

University of Wisconsin – Milwaukee
Human Research Protections Program
Department of University Safety and Assurances

Institutional Review Board (IRB) Guidelines

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1.0 The Role of the Institutional Review Boards

The role of the University of Wisconsin - Milwaukee Institutional Review Board (IRB) is to protect the rights and welfare of human subjects by reviewing research studies involving human subjects to ensure compliance with the ethical principles and Federal regulations related to human subjects research. To minimize risks and maximize the potential for benefit from human subjects' participation in research, the IRB ensures that the ongoing conduct of the research protects subjects at UWM, and at other sites as negotiated through Assurances. UWM has at least one local institutional review board designated in its HRPP and under its FWA.

These protections ensure that human subjects participate in research only after providing legally effective, fully informed consent when consent is required by law for the ethical and legal conduct of the research. The IRB's decisions are based on the ethical principles in the Belmont Report and the "Declaration of Helsinki". IRB operates under the rules of conduct established from the Code of Federal Regulations, most frequently 45 C.F.R. § 46, 21 C.F.R. § 50 and 21 C.F.R. § 56 as well as Wisconsin state laws, and from UWM policies.

The IRB is also responsible for ensuring that the standards of the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA) (45 C.F.R. Parts 160 and 164) is met when protected health information is used or disclosed for research purposes. The IRB reviews research authorizations, applications for the use or disclosure of limited or de-identified data sets, and applications for waiver of the Privacy Rule's authorization requirements. HIPAA's Privacy Rule is the first comprehensive Federal protection for the privacy of personal health information. Research organizations and researchers may or may not be covered by the HIPAA Privacy Rule. The UWM Office of Legal Affairs provides information and training for compliance with HIPAA.

The IRB exercises autonomy in decision-making. The Human Research Protection Program (HRPP) in the Department of University Safety and Assurances is the administrative home of the IRB and supports the IRB's independence from external influences. The IRB Chair fosters an environment that encourages the free and full participation of all IRB members in its deliberations. As an integral component of the HRPP, the IRB maintains an open line of communication with the IRB Manager and/or Administrator and the HRPP staff (individually and collectively, the "IRBA") who are the primary contact between the IRB and campus researchers, staff, and any others who require assistance or desire interaction with the IRB. The IRB also has a direct relationship with the Director of University Safety and Assurances, who serves as the Institutional Official (IO). The IO is the University officer, designated by the UWM Chancellor, who is ultimately accountable for the IRB and the HRPP. The IRB reports directly to the IO of the University of Wisconsin–Milwaukee and is supported by the IRBA and the University Safety and Assurances Department.

UWM has at least one local institutional review board designated in its HRPP and under its FWA.

2.0 IRB Authority

The IRB has the following authority:

- to approve research, require modifications to research protocols in order to approve research, or disapprove research;
- to require progress reports or other information from investigators in order to effectively oversee the conduct of the research and the informed consent process; and
- to place restrictions on, suspend, or terminate the approval of research that is not being conducted in accordance with IRB requirements or that has been associated with unanticipated problems that involve serious risks to subjects or others.
- The IRB is constituted by the IO and is registered with Department of Health and Human Services, Office for Human Research Protections (OHRP) under the UWM's Federal Wide Assurance (FWA #00006171).

3.0 IRB Functions

The IRB ensures the adequacy of human subject protections by taking the following actions:

- (1) Conduct the initial and continuing review of research protocols;
- (2) Report the IRB's determinations and decisions, in writing, to investigators and the institution, either directly and/or or through meeting minutes;
- (3) Determine which research protocols require review more frequently than once per year;
- (4) Determine which research protocols require verification from other sources, other than the investigator, that no material changes have occurred since the most recent IRB review and approval;
- (5) Require that proposed changes in research are promptly reported;
- (6) Require that changes in approved research are not initiated without prior IRB review and approval, *except*, when necessary to eliminate apparent immediate hazards to subjects;
- (7) Require that any unanticipated problems involving risks to subjects or others be promptly reported to the IRB Chair by the IRBA and, when appropriate, by the IO to pertinent federal agencies and/or internal University Administrators;
- (8) Require that any serious or continuing noncompliance with UWM HRPP Policies and/or federal regulations, or the requirements or determinations of the IRB, be promptly reported to the IRB, the IRBA, the IO, and, when appropriate, via the IO to pertinent federal agencies and/or internal University Administrators;
- (9) Require that any suspension or termination of IRB approval be promptly reported to the IO, the IRBA, and, when appropriate, via the IO to pertinent appropriate federal agencies and/or internal University Administrators;

4.0 IRB Jurisdiction

The IRB has jurisdiction only over the following categories of research when that research involves the use of human subjects or identifiable data or tissues derived from human subjects:

- (1) Research conducted by UWM faculty (any percent time appointment, including adjunct, emeritus and non-salary), staff or students under UWM auspices.
- (2) Research to satisfy a requirement imposed by UWM for the award of a degree or the completion of a course of study, including a capstone project, thesis or dissertation.
- (3) Research conducted by faculty affiliated with UWM, under UWM auspices.

5.0 IRB Membership

The IRB is composed mostly of members representing the University and includes members who are scientists, members who are non-scientists, and members who are not affiliated with UWM. The IRB has a balance of men and women, drawn from a diverse cross-section of the Milwaukee community racial and ethnic groups. (45 C.F.R. § 46.107 and 45 C.F.R. § 46.304).

The members bring sufficient experience, expertise, diversity of membership, (including race, gender, and cultural backgrounds) and sensitivity to issues such as community attitudes, to promote respect for the IRB's advice and counsel in safeguarding the rights and welfare of human subjects. The collective experience and the professional preparation of IRB members includes: expertise in a range of health and behavioral sciences; familiarity with relevant standards of professional conduct and practice; and knowledge of vulnerable or special populations, including children, prisoners, pregnant women, handicapped children, mentally disturbed persons and others (i.e., disabled persons). The members of the IRB possess the professional competence necessary to review the various kinds of human subject research that is conducted at UWM. The IRB composition meets the requirements of 45 C.F.R. § 46.107.

The IRB also has the competence to judge the acceptability of the research in terms of institutional commitments and regulations, applicable laws, and standards of professional conduct and practice. IRB involves *ad hoc* consultants as needed. The IRB has access to HRPP staff for interpretation of federal regulations regarding human subjects research and to UWM's Office of Legal Affairs for interpretation of applicable federal, state, and local laws.

5.1 Membership Appointment

The IRB conducts its business with the participation of the following persons: Chair, Vice-Chair, IRB voting members, alternate IRB voting members, and non-voting *ad hoc* consultants. All IRB appointments are made as follows: A slate of nominees for membership or officer positions on the IRB is presented to the IO. The IO consults with the Vice-Chancellor for Research and the Vice-Chancellor of Finance Administrative Affairs regarding the candidates for IRB membership. Once approved by the IO and Vice Chancellor(s), the IRBA will forward the list to the Chancellor who issues the appointment letter.

5.2 IRB Chair

The IRB has a Chair. The Chair is a respected, active member of the faculty or staff of UWM, who is concerned about human rights and ethical issues, and well informed of the federal and state regulations relevant to human subject research. The Chair is knowledgeable about the application of the ethical principles and regulatory requirements when reviewing human subject research, and sets an example for IRB members. The Chair also leads the IRB meetings and facilitates communication between investigators and the IRBA. As a representative of the institution and the IRB, the Chair exhibits high standards of moral integrity and ethical conduct.

A Chair may continue to serve three year terms at the discretion of the IO. The IO will consult with the IRB and the Vice-Chancellors of Research and Finance and Administrative Affairs regarding the nominee for Chair. The IRBA will forward the Chair nominee to the Chancellor's office where the appointment letter is issued. Acceptance of the Chancellor's Letter of Appointment carries with it the acknowledgement of the primacy of ensuring human subject protections.

