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# Abbreviations

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<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>CTN</td>
<td>Clinical Trial Notification</td>
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<tr>
<td>CTX</td>
<td>Clinical Trial Exemption</td>
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<tr>
<td>EC</td>
<td>Ethics Committee</td>
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<td>HREC</td>
<td>Human Research Ethics Committee</td>
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<tr>
<td>NHMRC</td>
<td>National Health and Medical Research Council</td>
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<tr>
<td>IP</td>
<td>Intellectual Property</td>
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<tr>
<td>MUHREC</td>
<td>Monash University Human Research Ethics Committee</td>
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<tr>
<td>PI</td>
<td>Principal Investigator</td>
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<tr>
<td>PICF</td>
<td>Participant Information and Consent Form</td>
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<tr>
<td>RGC</td>
<td>Research Governance Committee</td>
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<td>RGO</td>
<td>Research Governance Officer</td>
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<tr>
<td>SAE</td>
<td>Serious Adverse Event</td>
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<tr>
<td>SOP</td>
<td>Standard Operating Procedure</td>
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<tr>
<td>SPHPM</td>
<td>School of Public Health and Preventive Medicine</td>
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Clinical and public health research must be conducted in accordance with a large number of laws, regulations and conventions. These are designed to protect the participants, the researchers and the institutions where research is conducted.

Well-conducted research flourishes best in a culture that emphasises respect for research subjects and a focus on accuracy and honesty.

At the Monash University’s School of Public Health and Preventive Medicine (SPHPM), we are fortunate to have a number of our senior staff involved in ethics and research governance as well as in research. Over several years, we have developed activities designed to ensure that our research is conducted at the highest standard and that our working culture emphasises all of the attributes needed to support this goal.

In addition to producing this guide, we have focused on careful induction of new staff and ongoing education and quality assurance activities, all directed by our Research Governance Officer and an active research governance committee.

I would like to record my appreciation of the many people who have participated in the development of this guide and in the development of the research governance framework of the School. In particular I would like to thank Stephanie Poustie, Giuliana Fuscaldo, Megan Brooks and Liz Bishop, all of whom have provided outstanding support in their research governance roles. I also thank Andrew Forbes, Marina Skiba and Robin Bell for acting as Chair of our Research Governance Committee. I commend this work to all new staff of our School.

John McNeil  PhD FRACP
Head of School
2 Promoting High Quality Research

2.1 Purpose

The purpose of this document is to ensure that medical research conducted within our School meets the highest scientific and ethical standards.

This guide outlines a set of standards that must be adhered to by all those involved in any research capacity.

- If you identify any significant departure from these guidelines, you must bring it to the attention of your supervisor and/or the Research Governance Officer (RGO).
- Diligent supervision and monitoring of research projects by appropriately trained and experienced individuals is a core expectation within the School.
- Particular care must be taken to ensure full compliance with consent and privacy requirements. The highest level of confidentiality must be maintained with all research data at all times.
- Research misconduct in any form is totally unacceptable. This behaviour would have implications, not only for the individual researcher, but also for the School and the University.
- The position of RGO has been established to oversee the School’s research and to assist investigators in all aspects of good clinical research practice. The RGO has been authorised to conduct audits of all School research projects.
- The guidelines outlined in this booklet are available for quick reference. It is highly recommended that investigators enrol in programs and courses on ethics and good clinical research practice.

2.2 Risk Management

Although research misconduct has generally resulted from aberrant behaviour by individuals, the senior staff of the School have a responsibility to establish a culture and environment that reduces the likelihood of such an event.

Within SPHPM we have certain vulnerabilities to research misadventure that put us at risk. These include:

- A large number of research projects with responsibility dispersed among many senior investigators;
- A heavy reliance on relatively junior staff and PhD students to supervise research assistants and to analyse research results;
- A high level of investigator initiated research that is not monitored by external bodies such as pharmaceutical companies; and
- Some data collected off-site by research staff working away from direct supervision.

Because of these concerns the School has established a Risk Management Plan that attempts to foresee our major areas of risk. The School’s Risk Management Plan is Appendix E of this document.

2.3 Good Research Practice: Fundamentals

The following principles have been adapted from the United Kingdom’s Medical Research Council’s “Guidelines for good clinical practice in clinical trials” (see Appendix I).

- Clinical studies should be conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, The National Statement on Ethical Conduct in Human Research (see Appendix I) and the ICH/Good Clinical Practice Guidelines (see Appendix I).
- A study should only be initiated and continued if the perceived benefits for the individual participant or society justify the risks and inconvenience.
- The rights, safety and wellbeing of the participants are the most important consideration and should outweigh other considerations.
- Clinical studies should be scientifically sound and clearly described in the study protocol.
- Studies should be conducted in compliance with a protocol that has been authorised by an appropriate Human Research Ethics Committee (HREC).
- Individuals conducting the study should have an appropriate level of education, training and experience to perform their tasks.
- Freely given informed consent should be obtained from every participant prior to study participation.
- All study data should be recorded, handled and stored in a way that allows their accurate reporting, interpretation and verification.
- The confidentiality of participant records should be protected, respecting the privacy and confidentiality rules of the applicable regulatory authority.
- Systems that ensure the quality of every aspect of the study should be implemented.
2.4 Research Ethics: Fundamentals

It is important that researchers understand the approach taken by ethics committees to various types of projects. This is described in Appendix A. A brief description of the responsibility of researchers in dealing with ethics committees is provided below.

a. Ethics Committee Approval

Ethics committees have been established in all institutions that receive funds for medical research from the National Health and Medical Research Council. Their purpose is to look after the rights and safety of research participants. It is a requirement that researchers seek approval for any project that involves contact with individuals or uses their data. All research undertaken must comply with the authorising ethics committee’s requirements. In particular:

- Projects must not begin until ethics committee approval is obtained in writing.
- The authorised study protocol must be followed in all cases.
- Ethics committee approval must be sought for protocol amendments, even if they are relatively minor.

Projects must not run longer than the approved completion date, unless an extension has been obtained in writing.

Ethics committees require all study participants (or their legal representative) to be provided with an approved Participant Information and Consent Form (PICF) and to sign their name to signify their preparedness to participate in the project. These forms must be carefully filed and made available for scrutiny by auditors operating on behalf of the ethics committee or the study sponsors.

Any serious adverse events that occur during the study, whether considered to be related to participation or not, must be notified urgently to the appropriate ethics committee.

Exempt from Ethics Committee review:

There are some projects which are so low in risk (e.g. some Quality Control projects) that they may be exempt from review and approval by an HREC. However, SPHIM requires that researchers conduct an HREC and received written confirmation that formal review and approval is not required for their study.

The work of ethics committees is guided by:

- National Statement on Ethical Conduct in Human Research: http://www.nhmrc.gov.au/publications/synopses/e72syn.htm; and

Research institutions also have their own specific requirements that need to be observed. For example:


All Monash University staff and students must obtain approval from MUHREC even if they are conducting their research at another institution (e.g. a public hospital) and have received ethics approval from that institution, i.e. you must have MUHREC approval as well. Monash has a memorandum of understanding with a number of institutions to make this process as easy as possible (for details see the website under “multicentre research”).
It is also unethical to assign human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. "For the purposes of registration, a clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes."¹⁵  The ICMJE (International Committee of Medical Journal Authors) now require that a clinical trial is registered prior to enrolment of the first participant for most journals to consider the results of the project for publication. For this reason it is recommended that, if in doubt about whether or not your project is a clinical trial, you register it anyway. The registry you choose must meet the ICMJE criteria. Some registries that comply are: ClinicalTrials.gov is a US based registry: http://www.clinicaltrials.gov The NHMRC developed the Australian Clinical Trials Registry http://www.actr.org.au

**f. Plagiarism**

Quoting someone else’s work, or even quoting your own, without properly referencing it could be considered plagiarism. The universities policy on Academic integrity, plagiarism and collusion can be found at http://www.med.monash.edu.au/intranet/policies/academic-integrity-procedure.html. The student equivalent is http://www.monash.edu.au/students/policies/academic-integrity.html.

Learn how to reference properly and avoid plagiarism. The following link leads to a short tutorial entitled “Demystifying citing and referencing” which was developed by the University Library: http://lib.monash.edu.au/tutorials/citing/

### 2.5 Ethics Committee Review of Projects

The general focus of ethics committee deliberation is to protect the "rights and welfare" of human subjects. This goes beyond simply protecting them from egregious behaviour or undue risk. In general, it looks to ensure that research subjects are treated in accordance with three basic principles referred to in the 1978 Belmont Report (US)¹⁹ (see Appendix I). These are:

1. **Respect** – for the individual, ie individuals should have total control and authority over everything that happens to them;
2. **Beneficence** – refers to the obligation of carers and researchers to maximise benefits and minimise harm; and
3. **Justice** – a more general concept that includes the undesirability of certain disadvantaged groups taking all the risks of research while other groups benefit.

In practice these principles are put into operation as follows:

**Scientific validity:** Ethics committees now take the view that it is unethical to approve scientifically flawed research because individuals should not be expected to undergo the risks, inconvenience and expense of research that is unlikely to provide a scientifically valuable result. As a result, studies with substantial design errors or a major susceptibility to bias are unlikely to be approved until these deficiencies are remedied. Ethics committees are increasingly scrutinising sample-size calculations since underpowered studies are unlikely to provide scientifically useful results. Experience has also made most large ethics committees aware of the adage that “the devil is in the detail”. This is the reason for insisting on the provision of detailed protocols with every application.

**Scientific value:** It is also unethical to expect sacrifices from volunteers that are out of keeping with value of the potential findings.

**Credentials:** The ethics committee requires that a current curriculum vitae of all investigators on all submitted studies be held on file. The research credentials and previous experience of investigators are matched against the nature of the study and a judgement formed about whether the individuals involved are appropriately trained to be undertaking the proposed research. A research team may be asked to add a more experienced investigator, or someone...
A Guide to Good Research Practice

One particularly common form of risk is that arising from withdrawal of regular treatment (e.g., from anti-hypertensive or anti-asthmatic medication). Under such circumstances, ethics committees will require strict limits on the severity of illness involved and the duration of the period without therapy. Careful and frequent clinical monitoring and instructions to patients about procedures in case of emergency will also be mandated.

**Safety monitoring:** In many research studies, the risks are not fully established at the time the research commences. If substantial numbers of participants are involved in such studies, ethics committees commonly require a safety committee or safety monitor to be appointed. This committee or individual will regularly review the un-blinded study data and alert the investigators, and ethics committees, about safety concerns.

Proper safety monitoring during the course of clinical research projects is also required. For example, full blood exams or liver enzymes may need to be monitored regularly and in such circumstances it is imperative that arrangements are in place for the study co-ordinator to review such results immediately and bring abnormalities to the attention of the investigators and to the individual’s attending doctors.

**Inconvenience etc:** Many studies involve considerable numbers of trips to hospital and time away from work, which must be explicitly described in the PICF.

**Informed consent:** Participants in clinical research must be fully informed about the nature of any research project that they participate in and be free to choose whether or not to take part. Basic ethical principles dictate that:

1. Participants have an unambiguous right to decline participation or to withdraw their consent at any time without an obligation to provide a reason.
2. There is a full disclosure of any known risks that might influence their decision about whether or not to participate.

Participants involved are provided with the most explicit and accurate account of personal inconvenience and expenses likely to be encountered.

The PICF is the key document in the consent process (see section 4.4). Its purpose is to provide prospective participants with a simple and easily understood account of the rationale for the research and a detailed description of all foreseeable risks and benefits. Ethics committees are required to review these documents and to endorse their contents as providing a fair and balanced account of risks and benefits. In fact, much ethics committee time is spent adjusting the language of PICFs so that it can be understood by an average person. A checklist of contents is shown in section 4.4.

**Early cessation:** A study that continues well beyond the time that convincing evidence of benefit has been demonstrated, is denying many participants access to a superior therapy. Procedures are therefore regularly put in place with very large trials to stop a trial early in the event that a significant benefit (or risk) becomes evident before the scheduled end of the study.

**Adverse events:** All serious adverse events occurring in participants enrolled in clinical research projects must be reported to the ethics committee and any sponsor within 24 hours. For this purpose, “serious” refers to any event that is fatal, life threatening, results in (or prolongs) hospitalisation, results in a significant disability, takes the form of a birth defect or is a medically important event or reaction.

**Special Issues**

**Clinical Trial Notification/Clinical Trial Exemption (CTN/CTX) studies:** In the early 1990s, the Commonwealth Government introduced new procedures designed to speed up the approval process for clinical trials of new drugs. Essentially, companies could choose whether to introduce new agents to clinical research under a CTN scheme.
or a CTX scheme. If the CTX route was chosen, the company would submit the available data on their drug to the Commonwealth Department of Health and Aged Care where, for a substantial fee, an evaluation of its safety and suitability for use in clinical trials would be carried out.

Companies wishing to avoid the delays inherent in this process could alternatively introduce their drug through the CTN scheme, under which they are merely required to notify the Department of Health and Aged Care of their intention to undertake studies and the relevant ethics committees then assume responsibility for evaluating the drug. In practice, unless the ethics committee has the experience to evaluate the preclinical data, most committees will only approve CTN drugs if they have been evaluated through a CTX-type process in one of the three countries with similar drug evaluation standards to Australia (USA, UK or Sweden).

**Consent in Special Circumstances**

In some studies, special procedures are required for informed consent. These may include studies on:

- human genetics;
- vulnerable patients (eg mentally handicapped);
- minors; and
- participants unable to provide consent (eg unconscious, demented).

In these circumstances, advice must be obtained from the relevant ethics committee/s during development of the consent documentation. It is strongly recommended that researchers who may be recruiting from these special groups be familiar with the Guardianship and Administration Act 1986 (version incorporating amendments as at 1 August 2011) (see Appendix I).

**Emergency care research and research on unconscious patients:** In situations where an individual may be unconscious or in no position to provide informed consent, an ethics committee in Victoria is authorised to allow important research to go ahead on the basis of consent from a “responsible person”, normally the next of kin (with a carefully defined hierarchy).

Ethics committees will not approve such research unless it is clearly not to the disadvantage of the research participant and it could not be undertaken with consenting participants.

