This template for the development of a research protocol was created by Professors Colleen Aldous, Chris Rout and Doug Wassenaar.

The pages which follow make up a comprehensive protocol template which can be used as a guideline when preparing a new protocol. It is generic in nature and is open to tailoring for specific requirements.

Text in red is for information purposes only and should be deleted as the document is completed. Highlight the text in each section of the template, type what you wish in the final version then press enter. **Do not leave template instructions in your final version.**

Please delete this first page of the document prior to completing the protocol for submission.

University of KwaZulu-Natal
College of Health Sciences
School of Clinical Medicine

Title (This Must Be Short and Concise and Reflect Your Primary Aims)

Degree: for example MMed Surgery

Principal Investigator: name
Student number: xxxxx

Contact details:
Address: **XXXXXXXXX**
Tel: **XXXXXXXXX**
Cell: **XXXXXXXXX**
E-mail: **XXXXXXXXX**

Co-investigator: name if relevant or otherwise delete heading

Supervisor : name
E-mail address: xxxxxx

Co-supervisor: name if relevant otherwise delete heading

Date of Submission

EXECUTIVE SUMMARY

This must start with a statement of purpose.

Statement of purpose

The statement of purpose outlines exactly what is to be studied, how it is to be studied, in whom, where and when. Although this normally develops from the literature summary providing the background to the proposed research study, it is a useful initial declarative statement that crystallises the nature of the study in both the reviewer's and student's mind and directs the review to relevant questions that are best addressed by the student beforehand

The statement varies between quantitative and qualitative designs and the exact wording will depend upon the specifics of the study.

For a quantitative study:

The purpose of this …….. (observational/descriptive, comparative, correlational, survival, analytical etc) study ……. (is, was, will be) to ……. (Understand, describe, compare etc) the …….. (central focus, ie what you are actually measuring) for/of/in …… (population sampled) at /in/presenting to ……..(location) from/ over/ for the period ……...(Dates, time period etc)

(Adapted from Qualitative and Mixed Researcg, Creswell, JW. Presentation at UKZN 15 October 2008)

Example:

"The purpose of this double blind randomised controlled study is to compare the pH and volume of gastric contents in term parturients presenting for Caesarean section receiving preoperative glopatidine compared to saline controls presenting to St Elsewhere's Hospital for the period January to July 2015".

After the statement of purpose, an overview is provided which answers the following questions. Do not include the actual questions below in the summary and please note no references in the executive summary

The purpose of the overview is to provide the reviewer with a brief summary of the research. The summary must be approved by the supervisor of the dissertation.

IT MUST ANSWER THE FOLLOWING QUESTIONS (but don't include the actual questions in the summary). It can vary in length from one to three pages but must cover the following:

- Why is this project necessary? (show equipoise)
- What will you do?
- How will you do the project?
- What are the anticipated project outputs?
- What will be the impact of the project for patients, community or health system?

Example:

Road traffic crashes (RTCs) are a worldwide phenomenon, but a disproportionate number of deaths and injuries caused by RTCs occur in developing countries. A number of international organisations have drawn attention to the problem and called for a comprehensive public health response. Such a programme needs to be multi-faceted and use preventative and therapeutic strategies and also involve a wide range of stakeholders from government and civil society. In South Africa, the Province of KwaZulu-Natal (KZN) has the worst record for the number of deaths and injuries sustained on the roads. Despite the urgent need for such programmes in the Province there is a paucity of local research on the problem. *(answers: "Why is this project necessary? (show equipoise)")*

This project will be part of an ongoing systematic comprehensive quality improvement initiative. (answers: "*What will be the impact of the project for patients, community or health system?")*

A cohort of patients with injuries sustained in RTCs, presenting to a Regional hospital, will be identified gathering data on their injuries and the circumstances of the crash and costing their inpatient stay using micro-costing methods. *(answers: "What will you do?")* Data will be gathered close examination of hospital inpatient and outpatient records and paramedical reports made at the scene. *(answers: "How will you do the project?")*

Data from the study will be submitted for publication in an appropriate South African medical journal, and copies submitted to Provincial and National Road Traffic and Health Authorities *(answers: "What are the anticipated project outputs?")*