Whenever the Chair is not available, the Vice-Chair assumes the responsibilities of the Chair during the period of absence or other unavailability. If the Chair and Vice-Chair are unavailable, the IO may designate a temporary Chair following a discussion with the IRB, if possible.

The IO may remove an IRB Chair at any time, after consulting with the Vice-Chancellors for Research and Finance and Administrative Affairs. Before a Chair is removed, the IO will also consult with the IRBA and the IRB members.

5.3 Vice-Chair

The IRB has at least one Vice-Chair. The IO solicits recommendations from the IRB Chair and IRBA for any Vice-Chair.

The selection and appointment of Vice-Chairs is made by the IO for a term of one to three years. A Vice-Chair may serve consecutive terms at the discretion of the IO. The IO will consult with the Vice-Chancellors of Research and Finance and Administrative Affairs regarding the nominee for Vice Chair. The IRBA will forward the Vice Chair nominee to the Chancellor's office where the appointment letter is issued. Acceptance of the Chancellor's Letter of Appointment carries with it the acknowledgement of the primacy of ensuring human subject protections.

The position of Vice-Chair is a learning position with the intent of being Chair-in-Training. The potential candidate for this position should consider these responsibilities when accepting the Vice-Chair position. As a representative of the institution, and the IRB, the Vice-Chair must exhibit high standards of moral integrity and ethical conduct. The Vice-Chair is the person to whom complaints are directed.

As the Institution Official for human subject protections, the IO may remove an IRB Vice-Chair at any time, after consulting with the IRBA and the IRB Chair.

5.4 Primary Voting Members

As mandated by UWM policy and federal regulations, the IRB has at least five regular, voting members. The membership roster must include at least one IRB member who is a scientist, at

least one member who is a non-scientist and at least one member who is not otherwise affiliated directly or through any immediate family members with UWM.

The IRB members who are scientists are recruited from among both active and retired members of the faculty and academic staff of UWM and have had experience in research involving human subjects. The IRB members who are non-scientists may or may not be affiliated with UWM.

The unaffiliated members may be either members who are scientists or members who are non-scientists. They or their families do not have any affiliation with UWM, and they are recruited from the community of Milwaukee and its vicinity. These persons are included in the IRB in order to provide a perspective on the research that is from outside of the university community (as required by law).

The IRBA solicits member nominations through direct contact and via referrals from colleagues and/or IRB members about interested individuals within and outside the University for affiliated and non-affiliated members. These nominations are solicited as needed and typically when board members resign or take a leave of absence. A slate of nominees is presented to the IO for approval. The appointment procedures are described above in the Membership section of this document. Acceptance of the Chancellor's Letter of Appointment carries with it the acknowledgement of the primacy of human subject protections. As a representative of the institution, and the IRB, each member must exhibit high standards of moral integrity and ethical conduct.

All IRB members (voting and non-voting), including the IRB Chair and Vice-Chair, are instructed at the time of appointment and reminded at each meeting that activities related to research protocol review or other IRB-related activities performed during the time of an IRB member's appointment will be conducted in strict confidence and not discussed outside of the context of these duties.

IRB members are expected to attend the required initial education program, conduct reviews of research protocols in a timely manner, attend, and contribute to the IRB review and discussion of protocols during full board meetings, and attend any required continuing education for IRB members. The IO may remove an IRB member at any time after consulting with the Vice-Chancellors for Research and Finance and Administrative Affairs and consulting with the IRB Chair and the IRBA.

5.5 Alternate Voting Members

The IRB may recruit alternate members to substitute for any of the primary voting members of the IRB. Alternate members have voting rights, except that they may not vote at meetings attended by their respective primary members. Alternate members are included in determining or establishing quorum at IRB meetings, when the respective primary members are absent.

The procedures for appointment, the expectations for membership, and the procedure for removal of an alternate member are the same as that of a primary voting member.

5.6 Ad Hoc Consultant Reviewers

The IRB may invite scientists or non-scientists who have special expertise to assist the IRB in its review of research protocols. These *ad hoc* reviewers may be from within UWM or outside the

UWM community. *Ad hoc* reviewers have access to all documents submitted to the IRB relevant to the specific research protocol under review, may participate in the IRB meeting during discussion, and make recommendations on the research protocol, but they may not vote with the IRB. *Ad hoc* reviewers may also be asked to provide written comments in addition to, or in place of, attending the IRB meeting. *Ad hoc* reviewers may be compensated for their service. The *ad hoc* reviewer's identity and any documents they create may be kept confidential at their request.

All *ad hoc consultants* sign a statement of confidentiality prior to performing any review. This statement guarantees that activities related to research protocol review or other IRB-related activities performed during their course of consultancy are conducted in strict confidence and not discussed outside of the context of these duties.

5.7 Member Liability Protection

The actions of IRB members with respect to their official duties as IRB members are covered by the State of Wisconsin Self Funded Property and Liability Program (insurance) with respect to their official duties as IRB members, as described in this Policy.

5.8 Resignation from the IRB

Members who wish to resign from the IRB are requested to do so in writing to the IRBA. A member will be expected to attend all meetings and conduct all protocol reviews assigned up until the date their resignation takes effect.

5.9 IRB Member Education

IRB members participate in both initial and continuing education. These programs focus on the ethical principles and regulatory requirements underpinning human subject protections and how to apply those principles and requirements to the initial and continuing review of research protocols.

5.9.1 Initial Education Program

The initial education program consists of in-person training provided by the IRBA and on-line training found at: <https://www.citiprogram.org/>. All IRB Chairs and Vice-Chairs, members, and alternates must attend the training (or its equivalent) before actively participating in the IRB. The initial education program includes information about the following areas:

- (1) Ethical Principles and *The Belmont Report*
- (2) Regulatory Requirements
- (3) UWM Federal Wide Assurance (FWA)
- (4) UWM Institutional Policies and Procedures
- (5) IRB's Role and Responsibilities
- (6) Application of the Principles and Regulations to the Initial and Continuing Review of Research and Modifications
- (7) Research Protocol Review Criteria and Review Process
- (8) Informed Consent Process and Document

- (9) Vulnerable Populations: Pregnant Women, Fetuses, Prisoners, Children and Others
- (10) Investigator Responsibilities
- (11) HIPAA Policies and Procedures

5.9.2 Continuing Education Program

Continuing education programs may include scheduled short current topics (case studies and current events) and Just-in-Time (JIT) training that flows from issues raised in the course of the review of research protocols. IRB members are encouraged to attend regional and national educational conferences as appropriate. The IRBA will provide at least one continuing education program annually during a convened meeting.

6.0 IRB Operations

The IRBA supports the IRB by setting up the IRB meeting schedule, attending IRB meetings to provide assistance and record the IRB's discussion and decisions, managing the IRB records for the institution, and communicating the IRB's decisions, in writing, to investigators. The IRBA may be voting members of the IRB. In addition, the IRBA provides consultation to faculty, staff and students, coordinates the review of all protocols, and provides training to IRB members and researchers (faculty, staff and students).

6.1 Record Retention and Security

The Principal Investigator and IRB are expected to maintain and retain the appropriate records for each research study, consistent with federal regulations and UWM's records retention policies.

6.1.1 Principal Investigator Record Retention

Each Principal Investigator must retain records of all correspondence relating to the use of human subjects in research as required by UWM procedures and federal regulations. Copies of such items include, but are not limited to: the initial application, letters of approval (initial, continuing review, and amendments), and informed consent forms. All records of human subject research are subject to inspection by federal authorities and internal IRB audits. Copies of all research records must be kept for a minimum of three years after completion of the study. Studies that involve drugs or devices seeking FDA approval must be kept for three years after the FDA has taken final action on the marketing application.

