Standard Operating Procedure:

Submissions including new studies, clinical trials, amendments, annual renewals, serious adverse events, and others

This SOP was approved by resolution of the Faculty of Health Sciences Research Ethics Committee on 27 September 2023 and replaces all previous SOPs in this regard. It should be reviewed within 3 years after this date of approval.

_____ Date: 27 September 2023

Signed by the Chairperson

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1. Purpose of this document

This SOP gives effect to the Ethics Guidelines of the Department of Health (2015): Ethics in Health Research- Principles, Processes and Structure 2nd Edition (ISBN: 1-920031-04) (*www.doh.gov.za*)

In terms of international and national regulatory requirements (NHA Act No 6 of 2003, The National Bill of Rights of the Republic of South Africa and Guidelines for Good Practise in Conduct of Clinical Trials in Human Participants in South Africa, 2006/2019), all health research needs to undergo ethical review and approval, before such research may be done.

It is legally imperative that all health-related research needs to be reviewed by an independent research ethics committee. The Research Ethics Committee of the Faculty of Health Sciences University of Pretoria (REC FHS UP) is such and is accredited by the National Health Research Ethics Council. In the evaluation of study protocols and related documents, the Research Ethics Committee (REC) looks after the interests of all potentially affected parties, such as potential research subjects, researchers and the research site, in accordance with international research and ethics standards and guidelines.

The purpose of this SOP is to define the circumstances and the conditions that apply when UP personnel, pre- and post-graduate students, as well as external researchers not affiliated to UP, submit research proposals to the REC FHS UP for evaluation and approval.

2. Scope

This SOP covers the *submission processes to* the Research Ethics Committee for new studies, clinical trials, amendments, annual reports and renewals, serious adverse events, and other submissions.

This SOP should be interpreted within the Terms of Reference of the REC and other SOPs that may be relevant such as: SOP for Expedited Approval and the SOP for Informed Consent Process and Documents.

3. Definitions

3.1 Adverse Drug Reaction or Adverse Reaction: A response to a medicine or intervention which is noxious and unintended. The phrase response means that the causal relationship between the medicinal product/intervention and the adverse event is at least a reasonable possibility.

3.2 Adverse Events (AE): It is any negative or untoward occurrence that may present during the study intervention, but which does not necessarily have a causal relationship with the research undertaken.

3.3 Amendment: Any change made to the originally planned research proposal and that happens while the study is being conducted. No change may be implemented without first obtaining the necessary ethics approval.

3.4 Annual renewal: Yearly ethical clearance of all studies needs to be obtained at least 2 months before the current approval expires.

3.5 CONSORT criteria needs to be adhered to when planning a clinical medication trial.

3.6 Expedited approval: See the SOP for Expedited Review and Approval.

3.7 Health-related research: All health-related research done as defined in the National Health Act at the University of Pretoria, and all research done in the Faculty of Health Sciences. This includes research on health services, clinical research, clinical trials, education of students and workers in health matters, health practices, research on health personnel in the Faculty of Health Sciences. It is not confined to research on human participants but include research on chemicals or instruments, audits and surveys, health related laboratory research, in vitro and ex vivo health research, research on data already collected for clinical or educational purposes, secondary

research on data already collected as part of another research project, case reports, case series for publication purposes, and service delivery statistics for degree or publication purposes.:

3.9 'Health research' as defined by the National Health Act: In section 1 it defines health research as any research which contributes to knowledge of:

(a) the biological, clinical, psychological or social processes in human beings; (b) improved methods for the provision of health services; (c) human pathology; (d) the causes of disease; (e) the effects of the environment on the human body; (f) the development or new application of pharmaceuticals, medicines and related substances; and (g) the development of new applications of health technology.

3.8 Informed Consent Process and Document: See SOP regarding Informed Consent Process and Documents (ICD).

3.9 Material Transfer Agreement (MTA) No.41781 Goverment Gazette, 20 July 2019

3.10 Medication definition: A 'medicine' is defined in article 1 of the Medicines and Related Substances Act 101 of 1965 (as amended):

"medicine"— (a) means any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in—

(i) the diagnosis, treatment, mitigation, modification or prevention of disease, abnormal physical or mental state or the symptoms thereof in humans;

(ii) or restoring, correcting or modifying any somatic or psychic or organic function in humans; and

(b) includes any veterinary medicine: [Definition of "medicine" substituted by sec 1 (d) of Act 17 of 1979; sec 1(i) of Act 72 of 2008 and by sec 1(g) of Act 14 of 2015.]