TABLE OF CONTENTS

Remember to update this table once the protocol is completed

1. BACKGROUND AND LITERATURE REVIEW

1.1 Defining the Clinical Problem

The background declares and explains the clinical (or other) problem and summarizes existing knowledge generally (world literature) and in the context of local conditions (epidemiological, socioeconomic and health systems etc.). For example, the background would include evidence of a problem (for example acid aspiration syndrome) in this specific group of patients that is known to cause morbidity or mortality generally and its relevance to local conditions (for example as highlighted by enquiries into maternal deaths).

1.2 The literature review

Again starting globally and reducing to local experience, i.e. contextualization, write a critical, objective summary of the known extent of the problem. Reference should be made to the findings of studies performed internationally and locally to address the problem. Novel methods and those particularly suited to local circumstances should be highlighted. By the end of the review it should be clear that the researcher has a thorough understanding of the problem and why the proposed study design has been chosen, based upon gaps in knowledge and conflicting results (equipoise).

Content will be determined according to your protocol, but should include the following (do not use as subheadings):
Historical background.

- Why this subject is important?
- What is known from previous studies?
- Critically appraise and show limitations of previous studies, if any.
- What factors led to, and why you initiated research project?
- Justification/relevance/impact of your study (based on the above aspects: e.g. importance of subject, gaps in knowledge, request from the institution, what the anticipated impact of the research may be etc…)

NB:

This must clearly identify the research area, the research topic and the area of equipoise and lead any reviewer to the logical conclusion of your research question or hypothesis and aims.

Include references

Only use Vancouver style: see
http://0-www.lib.monash.edu.au.innopac.up.ac.za/tutorials/citing/vancouver.html
Try to avoid website references if possible.

The protocol literature review should be brief but incisive, and there may be stipulated requirements. However, investigators are encouraged to develop a more extensive review, kept as a separate document and repeatedly reviewed throughout the study (up to the day of submission of the report)

NB:

Do not cut and paste this literature review onto the ethics application form. A maximum of 1 page (500 words) and 5 references are sufficient for BREC)

1.3 The research question (or hypothesis)

This should naturally emerge from the background and literature but must also appear as an explicit statement under a separate sub-heading at the conclusion of this section.

In the case of an analytical/experimental study use a hypothesis. E.g. Hypothesis: Our hypothesis is that the type of day care centre is associated with risk of TB in 6-9 year olds.

In the case of a descriptive study, use a research question. E.g. why do patients not adhere to TB therapy regimens?

2. AIMS AND OBJECTIVES

Confusion may arise concerning these two terms; semantically they are so close as to be virtually indistinguishable and not all centres will insist on both. However, we value the distinction as it assists in clarifying thought processes within the research design.

Aims are what you hope to achieve in your research project and objectives are the steps you need to take in order to achieve your aims. Aims must directly relate to the research question or hypothesis. Objectives must relate to the aims.

Example:

Aim: To investigate risk factors for TB in children aged 6-9 years in Limpopo Province.

Objectives: To determine the relationships between:

1. birth weight and incidence of TB in 6-9 year old children
2. day care, type of care giver and TB…
3. socio-demographic factors and TB…

