreement (*pro forma* attached as Annexure 10)
- Questionnaires (if any)
- Copy of the Insurance Certificate
- SAPHRA approval or notification or letter of submission
- Proof of SANCTR registration
- Details and breakdown of financial arrangements with study doctors, and
- Information pertaining to patient recruitment e.g., advertisements, bulletins and information placed on the Internet. (Guidelines attached as Annexure 7)
- Justification for the use of a placebo
- *Curricula Vitae* of all study personnel according to the SAHPRA format (as a minimum format / requirement) copy of format attached as Annexure 3)
- Declarations by Trialists (Please refer to Annexures 8 for the declaration template)
- Proof of personal Malpractice Indemnity cover of study doctors, nurses, and pharmacists
- GCP certificates (SAMAREC recommends that site staff be trained in latest version of both ICH GCP and SA GCP)
- Dispensing License (if applicable)

Please ensure that submitted documentation includes the following information in footers "Protocol number/ Participant Information and Informed Consent Document, SAMAREC Version XX dated XXX." Furthermore, no product logos should be displayed on any documentation.

All documentation should be properly indexed, with the protocol number clearly visible on all the sections of each document. All relevant attachments with regard to the study staff **should be put together per person**, i.e., CV, Declaration, HPCSA / SANCTR Registration, Malpractice Insurance, GCP Certificate, Dispensing Licence etc. The manual and computer filing systems of the SAMAREC are based on the protocol number and not the name of the drug involved.

Submitting of additional site staff once approval obtained:

- Covering letter listing study staff must be presented with an indication of their submitted documents (example attached as Annexure 9)
- Relevant documentation as mentioned above.

3.2. Annual Renewal and 6-Monthly Progress Reports



For annual renewals, the following documents - with dates and version numbers - relevant to the proposed study need to be submitted:

- Covering Letter
- Progress Report

3.3. Site/Study Closure

For annual renewals, the following documents - with dates and version numbers - relevant to the proposed study need to be submitted:

- Covering Letter
- Site closure report

3.4. Additional Post Approval Notification

Additional post approval notifications may include resignation of site staff, additional site staff, additional translation of patient facing material, Development Safety and Update Report (DSUR), Investigational Medical Product Dossier (IMPD) etc. For additional post approval notifications, the following documents relevant to the proposed study need to be submitted:

- Covering Letter
- Relevant Report i.e., DSUR report

Documentation as per section 3.1

4. COVERING LETTER

The Covering Letter must be dated and contain the following details:

- A brief summary of the protocol
- Confirmation of the study sites
- The study doctor's assessment of any potential additional risks or discomforts to the participants
- Study staff must be listed with an indication of their submitted documents (example attached as Annexure 9)
- Details of documents submitted with dates and version numbers.

5. DECLARATIONS

Declarations by all study staff must reflect the name of the sponsoring company, protocol number and title, as well as the study staff's name and designation (*pro forma* attached as Annexure 8) Declarations must be properly completed and signed.

6. CURRICULUM VITAE

Although the *Curriculum Vitae* of all study personnel should be, as a minimum requirement, according to the SAHPRA format, the format shown in Annexure 3 would be preferred when submitting protocols to SAMAREC for evaluation.

The approval criteria for Principal Investigators are:

- must be a suitably qualified health care professional;
- must have participated in two completed trials as Sub-Investigator;



- must have proof of valid GCP training in the last 3 years; and
- The trial must be within the Principal Investigator's scope of practice.
- Note the Specialist Regulations of the HPCSA, states that:
"A medical practitioner or a dentist who holds registration as a specialist in terms of the Act, shall.
 - (a) in the case of a specialty, confine his or her practice to the specialty or related specialties in which he or she is registered;*
 - (b) in the case of a sub-specialty, confine his or her practice mainly to the sub-specialty in which he or she is registered."*

The approval criteria for Sub-Investigators are:

- must be suitably qualified health care professional such as a qualified medical doctor;
- must have proof of valid GCP training in the last 3 years or the intention to attend GCP training when required by the nature of the study/trial. Proof of completion thereof must be submitted before commencing the trial (same for PI).
- if not previously involved in a trial, they should work under the supervision of the Principal Investigator; and
- the trial should be within the Sub-Investigator's scope of practice.
- Note, the Specialist Regulations of the HPCSA, states that,
"A medical practitioner or a dentist who holds registration as a specialist in terms of the Act, shall-
 - (a) in the case of a specialty, confine his or her practice to the specialty or related specialties in which he or she is registered;*
 - (b) in the case of a sub-specialty, confine his or her practice mainly to the sub- specialty in which he or she is registered."*

7. MALPRACTICE INSURANCE

All healthcare professionals (psychologists, pharmacists, nurses, or other health professionals) who are clinically involved with the participant must, at all times, act within their specific Scope of Practice. They must also provide proof that they have adequate Malpractice Insurance; either independently, through a professional association (e.g., DENOSA) or as an employee of a medical practice (i.e., named under the Malpractice Insurance of the relevant practice).

8. ABBREVIATIONS

Abbreviations may not be used without initially writing the words out in full with the appropriate abbreviation in brackets. Words need to be written out in full in the PID, in the first instance, even if abbreviated elsewhere in other documents included in the application for approval. Only South African English abbreviations for Standard International (SI) units must be used (e.g., ml not mL).

9. PUBLISHING OF RESULTS

In the interest of transparency, it is preferable that the Principal Investigator may independently publish his or her results, subject to internationally approved conditions. However, where this is not the case, the agreed upon procedure for publishing the results should be explicitly stated in the application. The sponsor must be identified in all research publications.



10. LANGUAGE

The Committee will only consider and approve English documentation. South African English spelling should be used in all documents, including the Patient Information Documents. Should translations be required, the sponsor or investigator(s) (in non-sponsor driven research), must obtain the services of a professional translator, and keep a record of their certification as to the accuracy of the translation. Where research involves the participation of persons unfamiliar with the language in which the research is to be conducted the PID and related documentation must be translated into the participants' language.

