UNIVERSITY OF THE FREE STATE
UNIVERSITEIT VAN DIE VRYSTAAT
YUNIVESITHI YA FREISTATA
UFS·UV
HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

HEALTH SCIENCES RESEARCH ETHICS COMMITTEE

CONTRACT / CLINICAL RESEARCH
GENERAL SUBMISSION GUIDELINES 2017

All applications must be approved by the Health Sciences Research Ethics Committee (HSREC) BEFORE research is conducted / continued.

a. **New applications** can be hand delivered or sent by registered mail to HSREC Administration no later than the submission dates for 2017 listed below in order to be tabled at the next meeting.

b. **Subsequent submissions** (amendments, reports, notifications, etc.) can be hand delivered or sent by registered mail to HSREC Administration no later than **7 working days prior** to the meeting in order to be tabled at the next meeting.

IMPORTANT NOTE: *Late and incomplete submissions will stand over until the next meeting. Please contact HSREC Administration to arrange for a consultation if needed.*

SUBMISSION DATES 2017	MEETING DATES 2017
20 JANUARY 2017	31 JANUARY 2017
17 FEBRUARY 2017	28 FEBRUARY 2017
15 MARCH 2017	28 MARCH 2017
12 APRIL 2017	25 APRIL 2017
19 MAY 2017	30 MAY 2017
15 JUNE 2017	27 JUNE 2017
14 JULY 2017	25 JULY 2017
18 AUGUST 2017	29 AUGUST 2017
14 SEPTEMBER 2017	26 SEPTEMBER 2017
20 OCTOBER 2017	31 OCTOBER 2017
24 NOVEMBER 2017	05 DECEMBER 2017

HSREC ADMINISTRATION CONTACT DETAILS:		
The Chair: Health Sciences Research Ethics Committee Dr SM Le Grange For Attention: Mrs M Marais 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	Mrs M Marais *Head: Administration* Mrs J du Plessis *Administration*	051-401 7795 051-401 7794
	Fax number	051-4444359
	Email	ethicsfhs@ufs.ac.za
	Office hours	07h45 – 16h30

SUBMISSION REQUIREMENTS: NEW PROJECT APPLICATIONS:

Submit **TWO HARD COPIES** of the following to the HSREC office (Block D, Room 104, Dean's Division, Faculty of Health Sciences, Francois Retief Building).

(PLEASE SEE SUBMISSION REQUIREMENTS BELOW)

1. Application form

- Signed by the Supervisor/Head of Department/Principal Investigator/Students/Co- and sub investigators
- All applications must be **typed** or printed in black ink on the prescribed form (available on the HSREC webpage)
- **Completed Checklist** (in the application form)
- **Investigator declaration of conflict of interest for ALL investigators MUST be signed in the Application Form**
    - If the study is for degree purposes, a supervisor declaration should be signed by the study supervisor as well.

IMPORTANT NOTE: Signatures are **mandatory**. Applications will **not** be accepted for review if all required signatures have not been obtained.

2. Cover Letter

- All documents submitted are clearly listed with version numbers and dates on the cover letter.
- If the new application forms part of a sub-study, the main study's ethics reference number is quoted.

3. Study protocol

- Page numbers, version numbers and dates on protocol

4. Investigator's Brochure and other related material, if applicable

5. Protocol summary in layman's terms

Simple, clear language must be used (maximum Grade 8 reading level) and all medical and technical terms have to be explained.

Definition:
To put something in lay terms is to describe a complex or technical issue using words and terms that the average individual (someone without professional training in the subject area) can understand, so that they may comprehend the issue to some degree.

When submitting any research protocol for ethical approval, a lay term summary **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.

A summary of the research protocol in lay terms **must** be included as an addendum to the protocol, printed on a separate page (no longer than 1 A4 page).

IMPORTANT: It is **mandatory** to email the summary in Word format to ethicsfhs@ufs.ac.za **before or on the last date** for submissions. Please ensure that the Project title and Principal Investigator's name(s) is/are included in the document. Failure to comply might result in the project **not** being tabled on the agenda for the meeting and instead held over until the next meeting.