6.1.2 IRB Record Retention

The IRB (through the IRBA) maintains records of all protocols and correspondence submitted to the IRB and minutes from all full board meetings. The IRB retains such records for a minimum of three years after the completion of the study. All records will be accessible for inspection and copying by authorized representatives of OHRP, DHHS, FDA, Sponsors, university officials, and internal auditors, at reasonable times and in a reasonable manner.

6.2 Meetings

IRB members convene regularly to fulfill their mandate to oversee research involving human subjects at UWM. The IRB generally meets once per month, but meetings may be added or cancelled, if necessary. The IRB meeting schedule is available on the IRB web site.

The IRB has an agenda for the meetings. The agenda includes all research protocols awaiting action by the IRB and informs the members about research that has been approved by the Chair or other experienced reviewers through exempt or expedited review procedures. The IRB agenda and meeting packet is provided to IRB members (through the online submission system, IRBManager) at least 5 days before the meeting to allow them sufficient time to review the research protocols and contact investigators, if they wish, for any clarifications or other relevant information. The meeting packet contains a copy of each protocol, with any supporting documents including appendices, informed consent documents, assent documents, and recruiting materials.

6.3 Quorum and Voting

The IRB meets regularly to consider research applications submitted for review. With the exception of applications eligible for exempt and expedited review, the IRB, including at least one member who is a non-scientist, reviews all research protocols at convened meetings where a quorum has been established.

A quorum is defined as greater than 50% of the voting membership.

The approval of a research protocol requires the vote of a simple majority (greater than 50%) of the voting members present at the meeting.

Voting members may attend full board meetings of the IRB by teleconference or videoconference, if they have been provided a copy of all of the items for review in advance of the meeting, and the equipment permits meaningful participation in discussion and voting. There are no provisions for any other kind of proxy or written vote, since IRB members must be in attendance to vote. However, IRB members may submit written comments or questions in relation to the protocols or other issues under review, prior to the meeting, if they are unable to attend.

6.4 Conflict of Interest

IRB members must disclose any known potential conflicts of interest to the Chair at the start of the IRB meeting. IRB members will not participate in the voting on research protocols in which they may have conflicting interests. Whenever research, in which a member of the IRB has an apparent conflict of interest is being reviewed, that member may be asked to recuse him or herself from the meeting (leave the room) for the duration of the discussion and review of that research protocol if the member's presence could create a bias.

6.5 IRB Meeting Minutes

The IRBA prepares minutes of each meeting of the IRB, documenting the Committee's review of research protocols, policy discussions, and continuing education. The minutes are recorded in sufficient detail and include the following:

- (1) IRB Member attendance and the presence of any invited investigators or guests.
- (2) Motions to go into closed session, the reasons for doing so, the applicable statutory exemptions for closed sessions, and each member's vote on such motions.
- (3) IRB committee acknowledgement of administrative actions by the IRB Chair or designated representative taken for Expedited and Exempt protocols.
- (4) Summary of the discussion, in particular discussion of required modifications for each research protocol reviewed.
- (5) Decisions reached on each research protocol reviewed.
- (6) Votes on the decisions, including a tally of votes for, against, abstaining and total present for the vote. Recusal of members due to conflicting interests is also documented.
- (7) Reasons for requiring modifications to secure approval of a research protocol, for disapproving a research protocol, or suspending or terminating a research protocol.
- (8) If a waiver or alteration of informed consent or a waiver of documentation of informed consent is requested, the specific findings supporting the IRB's determination.
- (9) The level of risk involved in the research.
- (10) The review frequency for the next continuing review. If no shorter of review frequency is discussed, the study will be reviewed annually.

A copy of the minutes is provided to the IRB members for review prior to the next meeting, to give members an opportunity to request clarifications or suggest changes to the minutes. Suggested modifications to the minutes are discussed at a full board meeting and agreed to by consensus, the minutes are subsequently modified according to the IRB's recommendations by the IRBA.

6.6 Investigators and Guests at IRB Meetings

The IRB complies with the State of Wisconsin open meeting regulations.
(http://www4.uwm.edu/secu/open_meetings/)

The IRB may request the attendance of investigators at IRB meeting so that IRB members may ask questions and clarify information. Researchers' team members may, and often do, also

If any IRB member determines that the Committee should go into closed session, investigators and other guests will be asked to leave the room unless invited by the Chair to remain. The Chair will call for a motion to go into closed session.

All guests who attend an IRB meeting are reminded of the confidentiality required of IRB discussions and decisions. A confidentiality agreement should be signed by each guest at every closed session meeting or read to each guest and acknowledged in the meeting minutes.

6.7 Communication of IRB Findings and Actions to the Investigator and the Institution

The IRBA is charged with attending full board meetings of the IRB, and working with IRB members who conduct expedited reviews and reviews of claims of exemption in order to facilitate the communication of the IRB's findings and actions to the Principal Investigator and the Institution. All communication of IRB findings and actions is done officially in writing. Customarily a copy of the correspondence is sent to the Principal Investigator by e-mail and included in the study file in the online submission system. When projects are federally funded, the Principal Investigator is responsible for sending a copy of the approval letter to the Grants and Contracts Office and/or the funding agency.

7.0 IRB Research Protocol Approval Criteria

Before approving a new research protocol involving human subjects the IRB must determine whether all of the criteria from 45 C.F.R. § 46.111 (and 21 C.F.R. § 56.111 when appropriate) are satisfactorily met in the research proposal. Principal Investigators are responsible for ensuring that any other required reviews have been completed and should provide the IRB with documentation of the results of those reviews when complete. Principal Investigators may not start their research (e.g., recruitment, screening, etc.) until all the appropriate reviews have been completed and they have received written notification of IRB approval.

All PI's and Student PI's are required to complete human subjects training. On-line training through CITI (found at: <https://www.citiprogram.org/>) is offered through UWM, but equivalent training will also be accepted. Completion certificates must be submitted to the UWM IRB before final study approval will be issued. The PI is responsible to ensure all other research team members receive the appropriate human subjects and study specific training.

The approval of research protocols may only be given when all of the following conditions exist (45 C.F.R. § 46.111):

- (1) Risks to subjects are minimized (a) by using procedures which are consistent with sound research design and do not unnecessarily expose subjects to risk, and (b) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- (2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to individual subjects, or from the importance of the knowledge that may reasonably be expected to result from the research.
- (3) Selection of subjects is equitable (the risks and benefits from the research are evenly distributed).
- (4) Appropriate, legally effective informed consent will be sought from prospective subjects (or their legally authorized representative).
- (5) Informed consent/assent will be appropriately documented as required by the IRB.
- (6) When appropriate, the research protocol has adequate provisions for monitoring data collected to ensure the safety of subjects.

- (7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- (8) When subjects are likely to be vulnerable to coercion or undue influence, such as pregnant women, fetuses, prisoner, children, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards are included.

7.1 Informed Consent Process and Documentation

Respect for persons requires that potential subjects, to the degree that they are capable, be given the opportunity to choose what shall happen to them. The informed consent process is the primary mechanism by which respect for persons is ensured. The IRB reviews the informed consent documents that Principal Investigators will use to ensure that the Principal Investigators shall, at a minimum, do all of the following (45 C.F.R. § 46.116):

- (1) Provide the subject (or representative) sufficient information about the research and how the research may affect the subject for the subject to assess the risks and benefits of the research.
- (2) Deliver such information in a comprehensible manner, using a language and methods readily understandable by the subject.
- (3) Assure voluntariness of participation by providing sufficient opportunity to consider whether to participate, thus minimizing the possibility of coercion, undue influence, or harassment.
- (4) Disclose significant financial conflicts of interest to potential research subjects.
- (5) Assure that the process of informed consent is ongoing throughout the duration of the research.
- (6) State that the study involves research, explain the purposes of the research and the expected duration of the subject's participation, describe the procedures to be followed, and identify any procedures which are experimental.
- (7) Describe any foreseeable risks or discomforts the subject that may be reasonably expected from the research.
- (8) Describe any benefits to the subject or to others which may be reasonably expected from the research.
- (9) Disclose appropriate alternative procedures or courses of treatment, if any, which might be advantageous to the subject.
- (10) Describe the extent, if any, to which confidentiality of records identifying the subject will be maintained.
- (11) For research involving more than minimal risk, explain whether any compensation or medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- (12) Explain who to contact with pertinent questions about the research and the research subjects' rights, and who to contact in the event of a research-related injury to the subject.

