Health Sciences Research Ethics committee

HSREC Preparation Guide: Application for Ethics Clearance

Version 10.01

November 2023

HEALTH SCIENCES
UFS

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UNIVERSITY OF THE FREE STATE
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UFS HEALTH SCIENCES

Contents

General notes

The Health Sciences Research Ethics Committee (HSREC) uses an online ethics review management system, *Research Information Management System (RIMS)* to manage the application and review process.

The purpose of this document is to provide researchers with the information needed to comply with the administrative requirements of an ethics application to the HSREC. **Please read the whole document.**

In line with the Policy of the University of the Free State on Responsible Research Conduct[1], the following research is exempt from the formal ethics review process:

- Research relying exclusively on publicly available information or accessible through legislation or regulation (i.e. desktop studies or literature reviews);
- Research involving observation of people in public spaces and natural environments provided that there is no research related interaction, an intervention stages, a reasonable expectation of privacy is transgressed, nor findings that identify individuals or groups; and
- Research relying exclusively on secondary use of anonymised information.

The HSREC cannot grant retrospective approval in cases where data collection has commenced or is completed. Please ensure that you submit an application for ethics review well in advance.

Applications will only be accepted on RIMS (https://rims.ufs.ac.za/)

a) HSREC Administration reserves the right to not accept applications for review that are submitted in any other format.
b) New applications and all other subsequent submissions (amendments, reports, notifications, etc.) must be submitted to the HSREC on RIMS no later than the submission deadlines listed below.
c) Please note: RIMS has a scheduled maintenance window every Monday from 16:00 – 22h00. The system will not be available during this time. When logging in again on the next day, please press F5 for the page to refresh.
d) Annual RIMS maintenance window: RIMS closes during December of each year for maintenance. Access to the system is not possible for researchers and administrators during this time.
e) The HSREC advises anyone who is awaiting the outcome of an ethics application to check their junk/spam e-mail folder. If these e-mails are sent to the junk/spam folder, please unmark it as spam/junk.
f) Documents must be submitted in PDF format.
g) Researchers are welcome to make an appointment with HSREC Administration for consultation prior to starting their application process. Please see contact information above.

RIMS-compatible browsers

[1] Policy of the University of the Free State on Responsible Research Conduct. UFS Statute, Government Gazette, No 42337, 29 March 2019

Submission deadlines and Meeting dates

PLEASE NOTE: Dates for upcoming submission deadlines and meeting dates can be found on the UFS HSREC webpage.

IMPORTANT: Meeting the submission deadline does not guarantee the submission will be incorporated into a specific HSREC meeting agenda or review cycle. Some submissions might roll over to the next available HSREC meeting. Late and incomplete submissions will automatically roll over until the next review cycle and meeting. Please contact HSREC Administration to arrange for a consultation if required.

Contact details for HSREC Administration and the RIMS Office

HSREC ADMINISTRATION CONTACT DETAILS:		
The Chair: Health Sciences Research Ethics Committee Dr CL Armour Block D, Room 104, Francois Retief Building University of the Free State Bloemfontein 9301 PO Box 339 (G40) Nelson Mandela Drive Faculty of Health Sciences University of the Free State Bloemfontein 9300	Ms Yanga Mkuzangwe & Mrs Nomasonto Mochochoko *HSREC administrators* Block D, Room D112/ D115, Francois Retief Building University of the Free State Bloemfontein 9301	+27 51 401 9860 or +27 51 401 2650
	Email	ethicsfhs@ufs.ac.za
	Office hours	07:45-16:30

For all RIMS system related questions/concerns/creation of user profiles, please contact the RIMS office:

RIMS CONTACT DETAILS:		
Physical Address: Johannes Brill Building 111 Directorate Research Development RIMS IB 57 University of the Free State Bloemfontein 9300	Mr W Killian *RIMS Administrator* Mrs A Smith *RIMS Administrator* *(Tuesday, Wednesday and Thursday)* Mr Mpho Mashamba *RIMS Administrator* Mrs M Van Rooyen *RIMS Project Manager*	+27 51 401 3682 +27 51 401 2075 +27 51 401 9398 +27 51 401 9451
	Email	rims@ufs.ac.za
	Office hours	07:45-16:30

WHO TO CONTACT FOR HELP

Enquiries about the HSREC application and review process:	Contact the HSREC Coordinators
Experiencing technical difficulties with RIMS:	Contact the RIMS Administrators

Review Fee Structure

GENERAL INFORMATION:

- HSREC has a graded administrative fee structure in place, which is revised annually.
- **Student projects for degree purposes, self-funded projects and projects funded solely from a University of the Free State Departmental budget are exempt from fees.**
- **IMPORTANT NOTE:** HSREC reserves the right to not review a research application, or to withhold an HSREC letter if invoicing details have not been submitted to HSREC Administration with the application

INDUSTRY-SPONSORED CLINICAL TRIALS		
Item	**Description**	**HSREC Review Fee (incl. VAT)**
New application	Pharmaceutical / Industry driven company sponsors an investigator to conduct a new research project	R13,426.75
Extension / Roll-over study / Sub-study	Project is extended; study rolls over to open label; re-evaluation of protocol for continuation; sub-study	R10,070.07
Annual re-certification / Progress report	Annual evaluation of research progress report for re-certification	R1,208.39
Protocol amendment - Major	Relaxation of inclusion criteria; relaxation of exclusion criteria; change in objectives / rationale of study; change in the study design and number of participants; relaxation of standards for data analysis; any change to the protocol that requires full committee approval	R2,685.34
Protocol amendment - Minor	Tightening of inclusion criteria; tightening of exclusion criteria; changes in the Investigator's Brochure; changes in the background information; extension of study period; budget change or change to the contract; minor technical amendments; other changes that do not affect study design or analysis / results	R1,678.34
Informed consent / Information Leaflet amendment	Any change to the content of the original informed consent form / information leaflet	R1,342.68
Participant / Recruitment material	This includes all material to be handed out to participants, all forms of advertising and blanket approvals.	R1,342.68
Additional investigator	Any additional investigator (per investigator)	R671.34
Administrative changes	Name changes; additional sites; typographical changes; other administrative changes	R671.34
External Administrative Charge	General Admin required by HSREC e.g. copying of lost trial documentation, protocols etc.	R671.34
Expedited / Urgent review of documentation		R671.34

*Administrative Fees for the process of SAEs / Progress Reports / Safety Reports / Investigators' Notifications are incorporated in the pricing structure

INTERNATIONAL GRANT FUNDED RESEARCH		
Item	**Description**	**HSREC Review Fee (incl. VAT)**
New application	International grant funded research (Total project budget > R1m)	R10,070.07
New application	International grant funded research (Total project budget R500 000 to R1m)	R4,699.37
New application	International grant funded research (Total project budget R100 000 to R500 000)	R2,685.35
New application	International grant funded research (Total project budget < R100 000)	R1,208.41
Extension / Roll-over study / Sub-study	Project is extended; study rolls over to open label; re-evaluation of protocol for continuation; sub-study	R1,208.41
Annual re-certification / Progress report	Annual evaluation of research progress report for re-certification	R1,007.25
Protocol amendment - Major	Relaxation of inclusion criteria; relaxation of exclusion criteria; change in objectives / rationale of study; change in the study design and number of participants; relaxation of standards for data analysis; any change to the protocol that requires full committee approval	R1,208.41
Protocol amendment - Minor	Tightening of inclusion criteria; tightening of exclusion criteria; changes in the Investigator's Brochure; changes in the background information; extension of study period; budget change or change to the contract; minor technical amendments; other changes that do not affect study design or analysis / results	R805.64
Informed consent amendment	Any change to the content of the original informed consent form	R805.64
Participant / Recruitment material	This includes all material to be handed out to participants, all forms of advertising and blanket approvals.	R805.64
Additional investigator	Any additional investigator (per investigator)	R537.08

*Administrative Fees for the process of SAEs / Progress Reports / Safety Reports / Investigators' Notifications are incorporated in the pricing structure

NOTES:

- No Pro-Forma Invoices will be generated. Invoices will be generated after submission
- Purchase Order numbers (where applicable) must be provided with the application
- Please quote invoice number on electronic payments, and **send proof of payment to** ethicsfhs@ufs.ac.za
- Application documents must clearly indicate VAT numbers and to whom the invoice must be made out

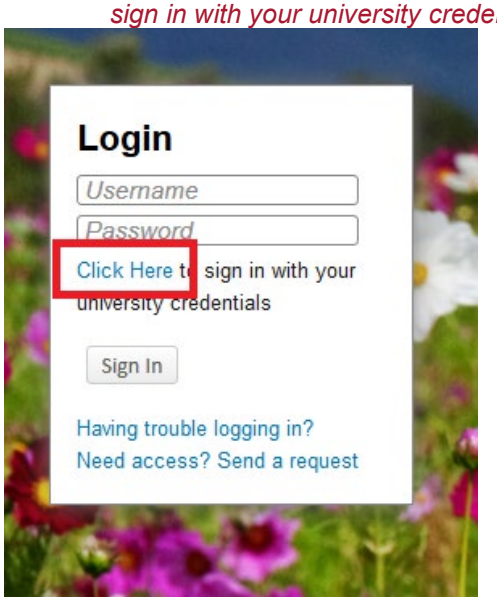
Getting started: UFS Affiliated Researchers

RIMS login

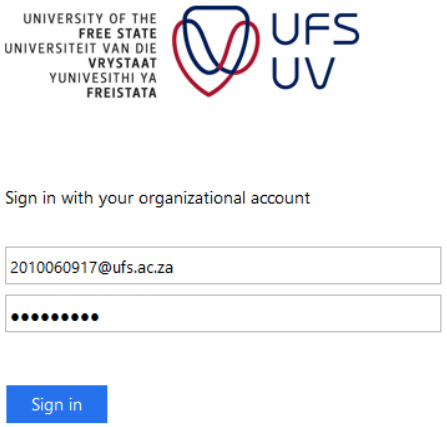
Please take note that the login for RIMS has changed. *Single sign-on* has been activated, which means that UFS students and staff should now use their own **university credentials** to access the system.