In some rare instances, an ethics committee is authorised to allow highly important research to take place without specific consent of either a participant or a “person responsible” using an approach referred to as “procedural authorisation”. HREC approval under this arrangement is typically restricted to low-risk research. After an individual has been entered into a study using procedural authorisation, it is necessary to complete and fax a Section 42T Certificate to the Office of the Public Advocate within two working days.

Detailed discussions should be held in advance with the Ethics Committee Secretariat if either approach is contemplated.

**Children:** When children are involved, there must be no risks greater than those of everyday living and permission must be obtained from both the participant and their parents.

**Long-term intellectual impairment:** Consent for involvement in clinical research must be obtained under special consent arrangements (“Person Responsible Consent”). The Ethics committee secretariat will provide details of what is required.

**Genetic research:** Collection of blood or other biological samples for genetic testing is a rapidly developing area of research with the potential to improve the diagnosis and treatment of many common diseases. It also raises a number of particular ethical issues that have led the NHMRC to develop a specific policy on this type of research. The policy incorporates the following principles:

1. Gene banks should be established within an academic research environment under the control of experienced and highly reputable researchers.

2. The researchers involved must be aware of the potential ethical issues associated with access to data and samples from the bank and have adequate resources and strategies in place to deal appropriately with them.

3. Committees typically, in the first instance, approve the establishment of the gene bank and the specific project linked to the application. Future research involving different markers will require further separate applications before approval will be given.

4. Individuals providing samples for a gene bank should be aware that they must disclose to life insurance and superannuation companies (upon request) any adverse information about their risk of future illness that is provided to them as a result of genetic testing. Possession of this information may increase their premiums or may have them denied cover (or employment) altogether.

5. Individuals should also be aware of the possibility that information held by the gene bank may be discoverable by a court of law.

6. The researcher in charge of the gene bank should also have a protocol to determine what information should be provided unsolicited to individuals as a result of findings generated by the research. Generally the ethics committee should be informed of such actions.

**Innovative therapy:** Increasingly, the introduction of new and innovative therapy is being handled in a fashion similar to a research project. Applications involve a justification and literature review, a protocol and a PICF. Commonly, new procedures are referred to an ethics committee and an innovations committee.

**Research in private doctors rooms:** Ethics committees are often asked to review projects conducted in private settings. There has been some reluctance to do this because some committees feel insufficiently familiar with the governance of research in such settings to be able to provide endorsement. Sometimes
there may also be unease about the financial arrangements involved. With the progressive decline in hospital outpatients it is likely that more and more research will move to such settings. Contact the ethics committee for details regarding special requirements such as access to the site for monitoring purposes, evidence of insurance that covers the research activities etc.

Audit: The NHMRC requires that, as a “minimum”, ethics committees monitor research conducted in their institutions by requiring a structured annual report. Some ethics committees supplement this by an audit program looking at such matters as consent forms, data storage, randomisation processes, bias control and source data verification.

Breaching Ethics Committee Requirements

Examples of serious breaches include:

- entry to a study of patients whose personal characteristics do not meet those of the approved entry criteria (this may also breach the contract with the study sponsor);
- failure to inform a participant of the risks of participation in a research project;
- alterations to a protocol without ethics committee approval; and
- failure to respect the privacy of an individual’s private information.

Vignette: A researcher was conducting a trial comparing two standard treatments for heart failure. He decided to commence with a pilot study without obtaining ethics committee approval or consent from the participants (like all other studies, pilot studies require ethics approval as the risks to the participants and the need for consent are the same). The ethics committee required the researcher to attend a meeting where he was reprimanded. It was made clear that it was unacceptable to conduct an unapproved pilot study.

Vignette: A researcher decided that since his research only involved the collection of some additional blood (during routine sampling) that it was reasonable to enrol participants without obtaining their consent. A member of the hospital staff notified their concern to the ethics committee and an audit was conducted. The researcher was reprimanded (participants always have the right to choose regardless of how simple the study is) and the ethics committee required that the study could continue only if that researcher was not involved.
3 Institutional Requirements

3.1 Conflicts of Interest
The School requires that all investigators pay careful attention to compliance with institutional policies regarding conflict of interest. Every significant conflict of interest must be declared both to the ethics committee (at the start of the study) and the journal (when the results are being published).

Ethics committees generally require a detailed account of the budget of a study and an explicit description of any personal benefits that an investigator will receive as a result of undertaking the research project. There is often a requirement for such matters to be mentioned in the PICF.

In addition to conflict of interest, the HREC will scrutinise the financial statement to determine whether the funding is sufficient to allow the study to proceed. In some instances, major issues will need to be considered by the senior administrators of an institution.

Most journals also require a detailed statement of conflicts of interest to accompany published manuscripts. Undeclared conflicts that are subsequently identified may require statements of contrition that are highly detrimental to a researcher, his/her colleagues and their institution.

The Monash University conflict of interest policy is provided at:

3.2 Participant Reimbursement
Compensation of study participants for incidental expenses is appropriate, as are small payments to compensate for inconvenience etc. Unlike the US, Australian ethics committees have generally been unwilling to allow more substantial payments in case they provide an inducement to participation against better judgement.

3.3 Intellectual Property
As an education and research facility SPHPM is involved in the generation of data by both staff and students. Students and staff are encouraged to identify new innovations or inventions that may arise from their work. Monash University has a policy to enable students and researchers to share in any commercial rewards that arise from such developments.

However, the rights and responsibilities differ between staff and students when it comes to IP.

Staff: The University owns the IP rights in research data generated by a staff member in their employment with Monash University. Staff are encouraged to engage in collaborative research but must ensure that an appropriate collaborative agreement is in place before to collaboration commences. Staff are advised to contact the University Solicitors Office for assistance in drafting the agreement. Staff are also reminded that the agreement should be between institutions not individuals i.e. Monash University, not the staff member, should be a party to the agreement.

Students: Within Monash University students own the IP within their research unless:
1. The University has made a specific contribution of funding, resources, facilities or apparatus to the research to create intellectual property AND the candidate has made or contributed to a patent worthy discovery or invention.
2. The intellectual property created by the candidate will use background intellectual property owned by the University.
3. The University has entered into an agreement under which the intellectual property created by the candidate is to be owned or partly owned by a person/party other than the candidate.

Due to the nature of the research conducted within SPHPM it is extremely unusual for one of the above criteria not to be met. For that reason, the default position with SPHPM is that student IP belongs to the University. Students are required to complete one of the 3 possible Deed of Assignments forms available (see http://www.monash.edu.au/migr/assets/documents/ipforms/ip-declaration.pdf for details). Students are required to make a case to the contrary if they feel they are an exception. Students are encouraged to engage in collaborative research but must ensure that an appropriate collaborative agreement is in place before the collaboration commences. Students are advised to contact the University Solicitors Office for assistance in drafting the agreement. Students are also reminded that the agreement should be between institutions not individuals i.e. Monash University, not the student, should be a party to the agreement.

Useful links:
Research Data, Ownership and Right: http://monash.edu/library/researchdata/guidelines/ownership/#Owner
Copyright at Monash University: http://www.copyright.monash.edu.au/

3.4 Research Agreements Between Institutions
Clinical and public health research increasingly involves a multi-institution collaboration where different aspects of a project are undertaken by different organisations. To avoid disputes it is essential that multi-institution agreements be accompanied by a document that specifies exactly what each institution (and employee of the institution) will be responsible for and what funds will flow as a result of these activities.

Agreements should also specify the composition of any committees involved in supervising the research activity and the approach to be taken in relation to authorship and financial reporting.
4 Essential Research Documentation

4.1 The Protocol

The study protocol is a document that describes the rationale, objective(s), design, methodology, and organisation of a study. The protocol provides the basis for ethics committee approval and up-to-date copies should be made available to every member of the study team. NO research activities, even relatively minor ones such as a pilot study, should be undertaken except in accordance with a protocol that has been approved by an ethics committee.

See Appendix B for details on what the protocol should contain.

Protocol changes: Once a project has been approved by an ethics committee, any change (eg changing the questionnaire to collect new information), should be immediately notified in writing to the ethics committee(s) where approval has been obtained. All protocol changes should be clearly identified on an updated version of the protocol and procedure manual. Changes to a protocol may also necessitate changes to the PICF.

4.2 Procedure Manual

All large studies require a detailed procedure manual that incorporates and expands upon the study protocol. The purpose of the procedure manual is to provide a detailed account of all study procedures. It is the day-to-day reference document for all staff involved in any large research project. It should provide enough information to allow a new staff member to take any role in the study at any time. Copies of the procedure manual must be provided to all research staff involved in a study (including updates or amendments agreed to at study meetings).

See Appendix C for details on what the Procedure Manual should contain.

4.3 Consent Documentation

Informed consent must be sought from all participants involved in medical research. The “consent process” typically involves a detailed discussion with each participant that includes the reason that the study is being undertaken, together with an explicit description of any risks or inconveniences involved. The person involved in discussions with the participant must be “manifestly capable” of describing the risks and benefits of the study. This means that the person involved in consent discussions must be either an investigator or a research officer who has become fully acquainted with all aspects of the study. The consent process must never be delegated to junior members of a study team unless the project is of relatively low-risk.

On occasions an ethics committee may vary the normal requirements for consent. For example, in very low risk settings a committee may approve opt-out consent, or even a waiver of consent. However such circumstances are only approved in situations where the ethics committee determines that consent is impractical, undesirable (eg by the likelihood of distressing participants) or would impair the scientific validity of the study.

4.4 The Participant Information and Consent Form (PICF)

The Participant Information and Consent Form (PICF) is an essential accompaniment of the consent process. It is given to all study participants at the time when their participation in the research is first discussed with them. It must be made available in the language of study participants.

This document should be written in language appropriate to the participant group/s. Technical terms and concepts should be described in lay language. It should describe the reason the study is being conducted, the demands to be made of the participant and any risks that may occur as a result of their participation. It should also describe arrangements to ensure the privacy of the information collected.

The PICF must be updated if significant new information becomes available during the course of the study. The ethics committee should approve the update, and only the most recent approved version should be provided to potential volunteers.

Section 4.8.10 of the ICH/GCP Guidelines (See Appendix I) and section 2.2.6 of the National Statement (See Appendix I) provides an outline of the information that should be included within a PICF. Many institutions also require that specific wording covering local requirements (eg privacy legislation) is included in a PICF.

Typically the information to be included in a PICF includes:

1. An invitation to participate.
2. The fact that the study is a research project.
3. The nature and purpose of the project.
4. A description of any randomisation procedures and the use, if any, of placebos.
5. A description of any medical procedures to be undertaken.
6. A description of any drugs or isotopes to be used.
7. The availability of alternative treatments.
8. An explicit account of what is involved in participating including changes in lifestyle required, the expected number and timing of follow-up visits and any monetary costs likely to be borne by the participant.
9. The anticipated duration of the study.
10. The approximate number of patients treated similarly to date (when the research involves a new drug or device).
11. The possible benefits to the subject and others, stressing when appropriate, that these benefits are not assured.
12. Foreseeable risks, side-effects and discomforts.
13. The requirement that the subject must advise the researchers of any other research in which they are participating or drugs they are taking.
14. Any requirement that current treatment being taken by a participant may need to be suspended.

15. Steps to be taken in case of therapeutic failure or adverse events.

16. Insurance and other procedures for compensation in case of injury due to the study.

17. The fact that participation in the research project is entirely voluntary and that the subject is free to withdraw at any time without any negative effects on his/her relationship with the researcher or influence on subsequent treatment.

18. The circumstances under which the subject’s participation may be terminated.

19. The fact that the participant’s records may be inspected for the purposes of source data audit by individuals from inside or outside the hospital.

20. The precautions that will be taken to protect the confidentiality of the participant’s medical information.

21. The names and telephone numbers of the person to contact for further information about the study and the person to contact in case of emergency.

22. A statement about the funding of the study and any payments to study personnel.

Ethics committees require that patients be given time to properly consider these PICFs (and discuss them with friends or relatives) before deciding whether to participate, particularly in long-term or invasive studies. Participants must also be given an opportunity to ask questions and should only be asked to provide consent when the researcher is confident that the participant understands what is required of them and is consenting willingly.

“Immediate consent” is increasingly restricted to low risk studies or those where immediate treatment is required. When there is urgency in commencing an intervention (as with research in acute stroke or myocardial infarction) patients are often distressed and not receptive to detailed explanations of a research project. In such cases, an abbreviated discussion may be acceptable if this approach has been approved by the ethics committee. However, in such circumstances, it is also important to seek the assent of relatives before any experimental interventions are commenced.

4.5 Advertising for participants

Advertising for participants to take part in studies must be undertaken with care and must receive HREC approval. This includes using the media, internet and flyers. Advertising should be targeted to the appropriate audience. Local newspapers may have advantages over state-wide newspapers, particularly for studies with multiple visits. It is important that any public advertising avoids wording that might imply endorsement of other institutions (such as hospitals).

4.6 The Study Document File

A Study Document File should be kept by the study coordinator/investigator as a central depository of all significant documents and correspondence involving the study.
5 Secure Maintenance of Study Records

5.1 Proper Document Management

All paper work relating to a study must be maintained in a neat and orderly fashion. Clinical research requires meticulous record keeping. Study documentation may be audited at any time, even some years after it has been completed.

- All study documentation must be kept for at least 7 years after the completion of studies not involving drugs and a minimum of 15 years for drug/device trials, although some institutions require indefinite archiving.
- It is recommended that the following documents be kept in the study document file:
  - ethics committee applications, including all correspondence and reports;
  - protocol and amendments;
  - PICF (all previous and current approved versions);
  - Participant Identification List;
  - CRFs (Case Report Forms) and/or questionnaires;
  - study brochures;
  - data dictionary;
  - correspondence with granting agencies;
  - contracts or agreements;
  - minutes of study meetings;
  - computer database specifications including data entry and verification procedures;
  - a record of any changes to data on computer files after data collection;
  - drug dispensing records;
  - randomisation schedule;
  - adverse events reported;
  - progress reporting forms;
  - quality control and/or monitoring reports; and
  - study reports and publications.

