AAHRPP®

Association for the Accreditation of
Human Research Protection Programs, Inc.®

Addendum: The Republic of South Africa

Governing Research Involving Human Participants

General Comments

Standards and Elements listed below address areas where policies and procedures must address specific requirements in the National Health Act (Act No. 61 of 2003), Regulations Relating to Research with Human Participants No. R719 ("R719"), the Children's Act, 2005 (Act No. 38 of 2005) ("Children's Act"), General Regulations Made in Terms of the Medicines and Related Substances Act, 1965 (2003), South Africa Good Clinical Practice (SA-GCP), and Ethics in Health Research: Principles, Processes, and Structures, Guidelines. The organization must follow the South African Department of Health (DH), the National Health Research Ethics Council, the Medical Research Council of South Africa (MRC), and the Human Sciences Research Council (HSRC) regulations and guidelines.

Domain I: Organization

Standard I-1: The Organization has a systematic and comprehensive Human Research Protection Program with appropriate leadership.

Element I.1.A. The Organization has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program.	A clinical trial or study is understood to be any investigation in human participants (including participants and other volunteers) intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining their safety and/or efficacy. (SA-GCP, Glossary) Health research may be understood to include, but is not limited to research that contributes to knowledge of: • Biological, clinical, psychological, or social welfare matters including processes as regards humans • The causes and effects of and responses to disease • Effects of the environment on humans • Methods to improve health care service delivery • New pharmaceuticals, medicines, interventions and devices • New technologies to improve health and health care (Ethics in Health Research, 1.1.3) For other non-health related research, organizations should define research as a systematic investigation designed to contribute to generalizable knowledge, or equivalent definition. Every organization, health agency, and health establishment at which health and health-related research involving human participants is conducted, must establish or have access to a registered Human Research Ethics Committee. (Ethics in Health Research: Principles, Processes, and Structures, Guidelines, 1.4.2) • Written materials describe the process in which IRBs or ECs that review research involving human participants register with the National Health Research Ethics Council (NHREC).
Element I.1.D. The Organization has and follows written policies and procedures setting forth the ethical standards and	The age of majority, where a child becomes an adult, is 18. However, under certain exceptions, children 12 years of age and older are allowed to consent to medical treatment. (Children's Act, Sections 17 and 129)

practices of the Human Research Protection Program. Relevant policies and procedures are made available to Sponsors, Researchers, Research Staff, research participants, and the Institutional Review Board or Ethics Committee, as appropriate.	• Written materials should define whether or under what conditions the organization allows children to consent to research related to medical treatment without parental permission. Clinical trials must be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practice and the applicable regulatory requirements. (SA-GCP 3.1; ICH-GCP E6)
Element I.1.F. The Organization has and follows written policies and procedures for reviewing the scientific or scholarly validity of a proposed research study. Such procedures are coordinated with the ethics review process.	The scientific review process must determine the available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial. (ICH-GCP E6)
Standard I-4: The Organization responds to the concerns of research participants.	
Element I.4.C. The Organization promotes the involvement of community members, when appropriate, in the design and implementation of research and the dissemination of results.	Protocols for clinical trials to be conducted in community settings must include a clear plan on how the communities will be consulted or involved in the research process, and how they will be kept informed. (SA-GCP 8.5) Sponsors of trials conducted in South Africa are required to provide the public with updated information on clinical trials being conducted in South Africa by registering their trials on the South African National Clinical Trials Network (http://www.sanctr.gov.za/). Where there is no sponsor, it is the responsibility of the Principal Investigator to register the trial. Written materials must describe the process and who is responsible for applying to the Department of Health for a South African National Clinical Trials Register (SANCTR) number and registering the clinical trial on the SANCTR website. (SA-GCP, 1.2.5 and I.6) Study results must be provided to the SANCTR within one year of completion of the study (SA-GCP 4.3, 4.22, 6.4)
Standard I-7: The Organization has and follows written policies and procedures to ensure that the use of any investigational or unlicensed test article complies with all applicable legal and regulatory requirements.	
Element I.7.A. When research involves investigational or unlicensed test articles, the Organization confirms that the test articles have appropriate regulatory approval or meet exemptions for such approval.	When research involves the use of non-registered medicinal substances and new indications of registered substances, written materials must describe the process for obtaining or verifying approval from Medicines Regulatory Authority/Medicines Control Council to conduct the research prior to initiating the clinical trial. (GCP 1.5.1. and the General Regulations Made in Terms of the Medicines and Related Substances Act)
Element I.7.B. The Organization has and follows written policies and procedures to ensure that the handling of investigational or unlicensed	Written materials must describe processes for control of investigational drugs and devices (ICH-GCP E6): • Written materials must describe manufacturing, handling, and storage in accordance with applicable good manufacturing practice.