3.11 National Health Act: Act 61 of 2003 (NHA): Provides statutory guidelines for "health research" and the necessary research ethics infrastructure.

3.12 National Health Research Ethics Council (NHREC): According to the NHA this committee sets norms and standards for health research involving humans and animals, determine guidelines for RECs and also register and audit all RECs .

3.13 Pilot study: A small scale preliminary study which aims to investigate whether components of a main study will be feasible or to clarify certain ethical aspects first.

3.14 Principal Investigator (PI) who takes full responsibility for the ethical conduction of the research study and to ensure that ethics clearance is obtained for the primary study as well as for any amendments.

3.15 Research Ethics Committee Faculty of Health Sciences University of Pretoria (REC FHS UP)

3.16 Serious Adverse Events (SAEs):

A SAE is defined as any negative or untoward occurrence that:

- Results in death;
- Is life-threatening;
- Requires participant hospitalisation or prolongation of existing hospitalisation;
- Results in persistent or significant disability/incapacity (social harm for displacement from the home);
- Any other experience that suggests a significant hazard, contraindication, side- effect, or precaution that may require medical or surgical intervention to prevent one of the outcomes listed above; and
- Is a congenital anomaly/birth defect.

Medical and scientific judgement should be exercised when deciding if other situations are serious. Such instances could include medical events that may not be immediately life-threatening or result in death or hospitalisation, but which may jeopardise the patient or may require intervention to prevent one of the outcomes listed in the definition above.

3.17 South African Health Products Regulatory Authority (SAHPRA): All clinical medical trials need to obtain SAHPRA approval, before ethics clearance can be given.

3.18 Sub study: Usually an undergraduate or honours-degree student's research proposal which are covered under the scope of a main study with ethical clearance. The sub study cannot add any new objectives or methodologies that are not covered by the main study. All sub studies need to be registered in the specific students' names.

3.19 Umbrella study: This is the main study that consists of various smaller studies, which are usually executed by students. The study proposal should identify all objectives, as well as, methodologies to be used by the specific students.

3.20 Unexpected Adverse Reaction: One in which the nature, specificity, severity and outcome is not consistent with the applicable product information (i.e. with the approved package inserts for registered products, or the investigator's brochure or other product information for unregistered products).

4. What is "health research" needs to be considered by the Research Ethics Committee of the Faculty of Health Science at the University of Pretoria?

All research that may be health related such as:

- Research with potential implications for the health of humans;
- Research in the domain of health regardless of using human participants (thus including research on e.g. chemicals or instruments);
- Clinical "audits" and surveys;
- In vitro, laboratory, non-human and human tissue research;
- Quality control procedures in laboratories, like assay validations and instrument calibrations, that are NOT for publication or for student research purposes are not considered as research and need not be submitted for ethics approval, unless human tissue, blood samples, and/or human bodily products need to be collected for these purposes in which case that should be incorporated into the research protocol of the relevant study(s) that depends on these quality control procedures;
- Research on data already collected for clinical or educational purposes;
- Secondary research on data already collected as part of another research project;
- Case studies for purposes of publication or conference presentations
- Case series for publication purposes;
- Service delivery "statistics" for research, scientific reports, degree or publication purposes;
- Reports and publications of health surveillance;
- Research on education in the Health Sciences Faculty;

- All research involving patients or materials from Steve Biko Academic Hospital, Kalafong Hospital, Tshwane District Hospital, the Dental Hospital, Weskoppies Hospital, or NHLS;
- All research involving healthcare workers or other personnel at Steve Biko Academic Hospital, Kalafong Hospital, Tshwane District Hospital, the Dental Hospital, Weskoppies Hospital, and NHLS;
- All research involving students of the Faculty of Health Sciences as research participants; and
- All research involving personnel of the Faculty of Health Sciences as research participants.

5. Researchers' Responsibilities

5.1 It is the responsibility of researchers to ensure that ethical approval is obtained in time before a research study can commence. Researchers need to take notice of the required *submission dates* for a specific monthly meeting. These are available on the REC web (www.up.ac.za/healthethics).