3. METHODS

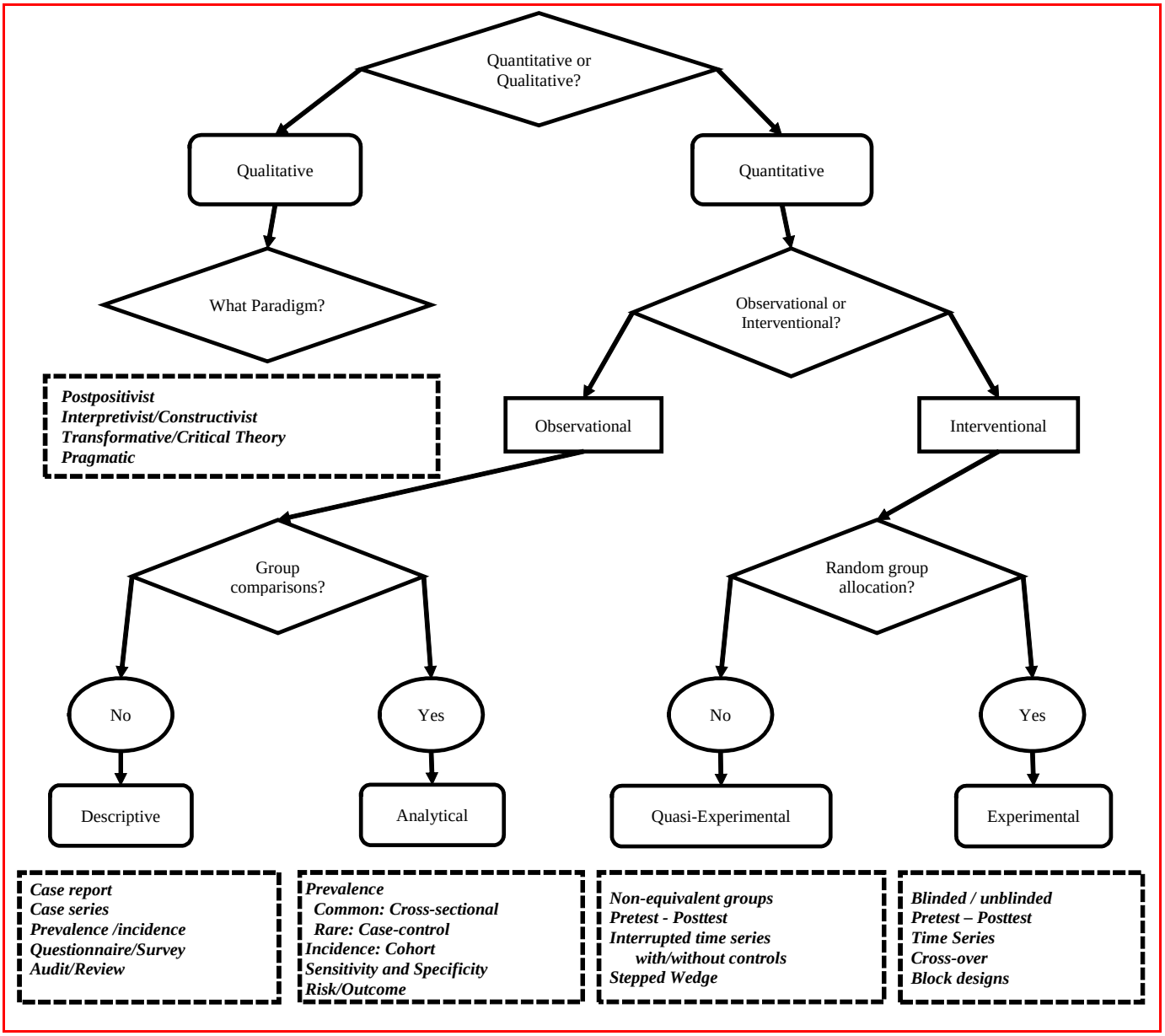
This is the most important section of the protocol. It must convey exactly what you are going to do, in whom, where, when, and how. Methods must relate directly to and only to the specific objectives of the study.

In the example above, recording the birth weight of all participants and a history of TB between the ages of 6 to 9 years would address objective 1. Testing for HIV status would not address any of the objectives as stated, so cannot be included in the methodology. If it is to be added as an “afterthought”, this can only happen if the possible role of HIV status is included in a rewritten background and literature and added as an additional objective of the study.

The methods section is written in the future tense in the protocol. It should be written in such a way that anybody can use it to reproduce your study exactly (although the results might turn out to be different). Scrupulous adherence to a well-written methods section enables complete “cut and paste” transfer to a paper or dissertation, simply changing the future to past tense. Each of the following must be addressed:

3.1. Study design

This adds detail to what has already been summarised in the statement of purpose. The following decision diagram can be used to define your possible research design.



Examples of study designs could be:
Quantitative, observational, analytical, cross-sectional
Quantitative, observational, descriptive, cases series
Quantitative, experimental, randomized control
Qualitative interpretivist.