test articles conforms to legal and regulatory requirements.	• Where allowed or required, the investigator may assign some or all duties for investigational articles accountability at the trial sites to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator. • The investigator, pharmacist, or other designated individual will maintain records of the product's delivery to the trial site, the inventory at the site, the use by each participant, and the return to the sponsor or alternative disposition of unused products. These records will include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational products and trial participants. • Investigators should maintain records that document adequately that the participants are provided the doses specified by the protocol and reconcile all investigational products received from the sponsor.
Domain II: Institutional Review Board or Ethics Committee	
Standard II-1: The structure and composition of the IRB or EC are appropriate to the amount and nature of the research reviewed and in accordance with requirements of applicable laws, regulations, codes, and guidance.	
Element II.1.A. The IRB or EC membership permits appropriate representation at the meeting for the types of research under review, and this is reflected on the IRB or EC roster. The IRB or EC has one or more unaffiliated members; one or more members who represent the general perspective of participants; one or more members who do not have scientific expertise; one or more members who have scientific or scholarly expertise; and, when the IRB or EC regularly reviews research that involves vulnerable participants, one or more members who are knowledgeable about or experienced in working with such participants.	The research ethics committee should consist of a reasonable number of members, who collectively have the qualifications and experience to review and evaluate the science, medical aspects, and ethics of the proposed trial. (SA-GCP 8.3): Research ethics committees should: • Be representative of the communities they serve and reflect the demographic profile of the population of South Africa. • Have at least nine members, with 60% representing a quorum. • Include members of both gender and not more than 70% of its members should either be male or female. • Include at least two lay persons who have no affiliation to the institution, are not currently involved in medical, scientific or legal work and preferably are from the community in which the research is to take place. • Include at least one member with knowledge of, and current experience in areas of research that are likely to be regularly considered by the research ethics committee. • Include at least one member with knowledge of and current experience in the professional care, counselling or treatment of people (e.g. medical practitioner, psychologist, social worker, nurse). • Include at least one member who has professional training in both qualitative and quantitative research methodologies. • Include at least one member who is legally trained. • Include at least one member who represents the general perspective of research participants. If the organization conducts or reviews research involving prisoners, the IRB or EC should include, at least on an ad hoc basis, a member with experience and knowledge of working with prisoners when deliberating on the protocol. The researchers must comply also with the requirements of the Department of Correctional Services.

