



GUIDELINES FOR NEW RESEARCHERS

Getting ethics approval for your project (Human Research: Health)

2008

**Faculty of Health Sciences
Stellenbosch University**





Website

http://academic.sun.ac.za/Health/support_services/research/index.htm

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I. RESEARCH ETHICS BASICS.

1. Introduction

Many human rights abuses have occurred in the name of research in the twentieth century. Some examples are the experiments conducted by the Nazis in the concentration camps during World War II, the Tuskegee Syphilis experiment, Radiation experiments conducted on soldiers in the USA, Willowbrook and many others. The World Medical Association published the Declaration of Helsinki in 1964 in response to these abuses. This document has been updated several times, the most recent in 2000 and is regarded internationally as the fundamental statement of the ethical principles of research. Every researcher should have read and be familiar with its contents. The Declaration of Helsinki can be found at www.wma.net/e/policy/b3.html

In 1976 The National Commission for the Protection of Human Subjects was signed into Law in the USA. The purpose of the Commission was to investigate the exploitation of Human Research Subjects. On April 18, 1979 the Belmont Report was published which identified 3 principles for ethical research:-

- **Respect for Persons** - by recognizing autonomy and upholding rules of informed consent, respecting privacy and confidentiality.
- **Beneficence** - the obligation to protect from harm and to do good
- **Justice** - ensure that the benefits and burdens of research are fairly distributed i.e. that vulnerable developing world populations are not targeted for high risk research from which they may never benefit.

The Belmont Report can be found at <http://ohsr.od.nih.gov/guidelines/belmont.html>

The following local and international guidelines should also be consulted and complied with:

- Ethics in Health Research: Principles, Structures and Processes. (Department of Health) Published April 2005 (This document is available on the Department of Health web site at <http://www.doh.gov.za/search/index.html>)
- SA GCP. Clinical Trials 2006. (2nd Edition) Department of Health (This document is available at <http://www.doh.gov.za/doc/policy-f.html>).
- Guidelines on Ethics for Medical Research. Books 1-5. MRC SA (refer <http://www.sahealthinfo.org/ethics/ethics.htm>)
- ICH- GCP (for clinical trials – refer <http://www.fda.gov/cder/guidance/959fnl.pdf>)
- CIOMS 2002. International Ethical Guidelines for Biomedical Research involving Human Subjects (refer http://www.cioms.ch/frame_guidelines_nov_2002.htm)
- CIOMS 2008. International Ethical Guidelines for Epidemiological studies http://www.cioms.ch/080221feb_2008.pdf



2. What Research must be submitted to a Research Ethics Committee for approval?

The National Health Act No 61.2003 requires that all “health research” is reviewed and approved by an ethics committee. (See Section 73 Health Research Ethics Committees)

All research (except animal studies and clinical trials) conducted in the Faculty of Health Sciences should be submitted to the Committee for Human Research (CHR) for registration and approval. This includes all research involving humans, as well as laboratory based studies that include the use of biohazards, or studies involving radiation.¹

“Research” is defined as “a systematic investigation, including research development testing and evaluation, designed to develop or contribute to generalisable knowledge. Any such investigation raises ethical issues. The issues themselves may be small, but because studies may involve subordination of at least the immediate interest of the individual participant to the objective of the advancement of knowledge, the studies must be submitted to ethical review.” (MRC Guidelines on Ethics for Medical Research: General Principles. 2.1.2)

All clinical trials that fall under the following definition should be submitted to the Committee for Clinical Trials (CCT) and not the CHR: *A prospective interventional study that involves a drug (registered or unregistered), a medical device, or an invasive procedure.*

“Human Subject Research”

A **Human Subject** means a living individual about whom an investigator (whether professional or student), conducting research, obtains:

1. Data through **intervention** or **interaction** with the individual or
2. **Identifiable private information.**

Intervention includes both physical procedures by which data is gathered and manipulation of the subject or his/her environment for research purposes.

Interaction includes communication or interpersonal contact.

Private Information includes information that has been obtained for a specific purpose, but that the individual can reasonably expect will not be made public, (eg a medical record, X-Rays etc). Private Information is **identifiable** information or is information that can be linked to a specific individual.

¹ The research ethics committee structures at Stellenbosch University may well change in 2009 with the scheduled implementation of a new university-wide Ethics Policy for Research.



The key words here are **systematic investigation** that will contribute to **generalisable** knowledge, i.e. all data collection that is for a **presentation, a degree** or a **publication** should get formal ethical clearance.

NB! It is essential to submit the research protocol and obtain the necessary ethical approval **BEFORE** a start is made on the research, not “after the fact”!