Examples of what Lay terms should describe:

- *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*
- *Risk and adverse effects of participating in the study*
- *Expected outcome of the research.*

**Note that a lay term summary with regard to contract research must be compiled by the Principal Investigator.*

*Guidance for simplifying medical terms can be found on the following webpage:
http://medicine.umich.edu/medschool/research/office-research/institutional-review-boards/guidance/simplification-guide-medical-terms#A

6. Questionnaires and/or other measuring tools/instruments

The questionnaire(s) can be submitted in either English or Afrikaans and must be written in layman's terms. Once the requested changes, if any, have been made, then the committee may request the researcher to submit translations in English, Afrikaans, Sesotho or other applicable languages. Questionnaires must be available in the main language(s) of the research setting.

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.

7. Recruitment material/ Advertisement(s)

If an advertisement for potential study subjects must be placed in the media, it must include the following information:

- Advertisement in its final form (logo etc.) must be presented to the HSREC
- Note condition/disease under discussion in the research proposal in layman's terms
- Category participants: Age, etc.
- Which method will be used, e.g. questionnaires
- Remuneration for transport and inconvenience
- Any costs payable by participant
- Contact person's name and cell phone number
- For further enquiries also note office hours, if applicable
- Voluntary participation and participant may withdraw at any time
- Patients currently on treatment will participation in the research study in conjunction with the treating physician
- Time duration of study

8. Material Transfer Agreement (if applicable)

9. Budget or Financial Contract

10. Letters of approval to conduct research

NOTE: If permission has been requested but not been granted by the time of submission, include the **letter of request** in this application.

Feedback on a letterhead of the institution and the name (printed) of the person granting approval has to appear together with the signature and must be submitted to the Ethics Committee in order to obtain final approval before conducting a study.

The following letters of approval must be submitted:

- **Head of Academic Department**
- **Institutional permission (other than public healthcare facilities)**
- 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** ethical approval has been granted. See HSREC webpage for relevant information.
- 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.
- Approval must be obtained from the UFS authorities if research is to be conducted among students, lecturers or other role-players on campus at the University of the Free State. Approval form: UFS authorities (EC42) must be used for this purpose.
- If research is to be conducted in a specific faculty, permission must be obtained from the Dean of the specific faculty and the Head of the School involved as indicated on the EC42 form. A copy of the protocol together with a cover letter must be attached to the EC42 form before it is submitted to the Dean of the specific faculty and the Head of the School for approval purposes.
- If research is to be conducted in the Faculty of Health Sciences, permission must be obtained from the Dean of the Faculty of Health Sciences and the Head of the School involved as indicated on the EC42 form. A copy of the protocol and the HSREC Application form must be attached to the EC42 form before it is submitted to the Head of the School and the Dean for approval purposes.
- When research are to be conducted in UNIVERSITY RESIDENCES, the consent of the Dean, Student Services as indicated on the EC42 form must also be obtained. A copy of the protocol must be attached to the EC42 form before it is submitted for approval purposes.
- When research is to be conducted among students, lecturers or other role-players on campus at the University of the Free State permission must be obtained from the Vice-rector: Research as indicated on the EC42 form. A copy of the protocol must be attached to the EC42 form in order to obtain approval.
- A progress report must be sent to the Vice-rector: Research after completion of the study.
- If your project is conducted at a school, consent/permission has to be obtained from the following:
    - Department of Education
    - Principal and Teacher
    - Parent/guardian
    - Learners

The following must be mentioned in the letter:

- Project/trial/study title
- Name and contact details of the researcher
- Brief description of the project/trial/study
- The relevant department/ward and whether patients and/or files are involved
- Number of patients, records/files, samples involved
- Duration of the study
- Whether the results of the project will be published and/or presented at a meeting/congress

11. Participant Information and Consent/Assent Form (ICF)

NOTE: The ICF can be submitted in either English or Afrikaans and must be written in layman's terms. 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.

The following must be mentioned in die **INFORMATION LEAFLET AND INFORMED CONSENT**:

- Purpose of the study (explanation in lay terms)
- Potential advantages of the study for the patient and the other persons
- Risks and foreseeable discomfort for the patient/subject
- That the patient/subject may withdraw from the study at any time
- That participation is voluntary
- Alternative methods for treatment available?
- Nature of preparations (+ placebo) in use
- That information obtained will be treated as confidential
- That insurance has been taken out to protect subjects
- The name of the contact person
- The reversibility or irreversibility of side-effects
- Number of studies that have so far been conducted with this substance on animals and also the number of persons that have been exposed to it
- Serious adverse effects
- Dotted line for signature and date
- That results may be published and/or presented at a meeting/congress
- That no costs will be payable by the participant
- Remuneration for patient/participant?
- In prospective ongoing studies where invasive procedures or new drugs are investigated, for an unregistered indication, the information leaflet and informed consent must be combined in one document. Participants of prospective drug or interventional (invasive) studies must receive a copy of the informed consent and information leaflet to ensure access to the document at all times. 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.
- Time that participant will have to give up to participate in the study
- Whether the product will be made available to participants on completion of the study and if so, whether there are any cost implications for the participant.