5.2 Maintaining Security of Study Record

Study participants are often asked to provide information of a personal and private nature. Sometimes research involves extraction and collection of personal data from hospital records or records held by other bodies. Confidentiality refers to the strict avoidance of disclosure of this information to anyone other than authorised individuals.

a. Privacy principles and guidelines

State and Federal legislation is in place to ensure privacy standards for the handling of health information. In December 2001, the Commonwealth Privacy Act (1988)\(^a\) was extended to cover all Australian private sector organisations. The Victorian Health Records Act (2001)\(^b\) applies to both private and public sectors that handle health information and took effect in July 2002. Together, these Acts impose a series of Privacy Principles that regulate the collection, use, disclosure and handling of personal information, including health information\(^c\).

Exemption from specific requirements of the Privacy Act may be allowed for a medical research study. Ethics committees have the authority to grant such exemptions provided certain criteria are met. These criteria include that:

- the research is of major public health significance;
- the research is being carried out by bona fide researchers with appropriate experience.
- the data will be kept secure and adequate privacy protection is in place;
- the data is not of a highly sensitive nature; and
- consent to access the information is obtained from each individual unless compelling reasons exist (typically that the requirement for consent would result in invalid results or cause distress).

If access to medical information is granted, it is the responsibility of the research team to ensure the participant’s privacy is adequately safeguarded. The following requirements apply:

- Information collected must be used only for the study for which approval has been given.
- Personal identifying information must be removed from all data collection forms and computer files. Typically, if identifying information is recorded in a data collection form it should be located on page 1, which is removed and stored separately from the rest of the form. Codes linking participant information to their data must be kept separately in a locked safe or filing cabinet. Access to data on computer should be under password control.
- Access to data should be available only to a limited number of individuals, directly responsible to the investigator(s), and each should sign a privacy declaration every year.
- The principal investigator or head of the appropriate unit should take responsibility for the destruction of records containing personal information (after the required archival period, as described above).
- No data capable of association with a particular participant should be published.
- Research data containing identifying information must never be kept on USB sticks, laptop computers or home computers.

Vignette: A researcher was undertaking some data analysis in an airport lounge. The data was held on a USB stick which contained names, addresses and laboratory test data (including HIV test results). In the rush to leave, the investigator left the unprotected memory stick in the publicly accessible computer. This was found by the next computer user and given to a journalist colleague.
b. Medical Record Access

In general, clinical records can only be accessed by employees of the hospital and with the permission of the ethics committee of the institution. University staff conducting research in a hospital typically require an honorary position in the hospital to be allowed to access clinical records. External individuals (such as pharmaceutical company monitors) who require access to medical records will need to obtain written approval from the institution (usually via the Ethics Committee and the Medical Director’s department). A statement that such access is likely should be included within the PICF provided at the commencement of the study.

5.3 Risks Associated with Serious Breach of Confidentiality

A serious breach of confidentiality could have serious consequences for:

- the research participant (e.g., resulting in legal action);
- future recruitment (e.g., fears about data security could significantly lessen the likelihood of future participants providing confidential information); and
- future research (e.g., the likelihood of an ethics committee approving future projects requiring collection of personal data would be jeopardised).

To minimise this risk the following requirements have been introduced:

- Staff must sign privacy declarations.
- New staff must attend an Ethics/Good Research Practice course soon after their commencement.
- Requirements for privacy and data-security are emphasised to new staff by unit head and the RGO.
- Data storage for all studies is reviewed periodically by the RGO.

Vignette: A research study was undertaken involving volunteers suffering from severe depression. They were recruited by advertising in the general community. The volunteers underwent nerve velocity testing, undertaken by a research assistant. One of the volunteers was the daughter of a neighbour of the research assistant’s mother. The research assistant told her mother about the volunteer’s illness ... who in turn mentioned the fact to the mother of the volunteer, commenting “I did not know your daughter was depressed.” A complaint was made to the hospital administration and the researchers were reprimanded (the importance of maintaining the participants confidentiality was highlighted).
6 Collecting and Recording Research Data

6.1 Principle

Most clinical and epidemiological research projects require a systematic gathering of information on data collection forms. In practice, these forms may be either paper based or electronic, the latter allowing direct entry of data into a database. All data collected for the study should be recorded directly, promptly, accurately and legibly. Also, the individuals responsible for integrating the data, both computerised and hardcopy, should be identified.

Important points to remember for all data collection

- **Good form design.** Badly designed data collection forms will seriously impair the quality of any research project. All questions must be clear and simple. Whenever possible it is advisable to create new forms by adapting others that have proven successful in other studies.

- **Standard questionnaires and coding.** Whenever possible, standard questions should be used. Examples are the SF36® health surveys for quality of life estimation, and the standard smoking questions adopted by the National Heart Foundation. Other standard codes that should be used include:
  - For disease coding – ICD10
  - For occupation coding – ASCO (Australian Standard Classification of Occupations) is available from the Australian Bureau of Statistics.
  - For industry coding – ANZSIC (Australian & New Zealand Standard Industrial Classification) is available from the Australian Bureau of Statistics.


- **For country and language codes – standard Australian Bureau of Statistics codes are also available.**

- **Identifiers.** All pages of a data-collection form should be prominently labelled with a unique numerical identifier that allows linkage to the name, address etc, if needed.

- **Questionnaire elements.** Whenever new questions are developed for a questionnaire or data collection instrument, it is essential that:
  - the options are comprehensive, i.e they cover all possible responses; and
  - the options are mutually exclusive, i.e they only one option can be chosen for any specific situation (unless it is designed as a multi-value field).

- **Special instructions.** Special instructions should be provided in small print on the data collection form (e.g. How to interpret or code specific responses). These instructions require great thought and considerable pilot testing prior to the introduction of the completed form.

- **Pilot testing.** Pilot testing is required for all data collection instruments. The nature and results of the piloting should be recorded in the study coordinator’s log.

- **Easy coding of forms.** Whenever possible forms should be self-coding, i.e those completing them should enter the data directly into coding boxes in the form. Decimal points should be clearly marked and each box must be large enough to allow legible recording. Particular care should be paid to having separate codes for ‘missing’, ‘not known’ and ‘refused to answer’ data; 99, 88, and 77 are often used for these, provided that they are not within the range of valid responses.

- **Training of data collectors.** Study coordinators must carefully explain every question and every response to new staff involved in data collection. When the form is to be completed at interview, the study coordinator must personally supervise the first interviews until he/she is confident that the information is being collected correctly.

- **Written comments.** Interviewers must also be encouraged to record comments with the data whenever a new or unusual situation is encountered. These should be brought to the coordinators attention at the regular study meetings.

- **Erasure of data.** Data collectors must be instructed not to erase any entry on a data collection form. If a mistake has been made, a line should be placed through the original entry so that it remains visible. The corrected value should be written in an adjacent space and a comment provided as to why the correction was made. Study coordinators are required to check every data collection form for completeness, as soon as possible after it has been completed and in no case more than one week after the interview. They must initial every form to indicate that it is ready for data entry.

- **Documentation.** Detailed quality control procedures must be used to verify and promote the quality and integrity of the data.
6.2 What can go wrong?

- A research assistant or student responsible for interviewing patients in isolation (e.g., in their homes) may falsify data rather than meeting the rigors required by the protocol.
- A researcher may falsify subject characteristics so that they meet eligibility criteria for a study.
- Research personnel may falsify data to make the results more likely to fit his/her preconceived idea about what results should show.

These risks are more likely under the following circumstances:

- Research personnel are collecting data without likelihood of their data being audited.
- Senior staff are overcommitted and do not have sufficient time to discharge their supervisory responsibilities.

These events could lead to the serious consequences including:

- Results of the study become un-reportable and un-publishable. If already published, the article may require a formal withdrawal with risk of severe reputation damage to both the researchers and their institution.
- A study may have to be repeated with the cost borne by the department. This may delay the results becoming available and lead to breach of contract (and liability to damages) especially if data is critical for the development of a drug or device.
- If grant funding is involved, the facts must be reported to the funding body with possibility of severe criticism of the level of supervision. A requirement to review previous data collected by the researcher may lead to high cost and interference with other work.

Vignette: A new research assistant was engaged in a project involving telephone counselling after traumatic stress. The assistant strongly believed in the value of the study and the certainty (in her mind) of a positive result. When the actual result of a test she undertook was unfavourable she recorded different data to make it appear that the result was positive in each patient. This was picked up during a routine quality control check, when it was found that her results were different to the results of the other research assistants employed. Falsification of data in this way can have the most serious results for everyone involved and would be grounds for instant dismissal. The research assistant might well find it impossible to gain employment in a health or research occupation.
6.3 Approaches used in other industries

The pharmaceutical industry pays particular attention to this risk because such an event could delay the program of development of a new agent resulting in large financial losses. Regulators also require rigorous data validation because of previous occurrences of fraudulent data collection.

As a result of these concerns many pharmaceutical studies are accompanied by rigorous data validation procedures. Monitors employed by the pharmaceutical company periodically visit participating centres and carry out source data verification. This involves the matching of trial data with information from patients’ medical records, original pathology reports etc.

Pharmaceutical companies also require units undertaking early phase drug studies to have a series of SOPs (standard operating procedures) that specify the procedures to be undertaken in deriving and recording all data elements.

6.4 Barriers to occurrence

Most institutions now attempt to establish a strong culture that emphasises care and accuracy in data collection. This will involve:

- ensuring that new staff are adequately trained in research methods/ethics;
- requiring all research protocols to have adequate quality control procedures that would be likely to detect falsified data;
- chief investigators having regular study meetings with their research team in which quality control measures are reviewed; and
- Standard Operating Procedures (SOPs) being required for most key data collection procedures including quality control procedures.

6.5 Database Management

Guidelines regarding requirements for data management are regularly updated and can be located at http://monash.edu/library/researchdata/file_links/storage_options_web_vers15_10_2013.pdf

a. Software packages

The principal software packages used for databases in the School are Microsoft Excel and Microsoft Access. Access is well supported, easy to learn, has good security and data checking features and is highly recommended for most studies. Monash University runs several short courses on database management with Access. In view of the fundamental importance of Access to our work, all staff should have familiarity with this package. SAS and Visual Basic may also be used but there is limited support from our computer staff for these programs. Epi-Info is occasionally useful for small studies involving fewer than 100 subjects and fewer than 50 fields.

b. Database documentation

Each database should be accompanied by a folder containing the following information:

- copies of the questionnaires and/or other data collection instruments;
- database information including an explanation of the various files, languages and data formats used, the directory structure and the key programs used to manipulate the data;
- the data dictionary which lists all variables, variable names, coding rules etc (see example below);
- coding manuals, eg listings of all occupation codes, drug codes etc; and
- the database log used by the study coordinator and database manager to record the nature of, and reasons for, all modifications, data cleaning etc.
c. Example of a Data Dictionary:

<table>
<thead>
<tr>
<th>TABLE NAME</th>
<th>PARTICIPANT DETAILS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comments</td>
<td>List of visit dates for each participant and their capsules Record count + 409</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FIELD</th>
<th>DESCRIPTION</th>
<th>VALIDATION</th>
<th>TYPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Number</td>
<td>Number that uniquely identified participants</td>
<td>Primary Key</td>
<td>Number</td>
</tr>
<tr>
<td>Mstat</td>
<td>Marital status of participant</td>
<td>1 = single, 2 = married, 3 = divorced</td>
<td>Number</td>
</tr>
<tr>
<td>Chol</td>
<td>Laboratory tested cholesterol result</td>
<td>&gt;0 and &lt;20mmol/L</td>
<td>Number</td>
</tr>
</tbody>
</table>

d. Data Log

It is the responsibility of the study coordinator to ensure that this log is maintained. In particular, he/she should ensure that the log shows the identity of individuals entering (or correcting) data onto the main database, any changes made to questionnaires or data entry screens, any auditing or checking undertaken and any difficulties experienced. Coding changes introduced and variables subtracted or added must also be documented.

When significant changes are made, notification should be circulated to all investigators and added as an appendix to the Procedure Manual.

e. Storage of data

All paper-based data must be correctly stored and a procedure to ensure the security of data must be developed. The exact procedures to be followed may depend on the sensitivity of the data set and on specific caveats imposed by the ethics committee. A storage site must be designated and security procedures established (e.g., responsibility for locking cabinets, location of keys, provision of passwords to key individuals and nomination of individuals with differing levels of access).

f. Privacy of computer files

Similarly, data files kept on computer should be separated from files containing identifying information and the data linked only by a numeric key. Access to all computer files should be under password control and a copy of the password made available to the Principal Investigator.

g. Commercial data entry

Data entry from paper forms is often achieved by sending batches to an external company. Written records outlining privacy assurance procedures of any external company should be obtained and stored. To avoid wasting considerable funds, it is essential that all forms are carefully checked in advance for completeness and legibility and that the nature of the task required is explained in great detail. The data entered should not need to interpret responses; i.e., they should never have to do more than simply enter the numbers provided. Double entry, whereby two independent people enter the same forms and any differences are reconciled, is a usual requirement.

h. Direct data entry

Data may be entered directly onto computer-based data entry screens, entered via Teleform or entered using marked sense cards which are read directly into a data base. These are more difficult to check and require special procedures for checking, mainly through the use of range and consistency checks (see below).

i. Range and consistency checks

Following data entry, and before finalisation of a data set, it is necessary to run a series of data verification procedures. These include range checks (to identify values that are likely to be outside a valid range), and consistency checks (e.g., checking that non-smokers do not have entries under “numbers of cigarettes smoked per day”). After these are complete, a sample of the paper records should be checked against the final data file and errors rectified until it is virtually certain that no errors exist in the key variables, and the error rate is less than (perhaps) one per cent in less critical fields. During this process it is critical to have changes made on a single copy of the database to avoid confusion in identifying the ultimate version. It is also critical that version control procedures are employed to document the current version of the database.
j. Back up

Clinical and public health research commonly involves the use of large computer databases that are continuously being updated as new data is added and older data is checked and edited. A highly organised and systematic process is needed to ensure that changes are being made to the appropriate (ie the latest) copy of the databases and that the most current copy of the database is backed-up regularly and kept in a secure location.

