

**THE UNIVERSITY OF WESTERN ONTARIO**

**HEALTH SCIENCES RESEARCH ETHICS  
BOARD (HSREB)  
FOR RESEARCH INVOLVING HUMAN  
PARTICIPANTS**

# **GUIDELINES**

**October 2009**

**HEALTH SCIENCES RESEARCH ETHICS BOARD (HSREB)  
FOR RESEARCH INVOLVING HUMAN PARTICIPANTS**

**GUIDELINES**

**TABLE OF CONTENTS**

1.0 INTRODUCTION.....	1
2.0 METHODOLOGY.....	1
3.0 RESEARCH INVOLVING INNOVATIVE THERAPY.....	2
4.0 ENSURING EQUITABLE PARTICIPANT SELECTION.....	2
4.1 INCLUSION OF WOMEN IN RESEARCH .....	2
4.2 IMPLICATIONS OF PREGNANCY AND BREAST-FEEDING .....	2
5.0 RISK/BENEFIT CONSIDERATIONS .....	3
6.0 DECEPTION .....	3
7.0 PRINCIPLES OF CONSENT .....	4
8.0 LETTER OF INFORMATION & CONSENT DOCUMENTATION .....	5
9.0 EXCEPTIONS TO PRIOR INFORMED CONSENT.....	6
10.0 PARTICIPANTS INCAPABLE OF GIVING INFORMED CONSENT .....	7
10.1 CHILDREN.....	7
10.2 INCOMPETENT ADULTS .....	9
11.0 COERCION OF PARTICIPANTS.....	9
12.0 DISCLOSURE OF INVESTIGATION .....	11
13.0 CONFIDENTIALITY .....	11
14.0 JURISDICTION OF THE REVIEW BOARD.....	12
15.0 CONDUCT OF MEETINGS .....	13
16.0 EXEMPTIONS AND DELEGATED REVIEW.....	13
17.0 PROTOCOL DOCUMENTATION .....	14
18.0 APPROVAL FORMS.....	14
19.0 REVISIONS TO APPROVED PROTOCOLS.....	15
20.0 ADVERSE EVENTS AND/OR INCREASES IN RISKS TO PARTICIPANTS.....	15
21.0 ONGOING SURVEILLANCE .....	15
22.0 STANDARD OPERATING PROCEDURES.....	16

## **ADDITIONAL GUIDELINES**

- 2-G-002 - Risk Equivalents
- 2-G-003 - Use of Radiation
- 2-G-004 – Use of Magnetic Resonance Imaging
- 2-G-005 - Information and Consent Documentation Guidelines
- 2-G-006 - Assent from Children
- 2-G-007- Categories of Review
- 2-G-008 - Sponsor Documents
- 2-G-009 – Alternate Wording Glossary
- 2-G-010 – Emergency/Compassionate Release
- 2-G-011 – Exercise Protocols
- 2-G-012 – Muscle Biopsy
- 2-G-013 – N of 1 Studies
- 2-G-014 – Open Label Extension Studies
- 2-G-015 – Reporting Protocol Violations, Deviations & Waivers
- 2-G-017 – Study Documents – Confidentiality, Access & Ownership
- 2-G-018 – U.S. HIPPAA Authorization forms & Consents
- 2-G-019 – Use of Alcohol in Research
- 2-G-020 – Compensation for Child Participants
- 2-G-023 – Placebos & Multiple Sclerosis Clinical Trials
- 2-G-024 – Protocols Already Approved by OCREB
- 2-G-025 – Recruitment of Healthy Volunteers
- 2-G-026 – Use Of Tissue And Biological Specimens And Cadavers In Research
- 2-G-027 – Release of Info Documentation

2-G-028 – Studies Involving Risks to Pregnant Women, Foetus, and/or Potential Fathers and Female Partners – September 2009

2-G-029 – CT Registration & dissemination

2-G-030 – HSREB Composition and Quorum

## 1.0 INTRODUCTION

It is the responsibility of the Health Sciences Research Ethics Board to oversee administration of ethics protocols for health related, biomedical and clinical research involving human participants for The University of Western Ontario and its affiliated hospitals and research institutes. In conducting these activities the Board ensures compliance with guidelines promulgated through:

- The Tri-Council Policy Statement: Ethical Conduct for Research Involving Human Subjects as mandated by the Natural Sciences and Engineering Research Council (NSERC), the Social Sciences and Humanities Research Council (SSHRC) and the Canadian Institutes of Health Research (CIHR),
- The Good Clinical Practice: Consolidated Guideline (GCP) of the International Conference on Harmonization which has been adopted by Health Canada,
- The U.S. Food and Drug Administration and,
- The Office for Human Research Protections, the U.S. Department of Health and Human Services.