When utilising the services of an interpreter, the investigator must ensure that the participant's informed consent is obtained and that an interpreter is present during discussions with the participants about the research study. As a rule, the interpreter should be an independent person and the patient should consent to the presence of the interpreter. Should a translator be present during the consent process, the information provided to the patient should clearly stipulate that the privacy of the consent will be compromised to that extent (DOH 2015). Translators should not unduly influence the consent process.

Submission Requirements:

A covering Letter and SAMAREC-approved documents translated into other languages must be sent to SAMAREC along with the translation certificates for record purposes.

11. SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY (SAHPRA) APPROVAL

Where SAHPRA approval for the trial is required, a copy of the approval letter must be submitted. If SAHPRA approval is pending, proof of application to the SAHPRA must be included. Where only SAHPRA notification is required, a copy of the notification must be submitted. Clients are requested to ensure that they abide with SAHPRA regulations, whether their projects need approval or only notification. SAMAREC Approval is subject to that of SAHPRA approval.

12. MAJOR AND MINOR AMENDMENTS

Amendments to be submitted to SAMAREC, the submissions will also be ratified by the full Committee at the subsequent meeting. The Amendment's will also be allocated to the original main evaluators of the first submission of protocol as main evaluators.

Major Amendment - (Ethical Changes) e.g., Protocol or PID, Changes in patient recruitment (Full Review – Committee Meetings), full committee review.

Minor Amendment – Sponsor Name Changes, Addresses, Administrative not involving ethical concerns (10 Working Days). Will be reviewed by the committee in between formal meetings, should the reviewer feel that the minor amendment needs formal Committee input, the amendment will be distributed to the entire Committee and added to the next scheduled meeting agenda for final approval.

Please ensure that submitted documentation includes the following information in footers "Protocol number/ Participant Information and Informed Consent Document, SAMAREC Version XX dated XXX." Furthermore, no product logos should be displayed on any documentation.



Submission Requirements:

Covering letters accompanying amended PIDs must state the date of their original approval. Please provide a brief paragraph or summary in your covering letter outlining the amendments. Amendments must be shown on the latest SAMAREC approved documents containing the changes recommended by SAMAREC, and the changes should be highlighted to facilitate review. A track changes copy and clean copy of the amended document must be provided. All amendments must be submitted electronically.

13. PRESENTATIONS

Presentations at meetings by sponsors and/or researchers who wish to explain and elucidate complicated and/or sensitive trials will be allowed to upon request, and at the discretion of SAMAREC. SAMAREC may also request the sponsor to present should they have any concerns regarding the trial.

14. REPORTING OF PROTOCOL DEVIATIONS AND VIOLATIONS

Protocol deviations and violations (Major and Minor) must be reported immediately to SAMAREC. The SAMAREC Chairperson will review the deviation within 48 hours should any urgent concerns be addressed, the reports will also be discussed and reviewed with the SAMAREC Meeting pack at the next meeting held and listed for discussion in the SAMAREC Supplement.

Submission requirements:

Accompanied by a Covering Letter, a description of the protocol deviation, rectifying action, and preventive action should be described. Further, SAMAREC must be provided with the date of the deviation, study site at which the protocol deviation took place, investigator of the site, subject ID of patient, and the severity of the deviation.

15. REPORTING OF ADVERSE REACTIONS AND EVENTS

SAMAREC holds to the SAHPRA definition of adverse events and reporting timelines.

Adverse Event: Adverse event is any untoward medical occurrence that may present during treatment with a medicine but which does not necessarily have a causal relationship with this treatment. An adverse event can be any unfavourable and unintended sign, symptom or disease temporarily associated with the use of a medicine, whether considered related to the medicine, or not.

Adverse Reaction: An adverse event which is assessed, by the Sponsor or Investigator, to have a causal relationship with the treatment.

Serious Adverse Event: any untoward medical occurrence that, whether drug related or not:

- Results in death,
- Is life threatening,
- Requires inpatient hospitalization or prolongation of existing hospitalization,



- Results in persistent or significant disability/incapacity or
- Results in a congenital anomaly/birth defect (see the ICH Guidelines for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting)

Reports of serious adverse events to SAMAREC must be reported immediately include a recommendation by the Principal Investigator regarding the continuance of the study trial, together with a brief motivation on whether, in his/her opinion, the SAE is trial related or not, and reasons for his/her opinion.

Unexpected Adverse Drug Reaction: is an adverse reaction in which the nature, specificity, severity, and outcome is not consistent with domestic labelling or holder of registration of certificate or expected from the characteristics of the medicine (i.e., the investigator brochure or product package insert).

Unexpected Serious Adverse Event: an event in which the specificity or severity is not consistent with the current investigator brochure (i.e., investigational drug or device). Serious Unexpected adverse events may be classified as “related” or “possible related.” An adverse event, which is related to the use of the drug, device, or intervention, is one for which there is a reasonable possibility that the adverse event may have been caused by the drug, device, or intervention. A “related” serious adverse event has a strong temporal relationship to the study drug, device or intervention and an alternative aetiology is unlikely or significantly less likely. A “possible related” serious adverse event is one that may have been caused by the drug, device, or intervention; however, there is insufficient information to determine the likelihood of this possibility. An If an unexpected serious adverse event proves terminal, SAMAREC must be notified immediately. Additionally, the study doctor must promptly report to the sponsor any unexpected adverse clinical event that may reasonably be regarded as caused by, or probably caused by the drug or device

Suspected Unexpected Serious Adverse Reaction: is the term used to refer to an adverse event that occurs in a clinical trial subject, which is assessed by the sponsor and or study investigator as being unexpected, serious, and as having a reasonable possibility of a causal relationship with the study drug

The timeframes and format for reporting of serious adverse events, adverse events and drug reactions are described in the SAHPRA guidelines and should be strictly adhered to.

All adverse reaction reports will be reviewed by the Chairperson and SAE Dedicated Clinical SAMAREC Member as received. Should it be of the opinion that a specific reaction must be discussed in detail by the Committee, detail of the specific reaction will be distributed to the entire Committee and the item will be added to the formal Minutes of the next scheduled Committee meeting. All adverse events are reported in the supplement and distributed to the entire Committee with the meeting pack.

Submission requirements:

A Covering Letter accompanied by a safety report (refer to *SAMAREC Report Form SAE*) should be submitted to SAMAREC.

