Standard **O**perating **P**rocedure

*Dated 11/11/2014
*This supersedes all previous documents

Faculty of Health Sciences
Research Ethics Committee
University of Pretoria

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31 Bophelo Road, HW Snyman South Building
Level 2 - Rooms 2.33; 2.34 & 2.35

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Web address:

http://www.up.ac.za/healthethics

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1. The responsibility of the Research Ethics Committee

The Faculty of Health Sciences Research Ethics Committee is tasked with the ethics of all health research and operates in terms of the **National Health Act (2003**), the **Code of Ethics for Research of the University of Pretoria,** and the **National Health Research Ethics Council.**

It is accredited nationally and internationally as follows:

- National Health Research Ethics Council of the South African Department of Health. REC-120208-018
- Office of Human Research Protection of the USA Department of Health & Human Services'
    - Federalwide Assurance FWA 00002567, Approved dd 22 May 2002 and Expires 20 Oct 2016.
    - IRB 0000 2235 IORG0001762 Approved dd 22/04/2014 and Expires 22/04/2017.

It is a legal imperative that **all health research** must be reviewed by the Research Ethics Committee in terms of the National Health Act as well as the policy (Rt 429/99) of the University of Pretoria

All health research must be considered by the Research Ethics Committee, where the section of the National Health Act 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) causes of the diseases;
(e) the effects of the environment on the human body;
(f) the development or new application of pharmaceuticals, medicines and
(g) the development of new applications of health technology.

The role of this Ethics Committee in reviewing health research is to ensure the safety, dignity, rights and well-being of all research participants, involved in any health related research.
The fundamental ethical principles are outlined in the Belmont Report. They provide a framework for ethical decision-making in research involving human any health related research. The three principles are:

- Respect for persons
- Beneficence
- Justice

1.1 Respect for persons

Respect for persons highlights the individual as an autonomous being, capable of making individual choices and decisions. Respect for persons includes allowing the individual to have the freedom to make his/her decision voluntarily. For those individuals with diminished capabilities – such as children or those with mental disabilities – extra protection must be granted to protect the individuals from any risk of harm.

1.2 Beneficence

The principle refer to the concept of maximizing potential benefits to society and/or to research participants and minimizing anticipated risks for the research participants. Beneficence includes protecting the individual form any undue harm (non-maleficence). In this way, the risks involved in the research can only be justified by the expected benefits.

1.3 Justice

Justice emphasizes the need for treating participants of research fairly. This means there must be equity in research among various classes of society. For example, prisoners should not be unfairly excluded or included in research without ethical or scientific justification.

2. The Ethics Committee

2.1 The General Attitude of the Research Ethics Committee

In line with international ethics standards for health research as well as the commitment of the University of Pretoria to ensuring ethically sound research, the Research Ethics Committee like to highlight the following points that are pertinent to us fulfilling our role diligently and accountably:

- The Research Ethics Committee upholds the principle that the **primary responsibility** for ethically sound research practice **resides with researchers**.
- The role of the Research Ethics Committee is to **support and guide** researchers towards **better/best ethical research practice**. The Research Ethics Committee is in this way a resource in the Faculty of Health Sciences for researchers.
- We approach the ethical review of proposals in a **collaborative spirit** in order to arrive at decision making that involves the researchers.
- The main purpose of questions or queries from members of the Research Ethics Committee is **to clarify or better understand** researchers' intentions in order to assist us working together with researchers towards solutions.
- The comments made and questions asked by any one member of the Research Ethics Committee are important to the deliberations of the Committee as a whole.

2.2 Research Evaluation Policy

The Ethics Committee reviews all health research that are connected to the Faculty of Health Sciences. No retrospective ethics approval can or will be granted (as enforced by the Senate Ethics Committee in January 2008). All personnel and pre- or postgraduate students affiliated to the University of Pretoria must apply to the Ethics Committee for the approval of their research proposals, before research may be undertaken.

The Faculty of Health Sciences Research Ethics Committee oversees research at the following sites, among others-:

• Department of Animal and Wildlife Sciences (Only where human participants are involved)	• Department of Veterinary Sciences (Only where human participants are involved)
• Faculty of Humanities, UP	• Hammanskraal Hospital
• Jubilee Hospital	• Kalafong Hospital
• Mamelodi Hospital / Campus	• Pretoria West Hospital
• School of Health Systems and Public Health, UP	• Steve Biko Academic Hospital
• Tembisa Hospital	• Tshwane District Hospital
• Weskoppies Hospital	• Witbank Hospital

2.3 What is "health research" that must be considered by the Research Ethics Committee?

All research that may be health related as such:

- All research using human participants
- Research not using human participants (e.g. research on chemicals or instruments)
- Clinical “audits” and surveys
- In vitro, laboratory, non-human and human tissue research:
  - The Faculty of Health Sciences Research Ethics Committee reconsidered the submission process for “in vitro” studies and resolved that it should be aligned better with the processes at other Faculties and the National Health Act: Act 61 of 2003. Accordingly, as from 26 May 2013 a full protocol must be submitted for consideration by the Committee for all research studies to be conducted through commercial cell lines, blood samples, human tissues, human bodily products and/or “in vitro” work.
  - Quality control procedures in laboratories, like assay validations and instrument calibrations, that are NOT for publication or 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 series for publication purposes
- Service delivery “statistics” for research, scientific reports, degree or publication purposes
- Reports and publications of health surveilance
- Research on education in the Health Sciences Faculty
- All research involving patients or materials from Steve Biko Academic Hospital, Kalafong Hospital, Tshwane District Hospital, Weskoppies Hospital, or NHLS.
- All research involving healthcare workers or other personnel at Steve Biko Academic Hospital, Kalafong Hospital, Tshwane District Hospital, Weskoppies Hospital, and NHLS
- All research involving students of the Faculty of Health Sciences as research participants
- All research involving personnel of the Faculty of Health Sciences as research participants

2.4 Independence of the Ethics Committee and relevant fees applicable

- The Ethics Committee of the Faculty of Health Sciences, is an independently functioning body.
- Both the University of Pretoria and the Steve Biko Academic Hospital are responsible for the financial support of the Committee.
- The Ethics Committee also generates funds by evaluating contract research or research proposals that are conducted in terms of a grant for a fee.