Steps to login:

- Clear the history and cache of your browser (Firefox/Chrome/Safari). **Please note:** *Do not use Microsoft Edge or Internet Explorer to access RIMS.*
- Click on the RIMS Web Portal link at https://www.ufs.ac.za/ufsresearch, or type the following URL in your browser's address bar: https://rims.ufs.ac.za
- Login steps for students and staff of the UFS:
  - Visit the RIMS Login page at https://rims.ufs.ac.za, then click on the blue link *('Click Here to sign in with your university credentials'*) as indicated below



  - University credentials: See screenshot below for example
  - Click the blue "Sign in" button



- If you forgot your password, please reset it by following the link below: https://selfservice.ufs.ac.za

Getting started: External Researchers

As received by the RIMS office

- External Researcher(s) seek approval from a UFS ethics committee for two reasons.
    - Reciprocal Approval; and
    - Gatekeeper's approval.
- If a researcher from an external institution wants to do research in a locale perceived to be under the auspices of one of the UFS ethics committees, he or she must have ethical clearance from an NHREC registered committee. In this instance, they apply for reciprocal approval from the relevant UFS ethics committee.
- In the event where an external researcher does not have ethical clearance, said researcher should send a request to the UFS RIMS office for a RIMS profile that will enable him or her to apply for ethical clearance.
- Applications for reciprocal approval are routed (sent) to members of an ethics committee to review and approve or disapprove, coupled with the sign off of the relevant ethics committees' chairperson, or an EXCO if deemed necessary.
- Gatekeepers' approval is a process through which a researcher seeks and receives – if approved, permission to make use of UFS staff and or students as participants in their research/study.
- This process also applies to UFS staff and student researchers. External researchers seeking this kind of approval will be subject to a similar process as those seeking reciprocal approval.
- Applications for Gatekeepers' approval are routed to (depending on the study and the nature of the request), the Dean of the specific Faculty (this will always vary depending on the nature and discipline of the study), Dean of Student Affairs (if the study requires UFS students as participants), Director of Human Resources (if the study requires UFS staff members as participants), and the Vice-Rector: Research.
- Please note: Gatekeepers will not review any study without ethical clearance, and in the case of UFS staff and student researchers, conditional approval is the minimum level of approval required for gatekeepers to review an application.

- **IMPORTANT NOTE:** Please ensure that your email address displays correctly in RIMS **before** completing your application. Incorrect email addresses will result in HSREC comments/decisions not reaching you. If incorrect, contact the RIMS office to update.

- RIMS Manuals: Please refer to the following RIMS manuals when applying for research ethics clearance (available from the RIMS office):
    - How to apply for ethics clearance on RIMS;
    - How to make modifications that are required on a RIMS;
    - How to respond when an application has received Conditional Approval;
    - How to submit a Health Sciences Historical Application.

- The Investigator Declaration and Conflict of Interest statements
    - All researchers as well as their main supervisor (if applicable) must sign the HSREC 19 form priot to the RIMS application process being initiated in the system. A signed document is a **mandatory** upload on the application form at the time of submission. A project will not be accepted for review if this signed document is not included.

- Lay term summaries:
    - The purpose of the lay summary is to inform the members of the Ethics Committee (that includes lay members) about the salient features of the proposal in a concise, yet structured way. It may also be required for auditing purposes. The lay summary is different from the information leaflet that is required for informed consent and should not be written as if for a participant.
    - Notes:
        - When submitting any research protocol for ethics approval, a lay term summary generated by the principal investigator must be included. This is a summary of the study in lay terms which is included in the agenda for notification of all members of the HSREC amongst which there are some who do not have medical background.
        - Simple, clear language must be used (maximum Grade 8 reading level) and all medical and technical terms have to be explained.
        - There are various websites which can be used to check the readability level of the lay term summary. (An example of such a website is https://www.online-utility.org/english/readability_test_and_improve.jsp). A Gunning Fog index of eight (8) is recommended for the lay term summary.
        - A summary of the research protocol in lay terms must be included in the application form (no more than 750 words).
        - A mandatory section regarding the ethical considerations of the project must be included in the lay term summary.
    - Lay terms should describe:
        - Project title
            - Explain in lay terms
        - Aim of the study
            - Exactly what you want to achieve
        - Methodology
            - Where the study will be conducted
            - What population will be included in the study
            - What method will be used
            - What treatment will be administered to participants
            - What control method will be used
        - Potential risk for participants
            - ALL risks, including ethical risks
            - Will patients receive remuneration?
        - What will happen with the outcome?
            - Will it be made known to the participants?
            - Will it be published/presented at a scientific congress?
        - Describe how the researcher will manage personal information
            - The protection of participants' personal information must be discussed in the informed consent and in the lay term summary.

- Protection of personal information should be addressed under "methodology" or "ethical aspects/considerations" wherever it fits the specific study best.

- Racial labelling:
  - In the rare instance when race is included in the data set and motivated by literature/scientific reason and required for a specific study, race/ethnicity should be described according to Statistics South Africa (https://www.statista.com/statistics/1116076/total-population-of-south-africa-by-population-group/):
    - Black African
    - Coloured
    - White
    - Indian/Asian
  - Race and ethnicity and culture are not synonyms. Be sure the consider this in your application.

- Good Clinical Practice
  - Formal Good Clinical Practice certification is *mandatory* for all clinical trials involving human participants. The term 'clinical trial' is inclusive and includes trials involving complementary medicines, African traditional medicines, and non-pharmacological interventions including surgical procedures, medical devices, cell therapy, genetics and genomics and imaging technology.[2]
  - TRREE (Training and Resources in Research Ethics Evaluation) GCP (Good Clinical Practice) (SA supplement), which is not equivalent to formal GCP training, is available at https://elearning.trree.org is *recommended* for the following scenarios:
    - Whenever human participants are prospectively involved in clinical research
    - Where identifiable personal information of human participants is involved
    - Human anatomy and medical anthropology research
    - Pathology-based research

- Permission from UFS authorities:
  - Approval must be obtained from UFS Authorities if research is to be conducted among students, lecturers and/or other role-players at the University of the Free State. This request for permission is completed in RIMS as a separate electronic application (Gatekeeper's Approval – Student/Staff Participation) **after** the HSREC grants conditional approval to a project.
  - Once the Gatekeeper's Approval letter is received by the researcher via RIMS, the letter must be uploaded to the RIMS HSREC application as a response to conditional approval.
  - Please contact HSREC Administration for guidance on the above process if anything is unclear.

- Completing the application on RIMS: Who is responsible
  - Postgraduate/Other research: The student/researcher is regarded as the Principal Investigator, and should complete the application
  - Undergraduate research: The student(s) supervisor is regarded as the Principal Investigator, however it is not the supervisor's responsibility to complete the application. If research will be conducted in groups, the group leader is responsible for completing the application. A field exists on the application form for supervisor details.

[2] Department of Health, 2000. South African Good Clinical Practice: Clinical Trial Guidelines. 3rd Edition. Pretoria, South Africa. P 9. https://www.sahpra.org.za/wp-content/uploads/2021/06/SA-GCP-2020_Final.pdf

Umbrella studies, basket studies and linked studies

Umbrella study:

Purpose of umbrella studies:

The umbrella study application is a single research study with a single Principal Investigator (PI) who takes full responsibility for all the administrative matters related to the umbrella study and a single RIMS number will be allocated to the umbrella study. It allows a PI to work with a number of researchers or student groups to work on various components within the research study. The components of the study need to be identified in the original application and can be activated with an amendment to the original application as researcher or student groups are identified to manage these components. These should not be loaded as sub-studies.