3. Retrospective Clinical Audits

Please note that all retrospective clinical audits that fall under the above definition of research must be submitted for ethics approval before the research starts.

1. A common prevailing misconception is that it is not necessary to get consent or ethics approval for all forms of retrospective research using clinical records. This is a false misconception and does not comply with international ethical research practice and regulations AND with the National Health Act 61. 2003. However it may not be necessary to get individual patient consent to use non-identifiable private information in research. [This means that the research information is collected anonymously or using a study code only and that no identifying information, such as a hospital number and name, is recorded. (See below)
2. A researcher can request the ethics committee to grant **a waiver of informed consent** under the following conditions:
 - Without an informed consent waiver it will be impossible to do the research because of the difficulty in tracing individuals.
 - The research to be done will produce valuable information that is likely to improve patient care in the future or will benefit the community.
 - The information will be collected in such a way as to protect patient confidentiality. This means that the data capture sheet or database will only contain a study code. Identifying information linked to the study code will be kept separately eg in a separate file or password protected database. Access to this information will be restricted to senior members of the research team.

NB! Section 7 Epidemiology Pages 35-37 in **Ethics for Health Research: Principles, Processes and Practice** addresses these issues in detail and with clarity. URL ref on page 11 allows an accessible file that can be printed as a paper copy.



II.

WRITING A RESEARCH PROTOCOL FOR ETHICS COMMITTEE SUBMISSION.

1. What are ethics committee members looking for when reviewing research protocols?

The following checklist is a useful indication of the ethical fundamentals that will be considered by the CHR when reviewing research protocols. It should be kept in mind, and frequently referred to, when planning and writing up and submitting research projects.

BENCHMARKS OF ETHICAL RESEARCH - A 7-POINT CHECK LIST (JID 2004:189 (1 March) 930-937)

1. Social and scientific value

- Is the research question relevant?
- Is the research that is going to be reported been done previously?

2. Scientific validity

- Is the design and methodology of the study sound?
- Has the statistical analysis been considered?
- Is the sample size adequate?
- NB! Research that is scientifically flawed is not ethical, because it is a waste of time and resources, and may raise expectation of benefit.

3. Fair Selection of study population

- Has the study population been fairly chosen?
- Have any groups been excluded that could benefit from the research, because of non-scientific reasons, such as non- English or Afrikaans speakers?
- Is the study population vulnerable in any way?

4. Favourable risk-benefit ratio

- Have the risk and benefit been assessed as accurately as possible?
- Is the risk/benefit ratio favourable?
- Are risks minimized?
- Are benefits maximized?

5. Independent review

- Will the research be submitted for independent ethical review?



6. Informed Consent

- Has the community been involved in any way in the informed consent process?
- Has sufficient information been disclosed in a culturally and linguistically sensitive manner? etc

7. Respect for Participants and Study Communities

- Do the participants know they can withdraw from the study at any time.?
- Have issues of confidentiality and privacy been adequately addressed, etc

2. A Stepwise Approach to Writing a Research Protocol for Ethics Committee Submission

Step 1.

Topic and title and key personnel

Once the area of interest has been identified, it will then be necessary to identify person(s) who will act as supervisor or mentor, co-investigators or sub-investigators as well as other people who may be able to be of assistance or play a valuable role in the research endeavour, eg a statistician. Together, the research “team” should draw up a preliminary research plan and develop the title of the study. It is important that the title is as concise and specific as possible. (See also Step 3).

All the key people involved in the study should be identified and their respective roles clarified. eg Co-Investigators, Sub-investigators, study coordinator (if applicable) etc.

Step 2.

Literature review.

Before proceeding further, the next crucial step would be to do a thorough literature review around the proposed topic. The following are some of the broad questions that must be answered in the literature review.

- What other similar research projects or studies have been undertaken in this field? (A search on www.afrosharingpoint.net is highly recommended).
- What were the results?
- How will the proposed study contribute to this field of knowledge?
- What makes this proposed research project different to ones that have preceded it?
- What is the scientific and clinical relevance of the proposed research?
- Is the research proposal of particular relevance to the community in which the researcher is working, or to the broader South African community?

As a final step in this preliminary process, ensure that a consistent and recognized reference



system is developed. The most commonly used reference system in medical journals is the Vancouver System. By consulting a journal such as the SAMJ, it is useful to see exactly how this system is structured.

Step 3.

Define the problem and develop a research question or hypothesis.

Some of the research projects submitted to the CHR give the impression that the researcher does not appear to have a clear idea what he/she wants to find out or prove. This is particularly true of studies that involve retrospective reviews of clinical records.