There are different interpretations of classification of qualitative designs that are often debated.

3.2. Setting

This states where you will be conducting your study, for example a tertiary care dermatology clinic. Remember that most research settings (and all that are institutional) will require site or gatekeeper permission to conduct your research. Have you obtained such? If not, why not? An acceptable reason might be “Hospital management has been approached, and they have deferred approval until provisional ethics approval has been granted.” (Remember to attach any correspondence as an appendix to your ethics application).

3.3. Participant selection and sampling strategy

This describes whom you are investigating (the population of interest, e.g. all people with hypertension) and should include your sampling strategy, with inclusion and exclusion criteria. It should be an appropriate match to your study design. For example, purposive sampling is not appropriate to an analytical (experimental) study comparing two groups, but may be ideal for a qualitative or quasi-experimental study. The sampling method determines the degree of external validity (or transferability in a qualitative study) of your findings and also the type of statistical analysis that should be used. Randomization and blinding procedures should be included if relevant.

3.4. Measurements

Here you provide details of what you are going to measure (the outcome variables), the methods of measurement to be used (including definitions if relevant) and what steps you are going to take to avoid measurement error (random and systematic error). These details determine the internal validity of the study. Remember that what you measure must relate to the objectives of the study and may not relate to an unstated objective.

3.5. Data collection and statistical analysis

This must be planned in detail. All outcome variables should be in a clear logical format on your data collection tool. Statistical analysis is part of the methodology and as such misuse, abuse, misapplication and inappropriate testing fall within the ethical domain. You are likely to require statistical advice, either from a professional statistician or an experienced, knowledgeable member of your department. Do not use vague statements such as “statistical analysis will be performed”. Be specific.

For example: “Descriptive statistics (mean and standard deviation or median and interquartile range as appropriate) will be used to describe the sample groups. Continuous variable group means will be compared using unpaired t-tests for normally distributed data, otherwise non-parametric (Mann Whitney U) methods will be used. A p value of < 0.05 will be regarded as statistically significant.”

3.6 Sample size, statistical power and variable selection

You should seek statistical advice. How this applies depends upon circumstances. For example:

1 You might have sufficient resources (personnel, time, funding and a high prevalence or incidence) and an estimate of the average value of your variable of main interest (mean, median, proportion) and its range (standard deviation, 95% confidence limits). In this case you can use statistical calculations to determine the required size of a comparative study to achieve a given

statistical level of significance for a predetermined difference of clinical importance between means. You will need to have an estimate of:

- The control mean
- An important clinical difference (**Δ** or effect size, **ES**)
- Standard deviation (**σ**, ***s.d.***) of your variable
- Your chosen **α** (probability of accepting a result as a statistically significant difference when in reality there is no difference)
- Required statistical power (probability that a study will detect an effect when there is an effect there to be detected)

The control mean may be known (e.g. from previous research, or a physiological value such as a systolic pressure of 120 mm Hg), and similarly the standard deviation. In which case, the "standard" chosen values of α of 0.05 and power of 0.8 might be used. (NB these "standard" values are by convention, not rule; there are situations, e.g. the incidence of cancer, where you would want to be more certain and therefore choose a smaller value of α and/or a higher power).

2 Alternatively, you may have few resources (limited funding and time constraints for whatever reason) and not know the size and range of the variable of interest and wish to describe it in a pilot study for future research. You should however, have some idea of how many potential participants you will be able to see in the time available (e.g. from clinic records). In this case statistical calculations can indicate how accurate your estimates of average and range will be. This is important in a descriptive study, and explains why protocols containing "this is a descriptive study only and requires no statistical analysis" are rejected.

One might add the following in your protocol after stating how many participants you think you will include: Post hoc power analyses will be carried out when the study is completed as the relevant estimates to base sample size on are not currently available.

Statistical treatment: what the reviewer will be looking for

1. The proposed statistical treatment must be appropriate to the study design and aims, and will depend upon issues such as randomisation, number of groups, whether repeated measures are to be used, possible confounding or interacting factors etc.