At every stage during the creation of the database it is necessary to employ a systematic backup procedure. This should be carefully described in the Procedure Manual and strictly observed. Documentation of files can be established with names in the format: <Database/StudyName>_<Bkp_Noeg. VECAT_Bkp_3.>

A record of who performed the backup, and at what date and time, should be kept on paper or in a text file (or both) with the backups. The IT manager will describe the best way to back up each dataset. Regular backup that are held outside the department is highly recommended. This precaution guards against the unlikely events of fire or theft.

k. Risks associated with loss of data due to inadequate back-up procedures

Things that can go wrong:

- A database can be destroyed in a computer ‘crash’ or via accidental erasure.
- A research assistant may accidentally erase the current version of the database.

How does this happen:

- The risk is greatest when databases are established and maintained by researchers without the close support of an experienced programmer or database manager.

- The risk is greater in large datasets where databases are constantly being updated, especially if more than one person is involved in data entry or if different people are involved in data entry and data editing.
- A high risk exists in the data checking/editing stage where it is often easy to lose track of which is the most current version of the database.
- Data may also be lost due to theft, malicious destruction or fire, if all copies of a database are kept in the one location or on the same computer.

Consequences include the following:

- Essential data can be irreversibly lost.
- A highly expensive and time-consuming process can be required to reconstruct databases.
- If not recognised or remedied, publication of inaccurate data could occur.

Preventing high-risk events:

- Develop detailed SOPs related to data management that are incorporated into the study documentation.
- Handle all large datasets within the data centre.
- The research auditor should review data management procedures.

l. Final “locked” dataset

When final corrections have been made and the database is finalised, it should be labelled accordingly and stored securely with the data dictionary and randomisation key. No analysis of the data should be conducted until the final database is created.

m. Statistical analysis of data

All research data should be analysed by a statistician. No original results should be published without the senior researcher being able to certify that either (a) a statistician has undertaken the analysis or (b) that the analysis of the data has been checked by a statistician or (c) a statistician has reported to the senior investigator that the head of biostatistics has sufficient confidence in the researcher undertaking the analysis to warrant that the requirements for checking are not necessary. All PhD students should have key results checked by a statistician.

Analysis of large data sets by computer requires high levels of expertise gained only from experience under adequate supervision. Mistakes are easy to make and may be difficult to detect because intuitive ‘feel’ for data is less than with small paper-based datasets. Modern computer packages allow sophisticated analytical procedures to be undertaken by inexperienced people with little understanding of what they are doing. Serious errors are more likely if analysis of large datasets is unsupervised and conducted by relatively junior researchers.

Serious error made in analysis of a dataset may lead to retraction of a published article or report. Under the worst circumstances, this could alter outcomes of research that had already been acted upon at considerable cost and lead to substantial legal liability.

This could have serious implications for the scientific career of a researcher and his/her colleagues and/or threaten the financial viability of the department.

To prevent this from happening, it is the School’s policy that all “final” data analyses should be checked by a statistician.
6.6 Digital Data Storage at Monash

At Monash, there are various digital storage solutions available to staff and students based on a tiered service arrangement. These aim to match services and/or solutions to the user’s needs, and range from user-empowered access options to mediated support via the eSolutions Service Desk, Library or eResearch Centre.

To assist staff and students in selecting the most appropriate storage to meet their specific needs, the Digital Storage Options Matrix [http://monash.edu/library/researchdata/file_links/storage_options_web_vers15_10_2013.pdf] has been designed to provide information around available storage services, and to simplify selection by asking a series of filtering questions related to data, the systems being used and who might need access. Based on the answers, the appropriate storage solutions are shown.

For example, a HDR student is undertaking research requiring access to their data on a daily basis. Their data is not sensitive, amounts to approximately 15GBs and will only be shared with their research supervisor (a Monash academic). The HDR student requires access to the data from home, and is using Monash Windows SOE equipment whilst on campus. Based on this scenario, the Matrix indicates that “Transportable devices”, “Google Apps” and “S: Drive – Yellow zone” are all potential and appropriate storage solutions.

Notes:

1. The Matrix is not all encompassing. Therefore, where circumstances are not covered, contact eSolutions Service Desk (SDO) for advice and/or referral (http://ServiceDeskOnline.monash.edu/).

2. By nature, technical and storage environments at Monash are considerably fluid and dynamic; as such, any print version of the Storage Matrix represents a snapshot in time, and may not be current. However, the online version at [http://monash.edu/library/researchdata/file_links/storage_options_web_vers15_10_2013.pdf] will be maintained and updated as changes to the environment occur.
7 Study Management

7.1 The Principal Investigator

A single individual, the Principal Investigator, must be specified as having ultimate responsibility for the conduct of the study. He/she has responsibility for the design, conduct, analyses and reporting of the study and should:

- ensure that all investigators are aware of their responsibilities and that they conduct the study in accordance with the study protocol;
- ensure that appropriate systems are in place to guarantee appropriate quality control of every aspect of the study;
- ensure that all persons involved in implementing the protocol are adequately informed about the protocol, the nature of the intervention and their study-related duties;
- ensure that clear lines of communications are present between all study investigators;
- ensure that the Case Report Forms (CRFs) are adequately designed to capture the required data;
- manage the resources for the study in a way that ensures that the study finishes within the available budget; and
- ensure that the results are analysed, written up, reported and disseminated appropriately.

Other key individuals fulfilling different roles in a study may include:

a. Study Co-Investigator

Each co-investigator has the responsibility for the conduct of the study within his/her participating centre and/or area of expertise.

b. Study Coordinator/Manager/Executive officer

This role is often filled by a senior research fellow, who may be responsible for the day-to-day management of the study or some aspect of the study.

c. Study Documentation

The School has a responsibility for the conduct, management and monitoring of all research undertaken by SPHPM staff and students. It is therefore necessary for the School to be able to access basic study documentation if and when needed. To facilitate this the management and storage of research records should be undertaken in accordance with section 5 of this document. If a senior member of the study team is departing SPHPM please see section 7.3 i. of this document. At a minimum, the following should be stored on the Monash shared drive with more than one person having access to the folder:

- the grant application;
- the protocol;
- the ethics committee approval and correspondence;
- letters of agreements/contracts between the Institution and the Sponsor;
- annual reports to granting bodies and ethics committees; and
- details of where the study has been archived, if applicable.

If there is an impediment to storing the research records on the shared drive a copy of the above files should be provided to the School Research Manager.

7.2 Finances and human resources

- Financial management of each study will be the responsibility of the Principal Investigator. He/she must keep accurate and timely records of all expenditure and inform the head of School and School manager of any concerns or irregularities.

- Job descriptions based on a generic proforma will list staff responsibilities and will be provided for all staff associated with the project. These should be signed by the principal investigator and the staff member.

7.3 Study meetings

a. Regular meetings

The Principal Investigator and Study Manager must arrange for regular meetings of the study staff. In the early stages, such meetings should be at least fortnightly and in the later stages, at least every two months. Formal minutes should be kept and circulated to all involved parties.

b. Study management committee (for larger studies only)

This committee should meet at specified intervals to review the progress of the study.

Decisions concerning changes to protocols, case report forms or modus operandi must be ratified and recorded at meetings of this group.

Minutes of these meetings should be made and circulated as soon as possible after the meeting and stored in the Study Document File (see above).

Each member of the supervisory committee should be provided with the protocol, the PICF approved by the Ethics Committee, the case report forms including any questionnaires and procedure manual and the minutes of the study committee.

The principal investigator will ensure that copies of all protocol amendments and minutes of all meetings are circulated to each committee member for inclusion in his/her folder.
c. Interviewer safety

If interviews are undertaken in a participant’s home, interviewers should notify someone, such as colleagues or reception, of the time and location of all interviews. For personal safety, calls should be made to the office after interviews are completed and the interviewer has left the home. Interviewers undertaking interviews after hours should always take a mobile phone and organise a call-in procedure. A compressed air horn should also be carried. Wherever doubts occur about the advisability of interviews, a second individual should accompany the interviewer.

d. Diaries

All study personnel must keep a diary. These should detail their contact (or attempted contact) with study participants, the hours of such contact and a record of any matters arising.

e. Randomisation

Randomisation or blinding codes must be kept by an individual totally separate from the study and must not be available to the study team. It must be emphasised to all staff that under no circumstances must a randomisation or blinding code be broken until the final cleaned data set has been produced. Any emergency un-blinding must be developed and have the approval of the ethics committee.

f. Staff management

It is the responsibility of the study investigator(s) and the study coordinator, to provide appropriate training for staff and to monitor the work performance of all those involved in data collection, management and analyses. This supervision should include specific instructions concerning privacy, data handling, quality control, security during interviews etc, and adherence to these guidelines must be monitored. All staff must sign a document acknowledging their willingness to abide by privacy guidelines before commencing work. All staff involved in the conduct of the study should maintain a daily log book in which they record details of their day-to-day activities, including such matters as patient interviews, attempts at contacting participants, travel for study purposes etc.
g. If things go wrong

If there is evidence of poor study practice, the study team should know how to deal with the problem in a positive way. Solving the problem at an early stage is the best way to reduce damage to study participants and researchers. Informal confidential advice from senior colleagues may be helpful in deciding what action to take. There may be times when it is not possible for the study team to deal with a problem alone. In these cases, they should share the problem with colleagues who are in a position to act. However, if there is a pattern of poor practice that could place participants at risk, that would be the time to refer the problem to a more senior level.

h. Follow up of abnormal pathology result

Many studies involve the measurement of physiological variables (such as blood pressure) and the undertaking of various pathology tests (such as full blood examinations or liver function tests). When large numbers of individuals are tested there is a strong possibility of finding abnormalities of clinical significance that may not be known to the individual or his/her medical practitioner. In some instances recognition of the abnormality may allow effective treatment to be introduced.

Each study must have a procedure to review the results of physical examinations and pathology tests and have an efficient procedure to pass on important clinical information. If failure to pass on crucial clinical information meant that a potentially curable illness was not detected, it could lead to legal action for negligence. These procedures must be documented in the protocol and procedure manual and adherence monitored by the RGO.

i. Emergency Procedures

Some clinical research projects, particularly those conducted on patients with conditions such as asthma or hypertension, may require special attention to monitoring and the availability of emergency care. For example clinical trials of new drugs may require withdrawal of usual therapy, with clinical monitoring to ensure the detection of deterioration. The risk of medical complications resulting from such actions may be significant. If emergency care was not immediately available and, as a result a study participant died or developed serious complications, repercussions would follow for both the investigator and the department.

This risk is most likely to be encountered in drug trials and in physiological studies. The risk is greater when studies are supervised by inexperienced staff and when senior clinical investigators are unavailable or not able to be contacted.

Management of this risk is handled by the development of SOPs that cover as many emergency scenarios as possible. At a minimum, they should make sure each participant knows who to contact in case of emergency. The RGO will monitor the adequacy and functioning of these procedures.

j. Staff departing SPHPM

Staff who leave SPHPM must follow the instructions in the Induction guide (Resignation/Departure from the school) and ensure that an exit checklist is completed. In addition, if the staff member is responsible for one or more research projects which are remaining with SPHPM, they must ensure appropriate, ongoing management of the research project(s).

If the project is not leaving with the staff member:

- Ensure an appropriate replacement researcher is identified. This person must agree to take responsibility for the project.
- Ensure the necessary documentation is submitted to the HREC, funding body, sponsor etc of the project to inform them of this change.

If the project is being relocated with the staff member:

- Ensure the HREC, funding body, sponsor etc of the project are notified.
- The departing researcher must discuss with the head of school whether the researcher will be taking the original data or a copy. If the original data is being relocated a full and complete copy of all data and research records including the protocol, ethics application and approvals must be retained by SPHPM. Alternatively, the departing researcher may take copies of the data and research records leaving the originals with SPHPM.
8 Quality Assurance

8.1 Quality Control (QC)

Quality control procedures should be conducted by the Principal Investigator or his/her nominee and will usually involve:

- Verification of the availability of signed consent forms;
- Verification that the protocol is being followed;
- Verification of appropriately secure data handling;
- Source data verification (e.g., checking the study database against original pathology records);
- Review of the completeness of Case Report Forms;
- Duplicate interviewing of a percentage of participants as a reliability check;
- Verification of an appropriate audit trail accompanying data changes;
- Verification of appropriate computer back up;
- Retention in storage of all "returns" (in the bottles that were provided to participants), if a study involves administration of medication. These can later be used to verify the medication provided;
- Verification that serious adverse reactions have been reported; and
- Verification that emergency procedures are in place and are operational.

8.2 Audit

An audit is a systematic and independent examination of study-related activities and documents to determine whether these activities were conducted according to the protocol, the applicable standard operating procedures, good clinical practice, and the applicable ethical and regulatory requirements.

SPHPM has an RGO whose role, in part, is to conduct audits of the projects being undertaken within the School. In addition to randomly selecting projects for auditing, the RGO will audit other projects on request of the Head of School or the Research Governance Committee.

Audits may also be undertaken after a request by an individual researcher. These requests are often helpful for inexperienced researchers and/or those working in isolation.

The School has also developed a brief self-audit tool. This is available from the RGO or on line at selfaudit.med.monash.edu. This tool has also been adopted by some local HRECs and is required to be completed for each study as part of the annual ethics progress report.

The brief self-audits are sent to each research coordinator and are to be completed by that person. Encouragement is given to identify any areas where compliance with Good Research Practice requirements is less than ideal. The completed form must then be given to the principal investigator to make comments, sign, and return to the RGO and/or ethics office.

Individual researchers are also encouraged to make use of this tool as a way of checking that their study procedures are in line with the School’s guidelines.

During a formal audit, particular attention will be paid to the completion of PICFs. The audit will also ensure that the signed PICFs and other documentation are stored securely.

While the study co-ordinator is responsible for the day-to-day conduct of a research project, the ultimate responsibility lies with the principal investigator. Investigators are therefore reminded to oversee the conduct of their studies and to ensure all activities are undertaken appropriately. Study staff are reminded to keep their supervisors informed at all times.

Study closure

On completion of the study, procedures must be put in place to:

- Notify participants and their doctors of the results, if applicable;
- Provide reports to the Ethics Committee(s) and funding bodies;
- Arrange storage of study documentation;
- Label storage boxes clearly with the title of the study, the principal investigator, the completion date and the date on which records can be destroyed; and
- Provide information about where documentation is stored to the School’s Research Manager.