16. REPORTS, POST-APPROVAL, AUDITING, SUSPENSION, NON-COMPLIANCE, PASSIVE AND ACTIVE MONITORING

Passive Monitoring:

Following approval of a protocol, six-monthly reports on the trial must be submitted to SAMAREC. Failure to forward these reports will result in suspension or termination of approval for the protocol, without any prior notification by



SAMAREC. Any decisions taken by SAMAREC after the review of the Progress Reports will be conveyed to the investigator.

Once the study has been completed, the final study report must be submitted in due course. Copies of the SAHPRA reports will suffice otherwise, *SAMAREC Passive Audit Report* may be submitted.

SAMAREC would also appreciate copies of relevant publications arising from reviewed work. All information will be placed on record and kept confidential at the offices of the SA Medical Association for at least three years after the completion of a trial.

Active Monitoring/Auditing:

SAMAREC, in accordance with the DOH Guidelines, must conduct active auditing and monitoring of sites. Audits may be conducted randomly or when there might be causes of concern to patients and participants.

- SAMAREC may be entitled to carry out audits, without prior notification to the principal investigators (Declaration of Helsinki 2013 part 23).
- SAMAREC may recommend and adopt any appropriate mechanisms for monitoring, including random inspection of research sites, welfare monitoring sheets, data and signed consent forms, and records of interviews.
- SAMAREC may request regular reports from principal investigators pertaining to progress to date, or outcome in the case of completed research, and/or current enrolment status.
- SAMAREC is entitled to request the following information: whether participant follow-up is still active or completed; information concerning maintenance and security of records; evidence of compliance with the approved protocol; evidence of compliance with any conditions of approval; negative reports from monitors or GCP inspectors; list all adverse events in the past twelve (12) months; list all amendments made in the past twelve (12) months. SAMAREC should inform principal investigators in writing of concerns arising from such monitoring activities.
- The audits must be conducted in accordance with the applicable laws, regulations, and ethical guidelines.
- The audit must be conducted by independent auditors – SAMAREC members - who are free from any conflicts of interest. The auditors will maintain objectivity and impartiality throughout the auditing process.
- A comprehensive audit plan that outlines the audit objectives, procedures, and timelines must be made available, which should specify key areas of focus, such as ethical review processes, decision-making, and adherence to regulatory requirements (refer to [SAMAREC Active Audit Form](#) for insight on some key areas of focus).
- SAMAREC must conduct frequent reviews of its documentation practices and record-keeping systems to ensure accurate and complete documentation. SAMAREC must assess the adequacy of records in terms of ethical reviews, decisions, and communications.
- SAMAREC must conduct a compliance assessment, which requires evaluating the committee's compliance with relevant laws, regulations, and ethical guidelines governing research activities. In addition, a review the SAMAREC's adherence to its own policies, procedures, and a Code of Conduct must be undertaken.
- SAMAREC must assess the effectiveness of its ethical review processes, including the evaluation of research proposals, protocols, and amendments. This includes, but is not limited to, evaluating the consistency and transparency of decision-making in granting approvals, providing feedback, and ensuring participant protection.
- A review the SAMAREC's procedures for identifying, assessing, and managing conflicts of interest among members must be conducted. This serves to evaluate the effectiveness of conflict-of-interest disclosure processes and SAMAREC's actions in mitigating conflicts.
- An assessment of SAMAREC's efforts in providing training and educational resources to members regarding research ethics, regulations, and emerging ethical issues. Must be undertaken. Reviewing the member's ongoing professional development initiatives to enhance members' knowledge and expertise is vital.
- A review of the SAMAREC's mechanisms for monitoring approved research projects must be done to ensure



ongoing compliance and research participant welfare. This includes assessing the adequacy and effectiveness of SAMAREC's reporting mechanisms, including reporting to regulatory bodies (NHREC) and relevant stakeholders.

- SAMAREC must identify any areas of non-compliance or deficiencies in the protocol and provide recommendations for improvement. It must monitor the implementation of corrective actions and follow-up on the progress made in addressing identified issues.
- SAMAREC must maintain proper documentation of audit activities, findings, and conclusions, and collect sufficient and appropriate audit evidence to support conclusions.
- SAMAREC must prepare clear, accurate, and concise audit reports that highlight findings, recommendations, and action plans, as well as communicate audit results to relevant stakeholders in a timely manner.
- SAMAREC must strive for continuous improvement within the auditing function. This requires regular reviews and enhancement of audit methodologies and processes to align with best practices.
- **Passive Monitoring & Auditing:** Following approval of a protocol, six-monthly reports on the trial must be submitted to SAMAREC. Failure to forward these reports will result in suspension of approval for the protocol, without any prior notification by SAMAREC. Any decisions taken by SAMAREC after the review of the Progress Reports will be conveyed to the investigator or sponsor. Once the study has been completed, the final study report must be submitted. Copies of the SAHPRA reports will suffice. SAMAREC would also appreciate copies of relevant publications arising from reviewed work. All information will be placed on record and kept confidential at the offices of the SA Medical Association for at least three years after the completion of a trial. All passive reports will be reviewed by the
- Chairperson and the Main Evaluators of the study, final comments and summarized report will reflect in the SAMAREC Minutes Supplement Report for the review of entire SAMAREC Committee.
- **Active Monitoring & Auditing.** SAMAREC will randomly select sites for auditing, or when there are ethical concerns. The SAMAREC Officer will notify the Sites or Sponsors of the audit. The Audit will be conducted by at least two members of the SAMAREC Committee and the SAMAREC Officer. The findings and feedback will be deliberated with the SAMAREC Chairperson. Feedback will be provided to the Site or Sponsor within 10 days of the physical audit.
- For more information on SAMAREC's auditing process refer to the *SAMAREC Auditing Guidelines*.

17. ANNUAL, CONTINUING REVIEW AND RECERTIFICATION RENEWAL

Protocols are approved for a maximum period of one year only. For projects, which continue beyond one year, it is the responsibility of the Principal Investigator or Applicant to submit to SAMAREC an Application for Annual Renewal supported by the latest study progress report. The SAMAREC Application for Annual Renewal must be submitted in time to allow for review and approval no later than 12 months from the initial review date. Upon receipt of the application for SAMAREC will review and approve, if appropriate, continuation of the project for the subsequent approval period.