It is thus very important that the research question or hypothesis is as clearly defined and as specific as possible. If the initial idea is vague, then the result may be similarly “vague”, lacking in substance and useful implication, and/or difficult to interpret in a meaningful way. Knowing exactly where the study direction lies and how a useful outcome can be derived in an articulate way, is the first and perhaps most important step to producing valuable results. The following are examples of vague, as opposed to specific research questions. (From Katzenellenbogen, Joubert, 1997 OUP. *Epidemiology: A manual for South Africa*. Pg 58)

Example 1.

To study the problem of measles in SA

OR

To study trends in measles notification in South Africa from 1995 –2004.

Example 2.

To investigate alcohol consumption as a contributor to adult death,

OR

To determine the proportion of adult deaths that is due to alcohol related conditions.

Example 3.

To study the health profile of children in Mitchell's Plain,

OR

To study the nutritional status of children under 5 years old, in Mitchell's Plain.

Step 4.

Consult a statistician and develop a written statistical analysis plan.

This is a most important and valuable step that many new researchers leave out, or address only at the end of their research. By consulting a statistician at this early point of hypothesis development you will get valuable input into methodological issues such as experimental design, study population, sample size, questionnaire techniques, etc. The



Centre for Statistical Consultation offers consultations to researchers, Prof Daan Nel is available Mondays and Prof. Martin Kidd on Wednesdays at the Tygerberg Campus. On the other weekdays they are based on the Stellenbosch campus. Contact them at 021 938 9181 on Mondays and Wednesdays or email Prof Kidd at mkidd@sun.ac.za or Prof Nel at dgnel@sun.ac.za.

It is important that you include at least one paragraph, usually after your methodology, on how you plan to analyse your results from a statistical perspective. This compels you to think ahead and consider whether or not the data you plan to capture will actually address your research questions. The CHR regards this aspect as an essential component of any research project and the committee may elect to return the protocol to the researcher without approval, if this element is missing or inadequate. (See step 8)

Step 5.

Aims and Objectives and Rationale

These components are similar to the research question, but should be formulated in more detail; preferably in point form. Each objective should 'stand alone', but also be connected to the others in some way. It may be appropriate to list "Primary Objectives" and "Secondary objectives". The objectives will ultimately determine the planning and methodological design of the study. For example, if your study involves a questionnaire, it is important to structure your questionnaire to ensure that your objectives will be met.

Step 6.

Definition of Terms (Optional)

It may be appropriate to include a list of definitions before describing the methodology. This will depend on the particular research project and field and may not always be necessary. This can also be included under the methodology heading.

If many abbreviations will be used, then it is also advisable to include a list of abbreviations, or a Glossary.

Step 7

Methodology

The methodology is a step-by-step detailed description of what is going to be done in order to obtain data that will be analyzable and permit conclusions to be reached, or research questions answered. Ensure that the chosen methodology will adequately address each of the listed objectives.

The following points should be included in the methodology:

- A description of the study design eg: This is a retrospective descriptive study; a prospective analytical case controlled study; a randomized controlled clinical trial, etc.
- Study population. Define the study population or study base as precisely as possible.



- Sample size and sampling methods. These should be explained and justified.
- Inclusion criteria. (Characteristics of participants that will make them eligible for inclusion and why)
- Exclusion criteria. (Characteristics of participants that will make them ineligible for inclusion and why)
- A detailed and precise description of all study procedures, including the informed consent process, if applicable.
- Pilot study description, if applicable.

Step 8.

Data management and statistical analysis.

(See step 4 above) Describe briefly how data will be recorded and processed. Also describe what statistical methods will be used.

Step 9.

Time plan and study logistics

- Study Flow Chart (optional, but often very helpful to include a graphical description of the study on one page)
- A time chart for all steps of the process could be included here, from writing the protocol, to preparing an article for submission for publication.
- It may also be useful to describe the responsibilities of different members of the research team, if applicable.

Step 10.

Ethical aspects

- Discuss all ethical issues that are considered relevant to the study and describe how these will be addressed. In particular indicate how participant privacy and confidentiality will be protected.
- If a Waiver of Informed Consent is being applied for, then a clear motivation should be provided at this point.
- The Informed Consent form must contain a statement to the effect that “this research study has been approved by the Committee for Human Research at the University of Stellenbosch and will be done according to internationally accepted ethical standards and guidelines”.

Step 11.

Resources

- Describe the resources that are available and also address resource limitations, if any.
- Declare the source of funding for the project
- Outline a realistic budget. (See an example of a budget on page 18)



Step 12.