HSREC application process for umbrella studies:

- *Initial registration for an umbrella study:*
  - The researcher will select "umbrella study" on RIMS.
  - For an umbrella study, a single protocol is required.
  - A single title will be registered on RIMS
  - In the protocol, the various components of the study must be clearly delineated by the PI. This includes the exact methodology used for these components as well as appropriate documents.
  - Such components should be described as COMPONENT A, COMPONENT B, COMPONENT C, etc.
  - At the time of HSREC application, the delineated components of the study **do not need to be allocated** to a named researcher. When researchers are allocated to a specific component of the umbrella study, that component will be opened by the HSREC (see below).
  - The HSREC registration of the umbrella study is based on the competence of the PI.
  - The HSREC number will be a standard HSREC number approving the umbrella study **registration** (e.g., UFS-HSD2021/1876/1002).
  - **Commencement of any research activity may only follow HSREC approval for that specific component of the study.**
- *Application to open components of the umbrella study:*
  - When a researcher is allocated to a specific component of the umbrella study, the PI should apply for an amendment to the HSREC on RIMS.
  - **A new protocol is not required to open a component of an umbrella study.**
  - In the amendment, the PI should mention:
    - The specific component of the study that is going to be amended in the SUMMARY OF CHANGES;
    - The component (e.g., COMPONENT B) of the study that the PI would like to "open" should also be mentioned in the cover letter to the HSREC;
    - Which researchers will be working on that component of the umbrella study;
    - An investigator declaration signed by all researchers working on that component of the umbrella study;
    - The relevant documentation of all the researchers working on that component of the umbrella study (CV and professional body registration if applicable);
    - Relevant approvals (head of department, study site, gatekeepers etc) in the case of a new site is being added;
    - Additional documentation as relevant to the component of the study.
  - The HSREC will then review the application and if all ethical conditions are met, an approval letter will be sent to the principal investigator.
  - The letter to the PI will mention the main title and HSREC reference number. Reference to the title of the specific component of the study will be made in the body of the letter.
  - Such approval only pertains to the specific component of the umbrella study which has been opened.

- All communication will be with the Principal Investigator, not with individual researchers.

Basket study*:*

Purpose of basket studies:

The basket study application also has a single Principal Investigator (PI) and all sub-studies (each with their own title and protocol) fall under the same PI. It allows several researchers to work on a single data set, or for a researcher to use the same data set to answer different research questions. The other researchers will be co-investigators to the sub studies registered, but the main administrative responsibilities for the studies and the data set will lie with the original PI. Sub-studies will each have their own separate protocol for approval and may be registered with the basket registration and may be applied for years after the original study. A suffix will be added to the RIMS number to indicate that the study is a sub-study.

HSREC application process for basket studies:

- *Initial application for a basket study:*
  - The PI will select "basket study" on RIMS.
  - The RIMS reference number of the original study will be required to register the new study as a sub-study of the original study.
  - A title or original study will be registered on RIMS.
  - The HSREC number will be a standard HSREC number approving the basket study registration (e.g., UFS-HSD2021/1876/1002).
- *Application process to register a sub-study or use data from the basket study.*
  - The researcher shall prepare a protocol for use of the data in the sub-study.
  - This protocol shall include a name for the sub-study that will be registered on RIMS.
  - The application should **include all the information as required for a new HSREC application process**, except for informed consent (as this would have been obtained when the data was collected).
  - The original informed consent documents must be reviewed so that the HSREC can evaluate whether the informed consent made provision for sub-studies in the basket study.
  - The HSREC will then review the application and if all ethical conditions are met, an approval letter will be sent to the principal investigator and co-investigators.
  - The RIMS number will be the original number with a suffix that reflects that this is a sub-study of a larger study (e.g., UFS-HSD2021/1876/1002-B).

Linked studies:

Purpose of linked studies:

The linked study application allows different PIs who wish to research the same patient population, each with their title, research questions and protocols to work together and to share data. The projects are linked by the fact that they have a single research theme and use same patient population or condition. Linked studies may be stand-alone studies, or may be part of a larger study. A researcher may link a study to an original study years after the original study was performed. There are a number of PIs and all linked studies will have their own PIs and RIMS reference numbers.

HSREC application process for linked studies:

- *Initial application for a linked study:*
  - The researcher will select "linked study" on RIMS.
  - The RIMS reference number of the original study will be required to link the new study to the original study.
  - A new title for the linked study will be registered on RIMS.
  - The HSREC number will be a standard HSREC number approving the linked study.
- *Application process to register a linked study.*
  - The researcher shall prepare a protocol for the linked study.
  - This protocol shall include the name of the linked that will be registered on RIMS.
  - The application should **include all the information as required for a new HSREC application process**.

- The HSREC will then review the application and if all ethical conditions are met, an approval letter will be sent to the principal investigator. A RIMS registration number will be allocated to this study.

Blanket approval

- The term Blanket approval is no longer used by the HSREC, and no such projects will be considered in future.
- Projects with expired blanket approval will not be renewed.

Application documents

Academic and contract research

The following documents should be prepared for submission to the HSREC.

- Some items in this list might not be applicable to a project, please select the N/A option on the form.

1. Cover letter
    a. Draft a letter addressed to the Chairperson of the HSREC. Contact details provided at the beginning of this document.
    b. If the new application is part of a main study, please quote the main study's ethics number in this letter.
    c. Contract research: Cover letter listing all submitted documents with version numbers and version dates

2. Study protocol
    a. Please upload the final protocol with exclusion of the appendices (this will be uploaded separately, please ensure that all appendices are saved as separate documents). Ensure that all track changes have been finalised.

3. Investigator's brochure and other related material
    a. Applicable to contract research/clinical trials.

4. Questionnaires
    a. The questionnaire(s) can be submitted in English and must be written in layman's terms. Once the requested changes, if any, have been made, the HSREC may request submission of translations in English, Afrikaans, Sesotho or other applicable languages. Questionnaires must be available in the main language(s) of the research setting.
    b. Please include the following introductory wording into questionnaires where **anonymous** participation in a study is relevant: "You have been asked to participate in a research study. Please note that by completing this questionnaire you are voluntarily agreeing to participate in this research study. You will remain anonymous and your data will be treated confidentially at all times. You may withdraw from this study at any given moment during the completion of the questionnaire. The results of the study may be published." In such cases signing an Informed Consent Form is not required but an Information Leaflet must still be available.
    c. Please note that standardised/validated questionnaires may not be translated.

5. Other measuring tools/instruments

6. Recruitment material/advertisement(s)
    a. If an advertisement for potential study subjects will be used, it must include the following information:
        i. Advertisement in its final form (logo etc.) must be presented to the HSREC
        ii. Note condition/disease under discussion in the research proposal in layman's terms
        iii. Category participants: Age, etc.
        iv. Which method will be used, e.g. questionnaires
        v. Remuneration for transport and inconvenience
        vi. Any costs payable by participant
        vii. Contact person's name and cell phone number
        viii. For further enquiries also note office hours, if applicable
        ix. Voluntary participation and participant may withdraw at any time
        x. Patients currently on treatment will participation in the research study in conjunction with the treating physician
        xi. Time duration of study

7. Budget

a. If the study budget is already part of the protocol, please save a copy of the complete budget (break it down) and upload it here, as it is mandatory. The application form cannot be saved if the budget has not been provided here

8. Permission letter from the applicant's Head of Department / Head of School of Nursing, if applicable
    a. If this letter is not submitted with the initial application, the project will not be taken in for review, but sent back to the researcher.
    b. The researcher's head of academic department must sign a letter printed on a letterhead confirming the researcher's project title.
    c. Do not submit a letter requesting permission from the HOD. It must be a final signed letter.
    d. **Exception**: In the case of MMed research, the letter from the HOD is not required, provided the HOD signed the Departmental Research Committee letter.

9. Permission letter from the Vice Rector: Research at UFS for research to be done among students and/ or employees of the UFS
    a. Note: This permission can only be obtained after receiving conditional approval from the ethics committee for your research by submitting a Gatekeepers application on RIMS

10. Permission letter from the institution where the study will be conducted
    a. This letter should be from the institution where research will be conducted, excluding institutions falling under the jurisdiction of the Free State Department of Health.
    b. If permission is still awaited, the researcher should upload the letter of request.

11. Approval from Radiation Committee
    a. Studies that involve radiation and humans (patients, employees or public) need to be evaluated by the Radiation Control Committee for exposure calculations and approval. Upload the permission letter from the Radiation Control Committee here (if applicable).

12. Informed Consent and Information Document for adults in the languages common to the research area
    a. The ICF can be submitted in either English or Afrikaans and must be written in layman's terms. The information leaflet is addressed to prospective participant and contains all information that a participant needs to know about the project in order to make an informed decision on whether to participate or not. Once the requested changes, if any, have been made, then the committee may request the researcher to submit translations. ICF must always be available in the main languages of the research setting.
    b. The following should be mentioned in the information leaflet and informed consent (where applicable):

Health-Related Research Informed Consent Form – essential elements
An introductory statement written as an invitation [You are being invited to participate….] • Project name • Project number (if applicable) • Summary of the project name in lay terms • Name of Principal investigator/researcher
Administrative area: • Space for a participant number • Informed consent version number and date of the version as a footer • The ethics approval date must be on the consent form
Opening statement: • The purpose of the research • The study involves research • The study involves experimentation (if appropriate)
A statement that explains whether participation is both or: • Confidential • Anonymous

A statement that participation is voluntary, and that

- the participant may refuse participation or to leave the study at any time by telling the researcher and will not be penalised or lose any benefits to which they are otherwise entitled.
- the participant may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

In the case of a survey:

- A statement that the responses are or are not linked to a participant's email address/name – must be clear
- Statement that reads that the participant is:
  At least 18 years of age
  Has read and understood the informed consent form
  Agrees to participate in the study
  That participation implies consent (if appropriate)

The expected duration of participation must be explained

Description of the procedures to be followed

[will I get paid to participate in this study?]

- Mention whether the participant will be remunerated for their time, inconvenience, and expense (TIE) related to the study.
- A breakdown of the actual reimbursement that will be offered
- An explanation of how (if any) additional costs to the participant that may result from participation in the study will be managed.