5.2 No late submissions will be accepted by the REC secretariat for evaluation for a specific REC meeting. The PeopleSoft system has a **cut-off-date** and will automatically allocate late submissions to the next REC meeting for evaluation.

5.3 Please note that the researcher, Head of Department and the student supervisor (where applicable) need to sign the electronic application form on the PeopleSoft electronic submission system, before the electronic system will forward it to the REC secretariat.

5.4 On this electronic application form the researcher needs to indicate that he/she will abide by the principles of the Declaration of Helsinki. The Declaration of Storage needs to be completed. Furthermore the Principal Investigator (PI) needs to complete the PI's commitment section.

5.5 **The PI is the only person** that can submit the research proposal and attached documents electronically, as this ensures that the PI takes *full responsibility* for all documents submitted and also for all research done.

5.6 Post-Graduate students, as well as **MPhil students,** first need to obtain written approval from a *Scientific or Academic Advisory Committee* (e.g.: MMed- Committee,

PhD-Committee, MSc-Committee, Postgraduate Committee School of HealthCare Sciences, Academic Advisory Committee, Academic Programme Committee). This approval letter needs to be attached to the research submission for ethical approval.

5.7 Where a researcher wants to do a pilot study first, before submitting the protocol to the scientific committee, he/she should submit a protocol to the Ethics Committee for the pilot study, and later, following the consideration by the scientific committee, submit to the Ethics Committee an amendment that will cover the full study.

5.8 It is all researchers' responsibility to take note of comments made by the REC after the Prelim Committee and the Main Committee meetings. These comments will be available on the electronic platform. This system will also forward an e-mail to the researcher to alert the researcher that comments made by the REC need to be addressed.

5.9 Researchers need to respond with a cover letter that addresses the REC comments in a-*point-by-point* letter format - each comment should be followed by a response addressing that comment specifically. This needs to be submitted before the deadline stipulated on the comments letter. All amended documents should be attached. Please submit the documents need to be submitted in track changed **and** clean format.

6. Submission requirements

- On the REC website (www.up.ac.za/healthethics), information and requirements are available regarding which documents to submit. Download the necessary documents

under “First Applications & Submissions”. The following options are available to choose from:

A. Post Graduate Research;
B. Under Graduate Research;
C. Medication Trials;
D. In Vitro, Lab, Non-Human and Human Tissue research;
E. Case studies; and
F. Other Research.

(Note that examples of all the templates of required forms are available underneath the above options).

- Thereafter a PeopleSoft electronic submissions should be done as follows:
    - On the Staff/Student and Guest Portal, search for the Research Grants & Ethics link, and click on the link;
    - Then click on the “Ethics Application & Approval” tile;
    - Then click on “My Ethics Application” on the left side of the page; and
    - Further instructions are available on the instruction manual on the above mentioned REC website.

Upon submission of your documents, the system would allocate you an “Application ID Number, e.g. XXX/2020”.

6.1 New Studies / First Applications

The following submission documents are required **together with** the *Scientific or Academic Advisory Committee* (e.g. MMed- Committee, PhD-Committee, MSc-Committee,

Postgraduate Committee, Academic Advisory Committee, Academic Programme Committee) Approval Certificate.

Please see the REC website: www.up.ac.za/healthethics for more details and templates.

6.1.1. Electronic Application Form (includes Declaration for Helsinki, Declaration of Storage and the Commitment by the PI)

6.1.2. Research Protocol

A protocol of any proposed research study should address the following:

- Introduction and relevance of the proposed research study;
- Background and problem statement (Literature references);
- Hypothesis / Aims;
- Objectives (primary / secondary);
- Methodology:
- Sample size and population- please explain in detail the recruitment process, control group and experimental group where applicable;
- Randomisation process: Explain in detail;
- Exclusion criteria / inclusion criteria;
- Procedures / frequency of visits;
- Quality assurance of specific tools to be used; and
- Data collection and analysis;
- Ethical aspects e.g. anonymising of data and participants;
- Assurance of data anonymity must be given. Details on how this will be done, must be written in the protocol under "Ethics."
- Statistical analysis with a statistical letter of support;
- Budget and funds allocated;
- Gantt timetable with correct/updated dates; and
- References.