KINDLY NOTE: 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.

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.

12. Evaluation Committee / other review committee approval: Masters (excluding M.Med.) and Doctoral degrees

13. Insurance Certificate, if applicable

14. <u>Short</u> Curriculum Vitae (CV) of all investigators

- Submit a short CV for the principal investigator, co-investigators, and sub-investigators (where applicable)
- **Each CV should not comprise more than 2 pages.**
- Undergraduate student groups: Mention full names, Student nr, course, language, ID nr and cell phone number

If the study is for degree purposes, a supervisor CV must also be included.

15. Approval by a Biostatistician

Please note the following when the Department of Biostatistics, Faculty of Health Sciences (Prof G Joubert Tel. 051-401 3117, Ms. M Nel Tel. 051-401 3116, Mr. FC van Rooyen Tel. 051-401 3114, Dr J Raubenheimer Tel 051-401 3115), CR de Wet Building, UFS will be assisting you with the protocol:

- In cases where protocols are submitted for the first time, these should be handed in at the Department of Biostatistics one month prior to the submission date of the HSREC.
- Protocols already verified by the Department of Biostatistics and which only need to be finally approved must be submitted to the Department of Biostatistics 2 weeks before the submission date of the HSREC.

Please note that, if the Department of Biostatistics, UFS is involved in analysing data, a letter of approval issued by the Department of Biostatistics must be attached to the protocol for submission to the HSREC.

Approval letters from biostatisticians/statisticians other than the Department of Biostatistics, Faculty of Health Sciences must also be submitted.

If no biostatisticians/statisticians are involved in a research study, the researchers themselves must provide sufficient information in order for reviewers to evaluate the ethical aspects of the statistics being used in the mentioned study.

16. GCP (Good Clinical Practice) certificate

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 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.

17. Membership registration HPCSA (Principal Investigator and/or Main Supervisor)

18. SUBMISSION REQUIREMENTS

TWO HARD COPIES:

- Arrange documentation in the order provided in this guide
- Two complete sets, including application forms, cover letters, letters of approval, etc., must be submitted.
- Make use of index cards, sticky notes, etc., to separate various documents.
- Please bind or file your applications (in two separate documents/files).

1.

ADDITIONAL DOCUMENTS REQUIRED FOR CLINICAL TRIAL SUBMISSIONS ONLY

If you are submitting a clinical trial application, please see the list below for *additional* documentation that must accompany clinical trial applications:

- A description of the study site, including the available infrastructure and the roles and responsibilities of study staff
- MCC approval or proof of application (if applicable)
- NHREC approval or proof of application
- Proof of insurance for participants (if applicable)
- Material for distribution to patients, including diary cards, QOL questionnaires etc.
- Recruitment material and advertisements
- Proof of GCP training
- SA approved package insert(s) of registered comparators
- Investigator's brochure

UNIVERSITY OF THE FREE STATE
UNIVERSITEIT VAN DIE VRYSTAAT
YUNIVESITHI YA FREISTATA
UFS·UV
HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

HEALTH SCIENCES RESEARCH ETHICS COMMITTEE

REVIEW FEE STRUCTURE 2017

- **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**
- **Application documents must clearly indicate VAT numbers and to whom the invoice must be made out**

HSREC REVIEW FEE STRUCTURE 2017		
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	R10000
Extension / Roll-over study / Sub-study	Project is extended; study rolls over to open label; re-evaluation of protocol	R7500
Annual re-certification / Progress	Annual evaluation of research progress report for re-certification	R900
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	R2000
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	R1250
Informed consent / Information Leaflet amendment	Any change to the content of the original informed consent form / information leaflet	R1 000
Participant / Recruitment material	This includes all material to be handed out to participants, all forms of advertising and blanket approvals.	R1 000
Additional investigator	Any additional investigator (per investigator)	R500
Administrative changes	Name changes; additional sites; typographical changes; other administrative changes	R500
External Administrative Charge	General Admin required by HSREC e.g. copying of lost trial documentation, protocols etc.	R450
Expedited / Urgent review of documentation		R450