Element II.1.B. The IRB or EC has qualified leadership (e.g., chair and vice chair) and qualified members and staff. Membership and composition of the IRB or EC are periodically reviewed and adjusted as appropriate.	Research ethics committee members must receive initial and continued education in research ethics, GCP and science, and are kept aware of current issues and developments in the broad area of ethics and science. (SA-GCP 8.5)
Standard II-2: The IRB or EC systematically evaluates each research protocol or plan to ensure the protection of participants.	
Element II.2.A. The IRB or EC has and follows written policies and procedures for determining when activities are exempt from applicable laws and regulations, when permitted by law or regulation and exercised by the IRB or EC. Such policies and procedures indicate that exemption determinations are not to be made by researchers or others who might have a conflict of interest regarding the studies.	South Africa law does not define categories of research that are exempt from applicable laws and regulations. However, Guidance provides that: • Research that relies exclusively on publicly available information or accessible through legislation or regulation usually need not undergo formal ethics review. (Ethics in Health Research, I.1.8)
Element II.2.E. The IRB or EC has and follows written policies and procedures to conduct reviews by the convened IRB or EC. **1. Element II.2.E.1. – Initial review** **2. Element II.2.E.2. – Continuing review** **3. Element II.2.E.3. – Review of proposed modifications to previously approved research**	In addition to other application materials, the reviewer is provided and reviews the investigator's current curriculum vitae or other documentation evidencing qualifications. (SA-GCP 1.2.3; ICH-GCP E6)
Element II.2.F. The IRB or EC has and follows written policies and procedures to conduct reviews by an expedited procedure, if such procedure is used. **Element II.2.F.1. – Initial review** **Element II.2.F.2. – Continuing review** **Element II.2.F.3. – Review of proposed modifications to previously approved research**	Research ethics committee may establish procedures for expedited review of clinical trials when this is in the public interest. For example, expedited review and approval may be considered for a trial where participants have a disease that may be rapidly fatal. (SA-GCP 8.7) Research with potential to cause physical or psychological harms should not be considered for expedited review. This includes drug trials, research involving invasive procedures and research involving sensitive personal or cultural issues. (SA-GCP 8.7)
Element II.2.G. The IRB or EC has and follows written policies and procedures for addressing unanticipated problems involving risks to participants or others, and	Problems researchers have to report to the IRB include (ICH-GCP E6): • New information that might affect adversely the safety of the participants or the conduct of the clinical trial. • Any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.

for reporting these actions, when appropriate.	
Standard II-3: The IRB or EC approves each research protocol or plan according to criteria based on applicable laws, regulations, codes, and guidance.	
Element II.3.A. The IRB or EC has and follows written policies and procedures for identifying and analyzing risks and identifying measures to minimize such risks. The analysis of risk includes a determination that the risks to participants are reasonable in relation to the potential benefits to participants and to society.	The IRB or EC should consider: • The risk-benefit analysis takes full cognizance 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. • Making specific recommendations regarding the continuation of treatments beyond the life of the study, or mechanisms to ensure that participants are fairly protected. • Whether the product will be made available to participants after the study ends, and if so whether there is any cost to the participant to continue treatment. • 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. (SA-GCP 2.2)
Element II.3.F. The IRB or EC has and follows written policies and procedures to evaluate the consent process and to require that the researcher appropriately document the consent process.	Consent documents must disclose, in addition to the requirements in Table II.3.F.1., Elements of Consent Disclosure, the following information (N719 and SA-GCP): • Information about the sponsor; • Any potential conflict of interests; • Information about approval from the health research ethics committee or the Medicines Control Council, where relevant; • Insurance in the event of research-related injury, for more than minimal risk research; and • The availability of beneficial products or interventions after completion of the research. • The alternative procedures or treatment that might be available to the participant, and their important potential benefits and risks. • That the monitor, the auditor, the IRB, and the regulatory authority will be granted direct access to the participant's original medical records for verification of clinical trial procedures or data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the participant or the participant's legally acceptable representative is authorizing such access. • The approval of the IRB.
Element II.3.G. The IRB or EC has and follows written policies and procedures for approving waivers or alterations of the consent process and waivers of consent documentation.	When research procedure precludes conformity to the principle of consent, and neither the prospective participant nor the participant's representative is able to give consent in advance, a research ethics committee may approve a research project without prior consent if it is satisfied that: • Inclusion in the research project is not contrary to the interest of the participant;