Continuation of projects beyond five years requires submission of a revised, updated SAMAREC Application, protocol, and consent/assent document. The Application for Annual Renewal must also be submitted to SAMAREC for approval via the SAMAREC Application form.

Annual Renewal applications must be accompanied by progress reports / reference to already submitted progress reports (within the last 6 months).

For more information on the requirements and review process, refer to the *SAMAREC Continuing Review Annual*



Renewal Recertification.

18. REPORTING PROPOSED CHANGES IN A RESEARCH PROTOCOL.

Any proposed change in a protocol which affects participants or patients must be reviewed and approved by SAMAREC prior to implementation except where an immediate change is necessary to eliminate a hazard to the participants. Study doctors/Sponsors should submit a document by way of an expedited review procedure.

If a change in protocol is relatively minor e.g., changes in statistical analysis, it is not necessary to have a revised PID or an addendum to the PID. If, however, the change is not minor and therefore changes the content of the originally signed PID, (e.g., addition of an intervention not addressed in the original PID, disclosure of a previously unidentified risk) the study doctor should have all new participants sign a revised PID. All currently enrolled participants should sign the revised PID or an addendum to the originally signed PID. See Major and Minor Amendment Process.

19. EXPEDITED REVIEW PROCESS

Expedited Review Process (Sub-committee review of minor ethical issues). SAMAREC has established procedures for expedited review of research when this is in the public interest. Expedited review will entail review of the lower risk studies (minimal risk), by a Lay and a Medical Committee Member and the decisions will be included in the following meeting of the whole committee for oversight. In general, research with potential to cause physical or psychological harm would not be considered for expedited review. This includes drug trials of new investigational products, research involving non-interventional research procedures and research involving sensitive personal or cultural issues. Expedited review applications must be accompanied by a covering letter detailing the request for expedited review. Should the evaluators feel that the study poses more than minimal harm or risk to the patients, the study will be referred to the entire committee for a full review during a formal meeting. Turnaround time for an expedited review is three working days. Please ensure "Expedited Review Process" is requested in the covering letter.

Risk Definitions:

- Lower Risk Studies: where the only foreseeable risk is one of discomfort.
- High/Medium Risk Studies: where probability and magnitude of possible harms implied by participation are no greater than those posed by daily life in a stable society or routine medical, dental, educational, or psychological tests or examinations.
- High Risk Studies: research involving highly sensitive topics and/or the participation of very vulnerable and marginalised individuals/groups.

20. RAPID REVIEW PROCESS

SAMAREC has established procedures for rapid review of research when this is in the public interest e.g., urgency of disease and value of research to society. Rapid review is done for research protocols where there is more than minimal risk to the subjects e.g., vaccine study of new investigational product. These more serious studies posing a higher risk must be reviewed by the whole Committee, but this can take place between meetings by way of "round robin" assessment and collation of inputs by the SAMAREC officer for final approval by ways of electronic approval. Rapid review and approval may be considered for research where participants have a disease that may be rapidly fatal. Rapid review applications must be accompanied by a covering letter detailing the request and motivation for rapid review clearly indicating the need for urgency. Should the evaluators feel that the study poses significant risk more than minimal harm or risk to the patients or participants, then the study will be referred to the entire committee as per



usual process for a full review during a formal meeting. Turnaround time for rapid reviews is ten working days. Please ensure “Rapid Review Process” is requested in the covering letter.

For more information on the rapid review process, refer to the *SAMAREC Rapid Review Guidelines*.

21. SITE/STUDY CLOSURE PROCESS

Upon completion of the trial, the Investigator must inform SAMAREC and provide a summary of the trial outcome. When a study is closed, cancelled for any reason, or is prematurely completed you must complete a Site Closure Report. This serves as notification to SAMAREC that continuing review of the study is no longer needed. A Notification Letter and Site Closure Report must be submitted. All Site/Study Closure Reports will be reviewed by all SAMAREC Members and noted formally in the SAMAREC Supplement to the Minutes Report.

22. REPORTING OF ALLEGATIONS OF MISCONDUCT/NON-COMPLIANT AND COMPLAINT PROCEDURES

Complaints may be lodged by researchers, or any other persons involved in the research being conducted. Complaints should be directed to the Committee first. Should the matter not be resolved, the complaint may be escalated to the NHREC.

Complaints may be lodged, in writing, with the SAMAREC Officer who will submit such complaints to the Chairperson or relevant bodies as soon as possible for investigation.

Formal written feedback will be provided to the complainant once received from the Chairperson.

Complaints against SAMAREC committee members can be lodged with the SAMA Governance Department at governance@samedical.org, the complaints will be handled by the SAMA Board or necessary authorities depending on the nature of the complaint.

23. WHISTLE BLOWERS

A SAMAREC Whistle-blower feedback form is available for all study staff and patients or participants at the following link: <https://www.samedical.org/cpd-hpcsaresearch>. The complaints will be handled by SAMAREC or necessary authorities depending on the nature of the complaint.

For further information on the whistleblower process refer to *SAMAREC Whistle Blower* guidelines.

24. APPEALS AGAINST DECISIONS

Appeals against decisions or REC members should be lodged, in writing, to the full Committee, who will then investigate the complaint and endeavour to deal with it to the satisfaction of the complainant at governance@samedical.org. All complaints will be reviewed in a confidential manner by the SAMA Company Secretariat. The complaints and decisions will be conducted by the SAMA Board or referred to the necessary Regulatory Bodies depending on the nature of the appeal.

25. EDUCATION

Research ethics committees must ensure that their members receive initial and continued education in research



ethics and GCP training and are kept aware of current issues and developments in the broad area of research ethics and science.

The current members of SAMAREC are qualified and experienced in these aspects and are afforded the opportunity of attending ethics and research ethics related courses, workshops and conferences as indicated.

26. RECRUITMENT

Additional members and new members to the Committee will be recruited regularly, to comply with the *DOH Ethics in Health Research Principles, Processes and Structures (2015)* REC Membership list.