A statement explaining the anticipated number of participants will be recruited for the study.

If appropriate:

- Statement that describes any potential benefit to the participant or to others/society which may be reasonably expected from the research [Will I benefit in any way by participating in this research?]
- Statement that treatment/procedures may involve risks to the participant that are not foreseeable at present. [Are there any risks to me if I choose to participate in this study?]
- Number of studies that have been done so far on the substance or device and number of people exposed to the substance or device. [how many studies have been done on this product? Approximately how many people have previously used this medication?]
- Serious adverse events previously recorded on the study drug [can I get any side effects if I decide to participate?]
- Whether anticipated adverse events are reversible or not [will any possible side effects be reversible?]
- What alternate methods of treatment are available [is there any other way that my condition could be treated?]
- A statement explaining the use of placebo [will I get the investigational product or placebo?]
- Nature of preparations used (as well as placebo) [what type of medication will I be getting on the study?]
- Whether there is insurance for the study participants [Will I be insured during the participation in this study?]
- Statement that treatment may involve risk to embryo/foetus should participant become pregnant. [is there any risk to my foetus/embryo if I get pregnant?]
- Statement that participants may be withdrawn from the study by the researcher without participants' consent, if they need other treatment, do not follow the trial plan, have a study-related injury, or for any other appropriate reason. [Could I be removed as a participant in this study?]
- Statement outlining the consequences of the participant's decision to withdraw from the research. [What will happen if I decide not to stop participating in this study?]
- The procedure for the orderly termination of participation by the participant [What process should I follow if I decide not to participate?]

- Statement that if a participant leaves the study for any reason, the PI may ask the participant to have some end-of-trial tests or procedures if applicable. [What will happen if I decide to stop participating in this study?]
- A disclosure of appropriate alternative procedures or courses of treatment that may be advantages or equivalent for the participant [Other than this study, are there any other treatment options that would be good for me?]
- Statement that significant new findings developed during the course of the research may related to the participant's willingness to continue participation [What could happen if the study shows that treatment needs to change?]
- Whether post-study access will be made available to participants? [will I still be able to get this produce after the study?]

Statement that findings may be published at the end of the study.

A statement that a signed copy of consent given to the participant

A section that asks and confirms whether the participant understands:

- Why the research is being done. [why are we doing this research study?]
- Which participants will be recruited. [who can participate in this research study?]
- What will happen during the study. [What will I be asked to do and what will be done to me in this study?]
- Any possible benefits? [Will being in this research study help me in any way?]
- The possible risks? [What are my risks of being in this research study?]
- Other options that they could choose instead? [is there another option? Do I have to be in this study?]
- How their personal health information will be used and treated during and after the study? [how will my personal information be protected?]
- What to do if they have any problems or questions about this study?

POPIA section:
A statement that explains:

- Which data is collected
- Purpose of data collected
- How data is collected
- How data is stored
- How the data will be de-identified and protected
- How data will be processed and destroyed/deleted
- If data will be shared with third parties, and who the third parties are
- The rights of the participant: (right to access, right to rectification, right to erasure, right to object to processing, right to portability/transferring of personal information)

Details of the:

- Responsible party
- Researcher
- Ethics Committee (HSREC)

[who can I talk to if I have questions or problems?]

Direction of POPIA relevant complaints:

- To the researcher, however at times the ethics committee (HSREC) may be the first point of call
- If unresolved via researcher – contact HSREC
- If unresolved via HSREC – contact NHREC (National Health Research Ethics Council)
- If unresolved via NHREC – contact ASSaF (Academy of Science SA)
- If unresolved via ASSAf – contact the Information Regulator

Direction regarding study-related injuries:

- Who should be contacted in the event of a study-related injury

Direction regarding general contact details for the research team for:

- Questions, concerns, or complaints about the research/study.

Direction to an independent person (not in the research team) who they can contact for:

- Questions, concerns or complaints about the research/study or any questions about their right to information/to offer input.

Space for:

- Participant full name and surname

• Participant Signature • Date and time • Researcher's full name and surname • Researcher Signature
Confirm that a copy of consent given to participant, including date and time given and researcher name, surname, and signature
Study participants must initial on each page of the document to confirm that they have familiarised themselves with the contents. The study participant and investigator obtaining the consent must both sign in full, print their names and indicate the date on the last page of the consent document.

13. Assent form for minors
    a. When children participate in research studies, an assent form together with an Information Leaflet (with the above information explained at the level of the children involved) must be available apart from the Informed Consent document that needs to be signed by the parents/legal guardian.
    b. **Note**: For "Non-therapeutic" health research with minors, as part of the statutory requirements, **Form A** (NHREC Operational Guidelines for Ministerial Consent: v19 Feb 2015 – included in this document) must be completed and must accompany your application. Non-therapeutic research is classified as research that includes interventions that do not hold the prospect of direct health-related benefit to the participant but may produce results that contribute to generalisable knowledge. This form must be uploaded on the application form.

14. Letter requesting permission from the relevant provincial department
    a. Submit a cover letter addressed to the provincial department. You may use the same letter you addressed to the HSREC, and change the address appropriately.
    b. If research is to be conducted in public healthcare facilities, approval from the Provincial Department of Health must be obtained. Note that this can only be applied for **after** the HSREC has granted **conditional approval** pending the submission of this permission. Do not apply for gatekeeper permission with any other approval status (e.g. modifications required).
        • Gatekeepers are the owners of the data
    c. If research is to be conducted in another province/country, the responsibility lies with the researcher to ascertain the appropriate permission required and inform the HSREC thereof.
    d. If research is to be conducted at schools within the Free State, see item 26 of this list.

15. Curriculum vitae:
    a. Student(s) CV(s)
        i. Mention full names, Student number, course, language, ID no and cell phone number
    b. Principal investigators CV
    c. Main Supervisor's abridged CV
    d. Co-supervisor's abridged CV (if appropriate)
    e. Sub/ Co-Investigator (s) CV(s) (if appropriate)

16. Evaluation Committee approval: Masters, M.Med and Doctoral degrees
    a. The final signed Evaluation Committee report (or Departmental Research Committee in the case of MMed) must be submitted at the time of application to the HSREC. If this document has not been submitted, the project will not be taken in for review.
    b. A letter from the supervisor is also required here. This letter should state that the comments from the Evaluation Committee Report have been implemented to the satisfaction of the supervisor (excluding M.Med applications).

17. Approval letter from a Biostatistician
    a. All studies that require statistical analyses must be accompanied by either:
        a. A letter from the Department of Biostatistics, UFS
        b. A letter stating who will be performing the statistical analyses.

b. Visit the UFS Department of Biostatistics webpage to find contact details and departmental policies and procedures: https://www.ufs.ac.za/health/departments-and-divisions/biostatistics-home

18. Good Practice (GCP)
    a. In the case of all intervention trials, such research protocols will be evaluated on merit and the risk will determine the need for the researcher to produce a current GCP certificate or attend a GCP course. The reviewers will evaluate the necessity for the researcher to attend a GCP course. The reviewers will make the appropriate recommendations to the HSREC. The final decision regarding the necessity to provide a GCP certificate of attendance of a GCP course will be taken at the HSREC meeting.
    b. All contract research/clinical trials require investigators to have current GCP

19. Professional Registration
    a. Proof of current professional registration (e.g. HPCSA, Nursing Council, etc.) must be submitted for all investigators, where applicable

20. Insurance Certificate
    a. Applicable to contract research/clinical trials or any research that involves an intervention that may result in risk beyond netlabel risk to the participant

21. Data management plan
    a. If any personal information is being processed.
    b.
22. Any other documents not mentioned above that need to be uploaded

23. Material transfer agreement
    a. If any samples will be transferred between labs, this needs to be included in your application.
    b. Not relevant in the case of contract research

24. Data transfer agreement
    a. If any data will be shared between institutions.
    b. Not relevant in the case of contract research

25. Documents required for clinical trials/contract research:
    a. List of documents for Sponsor
        i. Please list all documents that have been uploaded in the documents checklist (with version numbers and dates where applicable) in the text area proved. This list will be used to send a letter to your sponsor notifying them which documents have been submitted by you.
    b. NHREC Registration form
    c. SAHPRA application / approval letter

26. Free State Department of Education – Application
    a. All research conducted at schools within the Free State must be registered and approved at the Free State Department of Education (DOE).
    b. The department has its own application form for this purpose, which has now been integrated into the UFS RIMS ethics clearance application.
    c. The HSREC application form on RIMS now contains a question asking if the research will be conducted at schools in the Free State, which must be answered Yes/No.
        i. If Yes is selected a link which downloads the DOE application form in MS Word format will automatically appear along with a mandatory file upload field.
    d. After the DOE application form is filled out, the completed document must be uploaded in the mandatory field in the HSREC application form.
    e. Once the HSREC application form has been submitted, it will route directly to the HSREC Ethics Office Admin and after being accepted route automatically to the official at the DOE.
    f. The DOE official will decide if the application can be accepted for review by the HSREC or if it must be sent back to the PI for revisions, in which case the PI must edit the

application according to stipulations that will be provided by the DOE official (which will be visible on the record in RIMS) and re-submit it.

g. Acceptance of the application by the DOE official on RIMS will be regarded as full DOE approval and no approval letter or communication directly from DOE is required as part of the process as an application cannot be sent through the route in RIMS to the HSREC without the DOE official accepting it.
h. The full record of the application process, including proof that DOE has approved it will be present on RIMS.
i. Data collection can only commence after the HSREC has approved the application and issued the PI with a full ethics approval letter, as per usual.