6.1.3 Research synopsis/summary

6.1.4 Participant's Information Consent Document (ICD)

- Pro-formas of the ICDs are available on the website of the REC: **www.up.ac.za/healthethics.**
- See the SOP for Obtaining Informed Consent and Informed Consent Documents.

6.1.5. Curriculum Vitae (CV)

- An updated and signed Curriculum Vitae needs to be submitted electronically by all Investigators. Researchers doing frequent research only need to submit an updated and signed CV annually.
- Note that in collaborative research, the Principal Investigator must be South African based.

6.1.6 Promotion of Access to Information: Act No. 2 of 2000 (Permission to Access files/records) (where appropriate)

- Health information is regarded as confidential and is the property of the patient. Patient consent is therefore needed to access patient information. If it is not possible to obtain such consent from the patient, in the informed consent document, the custodian of the information, can give consent to access information.
- The Director of a Private Clinic or Hospital needs to give written permission for the research to be done at their premises.
- Where research is to be done at a state hospital or state clinic the REC suspended the need for researchers to submit the permission from the CEO of the relevant provincial health institution. The National Health Research Committee needs ethical approval before provincial registration and CEO permission can be given. **Please register online through the National Health Research Data Base (NHRD-website: http//nhrd.hst.org.za).** Enquiries can be made from Prof DJ Kocks daniel.kocks@up.ac.za, alternatively Dr TJ Sefala Tebatjo.Sefala@gauteng.gov.za
- Application to such custodian must be in writing, and reasons why the information is sought must be stated on the form.

- The pro-forma letter is available on the Research Ethics Committee website **www.up.ac.za/healthethics**

6.1.7 Statistical support letter (if applicable)

- For quantitative studies, a statistician should usually be consulted before submission of the final protocol to the Research Ethics Committee.
- Undergraduate and honours-degree research studies do not need a statistical letter of support, unless the complexity of the study would it.

6.1.8 Datasheet indicating all the variables to be collected. No patient name or identifiable information may be on this form.

6.1.9 Participant recruitment tools and gifts, with explanations when and why the gifts are necessary.

6.1.10 Advertisements to help with patient recruitment. These need to be approved by the REC. The PI's name and contact details may not be on this — rather use a research assistants or site's contact details.

6.1.11 Questionnaires which will be used. These needs to be specified in the ICD for the patient information and consent.

6.1.12 Any other relevant documents.

6.2 Clinical Medication trials

- A clinical trial is a research study or investigation intended to test safety (not harmful or dangerous to human health), quality (ingredients are of good quality), effectiveness (working to diagnose, treat, prevent or cure a disease condition) and efficacy (better/ best when compared with other treatment or medicine for a similar condition) of new

and/or existing or old medicines, medicine devices and/or treatment options, using human participants.

- The word "medicine" includes medicines that are used to treat diseases (therapeutic medicines), to prevent diseases (prophylactic medicines, e.g. vaccines), and medicines that are used in special investigations (diagnostic medicines, e.g. medicines used during special X-ray examinations to map out kidneys).

- Any health research or clinical trial in humans of an unregistered medicine or medical device must be approved by the South African Health Products Regulatory Authority (SAHPRA, previously the Medicines Control Council or MCC) in terms of the following: Regulation 34 [of the Regulations to Act 101 of 1965]:

- **Regulation 34. CONDUCT OF CLINICAL TRIALS FOR HUMANS**

  Regulation 34.1 A person desiring to initiate or conduct a clinical trial in respect of an unregistered medicine, a new indication or new dosage regimen of registered medicine or substance, shall apply to the Council on a form determined by the Council for authority to conduct such a clinical trial.

- Regulations for Medical Devices & IVDs: Publication 9 December 2016, Government Gazette No 40480, No 1515.

  Regulation 16: In the case of a medical device that is tested in a clinical trial: As of 1 June 2017 all protocols for clinical trials with medical devices must be approved by SAHPRA prior to initiation of the trial. This is done by means of the CTF 1 Form and applications are evaluated by the Clinical Trial Committee and the Medical Device Committee.

  'Any contravention of the above is guilty of an offence and upon conviction is liable to a fine, or to imprisonment for a period not exceeding 10 years.

