GUIDANCE

Ethics Clearance for Health-Related Research Conducted by non-FHS Researchers

Health Research in South Africa

In accordance with the South African National Health Act of 2003, **"health research"** includes any research which contributes to knowledge of:

- the biological, clinical, psychological or social processes in human beings;
- improved methods for the provision of health services;
- human pathology;
- the causes of disease;
- the effects of the environment on the human body;
- the development of new applications of pharmaceuticals, medicines and related substances; and
- the development of new applications of health technology.

Ethics Review Requirement

Health research that involves human participants must "undergo independent review by a registered health research ethics committee."
(*Dept. of Health, Regulations Relating to Research with Human Participants, 2(g)*).

Making an Application to the HREC

UCT Researchers who plan to conduct health research as defined broadly in South African law must seek and obtain the prior approval of the Health Research Ethics Committee (HREC), which is the registered ethics committee qualified to review and approve such research. Forms, instructions, and standard operating procedures are available at the HREC page on the Research tab of the Faculty of Health Sciences website:

http://www.health.uct.ac.za/fhs/research/humanethics/about

The HREC meets on a regular calendar throughout the year with submission dates set three weeks before scheduled meetings.

UCT Researchers who study health using methodologies of **non-clinical** and **non-therapeutic** character (as is common in social science scholarship) are not exempt from HREC review. However, their protocols often involve minimal risk and may be eligible for **expedited review**. Researchers should familiarise themselves with the criteria for expedited review as a key feature of protocol design, especially if they wish to conduct research on a compressed timeline.

Your Faculty-Ethics Committee Can Help!

Although the HREC cannot defer its review responsibilities to a faculty REC that is not registered, a faculty REC may defer to the HREC under the Terms of Reference or Standard Operating Procedures for the faculty REC.

Definitions

Research:
For health research review purposes, 'research' is defined as "a **systematic investigation**, including research development, and testing and evaluation, designed to develop or contribute to **generalisable knowledge**." US 45 CFR 46.102(d)

Research Participant:
A **living individual** (or group of living individuals) about whom a researcher conducting research obtains data through intervention or interaction with the person or **identifiable private information**. (*Department of Health. Ethics in Health Research: Principles, Structures, and Processes, 2004 p. 59.*)

Human Subjects:
'Human subjects' are defined as: living individual(s) about whom an investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information.

Minimal Risk:
A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests, accounting for all special participant vulnerabilities.

In addition, faculty RECs that require independent review of protocols under their purview (dual review) can use the faculty review process to facilitate best presentation of a research protocol to the HREC.

The HREC review process can proceed more efficiently if a faculty REC provides a cover letter indicating how its approval of a research protocol corresponds to the criteria for ethics approval and/or expedited review.

Tips

✦ Collaboration with a researcher or team based in the Faculty of Health Sciences is strongly encouraged.

✦ Protocols that involve privately identifiable data need a considered data management plan for ethics, legal compliance, and best practice purposes.

✦ Minimal risk studies, including non-clinical and non-therapeutic research studies, often present risks of information harms that should be specifically addressed. Such risk may relate to, for example:

- Reputation
- Shame/Disgust
- Employability
- Access to Insurance (medical)
- Liability (criminal)
- Misguidance
  (advice outside of professional communications: doctor-patient, attorney-client, etc.)
- Loss of time
- Recollection of trauma or stress
  (rape, torture, embarrassment)
- Perception of personal disorder
- Misapplication of hypothesis to self
- Depression (induced by participation)
- Environmental Exposures
- Boredom and Fatigue
- Repeated action injuries
- Loss of privacy

Expedited Review Criteria and Procedures

The type of review that the HREC conducts for a protocol depends on the level and type of risk involved. **Expedited review** is a valuable mechanism that allows the HREC to dedicate its time and resources in full committee meetings to protecting participants facing the greatest levels of risk or discomfort.

The **criteria** for approval by expedited review are the same as those of the full committee and the expedited review should be as substantive and rigorous as that of a convened meeting. The HREC Chair or Deputy Chair has the final responsibility for determining which new protocols, continuing reviews and amendments are eligible for expedited review and has the authority to designate one or more experienced Committee members to perform an expedited review. No member with a conflict of interest may serve as a reviewer for any expedited item. A monthly report of all research approved through an expedited procedure is distributed to members before the full committee meeting.

Eligibility for Expedited Review

Types of research that may undergo expedited review include:

- Research classified as no greater than minimal risk, depending on the details of the study.

Examples of research classified as no greater than minimal risk

1. Research conducted in established or **commonly accepted educational settings**, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

- The above classification is applicable to mentally handicapped individuals only if research involves changes in content, location, or procedures of instruction from those a subject would normally experience.

2. Research involving the use of **educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behaviour**, unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

- The above classification applies to research with children or mentally handicapped individuals only if research involves the use of educational tests.
- When children or mentally handicapped individuals are involved as subjects in research using a survey or interview procedures, the research may not satisfy minimal risk criteria.
- When children or mentally handicapped individuals are involved as subjects in research using observation techniques, the research may not satisfy minimal risk criteria if the investigator participates in the activities being observed.
- Sensitive survey research may not satisfy minimal risk criteria. A sensitive survey is one that deals with socially questionable or highly personal aspects of the subject's behaviour, life experiences or attitudes. Examples include chemical substance abuse, sexual activity or attitudes, sexual abuse, criminal behaviour, sensitive demographic data, detailed health history, etc. The principal determination of sensitivity is whether or not the survey research presents a potential risk to the subject in terms of possible precipitation of a negative emotional reaction. An additional risk consideration is, of course, whether or not there is risk associated with a breach of confidentiality should one occur (i.e., accidental release of drug use information to law enforcement). With respect to potential psychological risk associated with a survey, the presence or absence of subject identifiers is not necessarily a consideration, since the risk may be primarily associated with the sensitive nature of the survey as opposed to being dependent upon confidentiality. Subject identifiers do, however, become a factor when confidentiality is an issue.