IMPORTANT NOTE:

- HSREC Administration strongly recommends that all researchers who need to apply with the Free State Department of Education (DOE) submit their applications on RIMS at least two weeks prior to the HSREC submission deadline.
- The Free State Department of Education is the only province integrated into the RIMS system. For all other provinces, the ethics process should be completed prior to requesting permission from the relevant province.

Case studies/series

The following documents should be prepared for submission to the HSREC.

- Some items in this list might not be applicable to a project, please select the N/A option on the form.

1. Cover letter
    a. Draft a letter addressed to the Chairperson of the HSREC. Contact details provided at the beginning of this document.
    b. If the new application is part of a main study, please quote the main study's ethics number in this letter.

2. Article, Presentation or Both

3. Patient data

4. Anonymous laboratory data or imaging material

5. Copies of all images, videos, drawings or any other media, and all potentially identifying data that will be included in the publication/presentation.

6. Informed Consent:
    7.1 Adult Patient Consent form
    7.2 Child Assent form
    7.3 Parental / Guardian consent form is required if there is a Child Assent form
    7.4 Clear declaration if consent was not obtained including which measures were taken to seek consent from participant(s).
        a. If Informed Consent cannot be obtained from the patient, next of kin, etc. (due to death, lost to follow up, etc.) then the Clinical Head/Chief Executive Officer of the Institution must give consent.

7. Letter requesting permission from the institution where this case report/series will be conducted (other than public healthcare facilities), if applicable

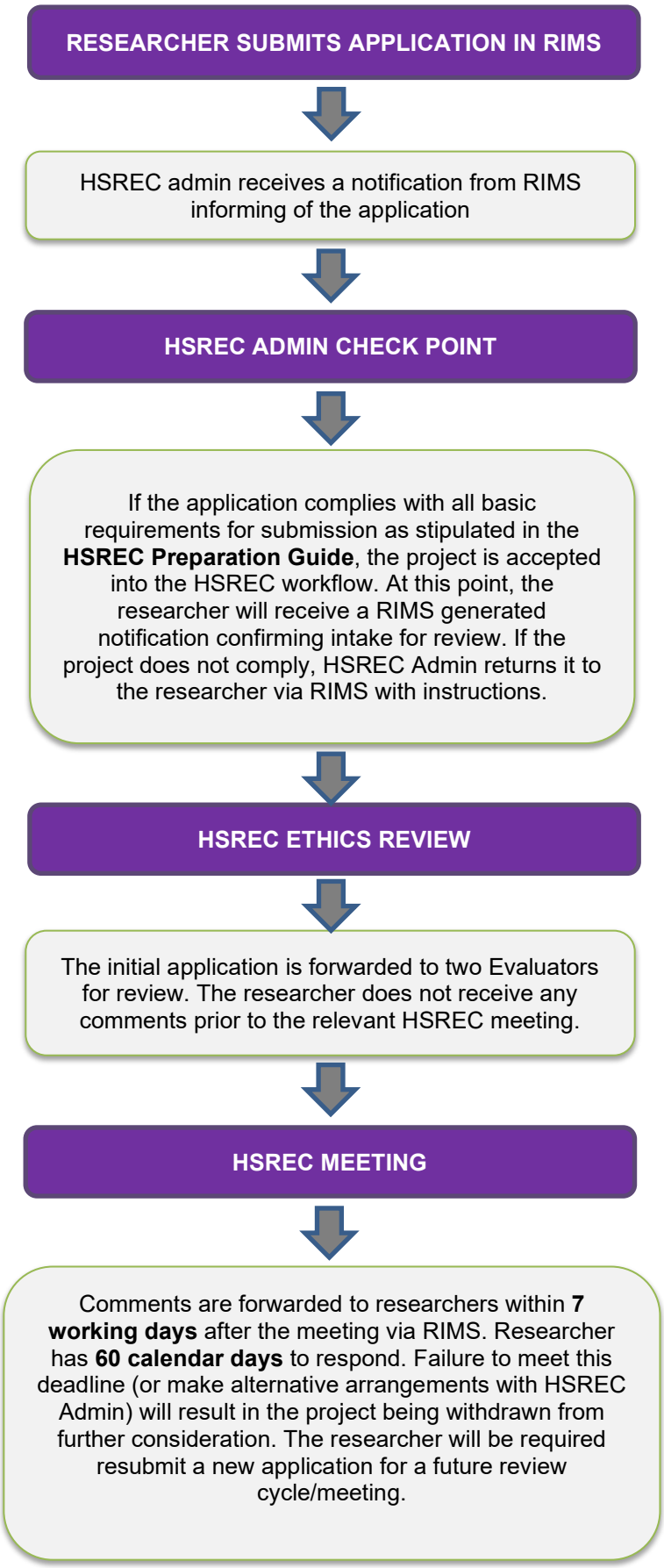
8. Letter requesting permission from the relevant provincial department
    a. Submit a cover letter addressed to the provincial department. You may use the same letter you addressed to the HSREC, and change the address appropriately.
    b. If research is to be conducted in public healthcare facilities, approval from the Provincial Department of Health must be obtained. Note that this can only be applied for **after** the HSREC has granted **conditional approval** pending the submission of this permission. Do not apply for gatekeeper permission with any other approval status (e.g. *modifications required*).
        - *Gatekeepers are the owners of the data*
    c. If research is to be conducted in another province/country, the responsibility lies with the researcher to ascertain the appropriate permission required and inform the HSREC thereof.

9. Permission letter from the Head of Department / School, if applicable
    a. If this letter is not submitted with the initial application, the project will not be taken in for review, but sent back to the researcher.
    b. The researcher's head of academic department must sign a letter confirming the researcher's project title.
    c. Do not submit a letter <u>requesting</u> permission from the HOD. It must be a final letter.

10. Abridged CV of all collaborators

11. Professional Registration
    a. Researcher and/or supervisor's proof of current registration must be submitted (e.g. HPCSA, Nursing Council, etc.)

What to expect after initial application submission



How to respond to comments from the HSREC

Possible review outcomes from a full convened meeting of the HSREC

Approval

a) The application is approved. Research activity may be conducted within the constraints (if any) established by the HSREC. No changes or additional information are required, and all of the applicable criteria for HSREC approval are met.
b) Final ethics clearance is valid for one year from the date of approval.
c) The official **ethics number** of the project is allocated.
d) **Response required from researcher:** Submission of progress report as specified in the final approval letter

Conditional approval

a) The HSREC has determined that the applicable criteria for approval have been met, based on the assumption that specific conditions will be met by the researcher and subsequently verified.
b) The application does not need to be presented at the next meeting, and can be granted final approval between meetings
c) The research activities under review cannot begin.
d) The project has not been allocated an official **ethics number** at this point, only a RIMS generated reference number which cannot be used as an ethics number.
e) **Response required from researcher**:
    - The HSREC requires as a condition of approval that the investigator: (1) make specified changes; (2) confirm specific assumptions or understandings on the part of the HSREC; and/or (3) provide additional or revised information or documents such that, based on the assumption that the conditions are satisfied, the applicable criteria for approval would be met and required determinations would be made.
    - Write a letter of response to the HSREC including a summary of changes (if applicable), and upload to RIMS as part of the response to conditions.
    - It is **very important** to highlight all changes made in documentation in order for the review to be finalised. Failure to comply with this request will delay approval.
    - Please note: All documents must be uploaded to/replaced on the HSREC Checklist. Documents submitted in any other location in RIMS will not be reviewed. Non-compliance to this request will result in the application being returned to the researcher to load the documents in the correct place.
    - The researcher has 60 calendar days to respond to the *Conditional Approval* determination, as stipulated in the official letter from the HSREC. If the deadline cannot be made, please inform HSREC Admin providing adequate justification.
        i. Failure to meet this deadline (or make alternative arrangements with HSREC Admin) will result in the project being withdrawn from further consideration. The researcher will be required resubmit a new application for a future review cycle/meeting.

Modifications required

a) The HSREC is unable to approve the research because it cannot make the determinations required for approval (i.e., the applicable criteria for HSREC approval have not been met.) The HSREC defers the item for further review after changes and/or additional information have been provided by the researcher.
b) The application does not need to be presented at the next meeting, and can be granted conditional/final approval between meetings
c) The research activities under review cannot begin.
d) The project has not been allocated an official **ethics number** at this point, only a RIMS generated reference number which cannot be used as an ethics number.
f) Response required from researcher:
    - Clarification, revised documents and/or additional information are required from the investigator in order to determine that the applicable criteria for HSREC approval are met.

- Use the Summary of Changes template (loaded onto RIMS as part of the HSREC Checklist) to draft your response to the HSREC. This is a mandatory form. Responses received without this form will be sent back to the researcher.
- Please note: All documents must be uploaded to/replaced on the HSREC Checklist. Documents submitted in any other location in RIMS will not be reviewed. Non-compliance to this request will result in the application being returned to the researcher to load the documents in the correct place.
- It is **very important** to highlight all changes made in documentation in order for the review to be finalised. Failure to comply with this request will delay approval.
- The researcher has 60 calendar days to respond to the *Modifications Required* determination, as stipulated in the official letter from the HSREC. If the deadline cannot be made, please inform HSREC Admin providing adequate justification.
    i. Failure to meet this deadline (or make alternative arrangements with HSREC Admin) will result in the project being withdrawn from further consideration. The researcher will be required resubmit a new application for a future review cycle/meeting.