The HSREB's primary responsibility is the protection of human participants from undue risk and from deprivation of personal rights and dignity while ensuring that they are participating in scientifically valid projects. This protection is best assured by consideration of two issues which are the touchstones of ethical research: 1) that voluntary participation is assured, indicated by free and informed consent; and 2) that an appropriate balance exists between potential benefits of the research to the participant or to society and the risks assumed by the participant.

The HSREB brings its collective experience to the review of each proposal - always conscious of its primary responsibility to protect the rights of human participants against exploitation, but within the context of the need for continued scientific - and therefore human - progress.

## 2.0 METHODOLOGY

It is not the role of the HSREB to evaluate and review the scientific methodology being proposed for any study submitted for consideration. Most research projects will be placed under scientific scrutiny by colleagues and peers in that subject area, and the validity of the design and the value of the research will be assessed during that process.

However, as a member of the scientific community, the HSREB has the right and the responsibility to monitor the methodology being proposed. With any research study involving people, the investigator enters into an ethical and moral contract with the study participants. In exchange for specific information from the participants, the investigator agrees to contribute to the advancement of scientific knowledge. If the research is poorly considered in its design, execution or analysis, it is unlikely to meet this commitment.

Thus, the HSREB takes the view that it is unethical to perform research which fails to demonstrate an adequate research methodology, and it may deny approval solely on methodological grounds. It is clearly seriously flawed designs which are being addressed here. The benefit of the doubt will ordinarily be given to the investigator, however, the HSREB will ultimately act in the best interests of the study participants.

### 3.0 RESEARCH INVOLVING INNOVATIVE THERAPY

In reviewing protocols that involve comparison between a new treatment and an established treatment (or between a new treatment and a placebo therapy), the HSREB considers it unethical to assess a new treatment in the setting where the efficacy of the treatment can not be rigorously tested scientifically. Although therapeutic research creates ethical problems, it is not ethical to proceed with new therapies in the absence of proper scientific evaluation as entailed in controlled trials. In such innovative therapy trials, the extension of treatment beyond three patients must be considered a formal research study and will be subject to review by the HSREB. In certain situations, it may be more appropriate to undertake a limited "pilot" study before entering into a larger controlled, randomized trial. In these cases, the HSREB will pay careful attention to the justification provided for choosing to proceed with the pilot study rather than a randomized trial. It will examine the sample size chosen and the method of data analysis.

### 4.0 ENSURING EQUITABLE PARTICIPANT SELECTION

#### 4.1 Inclusion Of Women And Other Populations In Research

The research subject/participant population should be as representative of the population as possible. It follows that women and other sub-group populations must be included in research. Mere inclusion, however, is not sufficient. There must also be valid sub-group analysis of the research data. Also, as appropriate, the research design must consider variability created by hormonal fluctuations.

Research that excludes women or other populations as research participants or ensures their under-representation should not receive HSREB approval unless the investigators provide a compelling justification of the decision to exclude, or limit their participation.

#### 4.2 Implications of Pregnancy and Breast-feeding

It is preferable not to have pregnant women as participants in studies involving, for example, radiation exposure, new drug use, etc. In such studies, the investigator should propose a means of assuring that no pregnant women are used as participants.

Please refer to HSREB Guideline 2-G-028 for details and considerations when research protocols may pose a risk to a foetus and/or subsequent child.

## 5.0 RISK/BENEFIT CONSIDERATIONS

One of the measures for determining whether research is ethically acceptable is a balance between risks and benefits. The potential participant must be informed of the risks involved, the potential benefit to the participant or other patients with his/her class of disease or society in general. The potential benefits must be in proportion to the degree of psychological or physical risk involved.

Participants for medical research may have strong altruistic motivation to participate in studies if they believe that the research will benefit others. Because of this, the HSREB gives consideration to the science of the protocol to determine whether the study is designed properly, and is capable of yielding the knowledge benefit which the proposal suggests. For this reason, the HSREB may draw on the expertise of the scientific community when the study involves technical issues not within the body of knowledge of the HSREB members.