- (13) State that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

The IRB has the authority to observe or have a third party observe the consent process and the research at any time.

7.2 Waiver to Obtain Informed Consent, Alterations of Informed Consent, Waiver to Document Informed Consent

Under certain circumstances, the requirement to obtain, document, or alter the informed consent form from subjects may be waived by the IRB.

7.2.1 Waiver to Obtain Informed Consent and Alterations of Informed Consent

The IRB may waive or alter the requirement to obtain informed consent, if the IRB finds (and documents with specificity) that **one** of the two sets of criteria below (either all of the A or all of the B criteria) are met.

A1. The research or demonstration project is to be conducted by, or subject to the approval of, state or local government officials, and is 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; and

A2. The research could not practicably be carried out without the waiver or alteration.

or

B1. The research involves no more than minimal risk to the subjects;

B2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;

B3. The research could not practicably be carried out without the waiver or alteration; and

B4. Whenever appropriate, the subjects are provided with additional pertinent information after participation.

7.2.2 Waiver to Document Informed Consent

An IRB may waive the requirement for the Principal Investigator to obtain a signed consent form for some or all subjects, if one or more of the following conditions exist:

- (1) The only record linking the subject and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.

- (2) The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the signed consent requirement is waived, the IRB may still require the Principal Investigator to provide subjects with a written statement regarding the research.

8.0 Recruitment and Other Study Related Materials

Printed or electronic materials developed for the sole purpose of recruiting human participants for research activities must be reviewed and approved by the IRB and must state on the document the UWM protocol number and IRB approval date. Noncompliant materials may not be posted or otherwise disseminated.

Electronic versions of printed recruitment materials or advertisements developed for printing in newspapers or other periodicals must be submitted through the online submission system for review and approval by the IRB. Any recruitment materials and advertisements must set forth the UWM protocol number and IRB approval date.

Copies of all approved recruitment materials will be stored in the study's file in the online submission system. Alterations to the approved, stamped recruitment materials must be submitted to the IRB as a protocol modification before use.

9.0 Review Process for New Research Protocols

Principal Investigators who intend to conduct research involving human subjects are responsible for submitting a research protocol and any other supporting documentation to the IRB for review and approval. No research with human subjects may begin (no data may be collected or subjects recruited/screened) until the IRB grants written approval.

9.1 Authorization Agreements

When research involves multiple institutions, the UWM IRB may agree to either defer its review to another IRB or accept IRB oversight for another institution depending on where and by whom the research activities take place. An IRB Authorization Agreement requires agreement from both/all institutions and an agreement signed by the IOs.

9.2 Exempt Human Subjects Research

Under 45 C.F.R. § 46.101 (b), certain types of minimal risk research qualify for exemption from IRB review if the research meets the requirements of one or more of the following categories:

- (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.

- (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, 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.
- (3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2) of this section, if:
 - (i) the human subjects are elected or appointed public officials or candidates for public office; or
 - (ii) federal statute requires, without exception, that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
- (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.
- (5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, 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.
- (6) Taste and food quality evaluation and consumer acceptance studies:
 - (i) if wholesome foods without additives are consumed; or
 - (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Research investigations conditionally qualifying under one or more of the categories for Exempt status must still submit a completed protocol form and supporting documents to the IRB. If the IRB or IRBA determines the research study does not meet the requirements for Exempt status, the Principal Investigator will be notified that the study will not qualify for exempt status and will be sent to the IRB for Expedited or Full Review. If the IRB or IRBA has determined the research study qualifies for Exempt status, a written letter will be issued to the Principal Investigator acknowledging the study is Exempt from review and under which of the six categories cited in 45 C.F.R. § 46.101(b).

Studies acknowledged by the IRB as Exempt do not need to seek Continuing Review approval unless otherwise requested by the IRB office. However, to keep the status of exempt studies accurate, the PI must respond to an email from the IRBA every three years to verify (via email) that the study is still active or if it can be closed. Any changes to the study protocol must receive prior approval from the IRB, as it may disqualify the study from Exempt status.

The IRB is informed of all exempt research protocols through inclusion of this information on the next available meeting agenda, and documentation in the meeting minutes in accordance with 45 C.F.R. § 46.110(c) and 21 C.F.R. § 56.110(c). An acknowledgement of research by exempt procedures is complete by itself and does not require any ratification by the convened IRB. However, the IRB may raise questions about any research that was previously acknowledged under exempt procedures.

Meeting minutes are sent to the IO monthly and made available to others within the institution upon request, so all can be aware of the IRB actions.

9.2.1 Exempt Review Process

The IRB and/or the assigned reviewer (IRBA or other IRB member) reviews the claim of exemption and determines whether the research meets criteria for exemption. The reviewers may:

- (1) Grant the Exemption,
- (2) Request further information or changes before a determination can be made,
- (3) Determine that the proposed activity does not meet the definition of research and/or does not involve human subjects.
- (4) Determine that the research does not meet exemption criteria and must be reviewed by the IRB under expedited or full board review processes.

The assigned reviewer ensures that all criteria for exemption are considered, met, and documented. The results of the review are subsequently communicated, in writing, to the Principal Investigator by the IRBA.

9.3 Expedited Human Subjects Research Review

Certain types of research protocols may be eligible for review under expedited review procedures. The research must involve no more than minimal risk and fit one or more of the categories for expedited review procedures as specified in the regulations [45 C.F.R. § 46.110 and 21 C.F.R. § 56.110].

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the 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. (45 C.F.R. § 46.102(i))

There are nine categories of research eligible for expedited review procedures. These categories are described below:

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met. **(a)** Research on drugs for which an investigational new drug application (21 C.F.R. Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.) **(b)** Research on medical devices for which (i) an investigational device exemption application (21 C.F.R. Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: **(a)** from healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the 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 **(b)** from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an eight-week period and collection may not occur more frequently than two times per week.
3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a non-disfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) 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 in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; or (j) sputum collected after saline mist nebulization.
4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

Examples: (a) 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 subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging,

doppler blood flow, and echocardiography; or (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 C.F.R. § 46.101(b)(4). This listing refers only to research that is not exempt.)
6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 C.F.R. §§ 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)
8. Continuing review of research previously approved by the convened IRB as follows: **(a)** where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or **(b)** where no subjects have been enrolled and no additional risks have been identified; or **(c)** where the remaining research activities are limited to data analysis.
9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where Categories 2 through 8 do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

The Principal Investigator may submit a new research protocol for review by specifying the relevant criteria/criterion that makes it eligible for expedited review. IRB members may choose to review a research protocol under expedited procedures if it meets the criteria, even if the Principal Investigator did not submit the research protocol for expedited review. In addition, IRB members may request a study be reviewed at a convened meeting if they are uncertain regarding its appropriateness for expedited review procedures.

9.3.1 Expedited Review Process

At least one member of the IRB is assigned as a primary reviewer. The IRB Chair and/or IRBA designates experienced members from the Committee to conduct these reviews. The IRBA conducts an initial review and then assigns study reviews to specific members. IRB members are assigned to review research protocols based on the nature of the research itself and on the expertise and experience of the IRB member.