Strengths and Limitations

Many research projects do have unavoidable limitations due to factors that are partly, but not entirely, beyond your control due to, eg budgetary, logistical or time constraints that affect the methodology, sample selection, etc. It is helpful for both researcher and the reviewer if the limitations have been clearly outlined and that any steps that could be taken to decrease the impact of the problems that have been identified, have been taken.

Step 13.

Reporting of Results.

Describe how the results will be reported or published and how they could be translated into action. Be sure to include a description of how feedback will be given to all relevant stakeholders, including participants and the community, if appropriate or feasible. Unpublished or unreported research can be considered a waste of time and effort and, as such, unethical.

Step 14.

References

These may also be included with the literature review if deemed appropriate.

Step 15.

Appendices

All additional documentation that will be used in the research study must be included in the protocol as a list of Appendices. Some examples are:-

- Questionnaires.
- Data capture sheets (optional).
- Interview structures or outlines.
- Rating scales eg for pain, anxiety, quality of life etc.
- Participant information and consent forms.
- Letters to authorities to request permission to do a study on their premises, eg to a school principal.
- Advertisements to attract participants.



III.

SUBMITTING A NEW RESEARCH PROTOCOL TO THE COMMITTEE FOR HUMAN RESEARCH (CHR)

The CHR meets once a month to review new and ongoing research. The dates for each meeting are circulated to all departments at the beginning of each academic year, and may be obtained from 021 938 9207. The dates are also posted on the website. The agenda usually closes 3 weeks prior to the meeting date, so ensure that the documentation is submitted in good time! Two paper copies of all documentation must be submitted.

An expedited (Fast Track) review process is available for minimal risk protocols, particularly for degree purposes. However, the demand for this service currently far exceeds the administrative and review capacity of the CHR. Researchers wishing to have their protocols “fast tracked” should provide some form of written motivation and, in addition to the hard copies, the protocol **MUST be submitted on a CD as well**. Please refer to the **CHR Standard Operating Procedures** on the web site for further information.

The application should include the following

1. An application form

Application forms and all other documentation are available electronically, either from the Division for Research Development and Support website or from 021 938 9207. Make sure that the application form is completed accurately. In particular PLEASE make sure that the supervisor and Head of Department sign the form.

2. The Checklist

This could be regarded as a nuisance, but it does help to be sure that everything has been considered and included.

3. A Protocol Synopsis or Summary

Very Important! No application will be accepted without a protocol synopsis that should comprise 800 to 1 500 words.

Not all committee members will get to see the entire protocol. Most committee members will only see the protocol synopsis and participant information leaflet and consent form. (ICF) The reason for this is that the committee usually reviews about 30 new protocols at each meeting and it is unfortunately too time consuming and costly to make all documentation available to every one. THUS it is VERY IMPORTANT that a good, clear protocol synopsis is submitted that clearly outlines the research rationale, objectives and methods.



The protocol synopsis should contain:

- Title
- A short introduction, motivation and literature overview (1 paragraph only)
- Research question or hypothesis
- Aims and Objectives
- A concise summary of the methodology
- A summary of the budget

4. Study Protocol (See Section II)

5. A Participant Information and Consent form(ICF)

Wherever possible, researchers are encouraged to use the available template and adapt it to the needs of the study. Templates are also available for research involving children and for DNA studies. Sections that are not relevant to the research project can be ignored. Sometimes it may be more appropriate to provide information to participants in the form of a letter. For example, if the study requests peers or colleagues to complete a questionnaire.

The ICF can be submitted in either English or Afrikaans. Once the requested changes (if any) have been made, then the CHR expects the researcher to submit translations in English/Afrikaans and Xhosa with a translation certificate or letter of authenticity, stating that the documents are an accurate translation of the original approved ICF.

NB! If it has been decided that Xhosa/Afrikaans/English consent documents are not necessary for the particular study, then the team leader is required to specifically justify this in the protocol under Ethical Considerations.

6. A Short CV of the Principal and Sub Investigators

This should not comprise more than 2 pages.

7. An Investigator Declaration

Investigators involved in the study must each sign an “investigator declaration” and declare any conflict of interest. Please read the form and complete it properly - don’t just sign it.

8. A budget (if not included in the protocol) and financial contract if applicable i.e. external funding.



IV. Submitting a new Research Protocol to the Committee for Clinical Trials (CCT)

The process is essentially the same as the Committee for Human Research. Please refer to the CCT Standard Operating Procedure on the website for details. Please note that, currently, the application form and checklist are different to those used in the CHR. The following documents should be submitted: (Those marked **if applicable** apply specifically to industry sponsored trials).