If participants may be exposed to radiation, the Letter of Information and Consent Documentation should follow examples provided in Guideline 2-G-003 - Use of Radiation.

If participants may be exposed to magnetic resonance imaging (MRI), the Letter of Information and Consent Form should follow examples provided in Guideline 2-G-004 - Use of Magnetic Resonance Imaging.

## 6.0 DECEPTION

Under most circumstances, research should not involve deception. Therefore, if researchers propose the practice of deception where participants are purposely misled, the deception must be justified as necessary to complete the research study. There must be no foreseeable risk of harm or potential for the perception of harm or embarrassment of the participant, and there must be a full explanation and debriefing soon after completion of the study.

Studies using deception withhold information or mislead participants about the purpose or process of the study. This conflicts with the requirement for informed consent. If there are legitimate reasons for withholding specific details about a study, it is the researcher's responsibility to provide the HSREB sufficient detail on the nature of the deception as well as a rationale for the use of the deception so that the HSREB can make a reasoned decision.

A study involving deception will not receive ethics approval if it is felt that a participant would not have agreed to participate had they known full study details. Participants in a study involving deception must attend a debriefing session at the end of their participation. This debriefing session will reveal the deceptions used in the research, provide participants with an explanation of why deception was required, answer questions regarding the deception, and obtain written consent to use all information obtained in the course of their participation in the study.

## 7.0 PRINCIPLES OF CONSENT

For participants capable of understanding the nature of the research, consent must be:

- freely given, without pressure or inducement,
- based on full knowledge of the risks and benefits of the research, and
- based on full knowledge of the processes involved.

The informed consent of participants must be documented by a signed Consent Form. As a major component of the ethics review process, the HSREB verifies that the Participant Letter of Information and Consent Form explicitly describe the voluntary nature of participation in the research.

In general, the HSREB may approve a protocol involving significant risk if the participant is well informed, appreciates the risk, and is under no duress or coercive pressure to participate. Where relevant, the investigator must demonstrate that:

- appropriate animal studies have been performed,
- that the results obtained from those studies indicate the likelihood of a significant positive risk/benefit ratio for participants who receive a therapeutic or diagnostic intervention,
- that there is sufficient background knowledge for presumptions of efficacy and safety, and
- that it is appropriate to proceed with an investigation involving human participants at the time.

Where appropriate, the investigator must demonstrate that the study has a sound scientific (including statistical) base. If the study is seriously flawed scientifically in concept or design, it would not be considered ethical to proceed with an investigation involving human participants.

The concept of informed consent must still be adhered to for those studies in which participants are not able to give personal consent. Here the Participant Letter of Information and Consent Form are addressed to those legally responsible for the well-being of the participant, for example the parents when the participant is a child. The HSREB is concerned with ensuring that the documents will assist legal guardians in making a prudent decision that is in the best interest of the participants in question.

The HSREB exercises special care when considering participants with diminished capacity to give free and informed consent, for example children and mentally incompetent participants. Other groups which require special care to ensure that there is no coercion and that consent is freely given include students, hospital or university employees, and prisoners. An area requiring careful consideration is the testing of new therapeutic procedures in patients with impaired capacity to consent, for example, in the treatment of unconscious stroke patients. The process of obtaining consent in these situations is discussed in detail in Section 10.

## 8.0 LETTER OF INFORMATION AND CONSENT DOCUMENTATION

In order that research involving human participants conform to ethical standards which respect the autonomy of the participant, that participant ideally must give free and informed consent to participation in the research protocol.

Generally, informed consent can be obtained by ensuring that the participant is given information in language that he or she is capable of understanding about the nature of the study, the risks to which he or she might be exposed and the potential benefits that might result both to the participant and to society in general as a result of the research.

In all cases, informed consent must involve a written Letter of Information, which will be read by the participant. In the case of a participant not able to give consent, the LOI will be read by the person giving consent for him/her, for example a parent, guardian, or designated other. HSREB approval of protocols involving guardian consent is contingent upon a highly favourable risk/benefit ratio. Information and consent documentation must adhere to Guideline 2-G-005 Information & Consent Documentation.

Information and Consent documentation should be designed to sufficiently inform the research participant so that an intelligent, voluntary decision may be made prior to participation in the study. For this reason:

- a) the form must be written in a straightforward fashion, well-organized and succinct,
- b) technical terms should be explained in simple language,
- c) the language used must be grammatically correct, and
- d) be understood by a research participant at a grade 8 reading level.