27. MATERIAL TRANSFER AGREEMENT (MTAS)

The SAMAREC MTA *pro-forma* must be used by all clients and sent through for approval. See Annexure 10 for template.

28. BIOLOGICAL MATERIAL

Informed consent to use biological materials in research must be obtained from the tissue donor. Human biological materials and their products may not be used for commercial purposes without the consent of the tissue donor. All information on Biological Material must be included in the applications and submissions.

Further considerations on using biological materials in research refer to the *SAMAREC Biological Materials, Databases, Registries and Repositories SOP*.

29. DATA BASES, REGISTRIES AND REPOSITORIES

The Informed Consent Documents should clearly explain the purposes and nature of Databases, Registries and Repositories.

The purpose and nature, the specifics for which consent is being sought, how and what types of research it supports must be included..

Further considerations on using databases, registries and repositories in research refer to the *SAMAREC Biological Materials, Databases, Registries and Repositories SOP*.

30. NON-COMPLIANCE CONSEQUENCES, SUSPENDED OR TERMINATED PROJECTS

The REC may withdraw approval of a study, should the study be non-compliant with the approved protocol. A due process must be followed for withdrawal of approval.

Once the REC becomes aware of an indication that warrants non-compliance with the approved protocol, the situation will be investigated, and all parties involved (Sponsor/CRA/Principal Investigator/ Researcher) will be expected to be transparent regarding their practices.

Findings during the investigation may warrant the study be suspended or discontinued.

The applicant and parties involved will be requested to comply with certain recommendations and provide evidence



that these have been implemented before the study is reviewed and may resume again.

31. THE SAMAREC REVIEW PROCESS

INTRODUCTION

The following description of the SAMAREC review process reflects the various ethical principles and regulatory requirements that study doctors should consider during the design phase of their project. For further insight into the principles, processes, and considerations of the review process, refer to *SAMAREC Decisional Analysis Guidelines*. In order to approve a research project involving participants, SAMAREC must assure itself of the following:

STUDY DESIGN

- The experimental design of the study is sound;
- Any risks associated with the research project are minimised to the greatest extent possible;
- The potential benefits are maximised to the greatest extent possible;
- The risks to the participant are outweighed or balanced by the potential benefits;
- The prospective participant population is appropriate in terms of characteristics and number;
- The investigators have the appropriate qualifications, experience, and facilities to conduct the research;
- Monitoring requirements are reviewed and adequate;
- Any other factors deemed appropriate.

VOLUNTEER PARTICIPATION

- The recruitment of participants is free of coercion;
- The method used to obtain informed consent is ethically and legally acceptable;
- The degree to which confidentiality is maintained is acceptable;
- Injury compensation is provided in accordance with the Association of British Pharmaceutical Industry (ABPI) Guidelines;
- Any other factors deemed appropriate.

32. REVIEW OF THE PROSPECTIVE PARTICIPANT POPULATION

The prospective participant population must be appropriate with respect to the nature and goals of the research. In addition, the study doctor should be guided by the principles that lead to an equitable selection of participants with regard to the potential risks and benefits of the research. Therefore, SAMAREC will carefully examine the characteristics of the participant population. Factors such as the required number of participants, age range, sex, ethnic background, and health status will be considered. The utilisation of any vulnerable classes of participants such as foetuses, prisoners, children, mentally incompetent persons, *non-compos mentis* persons, persons living with HIV / AIDS, frail and terminally ill persons, and persons of low socio- economic status must be clearly justified.

33. REVIEW OF METHOD(S) OF PARTICIPANT RECRUITMENT

SAMAREC will review the method of prospective participant identification and recruitment in order to be assured it is



ethically and legally acceptable. Advertisements used to recruit participants are considered an extension of the recruitment and informed consent processes, and therefore, must be reviewed by SAMAREC. All advertisements must adhere to the SAMAREC Guidelines for Clinical Trial Advertisements (Annexure 6).

34. REVIEW OF EXPERIMENTAL DESIGN

SAMAREC will review the experimental design in order to be assured that it is scientifically and socially sound and that the potential risks to the participants are minimised and the potential benefits maximised by using procedures consistent with acceptable research design.

The research design should be described in a clear and detailed protocol. Where applicable an investigational brochure detailing all relevant preclinical and clinical data to support the research should be made available.

The use of socially constructed categories (race, gender, religion etc.) in the research need to be justified, with the onus lying on the researcher to explicitly clarify the role of these categories in the research and risks and benefits associated with their description.

35. REVIEW OF THE POTENTIAL RISKS

A risk is a potential harm (injury) associated with the research that a reasonable person would be likely to consider significant in deciding whether or not to participate in the research or not. The concept of risk includes discomfort, burden, or inconvenience that a participant may experience as a result of the research procedures. Underlying the consideration of risk is the implicit moral guideline that all study doctors have a duty not to harm their participants and must minimise potential risk to the greatest extent possible.

The five major types of risk are: -

- **Physical risk** (e.g., pain, bruising and infection associated with venipuncture, adverse reactions to drugs, muscle soreness and pain as a consequence of exercise testing, heart attack induced by maximum exercise testing);
- **Psychological risk** (e.g., depression and confusion as a result of administration of drugs, feelings of guilt precipitated by a sensitive survey);
- **Social risk** (e.g., invasion of privacy, loss of community standing);
- **Legal risk** (e.g., compromising medical scheme benefits); and
- **Economic risk** (e.g., loss of employment, loss of potential monetary gain, cost to state or patient or medical scheme). Financial reimbursement of the research site or study doctor must not be excessive to result in a conflict of interest.

Risk can also be classified as minimal, greater than minimal and significant. The USA Federal Regulations define minimal risk, as “The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.” The term “minimal risk” is used as a base or standard by which the risk associated with research is judged.

Examples of “**minimal risk**” procedures include collection of urine, collection of sweat, weighing, pulse measurement, blood pressure measurement, voice recordings, electrocardiography, collection of blood by venipuncture from adults who are not pregnant, magnetic resonance imaging, skin fold body composition measurements, and any standard psychological testing without no stress.