All assigned IRB members review the research applications (including study protocol, recruitment documents, informed consent forms, data collection instruments, grant applications, etc.) to determine if the research meets the definition of minimal risk and the criteria of one or more of the eligible categories. IRB members reviewing a study may ask questions, seek clarification about the research, request modifications, or request additional IRB members to review the protocol.

If a reviewer believes that there is reason for disapproval or the nature of the project is not suitable for expedited review, then the reviewer may refer the application to the Full Board for full board review at a convened IRB meeting.

If two or more IRB members conduct an expedited review and their determinations are not in agreement, the IRB Chair also reviews the research protocol for a final decision or refers the matter to a full board review at a convened IRB meeting.

Under expedited review procedures, the determination options are:

- (1) **Approved:** Approve as submitted.
- (2) **Approved with Conditions:** Require specific modifications to the protocol necessary to secure approval. IRBA may review submitted revisions.
- (3) **Request modification(s).** A revised protocol and/or supporting materials must be submitted for additional expedited review.
- (4) **Request additional IRB member(s) to review.**
- (5) **Refer to the Full Board:** for review at a full board meeting of the IRB.

The IRB members assigned to review the proposal may not disapprove a research protocol under expedited review procedures.

IRB members use the IRB Member checklist/reviewer form to ensure all criteria for review are considered, met and documented. The IRBA communicates the determinations of the IRB, in writing via email, to the Principal Investigator and co-investigators, if applicable. If instructed by the IRB member that reviewed the study, the IRBA may review submitted revisions.

The IRB is informed of all research protocols reviewed and approved under expedited review procedures through inclusion of this information on the next available meeting agenda, which is documented in the meeting minutes in accordance with 45 C.F.R. § 46.110(c) and 21 C.F.R. § 56.110(c). An approval of research by expedited procedures is complete by itself and does not require any ratification by the convened IRB. However, the IRB does have opportunity and the authority to raise questions about any research that was previously approved under expedited procedures, and to re-review those research protocols at a full board meeting if it chooses to do so.

Meeting minutes are sent to the IO monthly and made available to others within the institution upon request, so all can be aware of the IRB actions.

9.4 Full Board Review of Research

Each IRB member will receive a copy of the meeting agenda and all full board review protocols, with supporting documents (appendices, informed consent documents, recruitment materials, etc.) prior to the meeting.

When research is reviewed at a full board meeting, at least two voting members of the IRB are assigned to be the primary reviewers. IRB assigned members review research protocols based on the nature of the research itself and the expertise and experience of the IRB member.

IRB members who are reviewing the research protocol are encouraged to contact the Principal Investigator to ask questions, or seek clarification about the research prior to the full board meeting.

Principal Investigators, Student Investigators and other researchers are invited to attend the meeting at which their full board review protocol will be reviewed. If present, a researcher will be asked to describe the research project and the IRB will ask any questions or request clarification of the study. If the researchers are not present, the primary reviewers will describe the research protocol. After sufficient discussion, the members vote on each research protocol and the votes are recorded in the meeting minutes.

The full board IRB may make the following determinations:

- (1) **Approved:** Approve as submitted.
- (2) **Approved with Conditions:** Conditional fulfillment is required to secure approval. The Principal Investigator's response may be reviewed through expedited procedures.
- (3) **Tabled:** Table the discussion of the research because additional information and/or protocol revisions are required.
- (4) **Disapproved:** The research protocol cannot be approved as proposed.

IRB members use the IRB Member checklist/reviewer form to ensure all criteria for review are considered, met and documented. The decisions will be based on the votes of the majority (more than 50%) of the voting members present at a full board IRB meeting. A scientist and non-scientist must be present at each meeting. In order to initiate a vote, a motion must be made by a voting member of the IRB and seconded. When a motion is not seconded, it does not go forward to a vote. Any motion that is seconded must go forward for a vote unless the person who made the motion withdraws it. If a motion does not pass, then the Chair will ask for another motion, and so on, until a motion passes or is withdrawn.

The IRBA communicates the determinations of the IRB, in writing via email, to the Principal Investigator and co-investigators, if applicable. Meeting minutes are sent to the IO monthly and made available to others within the institution upon request, so all can be aware of the IRB actions.

10.0 Approval with Conditions

When the IRB places conditions on the research protocol, informed consent document, or other research protocol documents, the Principal Investigator's responses and correspondingly revised documents may be reviewed under expedited review procedures. The IRB Chair, experienced designated IRB members, and/or the IRBA ensure that all criteria for review have been considered, and all requirements of the IRB have been met and documented. The IRBA will communicate, in writing, to the Principal Investigator.

11.0 Vulnerable Populations

11.1 IRB Review of Research Involving Fetuses, Pregnant Women, or Human In Vitro Fertilization

When the proposed research involves fetuses, pregnant women, or human in vitro fertilization, the IRB considers the additional protections outlined in Subpart B, of 45 C.F.R. § 46. In addition, the IRB will only review research involving fetuses, pregnant women, and human in vitro fertilization when there are members present who are uniquely qualified by their experience and training to review and approve the research. The IRB's discussions, findings, and determinations are documented in the IRB meeting minutes for each specific research protocol.

11.2 IRB Review of Research Involving Prisoners

When the proposed research involves prisoners, the IRB considers the additional protections outlined in Subpart C of 45 C.F.R. § 46. In addition, the IRB will only review research involving prisoners when there are members present who are uniquely qualified by their experience and training to represent the interests of prisoners in the review and approval of this research. The IRB's discussion, findings and decisions in regard to the requirements of 45 C.F.R. § 46.305 and 45 C.F.R. § 46.306 are documented in the IRB meeting minutes.

11.3 IRB Review of Research Involving Children

When the proposed research involves children, the IRB considers the additional protections and the parental permission and assent procedures outlined in Subpart D of 45 C.F.R. § 46. In addition, the IRB will only review research involving children when there are members present who are uniquely qualified by their experience and training to represent the interests of children in the review and approval of this research. The IRB discussion, findings and determinations in regard to the requirements of 45 C.F.R. § 46.404 through 45 C.F.R. § 46.408 are documented in the IRB meeting minutes.

11.3.1 Assent for Minors

In the State of Wisconsin, only individuals 18 years or older may legally consent to participate in research. Individuals who do not have this authority to consent must still provide assent. "Assent" is an active affirmation to participate in a research study. If the individual giving assent is able to read and write, then assent should be documented using an appropriate IRB Assent or Minor/Parental Consent form template; otherwise, assent should be obtained through dialogue with the subject. The assent discussion and form should be in language understandable

to the subject and contain the similar elements as those stated under “Informed Consent Process and Documentation (based on age and understanding)”

11.4 IRB Review of Research Involving Informed Consent by a Legally Authorized Representative

When the proposed research involves individuals who may not be able to provide informed consent for themselves, the IRB reviews the research to ensure the rights, welfare and autonomy of those individuals are respected. Wisconsin state law allows, under certain specific situations, designated persons to provide substituted judgments for others who may not be completely able to provide informed consent for themselves, specifically parents of minor children and legally appointed guardians. When reviewing research with vulnerable populations, including adults with diminished cognitive capacity and the potential need for other persons to provide consent for subjects, the IRB may seek legal counsel opinion or expert consultation from neuropsychologists or other professionals.

12.0 Continuing Review of Human Subjects Research

The initial approval of research is based on both the Principal Investigator’s presentation of information and the IRB’s assessment of the risks, benefits, and anticipated results of the research as set forth in the protocol application. At the time of initial review the IRB determines a period of approval and the frequency of any continuing review based on the kind and degree of anticipated risk for subjects and/or others. Depending on the degree of risk, the IRB may conduct continuing review at a fully convened meeting or under expedited review procedures.