The following fee-structure is applicable for 2014. Note: Researchers must budget for these expenses in their grant application. Researchers must budget accordingly for ethical evaluation fees:

A.

For all studies which are merely funded from Departmental budget and/or NAVKOM or any other University of Pretoria Grant the review is free.

B.

All research for degree purposes the review is free.

C.

Kindly complete the attached Agreement and submit together with your protocol (link)

Studies sponsored by outside grant organisations within South Africa such as the NRF (MRC, NIH, CSIR, ECOG, BCIRG), as well as research by non-UP faculty (below R500 000.00) are charged a reduced fee.

(**Note:** Researchers must budget for these expenses in their grant application.)

Description	Price excluding VAT	VAT	Price including VAT
Protocols	R2800.00	R392.00	R3192.00
Amendments	R800.00	R112.00	R912.00

D.

Kindly complete the attached Agreement and submit together with your protocol (link)

Research funded from International grants exceeding R500 000.00, all contract research and non-UP researchers with funding exceeding R500 000.00, the full fee is payable.

Description	Price excluding VAT	VAT	Price including VAT
Protocols	R10 000.00	R1400.00	R11 400.00
Amendments	R3300.00	R462.00	R3762.00

***Note:** Minor Amendments (e.g. advertisements, diary cards, posters, gifts, presents), no fee is applicable.

Please pay upon receipt of an invoice from our department. Please use the reference number for your deposit as reflected on this invoice. Please send proof of payment to deepeka.behari@up.ac.za

2.5 The composition of the Ethics Committee

http://www.doh.gov.za/docs/factsheets/guidelines/ethics

The composition of the Ethics Committee currently fulfills the guidelines proposed by the DOH as follows:

- ☑ A quorum is defined as 8 members attached plus 2 members not attached to the University of Pretoria.
- ☑ From the 1st May 2009, the Chairperson is Prof C W van Staden.
- ☑ Includes members of both genders.
- ☑ Includes at least 2 lay persons who have no affiliation to the institution, and are preferably from the local community.
- ☑ Includes members with knowledge and experience in research.
- ☑ Includes at least one member with knowledge and experience in professional care and counseling of people.
- ☑ Includes at least one member who has knowledge in both qualitative and quantitative research methodologies.
- ☑ Includes at least one member who is legally trained.

2.6 Appointment of Ethics Committee Members

- Nominations for a Chairperson and committee members are called for, when specific vacancies arises. Committee members and Faculty members are called on to submit in writing names of possible candidates who would be suitable.
- Nominations received by the Ethics Committee, are then evaluated by the current Ethics Committee members with regard to the suitability of the nominee to evaluate research protocols ethically. The committee members then vote to elect a new member.
- The nominated candidate's CV is then sent with recommendations to the Dean of the Faculty of Health Sciences, University of Pretoria for final approval. Committee members are then appointed by the Dean's office.
- Committee members serve for a non-specific time period.

2.7 Terms of Appointment

2.7.1 A member is obliged to declare any potential and/or conflicting interests, to any research protocol under discussion.

2.7.2 A member signs a confidentiality agreement annually regarding the meeting's deliberations, information and related matters.

2.8 Indemnity cover for Members and Lay Persons of the Committee

The University of Pretoria has taken out an Indemnity cover for Personnel and Committee members (Mr Marius Le Roux can be contacted on telephone number 012 – 4202731). *This document is still being evaluated by our Committee and lawyers.*

2.9 Members of our Committee

Members attached to the University of Pretoria		
1.	Prof MJ Bester	(female) BSc (Chemistry and Biochemistry); BSc (Hons)(Biochemistry); MSc(Biochemistry); PhD (Medical Biochemistry)
2.	Mrs N Briers	(female) BSc (Stell); BSc Hons (Pretoria); MSc (Pretoria); DHETP (Pretoria)
3.	Dr IK Dada	(female) BSc.HB; MB ChB; MA; MPH
4.	Prof R Delport	(female)BA et Scien, B Curationis (Hons) (Intensive care Nursing), M Sc (Physiology), PhD (Medicine), M Ed Computer Assisted Education
5.	Prof T W de Witt	(female) MBChB; MMed(Paed);DTE;
6.	Prof MM Ehlers	(female) BSc (Agric) Microbiology (Pret); BSc (Agric) Hons Microbiology (Pret); MSc (Agric) Microbiology (Pret); PhD Microbiology (Pret); Post Doctoral Fellow (Pret)
7.	Dr R Leech	(female) B.Art et Scien; BA Cur; BA (Hons); M (ECI); PhD Nursing Science
8.	Prof A Nienaber	(female) BA(Hons)(Wits); LLB; LLM; LLD(UP); PhD; Dipl.Datametrics(UNISA)
9	Dr C Oliphant	(female) MBChB, FCPHM (SA), MMed (Public Health), MPhil (Applied Ethics) (cum laude)
10.	Prof L Sykes	(female) BSc, BDS, MDent (Pros)
11.	Dr GP Stevens	LLB, LLM, LLD.
12.	Dr T Rossouw	(female) MBChB (cum laude); M.Phil (Applied Ethics) (cum laude), MPH (Biostatistics and Epidemiology (cum laude), D.Phil , PhD
13.	Dr R Sommers	Deputy Chairperson (female) MBChB; MMed(Int); MPharmMed
14.	Prof CW van Staden	Chairperson MBChB; MMed (Psych); MD; FCPsych; FTCL; UPLM