	• The research is intended to be therapeutic and the research intervention poses no more of a risk than that inherent in the participant's condition and alternative methods of treatment; • The research is based on valid scientific hypotheses which support a reasonable possibility of benefit over standard care; and • As soon as reasonably possible, the participant and the participant's relatives or legal representatives will be informed of the participant's inclusion in the research, and will be advised of their right to withdraw from the research without any reduction in quality of care. (SA-GCP 2.3.6.5)
Standard II-4: The IRB or EC provides additional protections for individuals who are vulnerable to coercion or undue influence and participate in research.	
Element II.4.A. The IRB or EC has and follows written policies and procedures for determining the risks to prospective participants who are vulnerable to coercion or undue influence and ensuring that additional protections are provided as required by applicable laws, regulations, codes, and guidance.	When reviewing research involving vulnerable persons, the IRB or EC must determine the research (R719): • May involve vulnerable persons only when non-vulnerable persons are not appropriate for inclusion; • Does not systematically avoid inclusion of vulnerable participants because to do so is unfairly discriminatory and vulnerable persons are potential beneficiaries of relevant research; • Is responsive to the health needs and the priorities of vulnerable persons; and • Receives special attention in ethical review to ensure that research-related risks are assessed and minimized and that appropriate consent procedures are followed. Research with children should only take place when: • Adults are not appropriate participants for the research; • The research interventions, including those in observational research, presents the participant with no greater than minimal risk (that is, 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 medical or psychological examinations or tests) (R719, 4.1; SA-GCP 2.3.1.); or • The research poses more than a minimal risk, but holds out the prospect of direct benefit to the minor (R719, 4.1; SA-GCP 2.3.1); or • The research interventions, including those in observational research, present more than minimal risk and do not hold out the prospect of direct benefit to the participant, but have a high probability of yielding generalizable knowledge. That is the risk should be justified by the risk-knowledge ratio. The risk should represent a minor increase over minimal risk. The intervention or procedure should present experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or education settings. (R719, 4.1; SA-GCP 2.3.1.) • The research poses a minor increase over minimal risk, and holds out no prospect of direct benefit to the minor, but is anticipated to yield

	generalizable knowledge about the condition under study. (RA719, 4.1; note this is not allowed under SA-GCP 2.3.1)
	
	In all cases, the protocol must provide sufficient information to justify clearly why minors should be included as participants. (GCP 2.3.1.)
	
	The organization must describe how it reconciles different requirements under South Africa law and ICH-GCP E6:
	
	• Research with adults with decision-making incapacity is appropriate when (R719, 4.2):
	  ○ The research cannot be conducted with adults who have decision-making capacity;
	  ○ The research poses no more than a minimal risk; or
	  ○ The research poses more than a minimal risk, but holds out the prospect of direct benefit to the participant; or
	  ○ The research poses a minor increase over minimal risk, and holds out no prospect of direct benefit but is anticipated to yield generalizable knowledge about the condition under study.
	• When reviewing clinical trials involving involves adults unable to consent, the IRB or EC determines (ICH-GCP E6):
	  ○ A non-therapeutic clinical trial (i.e. a trial in which there is no anticipated direct clinical benefit to the participant) should be conducted in participants who personally give consent and who sign and date the written consent document.
	  ○ Non-therapeutic clinical trials may be conducted in participants with consent of a legally acceptable representative provided the following conditions are fulfilled:
	  ▪ The objectives of the clinical trial cannot be met by means of a trial in participants who can give consent personally.
	  ▪ The foreseeable risks to the participants are low.
	  ▪ The negative impact on the participant's wellbeing is minimized and low.
	  ▪ The clinical trial is not prohibited by law.
	  ▪ The opinion of the IRB is expressly sought on the inclusion of such participants, and the written opinion covers this aspect.
	  ▪ Such trials, unless an exception is justified, should be conducted in participants having a disease or condition for which the investigational product is intended. Participants in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.
	
	Research with prisoners is appropriate when (R719 4.3):
	
	• The risk of harm posed by the research is commensurate with risks that would be accepted by non-prisoner volunteers;
	• The rights of prisoners, including but not limited to the rights to dignity, privacy, bodily integrity and equality, will be protected; and
	• The procedures and guidelines issued by the Department of Correctional Services will be followed.
	
	Prisoners may be enrolled as participants only when the clinical trial involves (SA-GCP 2.3.5):