The IRB may approve the research for a period less than one year when there are concerns regarding the risks of the study or the Principal Investigator’s level of experience or competency to conduct the research, or a history of non-compliance with IRB-approved protocols or institutional policies and procedures. If the IRB believes or finds that an investigator has not conducted the research according to the IRB-approved protocol, the IRB may require verification from sources other than the investigator that no material changes in the conduct of the research have occurred since previous IRB review and approval (e.g., auditing or monitoring of consent documentation). This verification should be in writing and submitted for IRB review along with the Continuing Review Form. Any requirement of verification will be communicated to the Principal Investigator by the IRB in writing with an approval notification for the research.

The IRB conducts continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year. This means that continuing review will occur on or before the one-year anniversary date of the previous IRB review, even though the research activity may not begin or support for the research may not be received until after the IRB approval date. When the IRB has approved the research for a period less than one year, continuing review will occur before the end of the approval period.

12.1 Content of Continuing Review

The IRB reviews the Continuing Review Form and the research protocol. Amendments to the research protocol, informed consent documents, or other supporting documents, may be submitted and reviewed concurrently with the continuing review. The Principal Investigators must submit all of the following for the Continuing Review:

- (1) The most current IRB approved protocol and informed consent document, including amendments.
- (2) The Continuing Review Form that includes:
 - (a) A summary of the progress of the research at UWM and other sites, if appropriate.
 - (b) A summary of any preliminary results or findings from this research at UWM and other sites.
 - (c) A summary of any recent literature, findings, or other relevant information that might affect the risks associated with the research, the risk-benefit analysis, or a subject's willingness to continue participation.
 - (d) The total number of subjects accrued since the initial approval or the last continuing review and the total number of subjects enrolled to date.
 - (e) A summary of recruitment and informed consent process information and mention of any problems.
 - (f) A summary of any unanticipated Adverse Events that have occurred since the initial review or the most recent continuing review, including whether they were of unanticipated frequency and/or severity, related to the research intervention itself, procedure, drug, device or biologic, and whether they modify the risk-benefit analysis, result in modifications to the research protocol to further minimize risk, and/or to the informed consent document.
 - (g) A description of any amendments to the research protocol or informed consent documents that have been reviewed and approved by the IRB since the most recent initial or continuing review approval.
 - (h) Any proposed amendments to the research protocol or informed consent documents.

12.2 Required Continuing Review Determinations

The IRB makes the following determinations in order to approve research for continuation:

- (1) That the research continues to satisfy the criteria set forth in 45 C.F.R. § 46.111 regarding minimizing risks, the anticipated risks remain reasonable in light of the potential for benefit, and there is a plan for an equitable selection of subjects, an adequate informed consent process and documents, provisions for monitoring the data for safety, and provisions to ensure the privacy of subjects and confidentiality of data collected.
- (2) Where applicable, the additional protections for vulnerable subjects such as pregnant women, fetuses, prisoners, and children as specified by regulations and the IRB, are in place and remain adequate.
- (3) That the informed consent documents are accurate and complete, and any significant new findings that may affect a subject's willingness to continue participation have been incorporated into the documents and communicated to research subjects in active treatment, if the IRB determines such information might affect their willingness to continue in the research.

- (4) Whether the research requires verification from sources other than the Principal Investigator (e.g., other institutional review boards, the FDA, Sponsors, or institutional sources or committees) that no material changes in the research have occurred since the previous review. The IRB may request an audit of study files to ensure adequate protections if there are concerns that there may have been material changes without prospective IRB review and approval.

12.3 IRB Continuing Review Processes

12.3.1 Continuing Review under Expedited Review Procedures

For research protocols the IRB initially approved under expedited procedures, the IRB conducts continuing review under expedited procedures unless new risks or information have been identified that warrant full board review. Research protocols previously approved by the full IRB may be eligible for review under expedited review procedures in accordance with 45 C.F.R. § 46.110, under either Category 8 or 9:

Category 8: Continuing review of research previously approved by the full board IRB as follows:

- (1) Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
- (2) Where no subjects have been enrolled and no additional risks have been identified; or
- (3) Where 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 2 through 8 do not apply but the IRB has determined and documented at a full board meeting that the research involves no greater than minimal risk and no additional risks have been identified.

The IRB is informed of all continuing reviews approved under expedited review procedures on the next available meeting agenda and this is documented in the IRB meeting minutes in accordance with 45 C.F.R. § 46.110(c) and 21 C.F.R. § 56.110(c). Meeting minutes are sent to the IO monthly and made available to others within the institution upon request, so all can be aware of the IRB actions.

12.3.2 Continuing Review by the Full Board IRB

For research that was initially approved by the full board IRB, continuing review will also be conducted by the full board IRB using the same procedures used during initial review.

The IRB may make the following decisions:

- (1) **Approved:** Approve as submitted.

- (2) **Approved with Conditions:** Conditional fulfillment is required to secure approval. The Principal Investigator's response may be reviewed through expedited procedures.
- (3) **Tabled:** Table the discussion of the research because additional information and/or protocol revisions are required.
- (4) **Disapproved:** The research protocol cannot be approved as proposed.

The decisions will be based on the votes of a simple majority (more than 50%) of the voting members present at a full board IRB meeting.

The IRBA communicates the determinations of the IRB, in writing via email, to the Principal Investigator and co-investigators, if applicable. Meeting minutes are sent to the IO monthly and made available to others within the institution upon request, so all can be aware of the IRB actions.

12.4 Study Completions and Closeouts

In order for the IRB to maintain accurate records of active studies, whenever a research study is identified by the Principal Investigator as being "completed" (the project has met its design goal) or "closed" (the project was not able to meet its design and unable to be completed as designed), the Principal Investigator must complete and submit the Continuing Review Form to the IRB. Once submitted, the IRB will acknowledge the completion/closing of the study and terminate IRB approval. If a continuing Review Form is not received by the IRB prior to the study expiration date, the study will be closed by the IRB and a close out notification will be sent, via email, to the PI.

13.0 Proposed Modifications to Previously Approved Projects (Amendments)

The Principal Investigator must conduct the research in accordance to the specific methods that were set forth in the application approved by the IRB. UWM policy and the federal regulations require that the Principal Investigator report proposed changes in a previously approved research project promptly to the IRB. No changes in approved research may be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to research subjects.

The IRB may review minor changes in previously approved research during the period for which approval has been given, under expedited review procedures (45 C.F.R. § 46.110 and 21 C.F.R. § 56.110). A '*minor change*' is a change in the research plan that does not increase the risks related to the study (including risks related to procedures and methods, and to modifications that might negatively impact the statistical analysis of the research) (45 C.F.R. § 46.110 and 21 C.F.R. § 56.110).

If the change affects two of the following three aspects of the research, (i) the purpose, (ii) the population or (iii) the procedures; the change cannot be considered '*minor*' and must be reviewed by the full board IRB (if originally approved by the full board as more than minimal risk) or by the IRB Chair or at least one experienced IRB member (if originally approved under expedited procedures or if the full board approved the study as minimal risk).

13.1 Expedited Review of Modifications to Previously Approved Research

Under an expedited review procedure, the review may be carried out by the IRB Chair or by one or more experienced reviewers designated by the Chair from among members of the IRB. The IRB Chair or experienced IRB members use a reviewer guide/checklist, after a pre-review by IRBA, to ensure all criteria for review are considered, met, and documented. The IRBA will communicate, in writing, the review determination to the Principal Investigator.

If the reviewer determines that the amendment involves significant changes or new risks that warrant review by the full board IRB, the amendment will be referred to a full board meeting. The IRB Members conducting the expedited review of the amendment make one of the following determinations:

- (1) **Approved:** Approve as submitted.
- (2) **Approved with Conditions:** Require specific modifications to the protocol necessary to secure approval. IRBA may review submitted revisions.
- (3) **Request modification(s).** A revised protocol and/or supporting materials must be submitted for additional expedited review.
- (4) **Request additional IRB member(s) to review.**
- (5) **Refer to the Full Board:** for review at a full board meeting of the IRB.