Members NOT attached to the University of Pretoria		
15.	Mrs S Bapela	(female) Dipl. Theology and Ministry
16.	Dr NE Khomo	(female) BSc (Pharm), MBChB, MMed (Comm.Health), post graduate diplomas in Public Health (DPH), Health Services Management (DHSM) and Tropical Medicine And Hygiene (DTM&H)
17.	Mr SB Masombuka	BA (Communication Science) UNISA; Certificate in Health Research Ethics Course (B compliant cc)
18.	Dr MP Mathebula	(female) MBCHB, PDM, HM
19.	Mrs MC Nzeku	(female) BSc(NUL); MSc(Biochem)(UCL, UK)
20.	Dr SAS Olorunju	BSc (Hons). Stats (Ahmadu Bello University –Nigeria); MSc (Applied Statistics (UKC United Kingdom); PhD (Ahmadu Bello University – Nigeria)
21.	Ms J Phatoli (sr)	(female) BCur(Eet.A); BTec(Oncology Nursing Science)
22.	Dr Y Sikweyiya	PhD (Public Health); MPH; SARETI Fellowship (Research Ethics); Postgraduate Diploma (Health Promotion); BSc (Health Promotion)
A quorum is defined as 8 members attached plus 2 members not attached to the University of Pretoria		

2.10 SAE Committee Members

- Dr NE Khomo — (female) BSc (Pharm), MBChB, MMed (Comm.Health), post graduate diplomas in Public Health (DPH), Health Services Management (DHSM) and Tropical Medicine And Hygiene (DTM&H)

All SAEs are listed on the monthly Agenda of the Main Research Ethics Committee. Members who would like more information, can evaluate the complete documents at the Ethics office.

2.11 Protocol Amendment Committee Members

- Mrs N Briers — (female) BSc (Stell); BSc Hons (Pretoria); MSc (Pretoria); DHETP (Pretoria)
- Dr R Sommers — Deputy Chairperson (female) MBChB; MMed(Int); MPharmMed
- Prof R Delport — (female)BA et Scien, B Curationis (Hons) (Intensive care Nursing), M Sc (Physiology), PhD (Medicine), M Ed Computer Assisted Education

Amendments are sent to the above four members. Their written comments are placed on the monthly Agenda of the Main Research Ethics Committee and discussed as necessary. Researchers need to respond to the comments, where after approval will be given.

2.12 Protocol Progress Report Committee Members

- Dr R Sommers — Deputy Chairperson (female) MBChB; M.Med (Int) PharMed

All Progress Reports are attached to the monthly Agenda of the Main Research Ethics Committee for notification to all members.

3. Terms of Reference to which this Ethics Committee adhere

3.1 International Guidelines

The International Guidelines that are applicable, are inter alia the following:

3.1.1 The Nuremberg Code (1946)
3.1.2 The Helsinki Declaration (1964; 1975; 1983; 1989; 1996; 2000): Updated with notes of clarification dated Washington 2002; and Tokyo 2004. The latest update was in 2008. (http://www.wma.net/e/policy/b3.htm)
3.1.3 The Belmont Report (1979) *http://ohsr.od.nih.gov/guidelines/belmont.html*
3.1.4 The WHO Geneva 2000 Operational Guidelines
3.1.5 The Code of Federal Regulations of the USA (Title 45 Part 46)
http://www.doh.gov.za/docs/factsheets/guidelines/ethnics/sec4.pdf
The US Offfice of Human Research Protections 45 CFR 46US
http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html
3.1.6 The International Conference On Harmonisation - Good Clinical Practice (1997) (ICH-GCP)
3.1.7 Council for International Organisations of Medical Science (CIOMS) Guidelines (1982, updated in 2002) *http://www.cioms.ch/frame_guidelines_nov_2002.htm*
3.1.8 Singapore Statement on Research Integrity

3.2 National Legislation

The National Legislations that are applicable:

3.2.1 National Health Act, Act No. 61 of 2003

Specific sections of Chapter 9 have direct relevance on the responsibility of Ethics Committees and Research Procedures. They are:

- Section 71 (a)(b):
  71 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.

- Section 72 (1):
  72 National Health Research Ethics Council (NHREC)
  (1) A council to be known as the National Health Research Ethics Council is hereby established.

- Section 73: **Health Research Ethics Committees**
  (1) Every institution, health agency and health establishment at which health research is conducted, must establish or have access to a health research ethics committee, which is registered with the National Health Research Ethics Council.
  (2) A health research ethics committee must-
  (a) **review research proposals** and protocols in order to ensure that research conducted by the relevant institution, agency or establishment will promote health, contribute to the prevention of communicable or non-

communicable diseases or disability or result in cures for communicable or non-communicable diseases; and

(b) **grant approval** for research by the relevant institution, agency or establishment in instances **where** research proposals and protocol **meet the ethical standards** of that health research ethics committee.

3.2.2 The Constitution of SA – Act 108 of 1996 / Chapter 2: Bill of Rights – Section 12 C

http://www.policy.org.za/pdf/NationalHealthB32D

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

3.2.3 Good Clinical Practice: Department of Health 2004/2006

Website address: *www.doh.gov.za*

3.3 Local Regulations:

3.3.1 University of Pretoria Senate Ethics Committee - Code of Ethics for Research

Website: *www.up.ac.za/healthethics*

3.3.2 Institutional Permission

- CEO to give permission
- Private Hospitals: Director to sign an approval letter
- Other Provincial Departments to sign an approval letter

Note: These approvals must be given to the investigator preferably prior to Ethics Committee evaluation.

3.3.3 Departmental Approval

- The research proposal must be approved by the Department or a specific Academic Committee, where applicable (see 5.3.1)
- Specific permission must be given that the study can be done in a specific Department.