Vignette: A PhD student finished her project, analysed the data and wrote her thesis. She then started looking for employment and found a new position, but her employment was contingent on successfully gaining the PhD. In the process of moving institutions, she disposed of anything she did not need, including her research documentation. Unfortunately, the examiners did have questions and asked for further analyses. With so much of the research documentation destroyed, the student was faced with the need to repeat much of her project.
a. Communication with a participant’s doctors
When enrolling a patient into a clinical research project, it is essential to:
- Communicate with his/her treating physicians to ensure there is no reason why the participant may not be suitable.
- With the patient’s permission, keep his/her general practitioner and other treating physicians informed regarding his/her involvement in the clinical trial.

b. Payments to Research Volunteers
Provision of appropriate compensation to research participants for expenses incurred is essential. These payments should be disclosed to the Ethics Committee(s). Other payments are sometimes approved, provided that it is judged that such payments are not an inducement for a person to participate against their better judgement.

c. Using drugs and other therapeutic agents during a trial
When clinical trials of therapeutic agents are undertaken, preparation of medication for patients must ALWAYS be done by a Pharmacy Department. Bulk medication must always be stored in the Pharmacy Department, never in the School.

d. Insurance Cover
Insurance provided by Monash University covers damage to study participants resulting from professional negligence in the design of the research protocol. It will also provide cover for non-medical research staff involved in clinical activities outside public hospitals.

Insurance cover against actions for medical negligence involving a patient from a public hospital is the responsibility of the Victorian Managed Insurance Agency. It is critical that all medical practitioners participating in clinical research involving such patients have an appointment (or adjunct appointment) at a public hospital to qualify for this cover.

When the study is being conducted in a general practice setting, the University will not provide insurance for negligent acts on the part of participating general practitioners. Those doctors would be required to have cover for their research participation included within the policy provided by their medical defence organisation or purchase their own additional insurance.

Alternatively the investigators may seek specific insurance to cover a particular research activity.

Externally sponsored studies are usually provided with an indemnity by the sponsor assuming liability for injury to participants in a clinical research project that they have initiated. Such arrangements agree to compensate injured participants on a no fault basis in accordance with Medicines Australia’s guidelines for compensation. However such indemnity may become void if the injury is sustained as a result of a protocol violation. However, if the study is investigator initiated, the employing institution takes on the role of sponsor and therefore the responsibility for providing insurance cover.

In some instances, injury to a research participant may result from the harmful effect of a product under investigation resulting from a defect in its manufacture (see Appendix I). This is usually the responsibility of the sponsor or manufacturer of the investigational project and is covered by a product liability agreement.

It must be emphasised that insurance cover may not be valid unless:
- a human research ethics committee, constituted in accordance with NHMRC guidelines, has reviewed and approved the clinical trial in question;
- the clinical trial is conducted in accordance with the terms of any human research ethics committee approval, and
- the practitioner’s involvement in the clinical trial comes within the category of practice for which the practitioner is insured (see Appendix I).

e. The Study Report
Completed studies must be summarised in a final report that accurately and completely presents the study’s objectives, methods, results and the principal investigator’s interpretation of the findings.

Funding agencies and/or sponsors must be informed of the study results in a manner that complies with applicable regulatory requirements. There is an ethical obligation to disseminate findings of public importance. Scientific peers shall be informed of study results by publication in the scientific literature or presentation at scientific conferences, workshops or symposia. Potential conflicts of interest should be disclosed. Authorship of publications should be determined in accordance with the School’s authorship guidelines (available from the “Department” folder of the S: drive). Ideally, authorship should be discussed prior to the commencement of the study.
Appendix A: Ethical Review Of Research Projects

The term “ethics” refers to the principles of good, desirable and/or acceptable conduct that should govern interactions in all spheres of human activity. Ethical guidelines related to medical research have been developed primarily to establish standards for the protection of the welfare and the rights of participants in research projects. They also provide assistance to researchers by providing guidance in how to conduct research in an ethically responsible manner.

Ethical review of research is a relatively recent phenomenon. The Judgement of the Nuremberg Military Tribunal on War Crimes contained a series of principles describing acceptable medical research practice. They were developed further by the World Medical Association in its 1964 publication “The Declaration of Helsinki”. Subsequently many countries have adopted these principles into their own guidelines, modifying them when necessary to accommodate new problems such as genetic testing.

In Australia, the NHMRC has released its own publication entitled “National Statement on Ethical Conduct in Human Research”. This was released in 2007 and can be downloaded from the NHMRC web site (http://www.nhmrc.gov.au/guidelines/ethics/human_research/index.htm). Australian ethics committees use this document to guide their decisions about the ethical acceptability of clinical research projects. The document has been supplemented by several other documents that give more detailed instructions about such matters as privacy, and Good Research Practice.

The NHMRC guidelines require that every institution in receipt of NHMRC funding must have an appropriately constituted ethics committee. As a result virtually all hospitals and universities and many research institutes have established ethics committees.

In some cases, specific legislation has been introduced covering areas such as confidentiality of medical information. Naturally, ethics committees will never (knowingly) approve a project that is in breach of the law or would place its home institution at legal risk. In the event that legal and ethical requirements both apply, the legal requirements will normally apply.

Ethics Committee Submissions

Membership of Ethics Committees

To comply with NHMRC guidelines, ethics committees (ECs) must have a minimum of eight members including a chair, layman, laywoman, two health researchers, clinical carers, a minister of religion and a lawyer. Most committees require more members to cope with the workload but retain a balance between non-researchers who can reflect community standards and researchers who can understand the clinical details.

Application process

HRECs or their institutions may have simplified review processes for some low-risk projects. For example, a review of patient records, simple questionnaires or studies on discarded tissues can be notified to the ethics committee via a simplified “low-risk” application process. In most cases, however, a full application is needed. Many HRECs now only accept the National Ethics Application Form (NEAF), which is normally accompanied by a Victorian Specific Module and an institution/site-specific assessment form. The Common Application Form (designed by the Victorian Department of Health) is another standard form that is still accepted by some Victorian Hospitals, although it is being phased out by many.

There is an increasing move towards streamlined ethics review, both at a State and a Commonwealth level. Under these arrangements, projects are submitted to a single hospital for ethics review. When this step has been successfully completed, the application passes to individual research institutions for a governance review. The governance review looks principally at the willingness of each individual institution to be involved. It considers aspects such as impact on the institution’s resources, the interest of staff, their workloads, the adequacy of the financial and insurance arrangements, conflicts of interest (if any) and whether staff are sufficiently trained.

Fees

Virtually all ethics committees now charge commercial entities for processing their applications. Many charge a reduced fee (or no fee) for grant funded projects and amendments.

Modus operandi

An increasing challenge for ethics committees is the increasing workload and the possibility of letting something “slip through” because insufficient time has been spent on the review process. One common approach to addressing this problem has been to stratify projects into different levels of risk. Lowest risk projects may be sent to a small number (perhaps one or two) of members who provide comments that are reviewed (if necessary) at the main monthly committee meeting. The low risk group included most questionnaire studies, student projects, quality assurance projects and studies requiring only clinical record reviews.

The remaining studies are typically reviewed by a research committee that is often a subcommittee of the main ethics committee. This committee typically consist of several experienced researchers. Its role is to flag problems and attempt to resolve them prior to the main ethics committee meeting. Occasional projects that raise special ethical issues may be flagged for interview. Typically CTN and “first in human” trials, studies with devices or invasive procedures, and studies involving the collection of sensitive patient data may require an interview (along with those flagged for attention by subcommittee members).

Documentation

The first step in the review process is typically a review of the documentation provided to ensure it is complete. The majority of problems occur with:

1. failure to provide a non-technical description of the project; this frustrates lay members;
2. failure to provide a budget with sufficient explicit detail;
3. failure to provide resource utilisation forms signed by the clinical services to be used;
4. failure to include essential CTN documentation, particularly that related to CTX approval in the US, UK or Sweden;
5. failure to include questionnaires; and
6. failure to provide details of an “after hours emergency contact”.

A Guide to Good Research Practice
Appendix B: Protocol Outline

Title Page
This page should include the following:
- title of the research project;
- names of the investigators;
- version number of the protocol; and
- date of completion of the protocol.
The title page should also include the signature of the Principal Investigator.

Background
This should include an explanation of why the study is being conducted
and the specific question being addressed. This section will comprise:
- a Literature Review describing previous relevant literature summarised
  in a fashion which explains the rationale for the research;
- the Study Hypothesis or Study Objectives; and
- the Study Aims and Purpose.

Study Design
This should be a description of the design of the proposed study including
(when appropriate) methods of treatment allocation and/or choices of controls.

Justification of Sample Size
This should be a description of sample size calculations demonstrating that
the study will have adequate statistical power or statistical precision.

Inclusion and Exclusion criteria
These should describe inclusion and exclusion criteria for participants.

Subject Recruitment
This should include the source of study subjects, how participants will be
recruited (advertisements in newspapers, notices around the institution etc),
the anticipated approach to subjects, procedures for establishing eligibility and
confirming entry criteria, procedures for handling consent, and a description
of any special measurements to be made (eg invasive and non-invasive
measurements, questionnaires).

Interventions
This should describe the exact nature of the study intervention(s) and
details relating to their preparation, stability, safety and, if necessary, a
rationale for the choice of dose(s).

Randomisation
This is the process of assigning study participants to treatment or control
groups using an element of chance to determine the assignments in order to
reduce bias. Details should include how randomisation will be conducted, what
allocation concealment will be used, who will be blinded, where the randomisation
code will be stored, and the circumstances when unblinding is permitted.

Study Endpoints (Outcome measures)
This should be an outline of the primary and secondary variables to be measured
to meet the study objectives.

Bias and Confounding control
Predictable sources of bias, variability and confounders should be addressed,
as well as measures taken to minimise them. Details of how blinding will be
conducted and maintained and who is blinded should be included. All study
staff must be informed that unblinding must never be permitted except
according to the Protocol. The decision to unblind a participant or the whole study
should only be made by the Principal Investigator, unless a contingency plan
has been established for emergencies.

Data Management
Include a description of how data will be handled, how privacy concerns will
be addressed and how storage and back-up of data will be undertaken.

Quality Assurance and Control procedures
Outline the quality assurance and control procedures to be employed to ensure
integrity and validity of the data.

Data Analysis
A specification of any “a priori” subgroup analyses and the statistical methods to be
used for data analysis should be included. For some studies, interim analysis of
data for safety monitoring and/or early study cessation will be required. Details
of such analyses should be provided.

Study Time Lines
This should indicate the anticipated time line for each of the major stages
of the study. Particular attention should be paid to participant recruitment.

Signature of the Principal Investigator
In all cases, the principal investigator should sign and date
the final study protocol and any
amendments to the protocol.
Appendix C: Procedure Manual Outline

Final Protocol
This is the Study Protocol as approved by the Ethics Committee(s) (see above).

Data Collection Documents
These include a copy of the approved Plain Language Statement, Consent and all data collection forms.

Study staff
This describes all members of the study team including their roles, responsibilities and reporting arrangements. Members of various study committees, together with their contact details should also be provided. Also, an appropriate schedule of training for staff involved in the project should be included. The need to maintain strict confidentiality in relation to any personal information concerning participants should be stressed.

Funding details
This details the sources of funding for the study as well as the expectation of funding bodies (e.g. timing of allocation of funds, deadlines for progress reports).

Study flow charts
A separate chart should be developed describing, in detail, the critical pathway for handling study participants and the sequence to be used in handling questionnaires, coding, data entry, data verification, cleaning and storage of hard copies and back-up of data files.

Clinical measurements of the study endpoints
These describe detailed procedures to be followed for clinical measurement of the study endpoints, e.g. blood pressure. Details of quality control of such measurements, maintenance of equipment, and methods of recording of results, calibration of equipment and the labeling and storage of biological specimens.

Compliance measures
These describe details, when appropriate, of compliance tests (including plasma measurements) and who will perform them.

Adverse events and contingencies
These describe the nature of any adverse events that might occur together with the approach that should be taken to manage them. Contingency plans for these events should be documented. Such events must be reported to all necessary agencies. These will vary from study to study but might include the ethics committee that originally authorised the study, other study personnel, the study sponsor, and the Therapeutic Goods Administration. In general, notification of serious adverse events should occur within 24 hours, should be in writing and signed by the Principal Investigator. Researchers should refer to the appropriate ethics committee for clarification of local requirements.

Clinical abnormalities
This describes follow-up of abnormal laboratory investigations, or other issues that require further action (including liaison with the participant’s medical practitioner).

Specific procedures
These should enable the study to cope with sick leave, holidays, occasional duties (e.g. equipment maintenance, cleaning, office supplies and tidying). Emergency contact details should be documented.

Data Management
The procedure manual will also provide detailed information about data management as outlined in section 6.5.
Appendix D: Ethical use of digital data in human research

Through the Carlton Connect Initiatives Fund (CCIF), the Centre for Epidemiology and Biostatistics at the Melbourne School of Population and Global Health developed the following document. It is included here with permission from by Associate Professor Jodie McVernon. An electronic version of the document can be found at http://www.carltonconnect.com.au/area/pervasive-it/.
Appendix E: Risk Management Plan

Introduction
Experience elsewhere has demonstrated that a serious misadventure in our research activities could have repercussions. This could result in disrepute of our entire research program and possibly compromise research activities elsewhere in our University.

Although such episodes have generally resulted from aberrant behaviour by individuals, responsibility for establishing a culture that reduces the likelihood of such an event rests with management of a research department or institution.

Within the School of Public Health and Preventive Medicine (SPHPM) we have certain vulnerabilities to research misadventure that puts us at risk. These include:

- Research projects with responsibility dispersed amongst several senior investigators.
- No single individual or committee with oversight responsibility for standards across our research program.
- Heavy reliance on relatively junior staff and PhD students to collect and analyse research results.
- High level of investigator initiated research that is not monitored by external bodies such as pharmaceutical companies.
- Data collected off-site by research assistants working without direct supervision.