*Administrative Fees for the process of SAE's / 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)	R7500
New application	International grant funded research (Total project budget R500 000 to R1m)	R3500
New application	International grant funded research (Total project budget R100 000 to R500 000)	R2000
New application	International grant funded research (Total project budget < R100 000)	R900
Extension / Roll-over study / Sub-study	Project is extended; study rolls over to open label; re-evaluation of protocol for continuation; sub-study	R900
Annual re-certification / Progress	Annual evaluation of research progress report for re-certification	R750
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	R900
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	R600
Informed consent amendment	Any change to the content of the original informed consent form	R600
Participant / Recruitment material	This includes all material to be handed out to participants, all forms of advertising and blanket approvals.	R600
Additional investigator	Any additional investigator (per investigator)	R400

*Administrative Fees for the process of SAE's / Progress Reports / Safety Reports / Investigators Notifications are incorporated in the pricing 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.

PAYMENT PROCESS FOR INDUSTRY-SPONSORED CLINICAL TRIALS or INTERNATIONAL GRANT FUNDED RESEARCH

- **NEW APPLICATIONS: Section 03** (*funding and grant information*) in the New Project Application form must be completed for all new protocols.
- You/your sponsor will receive an HSREC invoice.
- Payment reference: **"invoice number"**
- Please submit proof of payment to ethicsfhs@ufs.ac.za

POST SUBMISSION GUIDANCE

RESPONDING TO THE COMMITTEE'S FEEDBACK

- The submission deadlines are approximately **7 working days** prior to the HSREC meetings. Feedback will only be provided to applicants **after** the meeting.
- From **3-7 working days** after the meeting, HSREC Administration will forward comments from the Committee to your provided email address.
- Copy or restate the question or concern and then provide a detailed and thoughtful response. Incomplete responses are likely to trigger a repeat query from the reviewer.
- Address all points and queries, using examples, references and hard data where necessary.
- If the Committee's feedback is unclear or ambiguous, contact HSREC Administration and request clarification. If you disagree with a comment or recommended change, provide your rationale.
- If the response requires revisions to the protocol, recruitment materials and/or information sheets/ consent forms, revise the documents accordingly, submit **electronic** copies with changes highlighted in bold/color/italics so the evaluators can immediately determine where and what changes have been made. Include a summary of changes in your response.
- Proofread the final versions for grammatical, typographical and formatting errors.
- Feedback from the meeting will be communicated to researchers within **7 working days** after the meeting. You are welcome to contact the office for any information.

ANNUAL PROGRESS REPORTS (CONTINUING REVIEW OF ONGOING RESEARCH)

HSREC approval is valid for **one year**.

In line with international and national regulatory and ethical requirements, the HSREC must review active research at least annually. The Principal Investigator is responsible for submitting an annual progress report to the HSREC in a timely manner before the approval period for the study expires. The HSREC has the authority to **suspend** or **terminate** research which does not comply with annual reporting requirements.

The following forms and guidance are available on the HSREC web page:

- *Annual Progress Report and Guidance for **Clinical Studies***
- *Annual Progress Report*
- *Study Closure Report for **Clinical Studies***
- *Final Report*

***NOTE:** Only hard copies will be accepted when submitting your form(s) to the HSREC. (Hand-deliver or send via registered mail)*

ACTIVE PROTOCOLS

All changes to research protocols, including e.g. information/consent documents, advertisements, and study instruments must have HSREC approval **prior** to implementation except where necessary to eliminate immediate hazards to enrolled participants.

The following forms and guidance are available on the web page:

- *Amendment Form and Guidance*
- *Amendment Form and Guidance - Study Staff*
- *Adverse Events or Unanticipated Problems Reporting Form and Guidance*
- *Study Violation / Deviation Form and Guidance*
- *Study Exception Form and Guidance*

NOTE: *Only hard copies will be accepted when submitting your form(s) to the HSREC. (Hand-deliver or send via registered mail)*

TIMELINES FOR REPORTING UNANTICIPATED PROBLEMS OR ADVERSE EVENTS

Unanticipated problems	All unanticipated 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 unanticipated adverse device effects	All unanticipated 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.

TIMELINES FOR REPORTING PROTOCOL VIOLATIONS/DEVIATIONS AND STUDY EXCEPTIONS

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.