- A medical device is defined as:

‘Any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article including Group III and IV Hazardous Substances contemplated in the Hazardous Substances Act, 1973 (Act No. 15 of 1973) - intended by the manufacturer to be used, alone or in combination, for humans or animals for one or more of the following:

1) diagnosis, prevention, monitoring, treatment or alleviation of disease;
2) diagnosis, monitoring, treatment, alleviation of or compensation for an injury;
3) investigation, replacement, modification, or support of the anatomy or of a physiological process;
4) supporting or sustaining life;
5) control of conception;
6) disinfection of medical devices; or
7) providing information for medical or diagnostic purposes by means of in vitro examination of specimens derived from the human body; and
8) which does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human or animal body, but which may be assisted in its intended function by such means.

The following submission documents are required:

6.2.1 The South African Health Products Regulatory Authority Permission (SAHPRA)

In Summary: As stated in The SA Medicines and Related Substance Control Act – Act 101 of 1965 permission from SAHPRA needs to be obtained for the following indicated clinical medication trials:

a) If both the medication and the indication are registered SAHPRA must still be informed of the trial and the trial must be approved;
b) Trials done with unregistered medications;
c) Trials done with registered medications, but used for a new indication and;
d) If a trial is done on natural extracts/complimentary medication etc. for which a specific medicinal claim is sought

6.2.2 Electronic Application form (includes Declaration for Helsinki, Declaration of Storage and the Commitment by the PI);

6.2.3 Research protocol;

6.2.4 Summary of Protocol;

6.2.5 Participant's Information Consent Document (ICD) Questionnaires / Interview schedules;

6.2.6 Investigator's Brochure;

6.2.7 Obtaining written permission from the CEO of the hospital or institution to do research ((please see section 6.1.6) is the responsibility of researchers. Please register online through the National Health Research Data Base

NHRD-website: http//nhrd.hst.org.za). Enquiries can be made from Prof DJ Kocks daniel.kocks@up.ac.za, alternatively Dr TJ Sefala Tebatjo.Sefala@gauteng.gov.za

6.2.8 Researcher's Responsibility form for Principal Investigator and Sub-Investigator/s;

6.2.9 GCP Training Certificates (renewable every 3 years) of the Principal Investigator and Sub Investigator/s;

6.2.10 Other documents e.g. Advertisements (Advertisements to help with patient recruitment. These need to be approved by the REC. Also note that the PI's name and contact details may not be on this—rather use a research assistant or the site's contact details);

6.2.11 Participant recruitment tools and gifts, with explanations when and why the gifts are necessary;

6.2.12 Financial Contract: Financial contracts between an Investigator and Pharmaceutical Firm must be signed and submitted to the Head of the Financial Contract Committee;(will find out if it is Ms K du Preez)

6.2.13 Insurance Certificate (Clinical Medication Trials must have insurance coverage for research related complications, according to the ABPI Guidelines);

6.2.14 Material Transfer Agreement (MTA) for exportation of biological specimens (if applicable) -- see the required formatted and gazetted example on the REC website.

These documents will be signed after each Main REC meeting, by the chair or vice-chair/s;

6.2.15 Export permit of biological specimens (if applicable);

6.2.16 Statistical support letter (for non-contractual trials);

6.2.17 Registration at the National Health Research Ethics Committee (NHREC) All clinical medication trials need to be registered as a clinical trial, with the National Health Research Ethics Committee (*www.ethicsapp.co.za*). A unique number will be generated by the NHREC system;

Reference:

http://www.sanctr.gov.za/Resources/Whatisaclinicaltrial/tabid/175/Default.aspx

6.2.18 Any other relevant documentation and

6.2.19 A cover letter that explains the reasons should any of the above not have been submitted.

6.3 Material Transfer Agreement and Export Permit

- Please submit the MTA and Export Permit either together with the clinical trial or when the documentation is ready and signed by all parties.
- If submitted separately at a later stage, please submit as a post approval submission.
- The MTA will only be signed after each Main REC meeting, by the chair or vice-chair/s.
- See the required formatted and gazetted example on the REC website (No. 41781 Government Gazette, 20 July 2018).

6.4 Advertisements for patient recruitment

- Submit the advertisement, letters to recruit participants etc. on the UP STAFF PORTAL: LOGON to the Grants & Ethics link and click on the link. Then click on the "Ethics Application & Approval" tile.
- Note that the PI's name and contact details may not be on this—rather use a research assistant's name.