Because of these concerns the School has established a Risk Management Plan with the following components:

- Development of a “Research Governance Induction Session” which ensures that all new staff and students are aware of the expectations and support available within the school with regards to research activities.
- Development of “Good Research Practice Guidelines” that are distributed to all staff and students which sets a standard for research activities conducted within the school.
- Implementation of an online training package for all new staff and students. The training gives an overview of ethics and good research practice and should take about 2 hours to complete. Staff are required to pass the quiz associated with the training package.
- Development of a “Good Research Practice Course” which usually runs twice a year. This course must be attended by all PhD students. Although not compulsory, it is recommended for all SPHPM staff.
- Establishment of a “Research Governance Committee” and appointment of a part-time “Research Governance Officer” to assist in achieving/maintaining a high standard of research within the school by ensuring research projects comply with the Good Research Guidelines.
- Establishment of this “Research Risk Management Plan” that attempts to foresee our major areas of risk and ensure that barriers are in place to reduce the likelihood of occurrence.

Purpose of the Research Risk Management Plan
The purpose of the Research Risk Management Plan is to attempt to identify the most significant risks that we face in the conduct of research within the Monash School of Public Health and Preventive Medicine. The program also outlines approaches taken by department management and staff to reduce the likelihood of these risks eventuating. The document will be constantly updated as new risks are identified and new strategies are devised to counter them.
1. Fraud in Collection of Data

Description of risk

Data collected and used in the analysis of a research project must be accurate. Data may be inaccurate as a result of carelessness. It may also be inaccurate as a result of intentional falsification, manipulation or alteration. This is research fraud. Examples include:

- A research assistant responsible for interviewing patients in their homes invents data rather than taking the time to make the visits.
- A research student ‘adjusts’ a subject’s characteristics to make it appear that they meet the eligibility criteria for entry to a study.
- A senior researcher fraudulently adjusts data to fit his/her preconceived idea as to what the results should show.

Likelihood of occurrence

Data fraud is more likely to occur in the following “risk settings”:

- Research personnel are collecting data in remote locations with inadequate supervision.
- Research personnel responsible for data collection are new to research and have not been adequately trained or briefed.
- Situations where there is a low likelihood that data collection will be checked or audited.
- Situations where senior staff are overcommitted and do not have adequate time to discharge their supervisory responsibilities.
- The sponsor of a trial offers financial incentives to the researchers for recruiting participants or for recruiting quickly
- Settings where there is high pressure to recruit within specific time frames e.g. PhD, postdoc.

Likely consequences

- Results of the study may not be reportable and published. If the study has already been published the article will need to be withdrawn leading to the individuals involved losing their opportunity for a successful research career.
- If the study has influenced clinical practice patients may be treated with ineffective interventions or not receive effective therapy. This may potentially affect the health of very large numbers of individuals.
- If a change in clinical practice has resulted in the potential for harm to patients this may result in a police investigation which in turn could result in the person responsible for the fraud being brought up on criminal charges.
- Falsified data may lead to a breach of contract with an external research sponsor and liability for damages. The study may have to be repeated at a heavy cost to the department.
- The relevant ethics committees must be notified and additional penalties and restrictions may result.

Barriers to the occurrence of this risk within SPHPM

SHPHPM must establish a strong research culture that emphasises accuracy and integrity in data collection and all subsequent research procedures.

2. Carelessness or errors in the collection or analysis of data

Description of risk

The conclusion drawn from a published research project can alter clinical practice or public health policy. It is therefore important that every project is conducted and analyzed with utmost care.

- A serious error in the analysis of research data may lead to retraction of a published article which is likely to have considerable cost implications to the university as well as substantial legal liability, not to mention putting patients at risk of not receiving the best possible treatment.

Likelihood of occurrence

- Analysis of large data-sets requires considerable expertise with modern data-management packages. This expertise is obtained only form extensive experience gained under expert supervision. Modern statistical packages allow advanced analysis to be undertaken by junior researchers but at a high risk of inappropriate application.
- Serious errors are more likely when the analysis of data is delegated to unsupervised junior researchers or research students. Mistakes are easy to make, and are more often difficult to detect because the intuitive feeling for data is less than with small paper-based data-sets.
Likely consequences

- If the study has been published it may require formal withdrawal at substantial cost to the reputation of the research team. Other consequences may be similar to those listed above under ‘Fraud’.

Barriers to occurrence with SPHPM

- All research data should be analysed under the direction of (or in collaboration with) a biostatistician. All research projects should involve a member of the biostatistics unit and an appropriate allocation of research funds for statistical analysis should be included in all research grants.

- No significant original result should be published without the senior researcher being able to certify that a statistician has undertaken the analysis (or checked the analysis). The only exception is when a small project involving a statistician has reported (to the principal investigator) sufficient confidence in the statistician to make direct supervision unnecessary.

- Databases should be established with inbuilt warnings that are triggered by entering data outside the ‘normal’ or expected ranges.

- All basic frequencies should be checked prior to any analysis.

3. Loss of data due to inadequate filing or backup or as a result of malicious destruction

Description of risk

- Clinical and public health research commonly involves the use of large computer databases which are regularly being updated as new data is added and older data is checked and edited.

- A highly organised and systematic process is needed to ensure that changes are being made to the appropriate (ie the latest) copy of the databases.

- Portable data storage devices such as laptops, ipads and memory sticks increase the risk of security breaches due to theft or loss. If the data is not adequately backed up this can result in the loss of some or all of the database. In addition, if the portable device does not have adequate security e.g. password protection, participant and/or sponsor confidentiality may be breached resulting in adverse publicity.

- To avoid data loss the most current copy of the database stored and backed up according to University policy. For guidance see http://monash.edu/library/researchdata/file_links/storage_options_web_vers15_10_2013.pdf

- Irreversible data loss may destroy an entire research project and (in the case of sponsored studies) may lead to legal liability.

Likelihood of occurrence

Loss of particularly sensitive data is a high probability occurrence unless every member of the department with access to such data observes a series of specific precautions.

The risk of losing track of which is the latest version of the database is greatest:

- when databases are established and maintained by inexperienced researchers, without close support of an experienced database manager.

- when a low-cost database has been established by researchers themselves rather than experienced programmers. The risk is also higher than when data is constantly being added, especially if more than one person is involved with the data entry.

- a high risk exists in the data entry/checking/editing of stage where it is easy to lose track of the most current version of the database.

- when a researcher fails to develop a regular schedule of back-ups of every one of their active databases.

The risk of loss or theft of laptops, ipads or USB sticks is greatest when researchers fail to take basic precautions (e.g. leaving it in a car). However, occasional loss or theft is a common and almost predictable occurrence and must be addressed by security barriers on the device.

Data is less at risk when stored on a university server which is regularly backed up e.g. the S: drive. However, staff need to be aware that the backups of the S: drive are only stored for 30 days therefore if an issue with data or a document (e.g. damage, error, unauthorised manipulation etc.) is not identified within 30 days of its occurrence there will not be a back up available. The SPHPM is working with eSolutions to find a more robust solution for the long-term storage of data and research records.

By storing files on the S: drive there is a greater likelihood of continued access to the data in the future. Data stored on local and/or personal media e.g. floppy disks, may not be accessible in the future as technology changes. Portable hard drives can be damaged and the files rendered inaccessible.

The malicious alteration or destruction of a database is typically the result of actions of a hacker or a disaffected employee.

Likely consequences

- The likely consequences may range from irreversible loss of essential data to a highly expensive and time consuming process in reconstructing a database.

Barriers to occurrence within SPHPM

Because of the high likelihood of this problem arising it is necessary to have highly detailed procedures in place to lessen the risk. These include:

- Development of detailed SOPs which are incorporated into the Good Research Practice Guidelines and regularly updated. Compliance with guidelines must be regularly audited by the Research Governance Officer.

- Databases managed outside CIDMU must have patient identifiers, stored separately from the remainder of the databases. The identification key must
be encrypted and password protected. The two database components must be linked only by a common ID code.

- The School has an ABSOLUTE BAN on the holding of any patient identifying data (encrypted, unencrypted or code-protected) onto laptops, ipads and USB sticks. The only exception is when data is being transferred directly to the Data Centre (under which circumstances it must be encrypted and code-protected).

- During the establishment phase of new projects staff from the relevant units must meet with a representative of CIDMU for advice and verification of appropriate storage and back-up procedures and review the construction of the database.

- Data access privileges must be removed immediately by the unit from any staff member who is no longer responsible for a specific project.

- A yearly review will be undertaken (led by CIDMU) on data-management policies and testing of the data-recovery plan.

- It is not recommended that paper files containing data be taken off site as this can result in the loss of the data and can also lead to a breach of participant and/or sponsor confidentiality if the records are lost, stolen or damaged. If it is necessary to remove documents it is recommended that de-identified copies be used and the originals remain on site.

- Research records must be maintained in a way that not only ensures they are secure but also enables the tracking and retrieval of data and files. It is therefore important that computer files are named and stored in a consistent way as are paper documents and records. To assist with this the SPHPM has developed “Maintaining Research Records”. See appendix H for a copy of this document.

4. **Serious Breach of Protocol, Contract or Ethics Committee Conditions**

**Description of risk**

- All research involving humans must be endorsed by an appropriate ethics committee. Ethics approvals are specific to the particular protocol (including Participant Information and Consent Forms [PICFs]). Entry of patients to a study whose personal characteristics do not meet those of the approved entry criteria is a breach of the condition of ethics approval. It may also lead to a breach of contract with a study sponsor. If an individual who was ineligible for entry to a study experiences an adverse event they may have grounds for legal action that would not be covered by the institution’s insurers.

- Once approved, the study protocol must be followed closely throughout the study. Any changes must be presented to the ethics committee as an amendment and approval obtained before implementation. Failure to obtain approval for a change to the protocol may constitute a breach of ICH GCP and the National Statement.

- Ethics committees pay particular attention to circumstances of consent. They require all study participants to be provided with an approved Participant Information and Consent Form to sign to signify their preparedness to participate in the project. These forms must be carefully filed and must be made available for scrutiny by auditors. Should an individual claim that they had not been adequately informed of the risks and benefits of participation this documentation (in addition to a description of the consent process documented in the medical record) provides an important line of defence for investigators. Entry of patients to a study without consent is an egregious error which could lead to severe sanctions and highly adverse publicity.

- Serious adverse events affecting any study participant, and considered reasonably likely to have resulted from study participation, must be notified urgently to study sponsors and the appropriate ethics committee. Failure to do this may lead to sanctions by either of these agencies.

- Failure to adhere to contractual restrictions on the handling of study funding and/or restrictions regarding publication can result in the misuse of funds or restricted data e.g. commercial in confidence, entering the public domain.

Communication with study participants (or potential participants) by phone can pose a risk to confidentiality in a couple of ways:

a. Conversations by phone can be overhead by others nearby. It is therefore recommended that if you plan to call research participants that a huddle room is used.

b. If the research participant (or potential participant) is not the one to answer the phone when a researcher calls, leaving a message can reveal information that results in a breach of the participant’s confidentiality. Strategies for minimising this risk should be discussed on a study by study basis and senior researchers need to ensure that staff making and receiving phone calls are appropriately briefed with regard to appropriate protocol.

**Likelihood of occurrence**

- Due to the nature of the research that is undertaken within this school it is highly possible that this will occur unless specific precautions are put in place to prevent it.

- The areas of greatest risk are studies involving significant risk to participants such as drug trials and invasive studies.

- The risk is higher in investigator initiated research where there is no independent monitoring by a study sponsor.

- Under privacy law you will be required to notify each individual whose privacy may have been breached. This may be a major task.
Failure to meet ethics committee requirements is usually a result of a lack of knowledge of an ethics committee’s role in the regulation and monitoring of an institution’s research program.

Thus it is more likely amongst those who have not undertaken formal research governance training.

Likely consequences

- Failure to follow the appropriate process i.e. to adhere to the approved protocol, to obtain consent for each participant before they begin the study, to only include participants who qualify for the study and to ensure that all adverse events are appropriately reported; may results in the research being stopped by the ethics committee. The investigators may lose the protection of insurers. They may also lose the confidence of their ethics committee and the senior management of their institution. They may not be allowed to undertake further research.

- Adverse events that are not reported to an ethics committee may also result in a study being suspended.

Barriers to occurrence within SPHPM

SPHPM requires a strong culture that emphasises care and accuracy in the conduct of each clinical trial. This will involve:

- New staff and research students being required to complete the Research Governance Induction which is part of the SPHPM Onboarding process. Those without strong research background should be required to attend courses in research methodology and complete the Research Training (http://www.med.monash.edu.au/intranet/spphpm/research-training/index.html).

- All new staff must be briefed by a senior researcher about the need to adhere to the approved study protocol, report adverse events and follow carefully the approved processes for consenting participants.

- Compliance with these requirements will be monitored as part of the routine study audits.

When embarking on a new project all staff and students are reminded to be mindful of contractual restriction in regarding to funding and publication.

5. Serious Breach of Confidentiality

Description of risk

- Clinical and public health research commonly collects information of considerable sensitivity which is divulged only because of guarantees of confidentiality provided by the researchers. In other instances ethics committees may approve the use of health-related data without the consent of individuals when the public benefit is considered to substantially outweigh concerns regarding privacy.

- Ethics committees approve the collection of personal health-related data for research purposes if they are assured that the data (both paper records and electronic files) will be maintained under strict conditions that protect the confidentiality of the participants.

- Breaches of privacy legislation may result in criminal penalties.

- Modern, portable data storage devices such as laptop computers and memory sticks which are used to transport data also increase the risk that identified, confidential data may be revealed through loss or theft of the laptop or memory stick.

- A specific instance of risk is where:
  - a research staff member handles data from an individual known to the researcher and is tempted to mention this outside the department;
  - a staff member, leaves a memory stick in a public computer or has their laptop stolen

- Communication with study participants (or potential participants) by phone can pose a risk to confidentiality in a couple of ways:
  a. Conversations by phone can be overhead by others nearby. It is therefore recommended that if you plan to call research participants that a huddle room is used.
  b. If the research participant (or potential participant) is not the one to answer the phone when a researcher calls, leaving a message can reveal information that results in a breach of the participant’s confidentiality. Strategies for minimising this risk should be discussed on a study by study basis and senior researchers need to ensure that staff making and receiving phone calls are appropriately briefed with regard to appropriate protocol.

Likelihood of occurrence

- Due to the volume and nature of data handled by the school this is considered to be a high risk.

- Breaches of privacy are most likely in cases where there has been little attempt to create a culture of confidentiality and to reinforce it.