Examples of a “**greater than minimal risk**” procedure include the administration of drugs, intravenous (IV) catheterisation, radiology examinations (X-ray, CT scan), maximal exercise testing and stressful psychological testing.



Examples of “*significant risk*” procedures include chemotherapy, radiation therapy and major surgery.

For further considerations on SAMARECs review of risks and a risk assessment tool, refer to the *SAMAREC Risk Assessment SOP*.

36. REVIEW OF POTENTIAL BENEFITS

A benefit is a valued or desired outcome. Benefits associated with participation in research can be classified as those that accrue to the participant directly (e.g., improvement of the participant’s health status; acquisition of knowledge considered of value by the participant) and those that accrue to society (e.g., additions to the knowledge base). SAMAREC will review the anticipated benefits to both the participants and to others. In addition, SAMAREC will consider whether the benefits are maximised to the greatest extent possible through proper protocol design. Therefore, an underlying moral notion of “beneficence” should guide the study doctor.

Financial and other forms of compensation are not considered a benefit to be derived from research participation. Although the patient may consider financial compensation a desirable outcome this fact will not be used in the risk-benefit analysis and should not be mentioned in the. For example, the fact that patients may receive a certain sum of money per visit to defray travel expenses cannot be reflected as a benefit (see SAHPRA Guidelines). Please note that it may be stated in the protocol document that the patient would receive an exact amount for travel and / or other costs. However, the exact amount of money must not appear in the Patient Information and Informed Consent Document (PID) as this could be seen as coercive.

37. RISK-BENEFIT ANALYSIS

Once the potential risks and benefits are identified, an ethical review of research requires an examination of the relationship of the risks to the benefits. Risks and benefits cannot be considered parallel constructs and, therefore, no formula is applicable. The various ethical codes and regulations, however, require a favourable balance between harm and benefit. To assist the study doctor and SAMAREC in assessing the risk-benefit relationship the following is a series of principles, which take into consideration whether the research is therapeutic in nature:

- 1) In research that has no likelihood or intent of producing a diagnostic, preventive, or therapeutic benefit to the participant (non-therapeutic research), the potential risk to the participant must be outweighed or balanced by the potential benefit to the participant and/or by the potential benefit to society.
- 2) In research involving the study of the efficacy of a therapeutic or diagnostic method and the intervention is, therefore, not designed solely to enhance the well-being of the participant who is seeking a health benefit (therapeutic research), the potential risk should be primarily outweighed or balanced by the potential benefit to the participant. In addition, the relation of the anticipated benefit to the risk must be at least as favourable to the participant as that presented by alternate standard therapies available to the participant in the non-research context. No participant is allowed to continue participating in a research protocol if therapy of proven superior nature becomes available to the participant.
- 3) In research where a standard therapy, not part of the research protocol, is employed, the anticipated benefits of the therapy must not be used to justify exposing participants to the risks associated with the research procedures. Such risks can only be justified considering the potential benefits of the research procedures to the participant. However, the risks associated with the research procedures should be used in determining the risk-benefit ratio.



38. REVIEW OF PARTICIPANT COMPENSATION AND ASSESSMENT OF FINANCIAL ARRANGEMENTS

SAMAREC will review the amount of compensation (monetary as well as other forms) paid to the participants to ensure that the payment is not coercive (or deemed to be an enticement) and only covers reasonable actual expenses, e.g., relating to travel.

Financial arrangements involving participants and study doctors form part of the assessment by the Committee. Where participants or their medical schemes are requested to accept liability for any trial related costs, this must be clearly stipulated in the PID. Clear explanation of what are trial related costs and normal treatment (standard care) costs should be provided, and where participants are required to be responsible for normal treatment costs, this should be explained in terms of a cost breakdown in the PID or as an annexure to the PID.

Fees charged for dispensing medicines must be charged in accordance with the prescribed legislation (and regulations). Professional fees may only be charged by the health professional rendering the professional service.

39. REVIEW OF MEASURES TO PROTECT PERSONAL INFORMATION

SAMAREC will review the methods to be used to preserve confidentiality. If research data and participant identifiers will be made available to persons other than the listed study doctors or the sponsor, SAMAREC will review the justification for sharing this data and determine acceptability.

SAMAREC will also consider whether the appropriate consent has been sought for the retention and use of the confidential personal information in line with the requirements of the POPI Act, 2013.

40. REVIEW OF THE PATIENT/PARTICIPANT INFORMATION AND INFORMED CONSENT DOCUMENT (PID) PROCESS INCLUDING MINORS AND VULNERABLE PATIENTS

The Bill of Rights states that –

“Everyone has the right to bodily and psychological integrity, which includes their right - (c) not to be subjected to medical or scientific experiments without their informed consent”

Therefore, no research may be carried out on a person without his/her consent or the consent of the person’s legally authorised representative prior to the person’s participation in the experiment. The principal reason for informing participants about the experiment is that they have a right to know what would be done to them and what risk this entails, before they grant consent. Persons are regarded as autonomous, and the requirement of informed consent is designed to uphold the ethical principle of “respect for persons.” The use of humans as research participants is a privilege and a favour granted to the researcher. The researcher has no right to carry out health research without informed consent. An experiment differs from the usual medical practice where interventions are done solely for the



benefit of the patient.

SAMAREC takes the view that clinical trials compare to medical procedures and therefore, accepts that patients/participants older than 18 years may independently consent to participate in clinical trials. Patients/participants younger than 18 years may NOT consent independently to participate in clinical trials. Persons younger than 18 years are regarded as a vulnerable group and applications for clinical trials involving them will be carefully considered by SAMAREC to safeguard their interests. Such persons need to be assisted by their parents or their legal guardians. Where the research does not involve greater than minimal risk to the child and direct benefit is foreseen, SAMAREC may consider the consent of one parent sufficient. Exceptions to this rule would be where one parent is deceased, unknown, incompetent, and not available or only one parent has legal care and custody of the child. No other person, such as a caregiver or grandparent may give consent on behalf of parents or legal guardian. In addition to the PID to be signed by the parents or legal guardian, an appropriately worded **Patient Information and Assent Document** is needed to be read and signed by those minors who can observe and understand the circumstances relating to the clinical trial.