6.5 Sub-study / Umbrella study under a main study

For each Master's and Doctoral student an unique research protocol is required in the student's name. The Research Ethics Committee needs to consider these research protocols even if the study is a subset of another study, which has already been approved by the Ethics Committee.

For undergraduate and honours-degree research that is part of an ethically approved umbrella project, only an amendment needs to be submitted in the specific student's name.

Please indicate clearly and refer to the umbrella study title and protocol number.

As the latter submission needs to refer to the study already approved, it may consequently be less comprehensive (for example, the previously approved Participant Information and Consent Documents may suffice).

6.6. Laboratory/ In Vitro / Cell Lines Studies

The Faculty of Health Sciences Research Ethics Committee reconsidered the submission process for "in vitro" studies and resolved that it should be aligned with the National Health Act: Act 61 of 2003.

Therefore, a full protocol needs to be submitted for consideration by the REC for all research studies to be conducted with commercial cell lines, blood samples, human tissues, human bodily products and/or "in vitro" work.

6.7 Systematic Reviews

The FHS REC has resolved that even though this type of study may or may not have ethical implications and are of minimal risk, such research proposals need to be ethically approved. This type of research aims to provide a complete and extended summary of current literature which is relevant to the research question. Clearly stated objective/s with eligibility criteria for studies to be included and an explicit methodology needs to be written up.

For Post Graduate students a research proposal of this category needs to be ethically approved in the student's name, with an academic committee approval certificate.

A research proposal with all the required documents need to be submitted as described in section 6.4.

Also see: https://bestpractice.bmj.com/info/toolkit/learn-ebm/appraising-systematic-reviews/

For meta-analysis see: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2731030/pdf/1754-9493-3-16.pdf

6.8 Endorsements - Inter-Faculty Research: GIBS, EBIT, Faculty of Education and NASH

The REC FHS needs to endorse all health related research done on human participants, after the other Faculties, as mentioned above, of the University of Pretoria have approved the research themselves.

Please align the subsequent submission to the REC and be attend on the submission dates, requirements as described in Section 6.4 — especially the ICD requirements (See SOP on Informed Consent Procedures and Documents)

6.9. Not UP-staff member submissions

The Research Ethics Committee do, at the discretion of the Chairperson and vice-chairs, accept review of research protocols submitted to it, by researchers who are not UP staff members, students or affiliates.

A research proposal with all the required documents need to be submitted as described in 6.4.

6.10 Case reports and case studies

The application for Research Ethics Committee review should include:

- A cover letter outlining the rationale for the case report and steps taken to protect patient privacy and confidentiality.
- Signed consent from the patient(s) or their legally appointed representative, or an explanation stating why consent was not obtained. The Research Ethics Committee will consider clear and adequately motivated justification for the lack of formal informed consent.
- And the case report or draft article.
- Please submit the above mentioned documents on the UP STAFF PORTAL: LOGON to the Grants & Ethics link and click on the link. Then click on the "Ethics Application & Approval" tile.

6.11 Animal Ethics Research

All research from the Faculty of Health Sciences, involving animals, needs to be submitted to the REC FHS first. If human health is not implicated the study will be referred directly by The REC OF THE FHS to THE Animal Ethics Research Committee

7. Post Approval Submissions

Submission of Amendments, SAEs, Annual renewals, Letters and Notifications, as well as Line listings and SUSARS is via the PeopleSoft Portal System, as described above

Upon submission of your documents electronically, the system would allocate you an "Application ID Number, e.g. XXX/2020".

7.1. Amendment/s to an approved study

- An amendment is a change that is administrative in nature or has an impact on the safety or integrity of the participants, alters scientific value of the research or interpretation of the results, affects validity of data, the design of the study, planned statistical analyses or significantly alters other aspects of the research. Changes in the PI also constitute an amendment, and applications for such amendment should include information on the role and tasks of the persons involved.
- The Principal Investigator needs to describe and *explain the nature and reason / rationale for the amendment and also describe the ethical implication / risk of the changes on the electronic form.* Attached to the e-form all the amended documents (protocol and ICD etc.) need to be submitted in track changed and clean formats. This will ensure that the REC members can easily identify the changes, as well as the rationale of the amendment.
- Protocol Amendments cannot be implemented until the REC has reviewed and approved it at the monthly meeting.