3.3.4 HPCSA – Code of Conduct

- All health professionals registered at this Council, must adhere to the specific guidelines (website: *www.hpcsa.co.za*)

3.3.5 Additional requirements since 29th July 2005

- Dispensing licences for non-pharmacists (doctors) who are to dispense clinical trial medicine (Act 101 or 1965);
- The storage of such medicines should be consistent with the Pharmacy Act No 88 of 1974;
- Good Clinical Practice Courses (GCP) for researchers **doing clinical medication trials** must be updated every three years. The GCP certificate must be submitted to the Committee.
- **Note:** GCP courses must be applicable to local requirements – therefore must be based on South African conditions.

3.3.6 Archiving of Documents

- Ethics Committee: All documentation regarding protocols, Agendas and Minutes will be kept in the office for 5 years after a protocol has been completed. Thereafter, all files will be stored at Metrofile for another 10 years.
- Researcher's duties: Investigators must also indicate where they will store their documentation for 15 years after their research protocol has been completed. Supervisors are responsible to store their student's documentation. This is according to the National Health Act regulation.

4. The evaluation of research proposals

The Faculty of Health Sciences, Research Ethics Committee, University of Pretoria must satisfy themselves that all research proposals follows the Good Clinical Practice Guidelines.

4.1 The elements of the research proposal to be reviewed as prescribed by the South African Good Clinical Practice Document

http://www.doh.gov.za/docs/factsheets/guidelines/ethnics/sec2.pdf.

To enable the Committee, to ensure the protection of the rights, safety and well-being of research participants, as well as that of their communities, the following elements of the research proposal are to be reviewed:

- The prospective study population is appropriate in terms of characteristics and that vulnerable populations are protected – fair selection and inclusion / exclusion criteria must be used to ensure distributive justice;
- The design of the study is sound and thus scientifically acceptable (sample size, hypothesis and outcomes);
- The recruitment of subjects is free of coercion and the level of compensation (if any) is fair and non-coercive;
- Any risks associated with the research project are minimized to the greatest extent possible and the potential benefits are maximized to the greatest extent possible;
- That there is a favourable risk-benefit ratio;
- The degree and method to which confidentiality will be assured are appropriate;
- The method used to obtain informed consent is ethically and legally acceptable (individual and community consent where applicable);
- The Informed Consent Document contains all the necessary elements: (An assent document for children older than 7 years is necessary);
- The investigator has the appropriate qualifications, experience and facilities to conduct the research in an ethical manner;
- Post-study commitments are declared – the local standard of care must be discussed, where applicable; and
- That the dissemination of research results is discussed, eg publications, congress seminars or lectures.

5. Submission of research proposals and other documentation

5.1 Submission dates

- The website must be consulted to ensure timeous submission for a specific meeting during the year.
- The administrative secretaries may not distribute late submissions.

5.2. The submission details

- Protocol documents submitted for evaluation at a specific meeting are received and checked by the secretariat. Submission dates are available on the website *www.up.ac.za/healthethics*
- Researchers / applicants can now apply for ethics review via the electronic process.
- For electronic submissions, go to the following website: https://up.rims.ac.za
- Also obtain a username and password from: Ms Manda Smith – contact details: manda.smith@up.ac.za / fhsethics@up.ac.za and provide her with your personnel or student number, if you have one.
- Amendments, SAEs and Progress reports follow the same process and should be submitted henceforth electronically via the electronic process.
- Line Listings should be uploaded electronically in batches (with clear reference to the approved study).
- Upon submission of your documents electronically, the system would allocate you a "Temp Number, e.g. Temp2014-0000". Note that this "Temp Number" will be converted to a protocol reference e.g 000/2014 at our REC office.
- Also submit 1 hard copy of all documents uploaded electronically to the Ms Manda Smith at Faculty of Health Sciences Research Ethics Committee, H W Snyman South Building, Room 2.34
- Kindly note that it is the responsibility of the researcher to log onto https://up.rims.ac.za and keep track of the progress of your research study and check for correspondence from our REC office.
- When submitting the protocol and supporting documents, the Principal Investigator is the main responsible contact person.
- The necessary cover pages for the SAEs, Progress Reports and Amendments (available on our website), must be completed and signed by the Principal Investigator.
- Should two research sites submit the same protocol and supporting documents, the Principal Investigator from each site is responsible for his/her own submission process and communication with the secretariat. This is applicable only if the two research sites operates individually.
- **Note:** Researchers must complete all forms by themselves, as by signing these forms, they take responsibility for all the information.

5.3 Academic Committee Approvals prior to Ethics Committee Submission

Researchers may wonder **when should they submit their study protocols to other committees in relation to the submission to the Research Ethics Committee**. An appropriate answer would depend on the specific study as applied to the considerations below:

Internationally, the standard requirement is that research be conducted according to the research plan, contained in the particular version of a protocol approved by an independent ethics committee. This requirement has practical bearing where:

i) protocols also serve at one of the scientific committees (and consequently may be amended);

ii) research projects are related to or are subsets of other research projects.

- Where research is for degree purposes, the protocol serves at one of the scientific committees. It would ordinarily be best to have that committee consider the protocol first, unless the researcher is required to clarify particular ethical issues first.
- Should the researcher submit the protocol to the Ethics Committee first, the researcher will then need to re-submit amendments required and approved by the scientific committee, to the Ethics Committee for final approval.
- 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.

- Where research projects are related or a subset of another, the above-mentioned requirement applies.
    - It applies to all aspects of the research; and not merely to the data collection part of the protocol.
    - This means that any change in the protocol, whether a change or addition of a researcher or in the way that data are obtained or data are used must be considered for its ethical implications by the Ethics Committee.

- Practically, since the scientific committees require a unique research protocol for each post-graduate student, and that the postgraduate student will execute the research following that very protocol, the Ethics Committee needs to consider that protocol even if the study is a subset of another study that has already been approved by the Ethics Committee.
    - The latter submission needs to refer to the study already approved and may consequently be less comprehensive (for example, the previously-approved Participant Information Leaflet and Consent documents may suffice).

- Written approvals from the following Committees must be attached when submitting a protocol for Ethics Committee approval.
- It is **preferable** that the following approval first be obtained, before submission to the Research Ethics Committee.
- The reason being that should these Committees request changes, the amended documents must once again be submitted to the Research Ethics Committee for final approval.