Examples of research classified as no greater than minimal risk (continued)

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behaviour that is not minimal risk as described above, if: (i) the human subjects are elected or appointed public officials or candidates for public office; or South African law requires without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

- Same as those described under category 2.

4. Research involving the collection or study of **existing data, documents, records, pathological specimens, or diagnostic specimens**, if these sources are **publicly available** or if the information is recorded by the investigator in such a manner that **subjects cannot be identified**, directly or through identifiers linked to the subjects.

- The source of data, documents, records, pathological specimens or diagnostic specimens must be provided to the IRB.
- To qualify as minimal risk the study data, documents, records, or specimens must be in existence *before* the project begins.

5. Research and demonstration projects which are conducted by or subject to the approval of the authority of a ministry of government, and which are designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

Types of research that may undergo expedited review further include:

- Annual renewals of studies that initially qualified for expedited review or were determined to be minimal risk at a convened Committee meeting, provided no serious adverse events or ethical problems have occurred.
- Amendments to previously approved research where changes to the study protocol or consent documents do not result in significantly increased risk to participants.
- When, in the Chair's opinion, using an expedited procedure would be in the public interest.
- Additional categories of minimal risk research as defined by the HREC in a convened committee meeting.

Expedited Review of US Federally-funded or Supported Research

Protocols that may be reviewed under expedited review are limited to categories listed in 45 CFR 46.110(a) and 21 CFR 56.110(a) if the research involves no more than minimal risk and meets all the stipulated applicability criteria:

Applicability Criteria

- Research activities that:
  - Present no more than minimal risk to human participants, and
  - Involve only procedures listed in one or more of the following categories.
- The categories in the list below apply regardless of participants' age, except as noted.
- The expedited review process may not be used where identification of participants and/or their responses would reasonably place them at risk of criminal or civil liability; be damaging to their financial standing, employability, insurability, or reputation; or be stigmatising, unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- The expedited process may not be used for classified research involving human participants.
- Categories one to seven pertain to both initial and continuing review.

Research Categories

Category 1

Clinical studies of drugs and medical devices only under the following conditions:

- Research on drugs for which an investigational new drug application (21 CFR 312) is not required, but only if the research does not significantly increase the risks, or decrease the acceptability of the risks, associated with the use of the product.
- Research on medical devices for which (i) an investigational device exemption application (21 CFR 812) is not required, or (ii) the medical device is cleared or approved for marketing and the medical device will be used according to its cleared or approved labelling.

Category 2

Collection of blood samples by finger prick, heel stick, ear stick or venipuncture as follows:

- From healthy, non-pregnant adults who weigh at least 50 kg. Amounts drawn may not exceed 550 ml in an eight week period and collection may not occur more frequently than two times per week; or
- From other adults and children, considering age, weight and health, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. The amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an eight-week period and may not occur more than two times per week.

Category 3

Prospective collection of biological specimens for research purposes by non-invasive means. Examples:

- Hair and nail clippings in a non-disfiguring manner.
- Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction.
- Excreta and external secretions, including sweat.
- Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or applying a dilute citric solution to the tongue.
- Placenta removed at delivery.

- Amniotic fluid obtained at the time of rupture of the membrane prior to or during labour.
- Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished according to accepted prophylactic techniques.
- Mucosal or skin cells collected by buccal scraping or swab, skin swab, or mouth washings.
- Sputum collected after saline mist nebulisation.

Category 4

Collection of data through non-invasive procedures (that do not involve general anaesthesia or sedation) routinely employed in clinical practice, excluding procedures that involve X-rays or microwaves. Where medical devices are employed, they must be cleared or approved for marketing. Examples:

- Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the participant or an invasion of the participant's privacy.
- Weighing or testing sensory acuity.
- Magnetic resonance imaging.
- Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography.
- Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given age, weight and health of the individual.

Category 5

Research involving materials (data, documents, records or specimens) that have been collected or will be collected solely for non-research purposes such medical treatment or diagnosis.

Category 6

Collection of data from voice, video, digital, or image recordings made for research purposes.

Category 7

Research on individual or group characteristics or behaviour (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behaviour) or research that employs survey, interview, oral history, focus group, programme evaluation, human factors evaluation, or quality assurance methodologies.

Category 8

Continuing review of research previously approved by the HREC in a convened meeting as follows:

- The research is (i) permanently closed to the enrolment of new participants, and (ii) all participants have completed all research-related interventions, and (iii) the research remains active only for long-term follow-up of participants; or
- No subjects have been enrolled and no additional risks have been identified; or
- The remaining research activities are limited to data analysis.

Category 9

Continuing review of research, not conducted under an investigational new drug application or investigational device exemption, where categories two (2) through eight (8) do not apply, but the HREC has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Resources available at http://www.health.uct.ac.za/fhs/research/humanethics/about

Ethical and Regulatory Requirements for Human Research, Standard Operating Procedure, Human Research Ethics Committee, Faculty of Health Sciences, University of Cape Town

Definition of Health Research and Human Participants, Standard Operating Procedure, Human Research Ethics Committee, Faculty of Health Sciences, University of Cape Town

The Protocol Review Process, Standard Operating Procedure, Human Research Ethics Committee, Faculty of Health Sciences, University of Cape Town