	• The study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided; • No more than minimal risk and inconvenience to the participants; • The study of prisons as institutional structures or of prisoners as incarcerated persons, • Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on diseases that may be more prevalent in prisons and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) only after appropriate experts have been consulted; and • Research on practices, both innovative and accepted, that have the intent and probability of improving the health or wellbeing of prisoners. • Where some prisoners may be assigned to control groups that may not benefit from the research, the research may proceed only after appropriate experts have been consulted. (SA-GCP 2.3.5) Research with persons in dependent or hierarchical relationships (R719 4.4): • Includes but is not limited to research with users and their health-care workers; persons with life-threatening diseases and their care-givers, wards of the state and their guardians or caregivers, employees and their employers, prisoners and the relevant prison authorities and members of the national defense force and their superiors; and • Is appropriate when research-related risks of harm are minimized, and appropriate consent procedures have been followed No research involving pregnant women and fetuses may be undertaken unless: • Appropriate studies on animals and non-pregnant individuals have been completed; • The purpose of the activity is to meet the health needs of the mother of the particular fetus, the risk to the fetus is minimal and, in all cases, presents the least possible risk for achieving the objectives of the activity • Individuals engaged in the activity will have no part in 1) any decision as to the timing, method and procedures used to terminate the pregnancy and 2) determining the viability of the fetus at the termination of the pregnancy; and • No procedural changes which may cause greater than minimal risk to the fetus or the pregnant woman will be introduced into the procedure for terminating the pregnancy solely in the interest of the activity. (SA-GCP 2.3.2.1) No research involving fetuses in-utero as participants may occur unless: • The purpose of the activity is to meet the health needs of the particular fetus and the fetus will be placed at risk only to the minimum extent necessary to meet such needs; or • The risk to the fetus imposed by the research is minimal and the purpose of the activity is the development of important biomedical

	knowledge which cannot be obtained by other means. (SA-GCP 2.3.2.2) Until it has been ascertained whether or not a fetus ex utero is viable, a fetus ex utero may not be involved as a participant in any research activity unless: • There will be no added risk to the fetus resulting from the activity, and • The purpose of the activity is the development of important biomedical knowledge which cannot be obtained by other means, or • The purpose of the activity is to enhance the possibility of survival of the particular fetus to the point of viability. (SA-GCP 2.3.2.3) No nonviable fetus may be involved as a participant in any research activity unless: • Vital functions of the fetus will not be artificially maintained; • Experimental activities which of themselves would terminate the heartbeat or respiration of the fetus will not be employed; and • The purpose of the activity is the development of important biomedical knowledge which cannot be obtained by other means. (SA-GCP 2.3.2.3)
Element II.4.B. The IRB or EC has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question.	When research involves pregnant women, research may be conducted only if the mother and father are legally competent and have given their informed consent. (SA-GCP 2.3.2.1) However, consent of the father need not be obtained if: • The purpose of the activity is to meet the health needs of the mother; • His identity or whereabouts cannot reasonably be ascertained • He is not reasonably available; or • The pregnancy results from rape. (SA-GCP 2.3.2.1) When research involves fetuses in utero, research may be conducted only if the mother and father are legally competent and have given their informed consent. (SA-GCP 2.3.2.2) However, consent of the father need not be obtained if: • His identity or whereabouts cannot reasonably be ascertained • He is not reasonably available; or • The pregnancy results from rape. (SA-GCP 2.3.2.2) When research involves fetuses ex utero, including non-viable fetuses, research may be conducted only if the mother and father are legally competent and have given their informed consent. (SA-GCP 2.3.2.3) However, consent of the father need not be obtained if: • His identity or whereabouts cannot reasonably be ascertained • He is not reasonably available; or • The pregnancy results from rape. (SA-GCP 2.3.2.3) For research involving children, the following should be obtained (SA-GCP 2.3.1.1): • Consent from a parent or legal guardian in all but exceptional circumstances (e.g. emergencies). In exceptional circumstances a