Modifications required - Held over

a) The HSREC is unable to approve the research because it cannot make the determinations required for approval (i.e., the applicable criteria for HSREC approval have not been met, or critical documents, such as a data sheet, data management plan or informed consent document have not been provided.) The HSREC defers the item for further review after changes and/or additional information have been provided by the researcher.
b) The application will be presented at the next meeting for an updated determination.
c) The research activities under review cannot begin.
d) The project has not been allocated an official **ethics number** at this point, only a RIMS generated reference number which cannot be used as an ethics number.
e) Response required from researcher:
- Clarification, revised documents and/or additional information are required from the investigator in order to determine that the applicable criteria for HSREC approval are met.
- Use the Summary of Changes template (loaded onto RIMS as part of the HSREC Checklist) to draft your response to the HSREC. This is a mandatory form. Responses received without this form will be sent back to the researcher.
- Please note: All documents must be uploaded to/replaced on the HSREC Checklist. Documents submitted in any other location in RIMS will not be reviewed. Non-compliance to this request will result in the application being returned to the researcher to load the documents in the correct place.
- It is **very important** to highlight all changes made in documentation in order for the review to be finalised. Failure to comply with this request will delay approval.
- The researcher has 60 calendar days to respond to the *Modifications Required: Held over* determination, as stipulated in the official letter from the HSREC. If the deadline cannot be made, please inform HSREC Admin providing adequate justification.
    i. Failure to meet this deadline (or make alternative arrangements with HSREC Admin) will result in the project being withdrawn from further consideration. The researcher will be required resubmit a new application for a future review cycle/meeting.

Rejected/Disapproved

a) The applicable criteria for HSREC approval are not met, and the HSREC is not willing to re-consider the item.
b) An item is disapproved rather than deferred when the HSREC believes that it is very unlikely that:
- The applicable criteria for approval will be met even with substantial changes and/or additional information; or
- It is not possible to obtain (or the researcher is unwilling to provide) the substantial changes or additional information that would be necessary to meet the criteria for approval.

c) No actions proposed in the application may be initiated.
d) The project has **not** been allocated an official **ethics number** at this point, only a RIMS generated reference number which cannot be used as an ethics number.
e) **Response required from researcher:** None, the application is closed. The researcher may submit a new application after considerable updates have been made.

Subsequent submissions and reporting requirements on HSREC approved research

Definition

- Subsequent submissions refer to any and all applications, notifications, reports, etc., submitted to the HSREC for approval or notification after final approval has been granted for the initial application.
- All subsequent submissions and reports will only be accepted if submitted via RIMS. Hard copy and email submissions will not be accepted.

Paper vs electronic initial applications and RIMS

- All projects with an initial application **already on RIMS**
  - Log into RIMS and locate the relevant record. Choose the type of submission from the dropdown list. Electronic application forms have been created to accommodate all subsequent submissions. Please refer to page 16 of the 'How to apply for ethics clearance on RIMS' manual available on the HSREC webpage.
- All projects with an initial **paper** submission
  - Researchers require RIMS user profiles. If one has not been created, please contact the RIMS office (contact details at the start of this document)
  - Refer to the 'How to submit a Health Sciences Historical Ethics Clearance Application' RIMS manual (available on the HSREC webpage) for guidance on how to submit an historical application. This will enable you to submit your subsequent submissions (amendments, reports, notifications, etc.) on RIMS.

Progress and final reports

- Ethics approval is valid for one year from the date of approval on the official final approval letter. An annual progress report must be submitted to the HSREC before the ethics approval expiry date, so that the submission can be reviewed and the project re-approved for the next year. No research may continue without this process and re-approval.
- The progress report should contain sufficient information to allow the reviewer to conduct a substantive and meaningful review of the progress of the project, including any challenges or problems encountered.
- HSREC policy requires researchers to formally inform HSREC when a study is completed. A study is considered active while analysis of any data (human or other data) collected or resulting from the study is ongoing.

Amendments

- HSREC review and approval is required in advance of implementing any changes (amendments) to a protocol. Amendment applications may be submitted at any time after the study has been granted final approval.
- The changes made to applications as a response to HSREC comments (and prior to final approval of the initial application) are not considered an amendment, but part of the initial review.
- All applications for an amendment must include a letter to the HSREC with the rationale or justification for the proposed change(s). The justification for an amendment must clarify how it will change the study, how it will affect risks to participants and what safeguards will be introduced to protect participants from additional risks. If the revision requires a change in the informed consent process, a revised consent form must be submitted with the amendment.
- Submission requirement: please submit the updated documents in track changes or highlighted, in order for the review to take place. If the changes are not indicated/justified, the amendment will not be reviewed, but returned to the researcher.

  Minor amendments do not change the risk benefit profile of the study in any way.

  Examples of typical minor amendments:
  a) Additional investigators or study sites
  b) Small changes in the Informed Consent
  c) Change in background information or update of literature review

d) Extension of period of study
e) Other changes that do not affect study design and will not affect study outcomes or results
f) Administrative changes
g) Stricter inclusion or exclusion criteria

Major or substantive amendments require a change(s) to the study methodology or procedure that may result in an alteration of the risk benefit profile of the study.

Examples of typical major or substantive amendments:

a) Change in study aims, objectives or design
b) Resulting changes to consent documents
c) Additional study procedures
d) Easing of inclusion or exclusion criteria

Unexpected Problems and Adverse Events

- The HSREC requires researchers to promptly notify the HSREC of the following information and events, for any HSREC approved research:
    - Unexpected problem;
    - Unexpected adverse medical device effect;
    - Adverse Events and Serious Adverse Events;
    - Serious non-compliance by researcher (or allegation of serious non-compliance);
    - Continuing non-compliance (or allegation of continuing non-compliance);
    - Emergency deviation from HSREC-approved procedures made without prior HSREC review to eliminate an apparent immediate hazard to a subject or others;
    - Continuation of research procedures after HSREC approval has lapsed, because the procedures are of direct benefit to individual subjects or withholding the research intervention (if any) may increase risks to subjects;
    - Breach (or risk of breach) of subject confidentiality or privacy;
    - Complaint of a subject that cannot be resolved by the study team;
    - Audit, inspection, compliance-related inquiry, or safety-related inquiry from a regulatory agency;
    - New information that has implications for the risks of the research

When to report Unexpected Problems or Adverse Events: Table 1 on the next page includes a list of information and events that need to be reported as well as the timelines.

Table 1: HSREC required reporting timelines for unexpected problems or adverse events

Information or Event	When to report
Unexpected problems	All unexpected problems that increase the risk of harm to participants or others must be reported to the HSREC **within seven calendar days** after the investigator first learns of their occurrence
Fatal and life-threatening, unexpected adverse drug reactions	All fatal and life-threatening adverse drug reactions in clinical trials must be reported to the HSREC **as soon as possible but not later than seven calendar days** after the investigator first learns of their occurrence.
Serious and unexpected non-fatal adverse drug reactions	All serious unexpected drug reactions that are not fatal or life-threatening must be reported to the HSREC **as soon as possible but not later than fifteen calendar days** after first learning of their occurrence.
Expected adverse drug reactions	All adverse drug reactions that are expected but are judged to be occurring at a significantly higher frequency or severity than expected must be reported to the HSREC **within fifteen calendar days** after the investigator first learns of their occurrence. The basis for these assessments must be included in the investigator's report.
Serious and unexpected adverse device effects	All unexpected adverse device effects must be reported to the HSREC **as soon as possible but not later than seven calendar days** after first learning about their occurrence
New information that might impact the conduct of a clinical trial	Other unexpected adverse events, regardless of severity, that may alter the balance of risks and benefits in a study and as a result warrant consideration of substantive changes in the overall conduct of a clinical trial must be reported to the HSREC **within three calendar days** of first learning about their occurrence. The report could include individual case reports or a major safety finding from other sources.

Table 2: Timelines for Reporting Protocol Violations/Deviations and Study Exceptions

Information or Event	When to report
Major protocol violations/deviations	The Principal Investigator must report major protocol deviations to the HSREC **within seven calendar days** of first hearing of the incident
Minor protocol violations/deviations	If the principal investigator determines the deviation is **minor** and has **no impact** on the study or welfare of participants, **no further action** is necessary and the **deviation can be reported in the next annual progress report.**
Study exceptions	All study exceptions must receive HSREC approval **prior** to initiation and must be **listed** in the subsequent progress report.