When English is not the primary language of the research participant, an interpreter must be provided to guarantee that the participant is aware of and understands the details involved in participation.

Studies being reviewed by the Full HSREB require separate Letters of Information and Consent Forms, while minimal risk studies undergoing Delegated review may use a combined Information/Consent document. A copy of the Letter of Information or the combined Information/Consent Form must be provided to the participants to be retained by them.

In presenting information, it is important to avoid characterizations of the research project that are in any way coercive. The language of consent forms, as well as the circumstances of recruitment, must attempt to ensure that potential participants have a genuine choice about their involvement. Consent should not be sought under conditions of emotional or physical stress, but rather prior to the period of physical or emotional stress (for example, before rather than during labour, at a pre-operative appointment rather than immediately prior to surgery).

The Letter of Information or Information/Consent documentation should contain a statement that this participant agrees to be involved in the "research project" (or "research investigation" or "study") described, has had the project explained, and has had all questions answered to his/her satisfaction. It should provide a place for the participant's signature, and where appropriate, a place for the signature of the participant's parent, guardian, or designated other.

## 9.0 EXCEPTIONS TO PRIOR INFORMED CONSENT

There are a number of special circumstances outside of those involved in the diagnosis and treatment of acutely ill participants wherein free and informed consent may not be obtainable. In principle, in studies not targeted specifically to acutely ill or incompetent participants, participants who are incapable of giving free and informed consent should not be used in research. That is certainly the case where there are participants available who are independently capable of giving such consent.

It is appreciated that in some instances it may not be possible to obtain prior consent. The nature of the illness or trauma may preclude informed consent because of extreme pain, distress, loss of consciousness, or need for immediate treatment. Failure to conduct appropriate research regarding treatment of such individuals may ultimately disadvantage the entire class of individuals presenting with acute illnesses or trauma. Therefore, where the participant is conscious but distressed, it will be deemed appropriate for the investigator to proceed with the research with that particular participant, provided that the investigator has after a brief explanation of the nature of the research, obtained verbal consent in the presence of a witness. The investigator must obtain a signed post-hoc informed consent within 24 hours from either the participant, next-of-kin, guardian or designated other, and this process must be fully documented.

Where the participant is unconscious, or totally incapable of providing consent, the investigator should obtain written authorization from the next-of-kin, guardian, or designated other. However, where this is not feasible because of time constraints, verbal authorization, again in the form of consent may be obtained by phone if possible, and provided written consent is obtained within 24 hours. Specific details of the time, relationship, and telephone number of the individual who provides consent should be recorded carefully.

There may be areas of research where, because of the urgency of the patient's (participant's) situation, even verbal assent would not be feasible. This would apply, for example, to research evaluating different techniques for resuscitation of victims of a cardiac arrest. Particularly where this research involves victims of out-of-hospital cardiac arrest brought to emergency departments, prior identification of these participants, for the purposes of obtaining consent for the performance of this research, would not be feasible. The immediacy of treatment at the time of identification of the condition precludes the obtaining of either assent or consent from the next-of-kin, guardian, or designated other. To strictly adhere to the requirement of assent/consent

prior to undertaking research would prevent the development and/or improvement in treatments.

Particular care and scrutiny will be undertaken in the review and approval of such research protocols. For approval of these protocols, the protocol must be submitted to the full HSREB. Such protocols must involve a risk to the participant no greater than that currently involving available resuscitation techniques, and evidence must be provided of same or evidence that the risk is very small. In order to ensure that the protocol is scientifically sound, even in the case of external peer review having been completed, the protocol will likely be reviewed by a specialist from an institution not affiliated with the Principal Investigator. The reviewer would be asked to pay particular attention to the aspects of benefit that are likely to accrue by performance of such research, and particular attention to research methodology, sample size calculations and justification of the need to do the research.

The investigator must also inform in writing the survivor of cardiac arrest, or next-of-kin or guardian, of the performance of such research, and be available to answer any questions pertaining to the research itself, and the fact that it was conducted in the absence of consent.

## 10.0 PARTICIPANTS INCAPABLE OF GIVING INFORMED CONSENT

It is recognized that important studies would be impossible without involving participants who are incapable of giving consent, particularly studies which are designed to benefit those very participants. In such circumstances, participants who are incapable of giving consent may be enrolled provided that there is no significant risk or discomfort to the participant, or that any risk or discomfort that does exist is outweighed by the probability and degree of benefit that may accrue to that individual participant or to the group of which the participant is a member.