5.3.1 MMed Committee (All postgraduate students including Aerospace; Sports Medicine and Family Medicine) – Chairperson Prof P Rheeder (*www.up.ac.za*, click on Faculties, click on Health Sciences, click on School of Medicine, click on MMed Protocol Committee);
5.3.2 PhD Committee - Chairperson Prof B G Lindeque;
5.3.3 School of Health Systems and Public Health students must submit to the Academic Programme Committee (APC) - Chairperson Prof B Girdler-Brown (Secretariat Ms Elizabeth Rabotho);
5.3.4 Academic Advisory Committee (AAC) - Chairperson Prof K Voyi (Secretariat Ms Elizabeth Rabotho);
5.3.5 MSc. Committee: Chairperson Prof E Pretorius
5.3.6 Dental Research Committee (RESCOM) Chairperson: Prof P J van Wyk
5.3.7 A letter of approval from the HOD or the Supervisor from the Department of Radiographic Sciences; Department of Nursing; Department of Physiotherapy and Department of Dietetics must be submitted together with the protocol.

5.4 Which documents to submit

- Our submission instructions and documents can be found at www.up.ac/healthethics

5.5 Submission documents specifically (indicated specifically on the website)

5.5.1 Health Research Ethics Committee Electronic Application Form

https://up.rims.ac.za

5.5.2 Detailed Research Protocol

A protocol of the proposed 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
    - Randomisation process
    - Exclusion criteria / inclusion criteria
    - Procedures / frequency of visits
    - Quality assurance of specific tools to be used
    - Data collection and analysis
- Ethical aspects e.g. anonomysing 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." Any such study using data only, must be approved by the Ethics Committee.
- Statistical analysis to be done
- References (Vancouver style)

5.5.3 Patient / Participant's Information & Informed Consent Document

Different pro formas of the Patient Information Consent Document are available on our website www.up.ac/healthethics

- Ensure that **Layman Language** (Gr 6) be used
- Pages of the Patient Information and Consent Document must be **numbered** accordingly, ie, Page 1 of XXX, Page 2 of XXX, etc, to indicate that it is one document.
- **Questionnaires** (when appropriate) must be attached to the Patient / Participant's Information & Informed Consent Document and pages must also be numbered. NB: For anonymous Questionnaires, please use the Patient / Participant's Information & Informed Consent Document (PICD 4), as available on the website (adapt to your study)
- The following elements must be addressed: (when appropriate)
    - Do not use the first person address format
    - The title of the study must be inserted on the top of the page
    - State the study involves research and **invite** people to partake
    - The purpose of the research study, whether it is for degree purposes.
    - Different Treatment groups / Randomisation group
    - All procedures during the visits to be described
    - Benefits: Risk ratio discussion
    - Alternative treatments available
    - Voluntary participation

- Confidentiality aspects
- Anticipated expenses – who is to pay? Payment to participants
- Whom to contact for emergencies – Principal Investigator and telephone numbers (24 hr contact telephone number must be included)
- Provision for Witness to sign (independent)

- **Parental Information & Informed Consent Document :** If children (younger than 18 years) are research participants, the parents or guardians must give written consent as per approved document.
- **Assent Form:** Children older than 7 years must additionally give written Assent.
- Waiving of Informed Consent from specific participants for a research study can be requested in writing from the Research Ethics Committee.
- **Requirements for the signature of witnesses:**
  There is a distinction between a signature confirming that the consent process was performed on the one hand, and a contractual witness that merely confirms the authenticity of the signatures by the contracting parties but not the consent process. The UP Health Sciences REC requires that the consent process be witnessed (i.e., the former) and duly signed for subjects who are not fully capable of consenting or illiterate – we agree with GCP that for these cases, someone who is not research personnel would suit better as a witness. In other cases, however, where subjects are fully capable of consenting and literate, we **recommend** witness signatures of the latter kind (i.e., a witness signature that authenticates the signatures of the subject and the researcher but not necessarily the consent process)."

- **Translation of the Patient / Participant's Information & Informed Consent Document (PICD)**: Any other language translation other than English must be submitted to us **together** with a translation certificate, as this will be processed as a notification by our committee. This is subject to the English version being approved by our committee.

5.5.4 Curriculum Vitae (CV)

- An updated and signed Curriculum Vitae must be submitted **electronically** by all Investigators**.** Researchers doing frequent research can submit an updated and signed CV annually.
- In collaborative research, the Principal Investigator must be South African based.

5.5.5 The Declaration of Helsinki

This document must be read and signed by all Investigators, submit only the signature page.

5.5.6 The Declaration of Storage of Research Data

This form **must be** completed, as all research documents must be kept for 15 years.

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

- Health information is regarded as confidential and is the property of the patient. Therefore consent is needed to access patient information. If it is not possible to obtain such consent from the patient, the "custodian of the information ", usually the CEO or the Director of a Hospital/Clinic can give consent to access information.

- Application to such custodian must be in writing, and reasons why the information is sought must be stated on the form (pro forma letter is available on our website *www.up.ac.za/healthethics*).

5.5.8 Written permission from the CEO of the hospital or institution to do Research and access Records/Files and Data (when appropriate)

The CEO or the Director of the clinic or hospital must give written permission for the research to be done at their premises.

5.5.9 Statistical support letter (if applicable)

Not a requirement for an undergraduate degree.

5.6 For Medication Trials:

5.6.1 MCC Permission (when appropriate)

The MCC must give permission according to The SA Medicines and Related Substance Control Act – Act 101 of 1965.

The following drugs must be approved by the MCC:

- Trials done with unregistered drugs.
- Trials done with registered drugs, but used for a new indication.
- If both the drug and the indication are registered, the MCC must still be informed of the trial and the trial must be approved.
- Trial on other products, eg, natural extracts/complimentary medication etc. for which a specific medicinal claim is sought.