- Should an Amendment need expedited approval, as patient safety is at stake, a request for expedited approval can be submitted. In such cases the chair and vice-chairs can give provisional approval. This will then be ratified at the next REC meeting. (Please see the SOP for Expedited Approvals).
- In the case of **minor administrative modifications** (which do not have an impact on the safety of the participant and the protocol methodology) it can be submitted as a **notification only** to the ethics office and will be noted as such. If full ethical approval is needed then it needs to be submitted as above.

7.2. Annual renewals

- An *ethics approval certificate older than one year*, is not valid .
- Ethical renewals of all studies needs to be obtained *at least 2 months* before the current approval expires.
- The electronic form needs to be completed and the following needs to be described: a detailed description of progress to date, any protocol violations during the past year, any unforeseen risks that emerged during the past year and a confirmation that no changes were made to the study without obtaining prior ethical clearance.
- The REC rescinds the need to submit 6-monthly progress reports, except where it is mandatory by the SAHPRA for clinical medication trial research studies.

7.3 Serious Adverse Events (SAE's)

A SAE at the local site under the auspices of the UP REC, should be reported within 72 hours after first knowledge of the occurrence thereof.

- Reports on serious adverse events (SAEs) needs to be submitted by completing the e-form on the PeopleSoft Portal System.
- An attached cover letter from the PI should describe the following: the SAE as such, the site and country where the SAE happened, whether it is related or not the study medication.
- Furthermore, it needs to be stated if it is an initial SAE, a Follow Up (1/2/3) or a Final Report.
- Reporting requirements for **events occurring at Faculty of Health Sciences Research Ethics Committee's approved sites:**

  i. All deaths; and
  Serious, unexpected, adverse drug reactions which are fatal or life threatening:
  The PI should report this within 72 hours after first knowledge. The initial notification should be followed by as complete a report as possible within an additional 8 calendar days.

  ii. For serious, unexpected, adverse drug reactions which are not fatal or life threatening:
  Report as soon as possible and not later than 15 calendar days after first knowledge.

  iii. Non-serious unexpected adverse drug reactions:
  Report as part of the 6-monthly progress reports for clinical medication trials .

  iv. Serious, unexpected, adverse drug reactions occurring at other South African and Foreign sites:
  Report as part of the 6-monthly progress reports for clinical medication trials.

  v. New information which may affect the safety of participants or the conduct of a trial:

Report within 3 calendar days of first knowledge and in the six-monthly progress report for clinical medication trials.

vi. Change in the nature, severity or frequency of expected Adverse Drug Reactions. Report within 15 days after first knowledge and in the 6-monthly progress report for clinical medication trials.

The submitted documents will only be processed after delivery of 1 hard copy of all documents uploaded electronically, together with a copy of the Ethics Application form to Ms Manda Smith at Faculty of Health Sciences Research Ethics Committee, Tswelopele Building, Level 4, Room 4-59.

7.4 Other submissions

- SUSAR and Line listings (in 6 monthly batches) and all other correspondence eg. Advertisements, recruitment letters and general notices can be submitted here with the necessary description on the electronic form. All necessary documents need to be attached to this e-form.
- These submissions will be acknowledged by the REC secretariat and an acknowledgement letter will be sent out.

8. Protocol deviations and protocol violations

All protocol violations must be reported to the Ethics Committee as soon as the researcher becomes aware of the violation, or as part of the application for re-approval or on the progress report form; and

Protocol deviations and minor GCP violations must be reported to the Committee as soon as the researcher becomes aware of the violation; or as part of the application for re-approval or on the progress report form or for clinical medicine trials separately.

9. Suspension and termination of ethics approval

The REC may suspend or terminate approval of a study that is not being conducted in accordance with prevailing REC or South African Department of Health ethical requirements. The primary justification for suspension or termination of approval should be the safety of participants.

Such suspension or termination of approval must be authorised by the REC chairperson in minuted consultation with a REC subcommittee and/or other co-opted parties as soon as possible, but not more than seven days after receipt of relevant information by the chairperson. Such action must be reported to the REC at the next quorate meeting.

Should a research study be prematurely suspended or terminated, the PI must notify the REC. A summary must be communicated regarding the reasons for the suspension or termination, before the anticipated date of termination.

References

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