Participants who may be incapable of giving consent fall into two broad categories: children and the mentally incompetent.

### 10.1 Children

Children should not be exposed to greater risks than they face in their everyday lives and, while parents may consent to inspection of their children's records for research and may approve the collection and analysis of collected excreted materials, the method of collection must cause no pain or embarrassment.

Research protocols involving children that do not expose the children to any risks that are not faced in daily life may be submitted for Delegated review. Where there are greater risks, the protocol must be submitted for full HSREB review, will be subject to the same rigorous review as applies to incompetent adults and must indicate the need to perform the research with children (see

section 16.0 Exemptions and Delegated Review). The consent of a parent or guardian is required at all ages up to 18. If the HSREB determines that a research protocol is designed for conditions or subject populations for which parental or guardian permission is not a reasonable requirement to protect the participants, it may waive such requirement provided an appropriate mechanism for protecting the participating children is substituted. The choice of an appropriate mechanism should depend upon the nature and purpose of the activities described in the protocol, the risks and anticipated benefit to the research participants, and their age, maturity, status and condition. Furthermore, in all cases for research involving children, the child's assent must be sought in simple language that the child is capable of understanding from the age of 7 upwards in order to ensure that there is no coercion. If appropriate, the child should sign either the Consent form or a special Assent form as described in Guideline 2-G-006 Assent from Children.

A child's objection to participation in research should be binding unless the intervention holds out a prospect of direct benefit that is important to the health or well being of that child, and is available only in the context of research. The above conditions will hold for those protocols involving no greater than minimal risk.

In addition, the HSREB will take into account any potential for embarrassment and psychological risk as part of its evaluation. If the protocol involves greater than minimal risk from either an intervention or monitoring procedure, the risk must be justified by the anticipated benefit to the participant or participants with similar affliction, and the relation of anticipated benefit to such risk must be at least as favourable to the participants as that presented by available alternative approaches. (see Guideline 2-G-002 Risk Equivalents)

Investigators should as well:

- a) devote sufficient time to explaining the projects to parents and to child participants, preferably in the presence of a non-involved professional colleague, for example the child's nurse,
- b) listen to the anxieties that may arise,
- c) monitor whether research procedures produce any emotional or behavioural disturbances in the child participant,
- d) deal promptly with any emotional disturbance that does arise, either themselves or by appropriate referral, and
- e) devote sufficient time to explaining the projects to nurses and other staff involved with the child participants and their parents, and to discussing any problems that may arise from research procedures.

In general, research procedures on neonates, infants and children should not be undertaken in such a way as to keep parent and child apart; where possible, parent(s) should be encouraged to be present.

No financial or other inducement should be offered to a parent or guardian to persuade them to enter their children into a research project; any reasonable expenses incurred, however, should be reimbursed (e.g. transportation costs).

There may be circumstances in which a responsible adult may not give consent to the participation of a child in research where the child himself/herself desires to participate. In such cases, the competence of the potential participant must be carefully assessed to determine if the child is capable of independently authorizing participation in the study. Indication must be provided that a third party will be available to counsel the child in the event there is later difficulty with a parent or guardian and this third party must be named by the investigator on the protocol submission. Indeed, in some situations it may be an invasion of the child's privacy to seek parental consent, for example, where the child has received treatment for a venereal disease at a public clinic and is invited to participate in a study designed to improve the medical services offered in the clinic. Similar observations may be made with respect to research in which the investigator seeks to recruit children for research involving drug abuse. In these cases, consent for participation should be obtained from the child in the absence of a parent or guardian, and ongoing support as indicated above should be made available to the child.

## 10.2 Incompetent Adults

Similar considerations as presented in Section 10.1 will prevail with respect to research involving mentally incompetent individuals, both children and adults. Again, a restrictive approach to the circumstances in which such research could be conducted would deter and prevent investigators from pursuing important and potentially beneficial research. Thus, the HSREB may approve protocols involving incompetent adults where ample justification is provided for their inclusion as participants and the risk/benefit ratio is appropriate. Further, assent must be sought and obtained from the participant where possible and full information provided. Written authorization for this and all cases involving research on incompetent adults, excluding acute illnesses, must be obtained from the next-of-kin or designated proxy prior to the research project being initiated in individual participants. In general, in the absence of designated other or next-of-kin, research must not be performed.