In order for consent to be ethically and legally valid it must meet the requirements stated in the Principle (I) of the Nuremberg Code, which states, "The voluntary consent of the human patient is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the patient matter involved as to enable him to make an understanding and enlightened decision."

The PID and informed consent document are legal documents proving that informed consent was obtained. By signing the document, the participant declares that he/she gives consent to participate in the clinical trial. The study doctor signs the document to declare that he/she has guided the participant through the PID and explained the content to the satisfaction of the participant. The witness signs the document to testify that the participant and study doctor concerned have signed the PID. (The requirement for a witness for a literate patient will be determined by the Committee on a case-to-case basis) Where a participant is illiterate, verbal consent must be obtained and such verbal consent must be properly recorded. A witness must also confirm by signing the verbal consent document, that the participant understands the contents of the PID and has given free consent to participate in the trial **(See Annexure 4 for SAMAREC's preferred standard wording)**. The ethical and, indeed, legal validity of consent is, however, dependent upon the process of informed consent which requires the study doctor to engage in dialogue or negotiation with the prospective participant. The study doctor as an instrument to guide the negotiations with the prospective patient, therefore, should use the PID for this purpose. SAMAREC contact details must be provided on the PID. A paragraph informing the patient that the study received ethics approval should be included **(See Annexure 4 for SAMAREC's preferred standard wording)**. The SAMAREC will review both the PID and the process of informed consent in accordance with the provisions of the Guidelines for Good Practice in the Conduct of Clinical Trials published by the Department of Health in order to ensure acceptability.

The signatory section of the PID must be continuous with the rest of the PID to ensure that it is one document. Note that tick boxes are not suitable for participants' acceptance of various clauses in the PID. The clauses should rather be initialed by the participant.

For further considerations and SAMAREC guidelines, refer to *SAMAREC Informed Consent SOP*.



41. PRIVACY AND CONFIDENTIALITY REGARDING PARTICIPANTS AND THEIR HEALTH CARE INFORMATION FOR APPLICANTS

Privacy and confidentiality regarding participants and their healthcare information are of utmost importance in healthcare settings and research. Protecting the privacy and confidentiality of individuals and their health information is not only a legal and ethical requirement but also essential for maintaining trust and ensuring the success of healthcare services and research studies.

Legal Framework: Healthcare providers and researchers must adhere to relevant laws and regulations.

Informed Consent: Participants in healthcare research must provide informed consent, understanding how their information will be used and its potential risks and benefits.

Data Security: Implement robust data security measures to protect electronic health records, research data, and other sensitive information. This includes encryption, access controls, and secure storage.

De-identification: When sharing or using data for research, remove or encrypt personally identifiable information (PII) to protect the privacy of participants.

Data Minimization: Only collect and store data that is necessary for the intended purpose. Minimizing data reduces the risk of breaches and potential misuse.

Access Control: Limit access to healthcare information to authorized personnel only and establish protocols for granting and revoking access.

Audit Trails: Maintain records of who accesses healthcare information and when, which can be helpful in identifying unauthorized access.

Secure Communication: Use secure channels for communicating healthcare information, whether it's in electronic form or in conversations.

Training and Awareness: Ensure that all staff and researchers are trained on privacy and confidentiality policies and procedures. This includes regular updates to account for changing regulations and best practices.

Data Retention and Disposal: Establish guidelines for retaining healthcare data, and securely dispose of it when it's no longer needed.

Breach Response Plan: Develop a plan for responding to data breaches, including notification of affected individuals and appropriate authorities as required by law.

Third-Party Vendors: If using third-party vendors for data processing, ensure they also meet the necessary privacy and security standards.



Ethical Considerations: Beyond legal requirements, consider the ethical implications of using healthcare data. Ensure that research is conducted with respect for participants and their rights.

Patient Portals: Encourage the use of secure patient portals for accessing health information, allowing individuals to have control over their own data.

Regular Audits and Assessments: Periodically assess the privacy and security measures in place to identify potential vulnerabilities and areas for improvement.

Maintaining privacy and confidentiality in healthcare is an ongoing commitment, and it requires a multi-faceted approach involving technology, policies, training, and ethical considerations. The goal is to ensure that individuals can trust that their personal health information is being handled with the utmost care and respect for their privacy.

42. E-CONSENT

SAMAREC accepts Advanced Electronic Signatures (AES), in the place of wet signatures. Section 1 of the *Electronic Communications and Transactions Act No. 25 of 2002* defines AESs as “an electronic signature which results from a process which has been accredited by the Authority as provided for in section 37”. This form of E-Consent is also permitted through clause 10.9 of the South African Good Clinical Practice: Clinical Trial Guidelines (2020), which states that “An electronic signature is a computer data compilation of any symbol or series of symbols executed, adopted, or authorized by an individual to be the legally binding equivalent of the individual’s handwritten signature. In general, a signature may not be denied legal effect or validity solely because it is in electronic format, and a contract or other record relating to a transaction may not be denied legal effect, validity, or enforceability solely because an electronic signature or electronic record was used in its formation. To be considered equivalent to full handwritten signatures, electronic signatures must comply with all applicable requirements under 21 CFR part 117.

Electronic records that are electronically signed must contain information associated with the signing that clearly indicates the printed name of the signer, the date and time when the signature was executed, and the meaning associated with the signature. In addition, electronic signatures and handwritten signatures executed to electronic records must be linked to the respective electronic records to ensure that the signatures cannot be excised, copied or otherwise transferred to falsify an electronic record by ordinary means.”

43. REVIEW OF INVESTIGATORS

SAMAREC will review investigators and must be assured that they:

- Have the appropriate qualifications;
- Are licensed with the Health Professions Council or other appropriate statutory bodies to carry out procedures involving human participants with an acceptable degree of risk;
- Maintain adequate malpractice insurance cover;
- Carry out procedures involved in the clinical trial within their specialty/sub-specialty, if they are registered in that specialty or sub-specialty; and
- Have adequate facilities and equipment to conduct research with an acceptable degree of risk.



44. REVIEW OF MONITORING REQUIREMENTS

The SAMAREC will determine whether a research project requires review more often than annually and will establish an appropriate reporting and/or monitoring procedure which may include observation of the consent process, observation of on-going research and review of research records.