2. The types of data (continuous, discrete, nominal etc.) to be collected, to ensure that the proposed statistical analysis is appropriate, with clear identification of the outcome variable(s) of main interest on which any power analysis is based.

3. The number of outcome measures that are to be recorded, to avoid or adjust for issues of multiple testing.

4. Any power analysis to estimate required sample sizes for the outcome of interest must be based upon the statistical test identified for use in its subsequent evaluation

5. The information used in any power analysis (means, proportions, standard deviations, effect size, proposed alpha and power etc.) must be included to permit the reviewer to repeat the calculation.

6. Confirmation that the investigator has the required knowledge to perform the subsequent analysis, or whether assistance will be provided by a statistician or person with the necessary expertise.

4. ETHICAL CONSIDERATIONS

All studies must comply with SA DoH research ethics guidelines (2015) and the UKZN policy on Research Ethics (V). Researchers are required to be familiar with these and with the required documents available on the relevant research ethics committee's webpage (e.g. BREC see http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx). For special ethical issues consult relevant literature and guidance.

It is useful to use the following well-known international framework (Emanuel et al., 2004) for identifying and addressing ethical issues in the ethics section of your research proposal, rather than just stating that the project 'will be submitted for ethics review'. Not all of the points 4.1 to 4.8 may be appropriate in every study design. Where the point is not appropriate for your study state why.

4.1 Community participation

Have you had prior engagement with any communities/institutions/gatekeepers/affected parties to secure their interest in and provisional support for your research? Ideally research is done *with* persons rather than 'on' them. Community engagement is not necessary for all types of research (e.g. chart reviews; analysis of stored samples) but gatekeeper permissions are usually required. Communities must be respectfully engaged where relevant and they may have useful additional ideas for your research topic or enrolment plan.

4.2 Social value

There should be a few lines in your proposal outlining what the knowledge gained by your study contributes to the field of study and the world at large. On the other hand, do not overstate the benefits of the study, even if it is interventional.

4.3 Scientific validity

If the methodology is flawed the study is not worth doing and is unethical. The methods used must be scientifically valid and informed by current literature. This also applies to qualitative studies where the analytic method must be appropriate and rigorous.

4.4 Fair selection of participants

Avoid convenience samples. Participants selected must be relevant to the research question. Persons or groups of persons should not be unfairly excluded from research participation provided that they meet the inclusion criteria. Vulnerable populations (e.g. children, comatose patients, psychotic patients, prisoners etc.) should not be included in research unless the proposed study specifically explores a question about that specific population and that adequate steps have been taken to ensure legally acceptable proxy consent for parties unable to consent independently.

4.5 Risk/benefit balance

Do not assume that there are no risks of harm: Consider carefully a) **biological** (e.g., discomfort, pain, injury, reversible and irreversible adverse effects of the research procedures) b)

psychological (e,g, distress, anxiety, fear), c) **social** (breach of confidentiality, embarrassment, stigma etc.) dimensions of research procedures and then outline steps that will be taken to minimize these. Specified referral for foreseeable problems should always be considered and details mentioned in the information sheet. Researchers have an obligation to minimize harms and maximize benefits associated with research participation.

4.6 Independent ethics review

Recruitment may not commence until final written ethics approval has been received from an NHREC registered research ethics committee.

4.7 Informed consent

Ethical issues arise from direct participant contact (requiring a full explanation of what is to be done using simple language and an appropriately worded consent document). Use a standard information and consent form template from your local REC and do not use 'home-made' versions as these will have missing elements and cause delays. Consent requires the provision of information in appropriate non-technical language, in the preferred language of the participant, understanding of that information, and a voluntary decision to enroll. Persons may need time to consider enrolling in research, and should be encouraged to confer with significant others if they choose to.

4.8 Ongoing respect for participants

Confidentiality obligations pertain during and after completion of the research. Hard and electronic copies of data should be destroyed 5 years after the study has been completed, unless data curation and storage has been implemented and consented to. As a general rule all data should have identifiers removed and replaced with codes. They key to the codes should be retained separately from the data. All commitments to share study findings with individual participants or participating communities or institutions must be honored and in a format tailored to the specific audience in question. Post-study benefits (if any) originally approved must be delivered as promised. Reports on the study should take care to protect confidentiality and preserve anonymity of participants, appendices and footnotes included.