## 11.0 COERCION OF PARTICIPANTS

The requirement that consent be freely given and be well-informed dictates that those from whom consent is sought not be vulnerable to exploitation or open to coercion or over-inducement. The invitation to a prospective research participant must be made in a way that allows the individual freedom of choice.

There are a number of groups of potential participants who, because of their status and/or their relationship with an investigator, are vulnerable to undue influence to agree to participate. These groups include the following: patients, persons institutionalized in, for example, a correctional institution or a facility for the mentally ill, students, employees, and persons whose financial position is such as to render them prone to consenting to research as an aid to obtaining income. Persons in each of these groups are, to varying degrees, vulnerable to influence.

Consequently, care should be taken to ensure that the participant's independence is maintained. It should be made clear to participants who are vulnerable to influence that those invited to participate may refuse to participate and that those who agree to participate may withdraw at any time with no effect on their present or future medical care. Students must be assured that withdrawal will not result in any academic penalty; employees must be assured that withdrawal will not lead to any adverse employment consequences.

Similarly, care must be taken not to induce consent by the promise of reward. Thus, for example, students should not be promised academic reward and employees should not be promised employment advancement.

Research participants participate voluntarily in research studies. However, there are circumstances in which it is appropriate to offer financial compensation to participants for their participation in research. Such remuneration should be limited to compensation for expenses actually incurred, e.g. travel costs, child care. In addition some reimbursement for the time committed to the study and the inconvenience associated with participation in the study is acceptable provided that it is not of such a magnitude as to constitute an inducement to enter the study. Justification for compensation must be included in the protocol submission. There is no compensation for lost wages as a result of study participation. It is not possible for the Office of Research Ethics to specify exactly what amount of compensation will be appropriate. Each case must be determined on its own merits, and must be consistent with the principle of volunteerism.

Frequently, research is conducted by investigators who are also physicians in charge of the care of the patient/participant. Patients often bear a sense of dependency on their personal physician and may be anxious about their future health care. In this situation considerable care must be taken to avoid any undue influence on the patient/participant which will undermine the voluntary character of the consent. Where possible, the approach to the participant inviting participation in a research project should be made by another member of the health care team, preferably one who has no direct responsibility for the participant's future medical management.

Another important consideration to take into account in protecting the voluntary nature of the consent is the manner by which, and the time at which, a participant is approached to participate. Generally, participants should not be recruited at a time of stress or when their ability to comprehend the proposed procedure is impaired,

for example, by the administration of a sedative or tranquillizing agent. Moreover, they should be given sufficient opportunity and time to consider and reflect upon the request made of them before being required to make their decision.

Wherever possible, the family physician should be informed of the participant's participation.

## 12.0 DISCLOSURE OF INVESTIGATION

In all cases, where data have been obtained, research participants have the right to request and receive the results and interpretation of the grouped data. The specific results that apply to them individually can be obtained from their referring physician.

In protocols involving testing of blood samples for the HIV (AIDS) virus, all participants must be informed prior to their participation that they and their physician will be told of this test status. Additionally the Medical Officer of Health and other Public Health offices may be informed as directed by law. Further, the investigator must be available to provide initial counselling after notifying the participant of a positive HIV test result.

## 13.0 CONFIDENTIALITY

The general rule in research is that confidentiality cannot be breached without the participant's consent. This requires that care be taken at a number of stages in the research project:

- at the stage where the investigator is attempting to identify participants who will be suitable for the research
- during the conduct of the research on the participants, and
- during the period that the data obtained are studied, analyzed and reported.

In the hospital setting, where patients are to be recruited as research participants, it is inappropriate to identify potentially suitable participants by a random audit of patients' medical charts. Rather, the investigator should approach a member of the health care team treating patients who possess the characteristics for inclusion in the study to identify prospective participants. The initial approach to the patient to determine whether or not the subject is willing to participate should be made by the attending physician or member of the health care team and not by the investigator (where the investigator is not the participant's physician). If the patient consents to being approached, the investigator may then proceed to contact the patient and explain the research to the patient and seek consent.

Where participants give consent to research, access to personally identifying information and its use in research should be carefully guarded. Identifiable data should be coded at the earliest possible time. A minimum number of research staff, all of whom must be instructed about confidentiality requirements and completed hospital privacy sessions, should be involved. Where, in the conduct of research, it is necessary to consult medical records, the consent of the participant should be

obtained. It is recognized, however, that for some types of studies, e.g. epidemiological studies involving examination of hospital records, it may not be feasible to obtain the consent of participants.