5.6.2 Financial Contracts (when appropriate)

Financial contracts between an Investigator and Pharmaceutical firm must be signed and submitted to the Head of the Financial Contract Committee (presently Mrs Karen du Preez).

5.6.3 Registration at the National Health Research Ethics Committee (NHREC)

All clinical medication trials must be registered with the National Health Research Ethics Committee (*www.ethicsapp.co.za*). This has been implemented from 1st July 2005 (www.sanrr.gov.za).

5.6.4 Insurance Certificates

Clinical Medication Trials must have informed consent covering participants for research related problems, eg. ABPI coverage.

5.6.5 Summary of Protocol

5.6.6 Investigator's Brochure – 1 complete copy

5.6.7 Researcher's Responsibility Form for Principal Investigator and Sub-Investigator

5.6.8 GCP Training Certificate of the Principal Investigator and Sub-Investigator

5.6.9 Copy of eg. Diary cards, advertisements etc. (if applicable)

5.6.10 Questionnaires/interview schedules (if applicable)

6. The Review Process and Protocol Evaluation Procedure

6.1 The National Health Act (Act No. 61 of 2003) proposes the following functions for a Research Ethics Committee:

- Review of research proposals and protocols to ensure that research will be conducted
  in the spirit of endeavouring to promote health, and to prevent or cure disability and disease;
- Ensuring that humans involved in research are treated with dignity and that their well-being is not compromised;
- Ensuring that informed consent is obtained in the case of human participants; and
- Granting approval in instances where research proposals and protocols meet ethical standards.
  Note: This section should be read in conjunction with the Department of Health Ethics Guidelines, i.e. Department of Health (2004) Ethics in Health Research: Principles, Structures and Processes, ISBN: 1-920031-04, (*www.doh.gov.za*)

6.2 Types of Review

a) Full Board Review:

This is how the majority of protocols are reviewed:

- The committee has a meeting once a month, from January to November in each year.
- The researcher submits a protocol and all relevant documents which forms a properly collated document. Online submission is required as well.

b) Expedited Review:

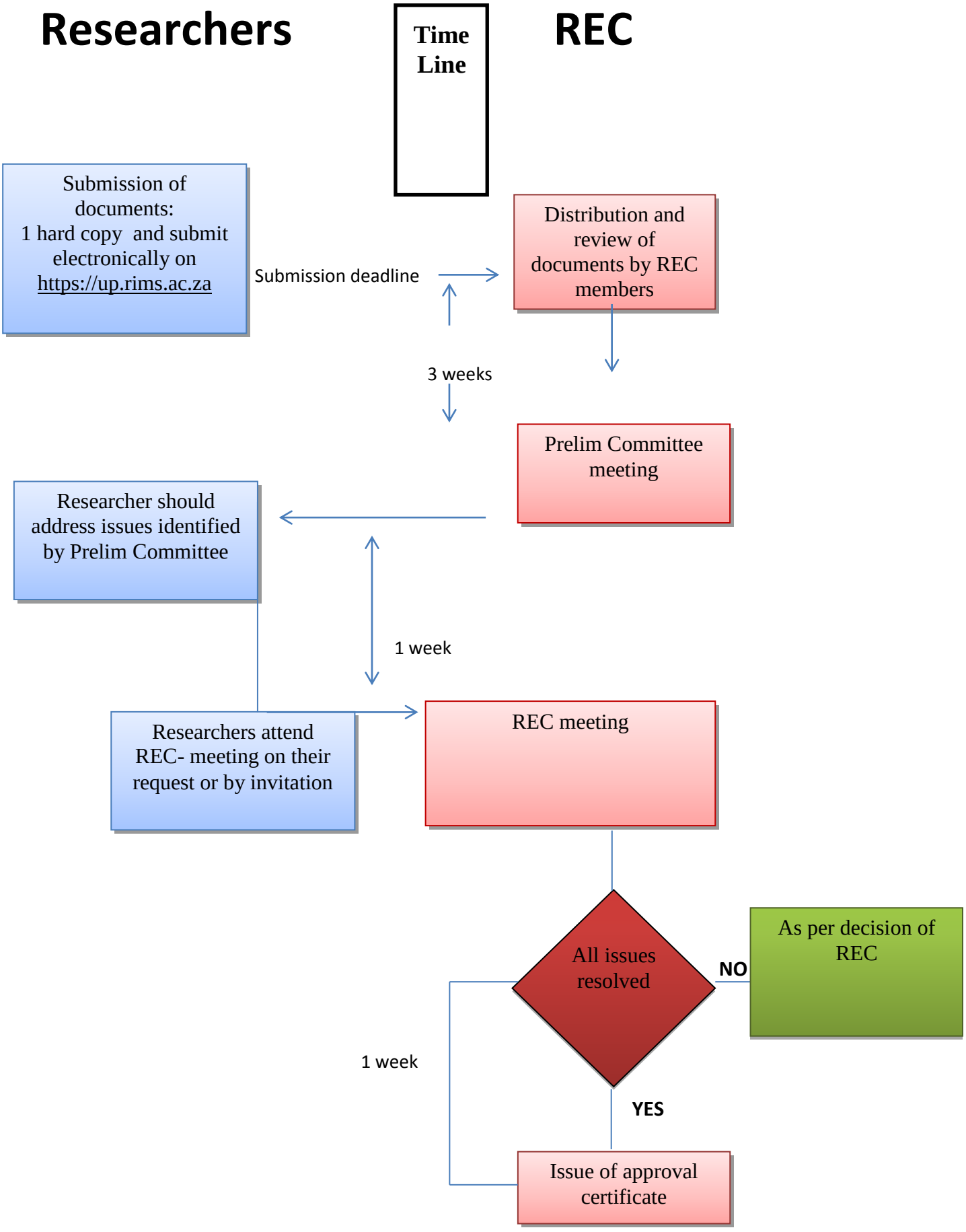
Note: A full protocol (1 hard copy plus online submission) still has to be submitted as soon as possible after the expedited approval has been granted. This will then be circulated to all the members.