The IRB members may not disapprove an amendment to a research protocol under expedited review procedures.

The IRB is informed of all modifications (amendments) to previously approved research protocols reviewed and approved under expedited review procedures on the next available meeting agenda and this is documented in the IRB meeting minutes in accordance with 45 C.F.R. § 46.110(c) and 21 C.F.R. § 56.110(c). Meeting minutes are sent to the IO monthly and made available to others within the institution upon request, so all can be aware of the IRB actions.

The date of approval of an amendment does not change the original approval period or the expiration date by which the regularly scheduled continuing review of the research project should be done.

13.2 Full Board Review of Modifications to Previously Approved Research

Proposed amendments which require review by the full board IRB will be placed on the agenda of one of its regularly scheduled meetings. The IRB makes one of the following determinations:

- (1) **Approved:** Approve as submitted.
- (2) **Approved with Conditions:** Conditional fulfillment is required to secure approval. The Principal Investigator's response may be reviewed through expedited procedures.
- (3) **Tabled:** Table the discussion of the research because additional information and/or protocol revisions are required.
- (4) **Disapproved:** The research protocol cannot be approved as proposed.

The decisions are based on the votes of the majority (more than 50%) of the voting members present at a full board IRB meeting. IRB members are requested to ensure all criteria for continuing review are considered, met, and documented. This also includes the information about the results of the review that the IRBA will communicate, in writing, to the Principal Investigator.

The date of approval of an amendment does not change the original approval period or the expiration date by which the regularly scheduled continuing review of the research project should be done unless the amendment increases the risk to benefit ratio, thus warranting the study to be reviewed more frequently.

14.0 Reporting of Unanticipated Problems Involving Risks to Subjects or Others (Adverse Event Reports)

The IRB is responsible for ongoing monitoring of the safety and welfare of human subjects. Part of this monitoring is ongoing review and assessment of Adverse Events related to participation in the research.

Adverse Events are any occurrences during the conduct of a research study that ultimately harm a subject. Adverse Events may either be related or unrelated.

Adverse Events may be the result of any of the following:

- (1) The interventions and interactions used in the research.
- (2) The collection of identifiable private information in the research.
- (3) An underlying disease, disorder, or condition of the subject.
- (4) Other circumstances unrelated to the research or any underlying disease, disorder, or condition of the subject.

Examples (1) and (2) are events which are related to the study, while (3) and (4) are not.

The Federal regulations at 45 C.F.R. § 46.103(b)(5) and 21 C.F.R. § 56.108(b)(1) require Institutional Review Boards to establish a procedure for “ensuring prompt reporting to the IRB, appropriate institutional officials, and the Department or Agency head, of any unanticipated problems involving risks to subjects or others....” Adverse Events must be reported to the IRB using a Reportable Event Form which can be found on the IRB website and/or on the Online Submission System.

The following three categories of Adverse Events must be reported to the IRB:

- (1) **Adverse Events that are serious, unanticipated, and related or possibly related to participation in the research.** Unanticipated deaths of study subjects should be reported within 24 hours. Other serious and unanticipated Adverse Events need to be reported within 10 working days.
- (2) **Serious Adverse Events that are expected in some subjects, but are determined to be occurring at a significantly higher frequency or severity than expected.** When monitoring a research study, an investigator, a data safety

monitory board/committee, a sponsor, or another entity assigned responsibility for monitoring the research data may detect that a particular type of serious adverse event is occurring in subjects with significantly greater frequency or severity than expected. Adverse Events under this category must be reported within 10 working days.

- (3) **Other unanticipated Adverse Events, regardless of severity, that may alter the IRB's analysis of the risk versus potential benefit of the research and, as a result, warrant consideration of substantive changes in the research protocol or informed consent process/document.** Examples of substantive changes that might need to be considered in response to this category of Adverse Events include: modification of inclusion or exclusion criteria to mitigate the newly identified risks; implementation of additional monitoring procedures of subjects; termination of enrollment of new subjects; modification of informed consent documents to include a description of newly recognized risks; and provision of additional information about newly recognized risks to previously enrolled subjects. Adverse Events under this category must be reported within 10 working days.

At the time of Continuing Review, the Principal Investigator must provide a summary of **serious Adverse Events and unanticipated problems (categories 1-3)** since the last continuing review. In many cases, an appropriate summary would be a statement that there have been no unanticipated problems and that serious Adverse Events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and/or the investigator brochure.

The Principal Investigator is responsible for knowing and adhering to the guidelines of the IRB, proper reporting, and maintaining copies of Adverse Events in the study file. Principal Investigators are also responsible for the accurate documentation, investigation, and follow-up of all possible study-related Adverse Events.

14.1 Adverse Events Review Process

The IRBA or IRB Members review the Adverse Event Reports to determine:

- (1) The effect of the Adverse Events on the risk-benefit relationship associated with the research, (i.e., no change in risks or benefits; increased risks with no change in benefits; or increased risk and decreased benefits).
- (2) Whether the research protocol requires modifications.
- (3) Whether the informed consent process and/or informed consent document requires modification to inform currently enrolled subjects or subjects who have completed their research participation.
- (4) Whether frequency of continuing review should be increased.
- (5) Whether additional safeguards should be implemented to minimize risk and/or maximize the potential for benefit.

14.1.1 When the Adverse Event is referred to the Full Board IRB for review the IRB may:

- (1) Acknowledge that the risk-benefit relationship has not changed and continue monitoring at the current continuing review interval.
- (2) Request further information from the Principal Investigator.
- (3) Require modifications to the research protocol and/or informed consent document or require an addendum to the informed consent document to notify currently enrolled subjects of the situation so they may decide whether they wish to continue participation.
- (4) Require modifications to the research protocol and/or informed consent documents or process for enrollment of new subjects.
- (5) Require notification of subjects who may have completed their participation in the research.
- (6) Shorten the period of IRB approval (decreasing the time interval for continuing review reporting and IRB review).
- (7) Implement additional safeguards (i.e., more frequent specific monitoring).
- (8) Suspend enrollment of new subjects.
- (9) Refer for further review as potential non-compliance.
- (10) Terminate the research.

The IRBA notifies the Principal Investigator, by email, of the IRB's determination and decisions.

If the IRB Chair/Reviewer and/or Full Board IRB determine that research activities should be suspended or terminated, the IRB will notify the IRBA and the IO. If appropriate, the IO will notify the Sponsor, and pertinent federal compliance offices and internal University Administrators.

If the IRB Chair/Reviewer and/or Full Board IRB determine that the event should be referred for review as potential non-compliance, the IRB will notify the IRBA and the IO. If appropriate, the IO will notify the Sponsor, and pertinent federal compliance offices and internal University Administrators.

15.0 IRB Role in Continuous Quality Improvement (CQI)

The IRB has a role in CQI from both the policy perspective and review process perspective to ensure that there is general consistency among the IRB members in applying human subject protections. The IO will meet with the IRB Chair and/or IRBA on a regular basis to identify common issues and concerns of the IRB, and to work towards improvements. In addition, the IO and IRB Chair will include groups of members or the complete IRB membership in activities when needed to improve the overall performance of the IRB review process.

The IRB has the authority to audit or review IRB approved research to ensure the continuing protection of human subjects and compliance with IRB policies and federal regulations.

16.0 IRB Role In Handling Allegations of Non-Compliance

Human subjects research that deviates from the approved protocol, policies, procedures, stipulations, decisions, state, or federal law is non-compliant and subject to further inquiry by the IRB and the IRBA. All reports and complaints of non-compliance should be directed to the IRBA (via email, phone, mail, or in person). The IRBA will investigate all allegations of non-compliance in collaboration with the Chair and the IO. If necessary the IRBA may, under the direction of the IO, send the investigator/s in question a notice requesting the immediate suspension of all specified research activities while the issue of non-compliance is reviewed, consistent with Federal Mandate 45 C.R.F. § 46.113. This initial notice will also include a statement detailing the rationale for the IRB's action. There are three categories of noncompliance: general, serious, and continuing.