Studies with a high degree of risk or harm may be requested to provide more frequent status updates. This might include:

- Progress Reports
- Enrolment status (including number of patients still actively participating in the study or who have completed the study)
- Maintaining security of records
- Supplying the Committee with evidence should there be any conditional approvals for the study.
- Any audit report results
- Adverse events lists
- List of any amendments

45. REVIEW OF INJURY COMPENSATION

Compensation for trial related injuries must be covered and set out in the PID. Compensation should be provided in accordance with the Guidelines of British Pharmaceutical Industry Compensation Guidelines (ABPI). Broadly speaking, these guidelines recommend that the sponsor, without legal commitment, should compensate the participant without having to prove fault. This applies in cases where it is likely that such injury results from giving any new medicine, or any procedure carried out in accordance with the protocol for the study. The sponsor will not compensate where such an injury results from any procedure carried out that is not in accordance with the protocol for the study. The participant's legal right to claim compensation for injury where the participant's negligence can be proven and is not affected. A copy of the ABPI Guidelines must be made available to the participant by the study doctor, on request.

The following should be present on the insurance certificate:

- Name and address of the insurance company.
- Name and address of the company who took out the insurance.
- Study title and protocol number of the insured study.
- Date of commencement and termination of coverage.
- Liability limit – per person and total.
- Insurance policy number.
- Number of participants covered by the policy.
- Countries for which the policy provides cover.

All healthcare professionals must provide proof that they carry personal professional indemnity insurance cover.

46. CONFLICT OF INTEREST

SAMAREC ensures that no member of the Committee adjudicates a clinical trial in which that member has any conflict of interest in relation to the research project under consideration. Members should declare before each meeting any real or potential conflicts of interest with any of the studies to be evaluated and offer to recuse themselves from the evaluation of the study concerned. The member in question may remain in the meeting for the discussion of the protocol (should the Chairperson feel that this is appropriate), however, the member may not be allowed to participate in the final decision-making of the specific protocol. (DOH 2015 Guidelines). Where the Chairperson is conflicted, the Chairperson will excuse themselves from the meeting and the Vice-Chairperson will take over the proceedings of the



meeting. Should a SAMAREC Member be an employee or Director of the Institute they must declare any possible conflicts and recuse themselves from voting should the need arise.

47. ACCESS TO AND PROTECTION OF INFORMATION/MAINTENANCE OF RECORDS

Protocol and trial information and documentation are regarded as confidential and are treated as such by SAMAREC and SAMA. In terms of the Guidelines for Ethics in Health Research, published by the Department of Health, all records and documentation relating to the functioning of SAMAREC are open to the National Health Research Ethics Council. All other requests for access must be done in terms of the Promotion of Access to Information Act. All personal information is treated as confidential and shall be processed in accordance with the Protection of Personal Information Act, 2013 (POPIA).

All documents are stored electronically for record keeping and are accessible only to current SAMAREC members. These records are available for audit, conflict, and query purposes. Records will be kept of the following:

- Main protocol and all supporting documents (study staff documentation etc.)
- Date of provisional approval and/or final approval
- If applicable – special conditions of approval
- Adverse events (with de-identified patient information)
- Additional sites and study staff applications
- Administrative, Minor and Major Amendments
- General Notifications
- Translation with translation certificates
- Annual renewal
- SAHPRA Approvals
- NHREC Approvals
- Protocol Deviations

The maintenance of records will be held in accordance with the latest DOH guidelines.

48. RECIPROCAL REVIEW PROCESS

SAMAREC may, at their own discretion, recognize prior review and approval of a research proposal by another registered REC to avoid duplication of effort.

- i. Reciprocal recognition means that two or more registered RECs decide to recognize each other's prior review.
- ii. RECs that recognize prior review in this manner must determine the nature of the documents to be filed locally, which must, at minimum, include a copy of the approval letter from the other REC.

The SAMAREC Chair will consider the application and the relevant reciprocal review documentation and decide on the most appropriate way forward. This may include:

- a. SAMAREC full committee review depending on amongst other factors, the risk level of the project, impact on the local community etc. or
- b. An expedited or rapid review (for example, in the time of Research in Emergencies) or
- c. The outcome of the review will be communicated to the local

The Chair of the relevant HREC will report to the full HREC meeting the process and outcome of the reciprocal review for ratification.



49. SAMAREC RESOLUTION

After noting and considering the submission, the Committee will resolve as follows

Approved: The Committee accepts the concept of the Study and has granted ethics approval. No further changes are required, and the Study may commence.

Provisionally Approved: The Committee accepts the concept of the Study; however, corrections must be made before final approval will be granted. The Study may not commence.

Not Approved: The Committee does not accept the concept of the Study. There are major scientific or ethical concerns. The Protocol should be revised. The Study may not commence.

50. DEVELOPMENT AND MANAGEMENT (REVIEW, MONITOR AND APPROVAL) OF SAMAREC SOP.

The SAMAREC SOP will be updated Bi-Annually or when regulatory or legislative changes are required.

51. ANNEXURES

The following annexures set out further information and pro-forma documentation, for the guidance of study doctors and sponsors:

- Annexure 1: SAMAREC Meeting Dates
- Annexure 2: SAMAREC Application Form
- Annexure 3: SAHPRA Format of Curriculum Vitae of Trialists
- Annexure 4: Guidelines Pertaining to the Patient Information and Informed Consent Document (PID) and SAMAREC Patient Information and Informed Consent Document (PID) (Including various consent Annexures to be used as relevant to a particular clinical trial)
- Annexure 5: Members of SAMAREC
- Annexure 6: SAMAREC Fees
- Annexure 7: SAMAREC Guidelines for Clinical Study Advertisements
- Annexure 8: Declaration by Investigators
- Annexure 9: List of Study Staff and their submitted documents.
- Annexure 10: Material Transfer Agreement



Approved by:

2024/07/02

X 

Signed by: 6a389e41-7404-4d00-ac2d-c6b576cd3bae

SAMAREC Chairperson:

Dr N Naidoo

Signed: 01 July 2024