- Only studies that present no more than minimal risk to the participants may be evaluated in this way. Minimal risk is difficult to define: The probability and magnitude of physical and psychological harm that is normally encountered in daily lives - defined as in a NORMAL STABLE daily live in a developed country;
- This must be discussed with the Chairperson or the Vice-Chairperson;
- Amendments with immediate effect on participants health and safety can also be submitted for expedited approval; and
- Any expedited approval will be ratified by the full committee at the following committee meeting.

6.3 Independent Consultants

- The Ethics Committee may call upon independent consultants who provide special expertise to the Ethics Committee on specific research protocols. These consultants may inter alia be specialists in ethical or legal aspects, specific disease or methodologies, or they may be representatives of communities, patients, or special interest groups.

6.4 Schematic Visualisation of the REC review process



6.5 The Prelim Committee Meeting

The electronic version of the protocol proposal and supporting documents will be sent to specific members. A prelim committee meeting will be held 3 weeks later. At this meeting the Chairperson and 2 Vice-Chairs as well as a specific committee member will be present. Researchers are not requested to attend this meeting.

The four identified committee members will assess the comments received from all the committee members together with the specific research protocol documents. At this prelim committee meeting, research protocols that can be approved at the main meeting will be identified and final approval will be ratified at the full committee meeting (the next week). All outstanding issues identified must be addressed by the researcher for the full committee meeting a week later. *Attendance by the researchers for the main meeting is by invitation only.* If a researcher wants to attend the main Ethics Committee meeting, a request can be lodged with the Secretariat.

6.6 At the Main Meeting

- During this meeting, the Minutes and recommendations of the Prelim meeting, as well as the requested amended documents are discussed by the committee members.
- The Principal Investigator **will be invited to attend** the meeting at a proposed time-slot (obtained from the secretary). If the Principal Investigator cannot attend, a sub-investigator must be appointed to attend the meeting.
- The outstanding issues can then be deliberated with the committee.
- Confidentiality is maintained, by discussing the relevant protocol with only the specific investigator/s present. (if indicated)
- Should amended documents be submitted at the meeting, be complicated or lengthy, specific identified members will evaluate such after the meeting. Feedback will then be sent to the secretariat.
- Further correspondence will be e-mailed to all the relevant investigator/s.
- It is the directive of the Ethics Committee that ethical approval can be granted and issued within 5 days after all outstanding documents are received by the secretariat.

6.7 Decision making rules

The following pertain:

a) Final decisions may only be made at meetings where a quorum (***A quorum*** *is defined as 8 members attached plus 2 members not attached to the University of Pretoria*) are present; if a quorum is not reached, then the protocols will be ratified at the next meeting.

b) The Committee usually makes a decision by consensus, but infrequently it is done by a voting process. In the Minutes, a final decision is indicated by a voting score.

c) An Ethics Committee member must indicate and withdraw from the final voting process, where a conflict of interest arises.

d) The following decisions can be made at the meeting:
   (1) Protocols are approved and an approval letter is issued within 5 days after the meeting;
   (2) Protocols are provisionally approved pending:
      (i) Outstanding documents or changes needed to be made by the investigator will be clearly indicated and conversed to the researcher.
      (ii) As soon as all these documents are received, it will be forwarded to a sub-committee indicated at the meeting for final approval.

(iii) If the sub-committee approves the amended documents, an approval letter will be forwarded to the researcher.
(iv) If the sub-committee still has difficulties, the protocol will be further discussed at the next Ethics Committee meeting.

(3) Should the protocol stand over from the previous meeting, the protocol will need to discussed at the next month's Ethics Committee meeting. The researcher will be invited to attend the meeting.

6.8 Communicating the review decisions

- After the Minutes have been drafted, the committee's final decision per protocols will be conveyed in writing to all investigators within 5 working days (as per schematic diagram).
- The committee approves a research study for a specific time period, as indicated on the electronic Application Form (1 to 2 to 3 years). This period will be stated on the final approval letter, with the provisio that six monthly reports and any amendments be submitted during the above granted period. This therefore omits the need for *applying* annually for permission to continue the research.
- The **final approval letter** will indicate that a quorum of members have evaluated and approved the research, the date of approval, as well as the period for which the approval is valid.

6.9 Follow-up Review

- Protocols reviewed before 2011: The Principal Investigator must write a letter to request re-approval for the estimated time duration still necessary to complete the research.
- Protocols reviewed from 2011: A protocol is approved for a pre-determined time period during the initial evaluation. This is indicated on the approval letter. No annual approval necessary.

6.10 Appeals Procedure

- Researchers have the right to appeal a decision of the Ethics Committee. The request to appeal must be submitted to the chair of the Ethics Committee via the secretary's office. The appeal must contain a clear motivation as to the reasons for the appeal. The documents must include an executive summary and motivation from a subject specialist other than the author of the protocol, stating clearly the reasons for appeal and why this protocol should be reconsidered. The chair will then approach outside consultants to evaluate the protocol and to furnish the Ethics Committee with a report and a recommendation. The Ethics Committee will then reconsider the entire protocol with new motivations at the meeting following the one at which the appeal was tabled. The decision of the Ethics Committee after the Appeals Process is final.

7. Post Approval Follow-up and subsequent submissions

So as to ensure ongoing communication between the Ethics Committee and researchers, the following should be taken into consideration:

7.1 Protocol Amendments

- An "Application for Approval of Amendment" form must be completed (form in the required format - available on our website).
- Amendments should be submitted henceforth electronically via the electronic process. (https://up.rims.ac.za)
- 1 hard copy of the Amendment plus an updated protocol needs to be submitted to the Ethics Committee.
- The Principal Investigator must motivate the amendment and also clearly mark the amended sections, as indicated on the form.
- Protocol Amendments cannot be implemented until the Ethics Committee has reviewed and approved it at the monthly meeting.
- Should an Amendment need expedited approval, as patient safety is at stake, it can be submitted as such to the secretariat. Provisional approval can be granted, which then needs to be ratified at the next formal Ethics Committee meeting.
- In the case of minor modifications (which do not have an impact on the safety of the participant and the protocol methodology) or administrative activities changes only, modification can be considered a minor notification, and these do not require formal approval. It can be submitted as a notification to the Ethics office and will be approved as such.