Appendix 1: Example of Cover Letter
Note: Customise to be project specific and upload to RIMS Document Checklist

[RESEARCHER ADDRESS]
[DATE]

The Chair: Health Sciences Research Ethics Committee
Block D, Room 104,
Francois Retief Building

PO Box 339 (G40)
Nelson Mandela Drive
Faculty of Health Sciences
University of the Free State
Bloemfontein
9300

Dear

PROJECT TITLE: [INSERT TITLE]

Enclosed please find the above research protocol for your evaluation and approval.
[PLEASE DELETE THIS SENTENCE. MENTION ANY OTHER DETAILS FOR NOTIFICATION BY THE HSREC THAT WAS NOT INCLUDED IN THE PROTOCOL OR APPLICATION FORM]

Yours faithfully,

_____
[INSERT NAME AND SIGNATURE OF RESEARCHER]

Email address
Cell phone number

*Appendix 2: Example of Head of Department permission letter – **must** be printed on the Department letterhead.*
Note: Customise to be project-specific and upload to RIMS Document Checklist

The Chair: Health Sciences Research Ethics Committee
Block D, Room 104,
Francois Retief Building

PO Box 339 (G40)
Nelson Mandela Drive
Faculty of Health Sciences
University of the Free State
Bloemfontein
9300
[DATE]

Dear

[STUDENT NAME AND NUMBER]
[PROJECT TITLE]

I, [HOD NAME] hereby grant [STUDENT NAME] permission to conduct the above-mentioned research project. The research will be completed in accordance with myself as Head of Department of [ENTER DEPT NAME] and [ENTER STUDENT SUPERVISOR NAME] as supervisor of this study.

Yours faithfully,

_____
[HEAD OF DEPT NAME AND DATE]

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

NATIONAL
HEALTH
RESEARCH ETHICS
COUNCIL

Private Bag X828, PRETORIA, 0001, Cnr Struben and Thabo Sehume Street
Tel: +27 (0) 12 395 8124/8113 Fax: +27 (0) 12 395 9249

MINISTERIAL CONSENT FOR NON-THERAPEUTIC HEALTH RESEARCH WITH MINORS: *OPERATIONAL GUIDELINES* 2015

1 PURPOSE

To provide guidance to health Research Ethics Committees (RECs) and health researchers regarding Ministerial Consent for 'non-therapeutic' health research with minors.

2 BACKGROUND

1. Section 71(3)(a)(ii) of the National Health Act (NHA) requires the Minister of Health to consent to 'non-therapeutic' health research with minors, after considering whether four criteria are met (see Appendix 1).
2. The Minister may delegate authority, in terms of s 92(a), to any person in the employ of the state, a council, board or committee established in terms of the Act to give this consent.
3. The Minister has delegated authority to provide Ministerial Consent for 'nontherapeutic' health research with minors to RECs who have been found to be compliant with the audit and have achieved full registration with the NHREC. Correspondence in this regard was sent to relevant RECs on 14 October 2014. As further RECs become fully registered, their authority to exercise the delegated power will be communicated by the NHREC through the Secretariat.
4. Regulations for research with human participants, published on 19 September 2014 (R 719; see Appendix 2), contain Form A that sets out the four criteria to be met for the additional review of 'non-therapeutic' health research with minors. Proper use of Form A should provide adequate evidence that these reviews are performed appropriately by RECs (see Appendix 3).

3 RECOMMENDATIONS FOR ***RESEARCHERS***

1. Researchers should consider carefully whether their planned research involving minors holds out the prospect of direct benefit to participants ('therapeutic' research); or whether it holds out no prospect of direct benefit to participants but holds out the prospect of generalisable knowledge ('non-therapeutic' research).
2. Researchers conducting 'non-therapeutic' research with minors must attach Form A to the application for ethics approval.
3. The content supplied in Form A should draw on relevant sections of the protocol or ethics application, for example, the sections that deal with the scientific justification for enrolling minors; how knowledge will be advanced by enrolling minors; the benefits to society in terms of knowledge gained by enrolling minors; and the potential risks to enrolled minors and risk minimisation.

4. Whether Ministerial Consent for 'non-therapeutic' health research with minors has been granted will be communicated, as part of the overall feedback about the application from the REC.

4 RECOMMENDATIONS FOR REGISTERED ***RECS***

1. RECs with delegated authority to grant Ministerial Consent must draw to the attention of researchers the following requirements:
   a) That researchers must consider carefully whether their planned research involving minors holds out the prospect of direct benefit to participants ('therapeutic research'); or whether it holds out no prospect of direct benefit to participants but holds out the prospect of generalisable knowledge ('nontherapeutic research').
   b) That 'non-therapeutic' research must meet four criteria to be eligible for Ministerial Consent.
   c) That the ethics application for 'non-therapeutic' health research with minors must include Form A completed appropriately.
   d) That where the REC judges that the research involves 'non-therapeutic' health research with minors, this view will be communicated to the researcher with a request to complete Form A accordingly.
   e) That the content supplied in Form A should draw on relevant sections of the protocol or ethics application, for example, the sections that deal with the scientific justification for enrolling minors; how knowledge will be advanced by enrolling minors; the benefits to society in terms of knowledge gained by enrolling minors; and the potential risks to enrolled minors and risk minimisation.
   f) That the outcome (whether consent for non-therapeutic health research with minors is granted) will be communicated by the REC, as part of the overall feedback about the application.
   g) That 'therapeutic' health research with minors does not require this additional review but is reviewed in the usual way to ensure norms and standards are met.
2. RECs should only grant Ministerial Consent after review of the application leads to the decision to grant ethics approval, and the careful review of Form A satisfies the REC that the four criteria are met.
3. RECs should maintain specific records of such applications, and outcomes, for reporting purposes. A traceable link to each application must be maintained.
4. RECs may devise Standard Operating Procedures (SOPs) to integrate the additional review into the overall ethics review process to facilitate efficient use of time.

5 RECOMMENDATIONS FOR NON-REGISTERED RECs

1. Two types of REC might not be registered with the NHREC.
2. The first type is an REC that reviews health research but has not been granted delegated authority because it is not (yet) fully registered with the NHREC. RECs that fall into this category are urged to complete the registration process as soon as possible.
3. The second type is an REC that does not review 'health research' with human subjects and is – because of the remit of its review and oversight authority – not registered and is unlikely to seek registration. While such RECs are not required to address the issue of Ministerial Consent, they should carefully review non-health research including the justification for the involvement of minors.

6 CONCLUSIONS

1. It is hoped that the delegation of authority from the Minister to fully registered RECs to grant Ministerial Consent for 'non-therapeutic' research with children will resolve an important issue in the short-term, while appropriate law reform of section 71 is pursued in the medium term.
2. RECs and researchers are requested to send feedback to the NHREC about the process of granting Ministerial Consent and the adequacy of these operational guidelines, so that improvements can be made.

Appendix 1: CURRENT WORDING: S 71 OF THE NATIONAL HEALTH ACT

Research on or experimentation with human subjects

(1) Notwithstanding anything to the contrary in any other law, research or experimentation on a living person may only be conducted- *(a)* in the prescribed manner; and
(b) with the written consent of the person after he or she has been informed of the objects of the research or experimentation and any possible positive or negative consequences on his or her health.

(2) Where research or experimentation is to be conducted on a minor for a therapeutic purpose, the research or experimentation may only be conducted- *(a)* if it is in the best interests of the minor; in such manner and on such conditions as may be prescribed;
with the consent of the parent or guardian of the child; and
if the minor is capable of understanding, with the consent of the minor.

(3) *(a)* Where research or experimentation is to be conducted on a minor for a non-therapeutic purpose, the research or experimentation may only be conducted- (i) in such manner and on such conditions as may be prescribed;
(ii) with the consent of the Minister;
(iii) with the consent of the parent or guardian of the minor; and (iv) if the minor is capable of understanding, the consent of the minor.
(b) The Minister may not give consent in circumstances where- (i) the objects of the research or experimentation can also be achieved if it is conducted on an adult; (ii) the research or experimentation is not likely to significantly improve scientific understanding of the minor's condition, disease or disorder to such an extent that it will result in significant benefit to the minor or other minors; (iii) the reasons for the consent to the research or experimentation by the parent or guardian and, if applicable, the minor are contrary to public policy;
(iv) the research or experimentation poses a significant risk to the health of the minor; or (v) there is some risk to the health or wellbeing of the minor and the potential benefit of the research or experimentation does not significantly outweigh that risk.

Appendix 2: CURRENT WORDING: S 7 OF THE REGULATIONS FOR RESEARCH WITH HUMANN PARTICIPANTS

Ministerial consent for non-therapeutic research with minors

7. Protocols for human participants' research that propose non-therapeutic research with minors 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.**

a) Applications for ministerial consent must be made on Form A;
b) the application should be considered by the Minister or the delegated authority after the protocol is reviewed by a registered health research ethics committee to assess whether it meets the required norms and standards of the health research ethics committee;
c) in granting ministerial consent, relevant bodies or experts may be consulted;
d) the researcher must be notified of the outcome in writing within 60 days; and
e) the researcher may appeal the outcome including by approaching the National Health Research Ethics Council in terms of section 72 (6) (d) of the Act.

Appendix 3: Application for Ministerial Consent for Non-Therapeutic Research with Minors (Form A)

*Note: Complete and upload to RIMS application form if applicable. **DO NOT** modify this form.*

DEPARTMENT OF HEALTH

APPLICATION FOR MINISTERIAL CONSENT FOR NON-THERAPEUTIC RESEARCH WITH MINORS

1. INSTRUCTIONS

1.1 This application form must be completed for all protocols that are classified as "non-therapeutic" and involve the participation of minors. *Non therapeutic research is defined in the regulations relating to research on human participants as "research that does not hold out the prospect of direct benefit but holds out the prospect of generalizable knowledge". Minors are defined as persons under the age of 18 by section17 of the Children's Act (No. 38 of 2005).*

1.2 This application form should be submitted with a copy of the protocol and supporting documents.

1.3 This application should be submitted to the Minister of Health or the delegated authority in terms of section 92(a) of the Act.