- Privacy breaches are also more likely where new researchers who have not been adequately educated about the rationale for confidential data handling are given responsibilities in this area.

- Under privacy law you will be required to notify each individual whose privacy may have been breached. This may be a major task.

- Transferring data or discussing a research participant via email can pose a risk to confidentiality. It is recommended that identified information should not be included in any email. However, protecting the participant identity can put the patient’s safety at risk e.g. communicating with a colleague that they need to review a particular participant, visit a specific patient on the ward, administer a test to a participant etc. When using email the need for identified information needs to be considered and, if deemed necessary, kept to a minimum. Researchers are encouraged to consider alternative ways of communicating.
The following link will provide guidance on appropriate data storage solutions to minimise the likelihood of confidentiality being breached: http://www.monash.edu/_data/assets/pdf_file/0008/160046/storage_options_web_vers15_10_2013.pdf.

- A secure portal and operating in the ‘red zone’ reduces the need for data transfer. Contact the data centre if you feel your project requires these measures.

**Likely consequences**

- A serious breach of confidentiality could result in serious adverse publicity that could significantly lessen the likelihood of future participants providing confidential information.

- It would probably reduce the likelihood of gaining ethics approval for future projects requiring collection of personal data.

- It might lead to legal action from the individuals whose privacy has been breached.

**Barriers to occurrence**

The procedures required for privacy protection include:

- restriction of access to personal data to a small number of individuals with a clear cut need for access.

- training of researchers at all levels on issues related to data confidentiality.

- provision of secure storage of confidential data which includes restricted access to areas where such data is stored, separation of identifying data from the other data elements, secure password access to data in computers and development of a specific protocol for destruction of identifying data when no further need exists to retain this information.

- To ensure that all staff and students understand the need for confidentiality they are:
  
  a. required to sign declarations of confidentiality.
  
  b. required to undergo good research practice training if they are involved in research (the schools good research practice course is compulsory for all students and staff).
  
  c. required to complete the Research Governance Induction as part of the SPHPM Onboarding.

- Requirement for privacy to be emphasised to new staff by unit head and research governance officer.

- Staff and students are discouraged from transporting identified, confidential information on devices such as laptops, ipads and memory sticks. If researchers are required to transport data on such devices they must ensure this is done in accordance with the university guidelines (http://monash.edu/library/researchdata/file_links/storage_options_web_vers15_10_2013.pdf) and are advised to meet with IT and Data Management staff to ensure the data is encrypted.

- Senior management must create a culture of confidentiality and respect for all patient-related data.

- Requirement for the development of standard scripts for leaving of messages on answering machines or with people when trying to contact research participants (or possible participants). Consideration needs to be given to not only protecting the participants confidentiality but also to ensuring that distress is not caused to the person on the phone (or listening to the message) by what is said or not said.

- Research staff who regularly have identified patient information, particularly sensitive information, on their computer screen are encourage to install a privacy screen on their monitor. This screen fits to the front of the monitor and ensures that the screen is only visible from directly in front but not from the sides.

6. **Failure to Identify and Follow-up an Abnormal Pathology Result**

**Description of risk**

- Many SPHPM studies involve the measurement of variables (such as blood pressure) and the undertaking of various pathology tests (such as full blood examinations or liver function tests). When large numbers of individuals are tested there is a strong possibility of finding abnormalities of clinical significance that may not be known to the individual or his/her medical practitioner. In some instances recognition of the abnormality may allow effective treatment to be introduced.

- If an abnormal result is not noted and flagged to the patient and/or the medical practitioner the patient may not receive the necessary treatment.

- This also applies to research projects that involve the collection of information around mental health issues such as depression and suicide. The implications and consequences of not following up on information pointing to a mental health issue are the same as for not following up on an abnormal pathology result. Consideration however, needs to be given to compliance with the Health Privacy act, duty of care and the approved study protocol. A distressed patient protocol is included in Appendix F.

- Registries are becoming more common place and are repositories not only of individual data but also collectively, provide extensive information on particular populations. As with any research, with the collection of data comes the responsibility of managing it appropriately and respectfully. This includes acting on group or individual data that may point to an issue. Therefore custodians of registries have the same obligations as researchers in a clinical trial, to monitor their participants for abnormal outcomes and to have a
process in place to act and/or manage this information as appropriate.

- All serious adverse event that occur in research participants must be promptly and appropriately reported. For details on reporting requirement please refer to ICH GCP1. An SAE template can be found in Appendix G.

Likelihood of occurrence

- There is a high likelihood of occurrence of ‘missed results’ in clinical research unless the issue is anticipated and a highly organised approach is developed to assess and handle abnormal results.
- The principal risk is where screening tests are being done on large numbers of individuals either as part of eligibility screening for a clinical trial or as part of an epidemiological study.

Likely consequences

- Failure to include an efficient procedure to pass on important clinical information may mean that a potentially curable illness is not detected. This could lead to legal action for negligence.

Barriers to occurrence within SPHPM

- All studies and registries involving physiological measurement, psychological measurements or laboratory testing must include specific procedures to review all abnormal results. These procedures must be documented in the protocol and/or procedure manual and adherence monitored during the study.
- Assessment of processes for reviewing abnormal results should be audited regularly by the research governance officer.
- Procedures for reviewing and managing abnormal results should include instruction to ensure anyone (individual or department) involved in the analysis, collection or interpretation of physiological, psychological or laboratory data are aware of who to contact in the case of an abnormal result. It is standard practice for pathology departments to contact the requesting doctor with any abnormal results and this process should be implemented for all research data.
- Registries should have a policy/procedure in place that outlines the steps to be taken with regards to practitioner outliers which should include the steps to be taken before it is reported and the reporting process.
- The existence of a procedure to manage abnormal results will be checked as part of the SPHPM audit process.

7. Failure of Emergency Procedures Leading to Death or Injury

Description of risk

- Some clinical research projects, particularly those conducted on patients with conditions such as asthma or hypertension, may require special attention to monitoring and the availability of emergency care. For example, clinical trials of new drugs may require withdrawal of usual therapy with clinical monitoring to ensure the detection of deterioration. The risk of medical complications resulting from such actions may be sufficiently high to mandate the availability of urgent medical assessment and/or emergency care.
- If such emergency care is not immediately available and, as a result, a study participant develops serious complications both the investigator and the school may face legal action.
- This also applies to research projects that involve the collection of information around mental health issues such as depression and suicide. The implications and consequences of not following up on information pointing to a mental health issue are the same as for not following up on an abnormal pathology result. Consideration however, needs to be given to compliance with the Health Privacy act, duty of care and the approved study protocol. A distressed patient protocol is included in appendix A.
- Registries are becoming more common place and are repositories not only of individual data but also collectively, provide extensive information on particular populations. As with any research, with the collection of data comes the responsibility of managing it appropriately and respectfully. This includes acting on group or individual data that may point to an issue. Therefore custodians of registries have...
the same obligations as researchers in a clinical trial, to monitor their participants for abnormal outcomes and to have a process in place to act and/or manage this information as appropriate.

- All serious adverse event that occur in research participants must be promptly and appropriately reported. For details on reporting requirement please refer to ICH GCP. An SAE template can be found in Appendix B.

- Emergency procedures may be difficult to implement if there isn’t appropriate staff available e.g. someone to care for the patient and a second person to call 000 and, if necessary, let paramedics into the building. For this reason staff are advised that no clinical work is to be conducted after hours unless there is more than 1 staff member present and security has been notified.

Likelihood of occurrence

- This risk is most likely to be encountered in drug trials and in physiological studies, particularly those involving the administering of medication or those involving elderly subjects. The risk is greater when studies are supervised by inexperienced staff and when senior clinical investigators are unavailable or uncontactable.

- It is important that research staff make participants aware of the way to get emergency assistance if required. In the case of a medical emergency you are required to call an ambulance on 000.

Likely consequences

- Injury to participant, legal action against researcher, adverse publicity.

Barriers to occurrence

- Appropriately trained staff available to review research participants.

- Emergency responses must be reviewed and tested. This includes the use of the defibrillation unit.

8. Loss of Biorepository Specimens

Description of Risk:

- A number of research projects within the SPHPM collect clinical data coupled with biological specimens (blood, urine, saliva, tissue) for long term storage and analysis throughout or at the completion of the project.

- Adequate and appropriate storage of the biospecimens is of the utmost importance to maintain the sample integrity and maximise the quality of the biospecimens for ongoing and future analysis.

- Loss of biospecimens due to a breakdown of storage facility equipment or staff mismanagement is a major risk to these projects. Having multiple storage sites may also pose a risk as it involves management of different physical locations and alarm systems.

Likelihood of occurrence:

- Storage systems are sourced from reputable suppliers with a good track record. The use of reliable storage systems along with adequate staff training and emergency back up plans makes the loss of biospecimens a medium to low risk.

Likely Consequences:

- Loss of partial or entire collections of biospecimens would be devastating for the research project for which it was collected. Biospecimens are collected at certain time points in a study or disease state and in most projects cannot be replaced.

- The loss of biospecimens from a small collection may result in a reduction in sample size that is too small for statistical analysis.

Barriers to occurrence within SPHPM:

- All research staff involved in the handling of biospecimens are trained in storage of samples at different conditions (room temperature, -80 freezers, Vapour Phase Nitrogen).

- Alarm systems are set up on all freezers so that in the event of an alarm due to temperature fluctuation, four key staff are contacted by SMS to ensure the alarm is attended to. Alarm systems are tested every 6 months to ensure they are working.

- Staff responsible for responding to the freezer alarms have access to SOPs at home and at the biospecimen storage location detailing the plan of action. All other staff handling biospecimens have access to the SOPs and have received training on how to respond.

- Duplicates of biospecimens are stored as backup in separate physical locations to avoid the loss of an entire set of biospecimens from one individual participant. For studies, units or groups where a second freezer is not practical, consider exchanging backup samples with another project. Even if the freezers are in the same location this provides a level of protection against loss of all samples due to freezer failure.

- All storage equipment is serviced in accordance with the manufacturer’s recommendations and back-up batteries are installed where appropriate.

- Equipment should be visually inspected regularly for signs of wear, deterioration or problems and the outcome of this inspection should be logged.
9. Attack on a Research Nurse or Research Assistant

Description of Risk:

- Several epidemiological studies involve visits to participants’ homes to conduct interviews or to collect samples. Often these visits are conducted by research nurses or research assistants after hours. Under these circumstances there is a risk to the safety of the research staff.

- From time to time research staff find themselves speaking with participants who have become upset or aggrieved. In some cases this may be anticipated due to the nature of the research but may be unexpected. This can cause psychological distress to the staff member. There needs to be a system of support for staff working with distressed patients. Depending on the project and situation this could be anything from an informal debrief to access to formal counselling.

- Sometimes researchers are disappointed with the outcome of their project. They may be tempted to exclude data to achieve a particular result or put pressure on statisticians to exclude data. That can lead the researchers to encourage the statistician to delete some data e.g. outliers so that the results conform to the expectations. Putting pressure on statisticians is unacceptable and may constitute bullying. Bullying will not be tolerated within the SPHPM or Monash University. Deliberate exclusion of data may constitute fraud.

- In many cases the research undertaken by SPHPM involves the collection of biological samples. The collection, handling and processing of these samples can present a danger to researchers. Appropriate handling of the samples will minimise the risk to staff.

Likelihood of occurrence

- There is a moderate risk of harm to staff if they conduct home visits, particularly after hours, without consideration for safety or back-up procedures.

- With appropriate training the risk to staff of contracting a disease from biological samples is low.

Likely consequences

- Injury to staff member with senior SPHPM management accountable for lack of appropriate preventive action.

- Mishandling of biological samples inappropriately can lead to infection of a staff member with a disease from the participant. Some diseases transmitted in this way are serious, may require lifetime treatment.

Barriers to occurrence

- Research staff will contact participants by phone in advance of visit to assess acceptability of visit.

- If there are any concerns visits will be undertaken with a companion and during daylight hours.

- The school will ensure that all research staff undertaking such visits have mobile phones or personal alerts. They will call a designated individual before and after the visit.

- Adherence to this protocol will be checked by the Research Governance Officer.

- All staff should have an understanding of the minimum steps to take if they find themselves speaking with an aggrieved participant. When this is anticipated the project/unit/group should develop a “Distressed participant protocol” (see Appendix F for a template) and ensure all staff are familiar with it.

- For projects/registries where it is anticipated that interaction with aggrieved participants is likely, this should be made clear during the hiring process so that a potential staff member can make an informed decision as to whether this is something they are willing to deal with.

- Staff required to collect, process or handle biological samples in any way must be appropriately trained to enable them to fulfil their role safely.
Appendix F: Distressed Participant Protocol

Distressed Procedure
1. Contact
   - If there is someone you can contact on your behalf, tell the participant.
   - Support person, partner, family member, etc.

2. GP
   - Ask if they would like to speak with a healthcare professional.
   - Offer to support them with the contact details.

3. Support
   - Ask if they have support at home with them.
   - Provide support if they need it.

Terminate all questions being asked
Remain calm; reassure patient; listen to their concerns
Not Alone

Remember to document all issues that have been offered or actions taken (GCOSE tool).
We can only offer advice; patient may need to seek additional support.
Appendix G: Serious Adverse Event report form

SERIOUS ADVERSE EVENTS REPORT FORM:

<table>
<thead>
<tr>
<th>Date of Birth</th>
<th>Gender (circle)</th>
<th>Ethnic Group</th>
<th>Weight</th>
<th>Height</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 = Male</td>
<td>1 = White</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = Female</td>
<td>2 = Black</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 = Asian</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 = Other (specify)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Study Title:
_________________________________________________________________________________
_________________________________________________________________________________
_________________________________________________________________________________

Study Sponsor: Protocol No: Project No:

SERIOUS ADVERSE EVENT DESCRIPTION:
_________________________________________________________________________________
_________________________________________________________________________________
_________________________________________________________________________________
_________________________________________________________________________________
_________________________________________________________________________________
_________________________________________________________________________________

SAE CATEGORY: circle all those relevant
1 = Death (date: dd/mm/y) ______/____/_____  2 = Life threatening  3 = Permanently Disabling
4 = Hospitalisation/prolongation  5 = Cancer  6 = Congenital Anomaly
7 = Overdose  8 = Other (specify)

Start Date dd,mm,yy __________
Stop Date dd,mm,yy __________

Intensity (1) Mild (2) Moderate (3) Severe
circle one

Relationship To Study Drug OR Study Procedure
(0) Not suspected (1) Possible (2) Definite
circle one
circle one

Study Drug Adjustment
(0) None (1) Modified (2) Discontinued
circle one
circle one

Treatment Required
(0) No (1) Yes if YES specify on conmed page
circle one
circle one

SAE Resolution
1 = Unresolved 2 = Resolved 3 = Resolved with sequelae
4 = Fatal 5 = Unknown circle one

Concomitant Drugs
Generic Name

Indication

Total Daily Dose & Route

Start Date dd,mm,yy

Stop Date dd,mm,yy

Ongoing Y = yes N = no

Suspect Drug (to SAE)
Y = yes N = no
SERIOUS ADVERSE EVENTS REPORT FORM: (page 2 of 2)

Relevant Medical History. Include relevant diagnostic/investigational data.
__________________________________________________________________________________
__________________________________________________________________________________
__________________________________________________________________________________
__________________________________________________________________________________
__________________________________________________________________________________
__________________________________________________________________________________

Report Information. Indicate when the following were notified.