7.2 Adverse and Serious Adverse Events (SAE), Line-listings, SUSARs

(i) A "Reporting of Serious Adverse Event" form must to be completed (required form available on our website) by the Principal Investigator. On the form, it is important that the **Principal Investigator interprets** the SAE and comments as to how the Ethics Committee should construe it.

Note:

- The Ethics Committee is guided solely by the content of this form, as completed by the Principal Investigator.
- Serious Adverse Events (SAE) from the local approved site must be submitted and will be noted per study, per site.

- SAEs should be submitted henceforth electronically via the electronic process. (https://up.rims.ac.za)
- One hard copy of the above form and SAE must be submitted.
- The Deputy-Chair will review the SAE and it will be put on the Agenda of the Main Ethics Committee's meeting.

(ii) • Line Listings should be uploaded electronically in batches (with clear reference to the approved study). Line listings for Clinical Trials can be submitted bi-annually. These listings will be considered a simple notification, which do not require formal approval.

(iii) Suspected Unexpected Serious Adverse Reactions (SUSAR Reports); Global Safety letters must be submitted to the Ethics Committee as a notification. Monthly to Six Monthly submissions are acceptable – as indicated by the specific sponsoring pharmaceutical company.

DEFINITIONS:

Adverse Event:

Any untoward medical occurrence that may present during treatment with a medicine/intervention but which does not necessarily have a causal relationship with this treatment

Adverse Drug Reaction or Adverse Reaction:

A response to a medicine/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.

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).

Serious Adverse Event or Serious Adverse Drug Reaction:

Any untoward medical occurrence that:

- results in death,
- is life-threatening,
- requires patient hospitalisation or prolongation of existing hospitalisation,
- results in persistent or significant disability/incapacity, or
- 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. Examples include blood dyscrasias or convulsions not resulting in hospitalisation, or development of drug dependency or drug abuse

REPORTING REQUIREMENTS FOR EVENTS OCCURRING AT FHS REC APPROVED SITES:

- **All deaths**
- **Serious, unexpected, adverse drug reactions which are fatal or life threatening**

Report within 7 calendar days after first knowledge.
The initial notification should be followed by as complete a report as possible within an additional 8 calendar days

- **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

- **All Serious Adverse Events**
- **Non-serious unexpected adverse drug reactions**

Report as part of the 6-monthly progress reports

OTHER REPORTING REQUIREMENTS:

- **Serious, unexpected, adverse drug reactions occurring at other South African and Foreign sites**

Report as part of the 6-monthly progress reports

- **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

- **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

***** Refer to : www.mccza.com

7.3 Progress Reports

(form can be downloaded from www.up.ac.za/healthethics

- Bi-Annual Progress Reports must be submitted in a typed format, pertaining to the progress of the envisioned research. Due dates for submission of same are 31st May and 30th September of every year.

7.4 New Information; Diary cards; Advertisements

Notification by completing an Amendment form.

7.5 Deviations;

- All protocol violations (instances where the selection criteria of the protocol was not adhered to must be reported to the Ethics Committee as soon as the researcher becomes aware of the violation,
- Protocol deviations (all other deviations from the protocol) and minor GCP violations must be reported to the Committee as part of the application for annual re-approval.

7.6 Premature Suspension/Termination of a research study

The researcher must notify the Ethics Committee and a summary of reasons must be communicated to the Ethics Committee.

7.7 Completion of a research study

The researcher must notify the Ethics Committee when the study has been completed. This should then be followed up with a **final** report.

7.8 Dissemination of Research Results

The researcher must state in the protocol how the results (positive or negative) will be disseminated for example:

- Publication (Article/Abstract)
- Congress Presentation / Posters
- How the community will be informed

Note: All research results must be put into the public domain

7.9 Monitoring of Research

- The Ethics Committee may from time to time monitor research sites. Should it be necessary an external auditor may be appointed to do an audit.
- Active monitoring becomes likely when research misconduct and/or complaints are received by the Ethics Committee.
- Passive monitoring is done by evaluating Progress Reports and Annual Review applications.

8. Education in Ethics and Capacity Building

8.1 Faculty and Institutional members

- Ethics lectures will be advertised on the UP Intranet.
- Researchers doing clinical medication trials, need to attend GCP courses. It needs to be reviewed every 3-4 years.

8.2 Ethics Committee members

- CPD accredited lectures / workshops / conferences / seminars will be identified and members can attend on an alternative basis. Request to attend such courses can be submitted to the Secretariat.
- All members will receive the following handbook: "Institutional Review Board Member Handbook", 2nd Edition. Authors Robert J, Amdur and Elizabeth A Bankert.

9. References

- National Health Act 61 of 2003
- 'Clinical trials medical research and cloning in South Africa' C van Wyk (2004) 67 *THRHR* 2004:67
- Ethics in Health Research; Principles, Structures and Processes. DOH 2004.
- South Africa Medicines and Related Substances Control Act 107 of 1965 – amended in 1974, 1979, 1981, 1991, 1997, 2002
- Code of Federal Regulations USA – Title 45 part 46 – Protection of Research Subjects
- 'What makes Clinical Research in Developing Countries Ethical?' E J Emanuel *et al* (2004) 198 *JID* 930-937
- Human Tissue Act 65 of 1983 as amended in 1984, 1989
- Constitution of the Republic of South Africa of 1996 - Bill of Rights; Chapter 2
- Guiding Principles – Department of Health South Africa