	caregiver (e.g. custodian, person providing long-term day-to-day care for the child) can act on behalf of a minor. • Assent from the child where she or he is capable of understanding. • A child's refusal to participate in research must be respected, i.e. such refusal settles the matter. If organizations conduct non-therapeutic research involving children, they must obtain ministerial consent prior to commencing such research. (R719, 71, 72, 92) Non-therapeutic research involving children must:. • Have ministerial consent in terms of Section 71(3)(a)(ii) of the Act or, where appropriate, consent from • A delegated authority in terms of Section 92(a) of the Act. • Ethics Council in terms of Section 72(6)(d) of the Act. For research involving adults with mental disabilities, or intellectual or mental impairment, consent to research must be obtained from (SA-GCP 2.3.3): • The person with the intellectual or mental impairment, wherever he or she is competent to give informed consent; • The person's legal guardian where the person is deemed not competent to do so; or • An authority, organization or person having that responsibility by law. • Proxy decision makers are not permitted for adult persons who lack capacity unless the proxy is a court-appointed curator.
Element II.4.C. The IRB or EC has and follows written policies and procedures for making exceptions to consent requirements for planned emergency research and reviews such exceptions according to applicable laws, regulations, codes, and guidance.	Research involving the initiation of emergency care without consent may be only be approved if: • Steps are being taken to ascertain the religious and cultural sensitivities of participants experiencing medical emergencies; • The condition of the participant precludes the giving of consent; • Inclusion in the trial is not contrary to the interests of the participant; • The research is intended to be therapeutic and poses no more risk than is inherent to the participant's condition or would be caused by alternative methods of treatment; • The participant and the participant's next of kin or legal representatives will be informed • As soon as is reasonably possible of the participant's inclusion in the study and of the option to withdraw from the research project at any time; • The participant will be informed, and consent obtained, once the participant who has undergone the necessary emergency procedures has regained consciousness; and • The research is based on valid scientific hypotheses and offers a realistic possibility of benefit over standard care. (SA-GCP 2.3.9)
Standard II-5: The IRB or EC maintains documentation of its activities.	
Element II.5.A. The IRB or EC maintains a complete set of materials relevant to the	Records are maintained for a period of at least 15 years after the completion of the study. (SA-GCP 8.8)

review of the research protocol or plan for a period of time sufficient to comply with legal and regulatory requirements, Sponsor requirements, and organizational policies and procedures.	
Domain III: Researcher and Research Staff	
Standard III-1: In addition to following applicable laws and regulations, Researchers and Research Staff adhere to ethical principles and standards appropriate for their discipline. In designing and conducting research studies, Researchers and Research Staff have the protection of the rights and welfare of research participants as a primary concern.	
Element III.1.A. Researchers and Research Staff know which of the activities they conduct are overseen by the Human Research Protection Program, and they seek guidance when appropriate.	Researchers: • Must ensure that they have the responsibility to make trial results (both positive and negative) publicly available within a reasonable timeframe. • Have the responsibility to share possible benefits of research results with participants. • Generate the information package for the participant, and where applicable with the sponsor. • Ensure proper safety reporting procedures. (SA-GCP 3.1)
Element III.1.C. Researchers employ sound study design in accordance with the standards of their discipline. Researchers design studies in a manner that minimizes risks to participants.	During and following a participant's participation in a clinical trial, the researcher ensures that adequate medical care is provided to a participant for any adverse events, including clinically significant laboratory values, related to the clinical trial. (SA-GCP 3.4; ICH-GCP E6) The researcher follows the clinical trial's randomization procedures, if any, and ensures that the code is broken only in accordance with the protocol. If the clinical trial is blinded, the researcher promptly documents and explains to the Sponsor any premature unblinding. (ICH-GCP E6) A qualified physician (or dentist, when appropriate), who is a researcher or a co- researcher for the clinical trial, is responsible for all clinical trial-related medical (or dental) decisions. (ICH-GCP E6) Researchers inform participants when medical care is needed for other illnesses of which the researchers become aware. (ICH-GCP E6)
Element III.1.D. Researchers determine that the resources necessary to protect participants are present before conducting each research study.	Researchers are responsible to (R719, 3): • Submit the research proposal for ethics review and approval to a registered health research ethics committee and, where applicable, to the Medicines Control Council or any other body required by law, before commencing with the research; • Consult with representatives from the participating community or other relevant research stakeholders, where appropriate; • Consult with and notify the affected institutional or governmental authorities where necessary;