Study Monitor Date: ___/___/____
Study Sponsor Date: ___/___/____
Ethics Committee Date: ___/___/____
Therapeutic Goods Administration Date: ___/___/____
Other: specify________________________ Date: ___/___/____

__/____/____
Principal Investigator’s Signature Name Printed Date
Appendix H: Maintaining Research Records

Maintaining Research Records
School of Public Health and Preventive Medicine
5th May, 2015

http://www.med.monash.edu/sphpm/research-governance-committee.html
PURPOSE OF THE GUIDE FOR MAINTAINING RESEARCH RECORDS

These guidelines have been developed to provide assistance to all School of Public Health and Preventive Medicine staff and students in the proper maintenance of research records. This document will provide guidance with regards to establishing a Study Document File (also known as a Site File or an Investigator File). It will also provide guidance with regards to the naming of electronic files. It is hoped that in providing this guidance that we will achieve the following:

1. Research records will be set up and maintained in an orderly fashion from the onset of the study.
2. Implementation of these guidelines will enable necessary research document to be easily identified.
3. All necessary documents will be locatable at the time of archiving ensuring that the study is archived as a whole and in a way that ensures easy retrieval of the study documents.
STUDY DOCUMENT FILE

All documents associated with a study must be stored securely in an orderly fashion so that documents can be located as needed. A study document file is the recommended way of doing this. The ‘file’ can be a single folder, multiple folders or an entire filing cabinet, depending on your trial. The following is a template for a study document file. Each of the section headings below represents a new divider in your folder (or filing cabinet).

In some cases additional information is provided. You may find it useful to print this on to your dividers. This will give you additional guidance regarding the contents of the section or actions that should be taking during the trial or at the end of the study i.e. as part of the archiving process.

Following this template will ensure that no important document are missed when maintaining your study records and will also ensure that others can locate documents as necessary.

REMEMBER – If your study document file contains identified information (signed PICF, subject identification list etc) then it is an ‘identified’ document and the whole file must be treated as such which means it must be stored securely (e.g. in a locked office or filing cabinet) at all times.
DIVIDERS

1 Ethics Committee Paperwork

1.1 Original ethics committee applications and all subsequent amendments
1.2 Ethics committee approvals
1.3 Annual reports to HRECs, progress reports
1.4 All correspondence to and from the relevant HRECs

2 Research Protocol

The SPHPM Guide to Good Research Practice states that no research activities, even relatively minor one such as pilot studies, should be undertaken except in accordance with a protocol that has been approved by an ethics committee.

A complete, signed and dated protocol should be filed in this section. Note any changes to the protocol should also be recorded and filed with appropriate version numbers.
3 Participant Information and Consent Form (PICF)

3.1 All approved versions of the PICF
3.2 Signed PICFs

During the study:

Where practical, signed PICFs should be stored in this section.

WHEN NOT IN USE THIS FOLDER SHOULD BE STORED SECURELY

If it is necessary to store the signed PICFs elsewhere please complete the following:

Are signed PICFs stored in the Study Document File? yes/no

If No, Where are PICFs stored?

_________________________________

_________________________________

At the completion of the study:

Signed PICFs should be placed in a sealed envelope before being placed in the archive box. The envelope should clearly state that it contains identified information (see section 18 - Archiving)
4 Subject Identification List

Where practical, subject identification lists should be stored in this section.  
*WHEN NOT IN USE THIS FOLDER SHOULD BE STORED SECURELY*

If it is necessary to store the subject identification lists elsewhere please complete the following:

Are subject identification lists stored in the Study Document File? yes/no

If No, Where are subject identification lists stored?

_________________________________

_________________________________

**At the completion of the study**

Subject identification lists should be placed in a sealed envelope and archived (see section 18 - Archiving)
5 Completed Data Collection Forms (Case Report Forms) or questionnaires

5.1 Blank copy of the data collection form/questionnaire

5.2 Completed data collection forms/questionnaires

If it is necessary to store the data collection forms/questionnaires elsewhere please complete the following:

Are data collection forms stored in the Study Document File?

Yes / no

If No, where are data collection forms or questionnaires stored?

_________________________________

_________________________________

DO NOT STORE CODED/RE-IDENTIFIABLE DATA COLLECTION FORMS TOGETHER WITH SUBJECT ID LISTS OR OTHER INFORMATION THAT COULD IDENTIFY PARTICIPANTS
6  Study brochure/investigator brochure/Product information Sheet (if applicable)

7  Data dictionary

8  Correspondence (general)

File in this section all (non HREC) correspondence relating to the study, e.g., letters, faxes, memos, phone logs, emails etc.

9  Contracts or agreements

Where practical, all contracts or agreements should be stored in this section

If it is necessary to store the contracts or agreements elsewhere please complete the following:

Are contracts or agreements stored in the Study Document File?

Yes / no

If No, which contracts or agreements are not in the Study Document File:

____________________________________________________

____________________________________________________

Where are the above contracts or agreements stored?

____________________________________________________

____________________________________________________
10. Minutes of study meetings (these must be circulated to all study team members)

11. DATA MANAGEMENT

11.1 Computer database specifications and details

Complete the following

Study computer file name______________________________

Database Name_______________________________________

Name of people with database access and password

11.2 Record and file of any changes to data on computer files after data collection

11.3 Record and file any Coding anomalies
12 Drug dispensing records (if applicable)

13 Randomisation schedule (if applicable)

14 Adverse events

All adverse event reports should be stored in this section

ALL SERIOUS ADVERSE EVENTS MUST BE REPORTED TO THE STUDY SPONSOR AND THE HREC

15 Quality assurance checks and documentation (if applicable)

16 Study Reports/publications

File in this section reports, audit reports, drug safety monitoring body reports and any publications resulting from the study

17 Additional Documentation

This may include:

CTN Clinical trial notification scheme
Indemnity documents
Budgets
Advertising
18 Archiving

To store or retrieve your documents archived by SPHPM, please email the Head of Schools Office regarding:

- the number of storage boxes required
- Primary Investigator's name, study name, specific contents list for each box, date for review of storage/destruction.

The Head of Schools Office will update the Archive database, create labels with allocated numbers and barcode, and arrange for collection and storage.

Please don't archive anything unless it has been entered into the database.
LIST OF DIVIDERS TITLES

The following is a list of the divider titles only.

1. Ethics Committee Paperwork
2. Research Protocol
3. Participant Information and Consent Form (PICF)
4. Subject Identification List
5. Completed Data Collection Forms (Case Report Forms) or questionnaires
6. Study brochure/investigator brochure/Product information Sheet (if applicable)
7. Data dictionary
8. Correspondence (general)
9. Contracts or agreements (if applicable)
10. Minutes of study meetings (these must be circulated to all study team members)
11. Data Management
12. Drug dispensing records (if applicable)
13. Randomisation schedule (if applicable)
14. Adverse events
15. Quality assurance checks and documentation (if applicable)
16. Study Reports/publications
17. Additional Documentation
18. Archiving
ELECTRONIC FILE NAMING POLICY

In order to ensure that electronic files can be identified and retrieved as necessary it is useful to have some consistency in the way files are named. Below is a recommended file naming policy to be used as a guide.

All studies must have a folder on a Monash University shared drive which is backed up regularly and password protected. The name of this folder should be an identifier easily associated with the study in question. The following folders should be located within the main study folder. These folders are suggestions. If a folder does not apply to your study you are not required to use it. If there is a component to your study not covered by the folder below you are welcome to add a folder and identify it accordingly.

It is recommended that file names begin with the identifier of the file e.g. ‘Protocol’, ‘PICF’ etc. rather than a study identifier. It is also recommended that the file name end with the version date of the file. To avoid confusion with the American date system we suggest ‘01Jan15’ for 1st January, 2015.

Ethics

This folder should include the following document types:

**Ethics application**

Whether you have used the NEAF, the Common application Form, the Monash University HREC Review form or a low risk application the application form should be stored here.

**Study Protocol**

All versions of the protocol should be stored here.

When a protocol is amended there should be a summary of changes document (stored in this folder) or a tracked version of the protocol.

The file name of the protocol should indicate the version number and date of the document.

**Example:**

Protocol V1 25Dec14.docx

**Participant Information and Consent Form**

All versions of the PICF should be stored here.
When the PICF is updated a tracked version of the document should be stored here.

**Example:**

PICF V1 01Jan15.docx
PICF V2 23June15 track.docx
PICF V2 23June15.docx

**Request for approval of amendment forms**

It is recommended that an amendment number and or a date be included in the file name for easy tracking.

**Ethics Committee Approval(s)**

Most HRECs provide their approval certificates electronically. However, they often arrive with varying file names e.g. ethics approval certificate, *project number* approval certificate, amendment approval certificate, approval just to name a few. It is recommended that you use a consistent way to name your approvals particularly if there a many amendments in your project.

**Ethics Committee Annual progress report**

Recommended naming:

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethics progress report 2015.docx</td>
<td>Completed form</td>
</tr>
<tr>
<td>Ethics progress report 2015.pdf</td>
<td>Signed and scanned version of the word document. You may wish to add ‘signed’ following the date.</td>
</tr>
<tr>
<td>Ethics progress report 2015 acknowledgement.pdf</td>
<td>Acknowledgement received back from the HREC</td>
</tr>
</tbody>
</table>

**Additional regulatory, ethics, governance documents**

Additional documents to be included in this section are:

- CTN form
- Indemnity form
- Investigators brochure
- Sponsor insurance certificate

**Mutual acceptance studies**
If your project is approved under one of the mutual acceptance schemes and you are the reviewing site you will have numerous documents for other sites that you will need to store and keep track of. It is suggested that you generate a folder for each site in which to keep the relevant files.

For larger studies and/or long running studies where there are numerous IBs, annual report, amendments etc. it may be useful to create separate folders within the Ethics folder e.g. all annual reports may be stored in a folder called 'Annual Reports' that sits within the 'Ethics' folder.

**CRF**

A copy of your Case Report Form (CRF) or data collection form should be stored here. Ensure you include the version number and/or date in the file name.

**Finance**

**Contract/agreement**

A copy of any agreement and a copy of any amendments to the original contract or agreement should be stored here.

**Supporting Department documentation**

It is quite common to have written agreements from groups within the institution who will support your study either for a fee or in kind. Documentation of such arrangements should be stored here.

**Study budget**

**Financial records**

This includes documentation of invoices requested, bills paid and balances of funds.

**Correspondence**

All correspondence (letters, faxes, memos, files notes etc.) should be stored here.
Label documents consistently. One method is to label files with the recipient’s name, the type of correspondence (if not a letter) and a date.

**Examples:**

- A letter sent to Rowan will be **Rowan 29Jun14.docx**
- A fax sent to her would be **Rowan fax 29Jun14.docx**

- **Database**

- **Report**

  This folder should include the final report (**Report date.docx**) and draft versions as well as files containing tables, figures etc. used in the report. Statistics may also be stored here for or may be stored in a separate folder (**Stats**) it this seems more appropriate.

- **SAEs**

  For interventional trials where Serous Adverse Events (SAEs) occur it may be useful to store these in this folder. Alternatively SAEs can be stored in the Ethics folder or in an SAE folder that sits in the Ethics folder.

- **Misc**

  Use this folder for any files that do not fit into any of the above folders e.g. advertising.

- **Archive**

  If you prefer to keep superseded documents separately to the current versions then create an Archive folder.
ARCHIVING

Once a study is complete all relevant documents should be archived. This includes not only paper records but electronic files also.

Archiving of study documents – paper

All paper based documents associated with your study need to be archived at the end of the trial. This includes everything listed in the “Study Document File” section of this document.

To store or retrieve your documents archived by SPHPM, please email the Head of Schools Office regarding:

- the number of storage boxes required
- Primary Investigator’s name, study name, specific contents list for each box, date for review of storage/destruction.

The Head of Schools Office will update the Archive database, create labels with allocated numbers and barcode, and arrange for collection and storage.

Please don’t archive anything unless it has been entered into the database.

Archiving of study documents – electronic

Once a study is complete the electronic files can be moved to LaRDS. This is a more secure environment for electronic data which does not need to be accessed regularly. To more your files please log a job with eSolutions.
Appendix I:
References / Useful Resources

1. Medical Research Council
“Guidelines for Good Clinical Practice in Clinical Trials 1998.”
http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002416


3. ICH/GCP Guidelines, an international ethical and scientific quality standard.

4. Monash University Human Research Ethics Committee (MUHREC).
http://www.monash.edu.au/researchofficelhuman/

5. Alfred Hospital Research & Ethics Unit (Alfred Hospital Ethics Committee).
http://www.alfredresearch.org/; Ext 79 63848 (9076 3848 for external calls)


8. ICD10: available from the World Health Organisation website:
http://www.who.int/en/


11. Health Services Commissioner,
Privacy Legislation.


16. Plagiarism tutorial
http://lib.monash.edu.au/tutorials/citing/

17. Academic integrity, plagiarism and collusion http://www.med.monash.edu/intranet/policies/academic-integrity-procedure.html

18. Student academic integrity

19. The Belmont Report
http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html