5. METHODOLOGICAL CHALLENGES AND STUDY LIMITATIONS

This should be a concise, realistic view of the challenges presented to the aims and objectives of the study. It should be long enough and detailed enough to demonstrate to the reviewer that the study team has insight into what it is doing, but not so long and detailed as to suggest that the project has no hope of success. Each challenge presented must be accompanied by a summary of how the protocol meets the challenge. For example:

- How have response rates to questionnaires been improved?
- What efforts have been put in place to select a representative sample?
- What was done to reach the target sample size?
- Can the results be generalised?

6. FEASIBILITY

6.1 Time lines and project management.

It must be demonstrated that the study can be completed in the time available. All stages of the research must be included and time allocated to literature search, protocol preparation and realistic turnaround time for necessary review following submission, recruitment and data collection, data collation and entry into electronic format, statistical analysis and review, and finally write up; use of a Gant chart is recommended. The project manager (usually the principal investigator) is responsible for ensuring timeous completion of each stage of the project. Realistic allowances must be made for ethics review times – RECs typically generate queries that need to be satisfied and this process can consume a few weeks or months. Because scientific and ethics review times are variable, it is useful to construct the study timeframe around X weeks from full ethics approval and further steps in x weeks/months after previous step. Other aspects of the study can be developed while awaiting final ethics approval – e.g. literature review.

6.2. Study team, contributors and authorship.

From the outset it should be clear who is responsible for each component of the study and who should be acknowledged and who should be an author on any papers published from the research. This not only clarifies everybody's role in the project but also avoids possible future embarrassment or acrimony. Also, naming individuals responsible for each part of the research project can ensure that everything gets done. For example, any laboratory analysis requires identification of the individual responsible for the analysis additional to permission to use the laboratory facilities for the project.

Regarding authorship, guidelines from the International Committee of Medical Journal Editors (ICMJE) should be followed as outlined in the UKZN Research Ethics Policy (V). Criteria for authorship are:

- Substantial contributions to: the conception or design of the work (individual study); OR the acquisition, analysis, OR interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content (comment during writing the dissertation or paper); AND
- Final approval of the version to be published (email approval acceptable); AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Contributions not complying with all the criteria merit a detailed "Acknowledgement" at the end of the dissertation or paper.

Proposed authorship need not be cast in stone, as required roles may change during the course of the study but changes to the study personnel usually require notification (amendment) to the Research Ethics Committee.

Name	Department	Contribution	Author or acknowledgement

6.3. Participating Centres

If the study is to be conducted in more than one centre, all centres should have the requisite resources (time, personnel, equipment and expertise) to fulfil study requirements, usually requiring additional gatekeeper permission letters.

6.4 Study Funding and Progress

Protocol submission for a study that will never bear fruit without adequate funding is a waste of everybody's time. However, it is acceptable to submit a realistic budget with the protocol before a grant has been awarded, as most grants will be subject to ethical (and in the case of a degree, postgraduate committee) approval. This section of the protocol must be completed even if there are no direct costs (e.g. a retrospective chart review) or the stationery etc. can be covered by departmental resources. Costs must match funds. State reasons why grants are delayed or deferred if that is the case.

Item Description	**Cost**	
Total Project Cost		

7. STUDY SIGNIFICANCE

A brief concluding paragraph as to the expectations of the study in terms of improving knowledge and how the results can be applied to the underlying clinical problem addressed by the study.

8. APPENDICES

These should include your research instrument (e.g. questionnaire or data collection tool), patient information sheet and consent form (based on template available from the REC website), ethics approval letter, gatekeeper permissions, certificates of recent approved research ethics training (e.g. TRREE), and clinical good standing (where applicable) and brief curriculum vitae of the Principal Investigator, any co-investigators, supervisors and co-supervisors etc. Ensure that all required documentation is included with your protocol and HREC submission, using any check-list provided.