	• Assess the ongoing welfare of participants and take appropriate steps in the event that participants experience harms; • Disseminate research results, whether negative or positive, to research stakeholders, in a timely and competent manner including to participants and participating communities as far as possible; and • Register the research in the South African National Clinical Trials Register, if classified as a clinical trial.
Element III.1.E. Researchers and Research Staff recruit participants in a fair and equitable manner.	Researchers are responsible to (ICH-GCP): • Inform the participant's primary physician about the participant's participation in the clinical trial if the participant has a primary physician and if the participant agrees to the primary physician being informed. • Although a participant is not obliged to give his or her reasons for withdrawing prematurely from a clinical trial, the researcher makes a reasonable effort to ascertain the reason, while fully respecting the participant's rights.
Standard III-2: Researchers and Research Staff meet requirements for conducting research with participants and comply with all applicable laws, regulations, codes, and guidance; the organization's policies and procedures for protecting research participants; and the IRB's or EC's determinations.	
Element III.2.A. Researchers and Research Staff are qualified by training and experience for their research roles, including knowledge of applicable laws, regulations, codes, and guidance; relevant professional standards; and the organization's policies and procedures regarding the protection of research participants.	Researchers fulfill responsibilities under South Africa law (SA-GCP 3.1): • Clinical trials must be conducted by a local, South African-based scientist. • The researcher must ensure that approval(s) from the relevant accredited local research ethics committee, and, if applicable, the Medicines Control Council (MCC) are obtained and that the trial is issued a South African Clinical Trial Register number by the Department of Health. • Have read and accepted the relevant information package developed by the sponsor for clinical studies. • Have good knowledge of the protocol, related documents and the regulatory requirements of the MCC and other relevant legislation. • Have read, understood and agreed to work according to the protocol, the Declaration of Helsinki, ICH Guideline for Good Clinical Practice, these Guidelines and other relevant legislation; undertake to use the investigational and comparator product(s) only for the purposes of the study as described in the protocol. • Take responsibility for accountability of the investigational product(s). • Ensure that they have the responsibility to make trial results (both positive and negative) publicly available within a reasonable timeframe. • Have the responsibility to share possible benefits of research results with participants. • Ensure proper safety reporting procedures.

	Researchers are qualified by education, training, and experience to assume responsibility for the proper conduct of the trial (SA-GCP 3.2): • The researcher provides evidence of his or her qualifications through up-to-date curriculum vitae or other relevant documentation requested by the sponsor, the IRB, or the regulatory authority. (SA-GCP 3.2) • The researcher is familiar with the appropriate use of the investigational product, as described in the protocol, in the current investigator brochure, in the product information, and in other information sources provided by the sponsor. (SA-GCP 3.2) • The researcher permits monitoring and auditing by the sponsor and inspection by the appropriate regulatory authority. (Not applicable to independent IRBs in South Africa.) (SA-GCP 3.2) • A qualified physician (or dentist, when appropriate), who is a researcher or a co-researcher for the clinical trial, is responsible for all clinical trial-related medical (or dental) decisions (not applicable to independent IRBs). (SA-GCP 3.4) • During and following a participant's participation in a clinical trial, the researcher ensures that adequate medical care is provided to a participant for any adverse events, including clinically significant laboratory values, related to the clinical trial. (Not applicable to independent IRBs in South Africa.) (SA-GCP 3.4)
Element III.2.C. Researchers and Research Staff follow the requirements of the research protocol or plan and adhere to the policies and procedures of the organization and to the requirements or determinations of the IRB or EC.	The researcher must maintain a list of appropriately qualified persons to whom they have delegated significant clinical trial-related duties. (SA-GCP 3.2; ICH-GCP)
Element III.2.D. Researchers and Research Staff follow reporting requirements in accordance with applicable laws, regulations, codes, and guidance; the organization's policies and procedures; and the IRB's or EC's requirements.	Researchers fulfill all reporting requirements (ICH-GCP E6): • The researcher reports all serious adverse events (SAEs) to the sponsor except for those SAEs that the protocol or other document (e.g., investigator's brochure) identifies as not needing immediate reporting. The researcher follows regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB. • The researcher reports adverse events or laboratory abnormalities identified in the protocol as critical to safety evaluations to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol. • For reported deaths, the researcher supplies the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports). • The researcher provides written reports to the sponsor, the IRB, and, where applicable, the organization on any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.

	• If the researcher terminates or suspends a clinical trial without prior agreement of the sponsor, the researcher informs the organization, sponsor, and the IRB. • If the IRB terminates or suspends approval of the clinical trial, the researcher promptly notifies the sponsor. • Upon completion of the clinical trial, the researcher informs the organization; the IRB with a summary of the trial's outcome; and the regulatory authority with any reports required.