1. Covering letter (optional)
2. CCT application form
3. CCT checklist
4. Protocol synopsis/flow chart
5. Clinical trial protocol
6. Site specific patient information leaflet and consent form
7. MCC approval or proof of application **if applicable**
8. Clinical trial financial agreement, with a clear indication of where funds are to be deposited, and budget. **if applicable**
9. Detailed budget
10. Proof of insurance **if applicable**
11. Letter of legal indemnity, extended to Stellenbosch University and Tygerberg / Stikland Hospital, **if applicable**
12. Material for distribution to patients, including diary cards, QOL questionnaires etc
13. Recruitment material and advertisements if to be used.
14. CV's of investigators (List names)
15. Investigator declarations
16. Proof of GCP training
17. SA approved package insert(s) of registered comparators
18. Investigator's brochure **if applicable**
19. Payment instruction form **if applicable**



V

USEFUL INFORMATION.

1. Documents

All documents listed below are available on the updated Division for Research Development and Support Website or from the Ethics Admin Office. (Tel 021 938 9207)

- Standard operating procedure
- Guidelines for new researchers
- Application forms
- Checklists
- Investigator declaration
- Informed consent templates for general use, studies involving children or where legal guardians must sign consent, DNA studies.
- Adverse event report forms
- Study progress report

2. Example of a Budget

See page 16, OR contact 021 938 9156, for assistance with a budget spreadsheet.

3. Useful References and Urls

Codes and Guidelines

- WMA Declaration of Helsinki 2002 <http://www.wma.net/e/policy/b3.html>
- Health Act No.61 2003. South Africa. <http://www.info.gov.za/gazette/acts/2003/a61-03.pdf>
- The Belmont Report. The National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research. April 18th 1979. at <http://ohsr.od.nih.gov/guidelines/belmont.html>
- ICH Guidelines 1996. www.ich.org go to Publications, Guidelines, Efficacy Guidelines, E 6
- Guidelines on Ethics for Medical Research: General Principles. MRC - SA 4th Edition www.mrc.ac.za or <http://www.sahealthinfo.org/ethics/ethics.htm>
- SA GCP Guidelines Dept of Health 2006. www.doh.gov.za
- Ethics in Health Research: Principles, Structures and Processes. 2004 Dept of Health <http://www.doh.gov.za/docs/index>
- CIOMS International Ethical Guidelines for Biomedical research Involving Human Subjects. 2002 http://www.cioms.ch/guidelines_nov_2002_blurb.htm
- CIOMS 2008. International Ethical Guidelines for Epidemiological studies http://www.cioms.ch/080221feb_2008.pdf



Books

- Abramson. Survey methods in community medicine. 1999. TYG W 84,5 ABR
- Beauchamp T. Childress J. Principles of Bioethics. 5th Edition. 2001. Oxford University Press.
- Federman, Daniel D. Hanna Kathi E and Rodriguez, L. Editors. Responsible Research: A Systems Approach to Protecting Research Participants. 2003. National Academic Press.
- Joubert, Gina. Ehrlich, Rodney Editors. Contributing Editors Katzenellenbogen JM, Karim, S Epidemiology :A Manual for South Africa. 2nd Edition Oxford Southern Africa.
- Mitchell H Katz Study design and Statistical Analysis. A practical Guide for Clinicians. 2006 Cambridge.

Other

- US Dept Health and Human Services, Office for Human Research Protections. (OHRP) <http://www.hhs.gov/ohrp/>
- US National Institutes of Health (NIH): <http://www.nih.gov/>
- The National Health Research Ethics Council: <http://www.doh.gov.za/nhrec>



Committee for Human Research: Budget Example

(Provided by Phillane Groenewald, RDS)

Budget		Period:	
Personnel Compensation			
Principal investigator	R	-	
Project coordinator	R	-	
Research nurse	R	-	
Data typist	R	-	
Data typist	R	-	
Consulting services			
Training services	R	-	
Database programmer	R	-	
Statistical services	R	-	
Travel			
Airfare	R	-	
Accommodation	R	-	
Meals & incidentals	R	-	
Travel to clinics	R	-	
Equipment & furniture			
Computer & printer	R	-	
Cell phone	R	-	
Office furniture	R	-	
Other Direct Costs			
Telephone, cell phone & fax	R	-	
Internet & email	R	-	
Office supplies	R	-	
Courier & postage	R	-	
Printing & copying	R	-	
Ethics committee fee	R	-	
Staff training	R	-	
Total direct costs	R	-	
Indirect costs (12%)	R	-	
Total Expenditures	R	-	

Notes



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