Where participants are offered the protection of confidentiality, care should be taken to inform patients that, while the investigator will not voluntarily breach confidentiality, research records may well be subject to subpoena, to disclosure by operation of law, and to the sponsoring agency, including for monitoring purposes, and where applicable Health Canada, and the US Office of Human Research Protection and Food and Drug Administration. If data are being sent to sponsors or other off-site investigators, investigators must ensure that names and identifying information are removed before this occurs.

Data once obtained should be kept secure from theft, copying, interception and/or casual release. Records should be kept in locked cabinets to which access is restricted to as few members of the research team as is reasonably possible. Similarly, data which are stored on computerized databases should be rendered secure from access by other users of the system. The method of disposal of research data must be clearly described.

Where the research is of such a nature as to require contact with relatives of the participant, access to relatives must in principle be controlled by the participants themselves. No approach for research purposes can be made without a participant's consent. If participants consent, they should approach family members first because individuals must not be approached by strangers bearing intimate information.

Confidentiality requires that when researchers publish their results, they preserve the anonymity of the participants used in that research. In rare cases where disclosure of the identity of the subject cannot be avoided, consent to such disclosure must be obtained.

#### 14.0 JURISDICTION OF THE REVIEW BOARD

***COMMENCING RESEARCH WITHOUT THE PRIOR WRITTEN AND SIGNED APPROVAL OF THE REVIEW BOARD IS UNACCEPTABLE AND WILL RESULT IN ACADEMIC AND OTHER PENALTIES.***

Research refers to the generation of data, using scientifically valid protocols, about persons, through intervention or otherwise that goes beyond that necessary for the individual person's immediate well-being. Intervention is not just medically defined, but includes acts which affect a participant's interests in, for instance: physical, psychological, intellectual and behavioural integrity, and privacy.

The HSREB must review all research protocols involving human participants in

which the research is to be carried out by a full-time or part-time member of the University or by an undergraduate or graduate student of the University or any research conducted within the University and affiliated Hospitals or Institutes. In any case in which the research is to be carried out by a student, a Faculty Advisor must be involved in the research and be named on the protocol submission as the principal investigator.

Investigators involved in multicentre trials require the specific approval of the UWO HSREB for the component carried out under UWO jurisdiction. In addition, the HSREB, at its discretion, may review protocols from outside the University upon request submitted to the Office of Research Ethics.

Once a protocol has been approved by the HSREB, the Investigator will receive a signed notice documenting such approval. The title on the approval form will be identical with that on the approved protocol submission form 2-G-001.

## 15.0 CONDUCT OF MEETINGS

The HSREB meets to consider protocols twice monthly, except once monthly during August and December. The HSREB may hold additional meetings as required by the volume of protocols or to consider specific issues. The HSREB may request that a researcher or research team attend a meeting, to discuss certain aspects of the protocol. Investigators may make a request to appear before the HSREB.

It is the investigator's responsibility to ensure that all documentation in support of requests for approvals are made sufficiently in advance of any deadlines as posted on the University's Research Ethics website.

A simple majority of affirmative votes are required for approval of protocols of the HSREB. The proceedings and minutes of HSREB deliberations are to be kept strictly confidential. In general, the HSREB strives to reach decisions by sufficient discussion to reach a consensus.

All decisions made by the HSREB will be communicated to the Principal Investigator within 7 working days of the HSREB meeting/decision. Correspondence or communication to the HSREB by the Investigators should be made to the Office of Research Ethics.

## 16.0 EXEMPTIONS AND DELEGATED REVIEW

Depending on the nature of the research, a protocol may have a Delegated review (non-interventional minimal risk studies), or a full review by the entire HSREB (interventional studies) and certain studies will not require HSREB approval. Guideline 2-G-004 - Categories of Review - outlines this process in detail.

Delegated review may be performed on those protocols involving minimal risk, meaning that the risks anticipated in the proposed research are not greater than

those ordinarily encountered in daily life or during the performance of routine physical or psychological examination, or by non-invasive tests without the use of ionizing radiation. Other investigations, primarily epidemiological in nature and where persons are not identified, involving the study of existing data, documents, or records may also receive Delegated review. Where the Delegated reviewer(s) has concerns about a specific protocol, the protocol may be directed to the HSREB for a Full Board review. All other investigations involving human participants, including all research involving drug administration, DNA banking and research on embryos or incompetent participants, must be submitted to the HSREB for Full Board review.