1.4 This application form should describe how 'non-therapeutic' research protocols with minors meet the conditions set out in section 71 (3)(b) of the Act (described below).

1.5 All sections of the form must be completed in full.

1.6 Ministerial Consent may be granted for non-therapeutic health research with minors when certain conditions set out in section 71 (3)(b) of the Act are met and these conditions are:

(a) The research objectives cannot be achieved except by the enrolment of minors;

(b) The research is likely to lead to an improved scientific understanding of conditions, or disorders affecting children;

(c) Any consent given to the research must be in line with public policy; and

(d) The research does not pose a significant risk to minors, and if there is some risk, the benefit of the research outweighs the risk.

2. INVESTIGATORS' DETAILS

Name of principal investigator	
Title of research protocol	
Institutional affiliation	
Postal Address	
Physical Address	
Email Address	
Phone	
Fax	
Date of Application	
Signature of Applicant	

3. APPLICATION

3.1 Condition 1: The research objectives cannot be achieved except by the participation of minors

Describe the scientific justification for the enrolment of minors. Explain why this research must be done with minors as participants:

3.2 Condition 2: The research is likely lead to an improved scientific understanding of certain conditions, diseases or disorders affecting minors

Describe how the research might, or aims to, advance knowledge affecting the health and welfare of minors as a class. Note that 'condition' is defined in the Regulations as 'physical and psychosocial characteristics understood to affect health' allowing that this research does not only involve children with an illness.

3.3 Condition 3: Any consent given to the research is in line with public policy

Consent given by authorised persons must be in line with public policy considerations. Describe how consent to the research will be in line with public policy or would be acceptable, for example, show how the research poses acceptable risks and promotes the rights of minors:

3.4 Condition 4: The research does not pose a significant risk to minors; and if there is some risk, the benefit of the research outweighs the risk.

Describe how the potential risks from the research procedures and/or intervention to minor participants will be minimised and describe any possible benefits from the research to society in the form of knowledge:

Appendix 5: Broad Ethical Principles for Ethics Review (DOH2015)

THREE BROAD ETHICAL PRINCIPLES

Beneficence and non-maleficence

- Maximise benefit and minimise harm, risks of harm posed by the research must be reasonable in light of anticipated benefits.
- Research design must be sound; researchers must be competent to carry out the proposed research activities.
- Research involving human participants should seek to improve the human condition. If the research cannot do this, then it is unlikely to be ethical.

Distributive justice (equality)

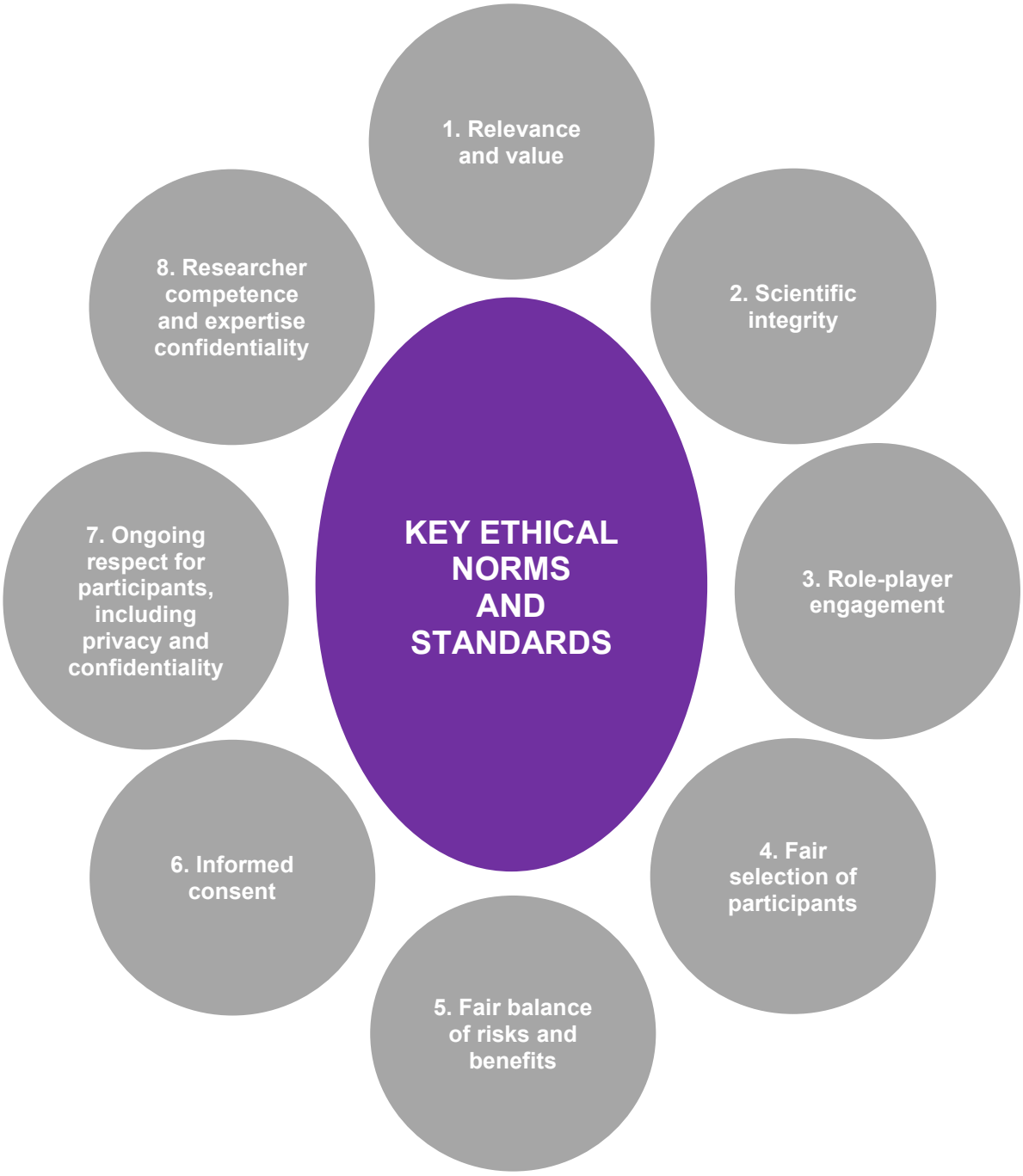
- Fair balance of risks and benefits amongst all role-players in research;
- Principle of equality is expressed in the research context.
- No segment of the population to be unduly burdened by the harms of research or denied the benefits of knowledge derived from it.
- Reasonable likelihood that the population from which participants are drawn will benefit from the research results, if not immediately, then in the future.

Respect for persons (dignity and

- Persons capable of deliberation about their choices must be treated with respect and permitted to exercise self-determination.
- Persons who lack capacity/ diminished capacity protected against harm from irresponsible choices.
- Dignity, well-being and safety interests of all research participants are the primary concern
- Interests of participants should outweigh the interests of science and society. Consequently, involvement of persons or particular categories of people in the research should be justified in research proposals.
- Respect for persons means also that the interests of researchers must be considered. These include welfare and safety interests, authorship and intellectual property interests, and collegial and professional interests.

Appendix 6: Eight Key Ethical Norms and Standards for Ethics Review (DOH2015)

KEY ETHICAL NORMS AND STANDARDS



Version history

Version 07.01_Feb 2019	• Changes as per branding guidelines • Deadline of 30 days to respond to review comments from the HSREC was extended to 60 days • M.Med research added to list requiring Evaluation Committee reports • DOE-required steps were added to post- and undergraduate research sections as well as case report section. • MCC updated to SAHPRA • HSREC 17 form/requirements updated to reflect the new system • Updated dates for 2019 • Ethical considerations inclusion for lay terms summary • Inclusion of the mandatory Summary of Changes form when responding to comments from the HSREC. • Adjusted fees. • All documents must be uploaded to/replaced on the Documents Checklist. Documents submitted in any other location in RIMS will not be reviewed. Non-compliance to this request will result in the application being returned to the researcher to load the documents in the correct place. • Update of the RIMS login procedures for UFS students and staff – Single sign-on
Version 07.02_12Feb2020	• Updated submissions, workshop and meeting dates. • Documents Checklist name change to HSREC Checklist. • Updated fee structure for 2020. • Updated Department of Education application process. • Updated External Researcher process
Version 07.03_01Jan2020	• Biostatistician contact details updated • Submission and meeting dates updated • Supervisor's letter of support – Evaluation Committee Report • Changes as per branding guidelines
Version 08.01_SEP2021	• Updated Investigator Declarations • Updated General Notes section • Updated Lay term summary guidelines • Section on Racial Labelling added • Section on GCP added
Version 09.01_AUG2021	• Consolidated and edited the Application Documents section (no longer differentiated for undergraduate and postgraduate and contract research) • Remove HSREC 18, 20 • Update HSREC 19 • Refer researchers to Biostatistics webpage • Updated meeting dates
Version 10.01 Nov 2023	• Updated informed consent • Minor editing • Remove HSREC 19 – to be a separate document • Remove dates for meetings – to be a separate document