- (1) Non-compliance: Any deviation from University of Wisconsin-Milwaukee IRB policies and procedures, federal regulations, or state law is “non-compliance”.
- (2) Serious Non-compliance: All non-compliance substantially affecting participants' rights and / or welfare, or impacting upon the risks or benefits is serious non-compliance.
- (3) Continuing Non-Compliance: Is a pattern of non-compliance that indicates an inability or unwillingness to comply with the regulations or the requirements of the IRB.
- (4) Allegation of Non-Compliance: An unproven assertion of non-compliance.
- (5) Finding of Non-Compliance: Non-compliance that is true in fact. A finding of non-compliance may exist because there is clear evidence, an admission, or an investigation into an allegation has determined the allegation to be true.

All non-compliance will be brought to the attention of the IO. If the general non-compliance is clearly neither serious nor continuing, and there is a corrective action plan that can be readily implemented to prevent recurrence, then the matter may be filed and no further action is needed (for example, failure to sign the application or lost consent forms). Otherwise, the IO will refer allegations and findings of non-compliance to an IRB Non-Compliance Sub-Committee for evaluation. This committee, composed of two members of the IRB and one staff member from the University Safety and Assurances Department, will review the nature of the non-compliance, complete a reviewer form/checklist, and make a recommendation based on each specific case and report to the IRB at the next meeting or within six weeks. The sub-committee will issue recommendations to the IRB for a vote. For allegations of non-compliance the sub-committee will recommend whether the allegation is true or false. For findings of true allegations, the sub-committee considers the following recommendations: modifying the research protocol; modifying the consent process; contacting past or current participants with additional information (for current participants whenever that information might affect their willingness to continue to take part in the research); re-consenting participants; modifying the approval period; suspension; or termination. The IRB non-compliance sub-committee will also recommend whether the non-compliance was serious or continuing.

For serious and/or continuing non-compliance issues, the IRB will review the recommendation of the IRB non-compliance sub-committee at a full board meeting. All IRB members will be provided with a copy of the approved protocol, current consent documents, and the report of the

IRB non-compliance sub-committee with any supporting documents. A member of the IRB noncompliance sub-committee will serve as a primary reviewer. The relevant IRB files, if any, will be made available at the meeting. The IRB may accept or reject the sub-committee's recommendations. If the IRB rejects the subcommittee's recommendations then the IRB may modify the recommendations for successful resolution described by the IRB non-compliance sub-committee. The IRB will assess and vote, within two meetings, upon whether any allegations of noncompliance were true, and whether any findings of non-compliance were serious or continuing. If necessary, the IRB may request additional information before issuing determinations. The IRB reserves the right to request any appropriate additional consultation and expertise to resolve non-compliance.

The IRB functions solely in the role of deciding whether non-compliance of human subject research has occurred and is limited to requiring: modifications to the research protocol and/or consent process; contacting past or current participants with additional information (for current participants whenever that information might affect their willingness to continue to take part in the research); re-consenting participants; modifying the approval period; suspension; or termination of research projects involving the use of human subjects. Any disciplinary actions (against the faculty/staff involved) will be governed by the University Policies and Administration.

All cases of non-compliance which are HHS conducted or supported research where the IRB determines to be serious or continuing noncompliance will be promptly reported to the IO, who will then report the incident to the appropriate federal agencies (e.g., Office of Human Research Protections, Food and Drug Administration, etc.), to appropriate internal University Administrators and to the Graduate School, as potential research misconduct under the Research Misconduct Policy.

All cases of non-compliance which are not HHS conducted or supported research where the IRB determines to be serious or continuing noncompliance will be promptly reported to the IO, who will then report the incident to the Graduate School as potential research misconduct under the Research Misconduct Policy and appropriate internal University Administrators.

17.0 Study Related Complaints

Complaints related to studies will be referred to the IRBA for investigation. The IRBA will consult with the IRB Chair and/or IO for further action.

18.0 Student Investigators

A student who submits an application for new protocol review by an IRB must list a faculty member or academic staff as the Principal Investigator.

Appendix A Glossary

ADVERSE EFFECT An undesirable and unintended, although not necessarily unexpected, result of therapy or other intervention (e.g., headache following spinal tap or intestinal bleeding associated with aspirin therapy).

ASSENT Agreement by an individual not competent to give legally valid informed consent (e.g., a child or cognitively impaired person) to participate in research.

ASSURANCE A formal written, binding commitment that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved [Federal Policy § ____.103].

AUTHORIZED INSTITUTIONAL OFFICIAL An officer of an institution with the authority to speak for and legally commit the institution to adherence to the requirements of the federal regulations regarding the involvement of human subjects in biomedical and behavioral research.

CONFIDENTIALITY The treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure.

EXPEDITED REVIEW Review of proposed research by the IRB chair or a designated voting member or group of voting members rather than by the entire IRB. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research [Federal Policy § ____.110] The research must involve no more than minimal risk and fit one or more of the categories for expedited review procedures as specified in the regulations [45 C.F.R. § 46.110 and 21 C.F.R. § 56.110].

CATEGORY #1:

Clinical studies of drugs and medical devices only when condition (a) or (b) is met. **(a)** Research on drugs for which an investigational new drug application (21 C.F.R. Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.) **(b)** Research on medical devices for which (i) an investigational device exemption application (21 C.F.R. Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

CATEGORY #2:

Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: **(a)** from healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the 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 **(b)** from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an eight-week period and collection may not occur more frequently than two times per week.

CATEGORY #3:

Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a non-disfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) 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 in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; or (j) sputum collected after saline mist nebulization.

CATEGORY #4:

Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

Examples: (a) 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 subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; or (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the 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 as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 C.F.R. § 46.101(b)(4). This listing refers only to research that is not exempt.)

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 behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 C.F.R. §§ 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

CATEGORY #8: (Continuing Review Only)

Continuing review of research previously approved by the convened IRB as follows: **(a)** where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or **(b)** where no subjects have been enrolled and no additional risks have been identified; or **(c)** where the remaining research activities are limited to data analysis.

CATEGORY #9: (Continuing Review Only)

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

FULL BOARD REVIEW Review of proposed research at a convened meeting at which a majority of the membership of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting [Federal Policy § ____.108].

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

- (1) Data through intervention or interaction with the individual, or
- (2) Identifiable private information.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. (45 C.F.R. § 46.102(f))

INFORMED CONSENT A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution, or agents thereof from liability for negligence [Federal Policy § 116; 21 C.F.R. §§ 50.20 and 50.25].

INSTITUTIONAL REVIEW BOARD A specially constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research [Federal Policy §§ ____.102(g), ____.108, ____.109].

MINIMAL RISK Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the 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. (45 C.F.R. § 46.102(i))

OFFICE FOR PROTECTION FROM RESEARCH RISKS (OPRR) The office within the National Institutes of Health, an agency of the Public Health Service, Department of Health and Human Services, responsible for implementing DHHS regulations (45 C.F.R. Part 46) governing research involving human subjects.

PRINCIPAL INVESTIGATOR The scientist or scholar with primary responsibility for the design and conduct of a research project.

PROTOCOL The formal design or plan of an experiment or research activity; specifically, the plan submitted to an IRB for review and to an agency for research support. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data.

RESEARCH A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. (45 C.F.R. § 46.102(d))

RISK The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only “minimal risk.”

VOLUNTARY Free of coercion, duress, or undue inducement. Used in the research context to refer to a subject’s decision to participate (or to continue to participate) in a research activity.