## 17.0 PROTOCOL DOCUMENTATION

All applications for review of protocols must be on the appropriate UWO form available on the Office of Research Ethics website. Requests for exemptions or Delegated review should be submitted on Form 2-F-002–Delegated Review submission form. All others should be submitted on Form 2-F-001, Full Board submission form. Sponsoring agency documents are received and retained solely as resource documents as outlined in Guideline 2-G-008 – Sponsor Documents. It is expected that all the relevant material in those documents will be incorporated succinctly by the Principal Investigator into the UWO protocol.

Investigators are encouraged to call the Office of Research Ethics with any questions. The principal investigator must sign the application form attesting to the fact that he/she and all listed co-investigators have reviewed the protocol as submitted and are in agreement with the protocol.

On receipt of the protocol in the Office of Research Ethics, an Ethics Officer will check the protocol. If the protocol is deemed by the Ethics Officer to be incomplete, it will be returned to the Investigator without review, but with comments made as to which items remain outstanding.

## 18.0 APPROVAL FORMS

### ***RESEARCH MAY NOT COMMENCE WITHOUT WRITTEN AND SIGNED APPROVAL FROM THE OFFICE OF RESEARCH ETHICS.***

Once a protocol has been approved, the Office of Research Ethics will provide an approval notice to the investigator documenting such approval. The title on the approval form will be identical to that on the submitted protocol form. The Office of Research Ethics does not sign sponsoring agency approval forms.

If an updated approval is required and there are no changes to the approved protocol, it is necessary for the investigator to complete a Request for Updated Approval form 2-F-011 and submit it to the Office of Research Ethics prior to the deadline as noted on the Research Ethics website. Upon receipt of the completed form and after a review of the file by a member of the HSREB to ensure there are no outstanding issues, an Updated Approval will be issued. In the instances where

the sponsor requires that an Updated Approval receive Full Board sanction and there are no outstanding issues, a recommendation will be made to the HSREB that updated approval be granted. The HSREB's decision will be documented in the HSREB minutes and upon Full Board approval an Updated Approval Notice will be issued.

## 19.0 REVISIONS TO APPROVED PROTOCOLS

During the course of the research, no deviations from nor changes to the protocol or consent form may be initiated without prior written approval from the HSREB, except when necessary to eliminate immediate hazards to the participant. An investigator must complete a Request for Revision to an Approved Protocol (form 2-F-004) and submit it along with the relevant documentation to the Office of Research Ethics. Delegated review of minor changes will be considered.

## 20.0 ADVERSE EVENTS AND/OR INCREASES IN RISKS TO PARTICIPANTS

Investigators must promptly report to the Office of Research Ethics:

- all adverse experiences or events that are both serious and unexpected
- new information that may adversely affect the safety of the participants or the conduct of the study, and
- changes increasing the risk to the participants and/or significantly affecting the conduct of the study.

If these events or changes require a revision of the consent form and/or recruitment advertisement, a Request for Revision Form 2-F-004 should be submitted with the newly revised consent form and/or advertisement.

## 21.0 ONGOING SURVEILLANCE

It is expected that investigators will conduct their own monitoring of ongoing trials for the detection of a clear pattern of side effects and complications or clear demonstration of benefit, or lack of benefit, in the therapeutic arm prior to the planned termination of the study. In such cases, premature termination of the study would be considered as the ethical course of action, and the HSREB must be notified.

If the investigator finds information which indicates a cognitive or health impairment detrimental to the participant's well-being, and this information is unknown to the participant, the investigator has an obligation to make the participant and the participant's physician, if authorized by the participant, aware of the problem.

All studies will require the completion of the Continuing Ethics Review form (2-F-010) at least annually and a final completion report which should include a brief summary of the results of the research. The Office of Research Ethics will send out the Continuing Ethics Review form when they are due. Failure to respond in a complete and timely manner may result in suspension of the HSREB approval until

the documentation is complete.

## 22.0 STANDARD OPERATING PROCEDURES

As general and day-to-day operating policies and procedures are required and evolve, the Office of Research Ethics will issue Standard Operating Procedures (SOPS) and append them on an ongoing basis

