POLICY ON RESEARCH INVOLVING HUMAN SUBJECTS AND THE MDH INSTITUTIONAL REVIEW BOARD (IRB)

I. EXECUTIVE SUMMARY

The Institutional Review Board (IRB) is the unit within the Maryland Department of Health (MDH) (Department) responsible for reviewing research to ensure that the rights, safety, and dignity of human subjects are protected. This policy outlines the processes the IRB will follow in reviewing research protocols and otherwise acting to protect the rights, safety, and dignity of human subjects. It specifies the requirements for protocol submission and approval and details the requirements a researcher must meet when conducting human subject research.

II. BACKGROUND

The IRB was established by the Department in 1977 in response to federal regulations requiring that an organization conducting human subject research with United States Public Health Services funding have that research reviewed and approved by an IRB.

The requirements and procedures in this policy are taken and reprinted, in part, from the Code of Federal Regulations, Title 45, Public Welfare, Part 46, (45 CFR 46). Except where State case law is more protective, for example, in the case of children as research subjects, Title 45 guides the IRB in its deliberation. Additionally, on October 1, 2002, Maryland House Bill 917 *Human Subjects Research-Institutional Review Boards* became effective and was codified at Health General §13-2001 *et seq.* This law makes clear that an individual may not conduct research in Maryland using a human subject unless the research complies with the federal regulations on the protection of human subjects. The IRB also relies on this State statute in its review of research. Further, all clinical investigations using investigational new drugs are reviewed by the Board using the criteria set forth in Title 21 Protection of Human Subjects, Part 50 (21 CFR 50); and Title 21, Institutional Review Boards, Part 56 (21 CFR 56). Each of these documents is hereby incorporated by reference.

All research involving human subjects shall be reviewed by the IRB if any of the following conditions are met:

A. Research is funded with federal, State, or other funds available from or through MDH;

B. Human subjects are patients or clients of MDH;

C. Data sought by the investigator is data held or compiled by or for MDH; or

D. Investigator is an employee of MDH or a student in a residency program at MDH if the employee or student is conducting the research as a function of his employment or training.

This policy version supersedes DHMH 01.03.02 dated December 8, 2014 and September 25, 2012. This version includes numerous changes resulting from revisions made to the federal regulations 45 CFR 46.

III. POLICY STATEMENTS

A. DEFINITIONS.

In this policy the following words have the meaning indicated.

1. **"Assent"** means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

2. **"Children"** means persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable laws of Maryland.

3. **"Clinical trial"** means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

4. **"Conditional approval"** means an action taken by the IRB that involves approving a protocol contingent upon certain minor modifications being made to the protocol or additional materials being submitted for review and approval. A conditional approval may not be granted if basic required elements of a research proposal are omitted.

5. **"Cooperative research projects"** means those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of a human subject and complying with this policy.

6. **"Dead fetus"** means a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

7. **"Delivery"** means complete separation of the fetus from the woman by expulsion or extraction or any other means.

8. **"Fetus"** means the product of conception from implantation until delivery.

9. **"Guardian"** means an individual who is authorized under applicable Maryland law to consent to general medical care on behalf of another individual.

10. **"Human subject"** means a living individual whom an investigator (whether professional or student) conducting research:

a. Obtains information or biospecimens through intervention or interaction with the individual, and uses studies or analyzes the information or biospecimens; or

b. Obtains, uses studies, analyzes or generates identifiable private information or identifiable biospecimens.

11. **"Identifiable biospecimen"** means a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

12. **"Identifiable private information"** means private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

13. **"Interaction"** means communication or interpersonal contact between investigator and subject.

14. **"Intervention"** means both physical procedures by which data is gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

15. **"IRB approval"** means the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional, State and federal requirements.

16. **"Legally authorized representative"** means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in a procedure involved in research. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research

17. **"Minimal risk"** means that the probability and magnitude of risks 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.

18. **"Neonate"** means a newborn.

19. **"Nonviable neonate"** means a neonate after delivery that, although living, is not viable.

20. **"Parent"** means a child's biological or adoptive parent.

21. **"Permission"** means the agreement of a parent or guardian to the participation of his or her child or ward in research.

22. **"Prisoner"** means any individual involuntarily confined or detained in a penal institution including an individual:

a. Sentenced to such an institution under a criminal or civil statute;

b. Detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution;

c. Detained pending arraignment, trial, or sentencing; and

d. Confined in hospitals as a result of a finding of not criminally responsible.

23. **"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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record),

24. **"Program Director"** means a health officer of a local health department, an MDH Administration Director, or designee of either.

25. **"Research"** means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities.

For purposes of this part, the following activities are not deemed research:

a. Scholarly and journalistic activities (e.g., oral history, journalism biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

b. Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

c. Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

d. Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

26. **"Table the Proposal"** means an action taken by the Board whereby a protocol is neither approved nor disapproved, usually occurring because the protocol requires such significant change that it cannot be conditionally approved.

27. **"Viable"** as it pertains to a neonate, means surviving after delivery (given the benefits of available medical therapy) to the point of independently maintaining heartbeat and respiration.

B. AUTHORITY.

1. Code of Federal Regulations, Title 45, Public Welfare, Part 46 (45 CFR 46). This title is the basic Department of Health and Human Services policy for the protection of human research subjects. It contains the standards for the composition and operation of an IRB and provides for the protection of human research subjects in general;

2. Code of Federal Regulations, Title 21, Protection of Human Subjects, Part 50 (21 CFR 50). This Title provides for the protection of human subjects involved in clinical investigations regulated by the Food and Drug Administration;

3. Code of Federal Regulations, Title 21, Institutional Review Boards, Part 56 (21 CFR 56). This Title contains the general standards for the composition and operation of an IRB that reviews clinical trial investigations regulated by the FDA;

4. Maryland Annotated Code, Health General Article §13-2001 *et seq*. This State statute requires that all research conducted in Maryland involving human subjects be conducted according to federal guidelines, regardless of the funding source.

C. BOARD ESTABLISHMENT AND ORGANIZATION.

1. **Establishment.** There is an Institutional Review Board in the Department.

2. **General Membership Qualifications.**

a. The IRB shall be sufficiently qualified through the experience, training, expertise, and diversity of its members to ensure the rights, safety and dignity of human subjects are protected.

b. The IRB shall include as members persons qualified to ascertain the acceptability of proposed research in terms of MDH commitments (including policies and resources), regulations, law, and standards of professional conduct and practice.

c. If the IRB regularly reviews protocols involving category of subjects that are vulnerable to coercion or undue influence, such as populations of children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged individuals, consideration shall be made to include IRB members with knowledge or experience in that area.

d. When appointing members, the Secretary shall strive for diversity and consider potential members' racial and cultural background, gender, profession, and sensitivity to such issues as community attitudes.

3. **Specific Membership Requirements.**

a. The Board shall have at least five (5) and no more than nine (9) members

b. At least one member shall not be affiliated with the Department or have an immediate family member who is affiliated with the Department.

c. At least one member shall have experience, training, or expertise in a scientific area.

d. At least one member shall have experience, training, or expertise in a nonscientific area (e.g. law, ethics, and religion).

e. At least one member shall have knowledge, understanding and appreciation of prison conditions from the perspective of a prisoner.

4. **Appointment and Removal of Members, and Terms of Membership.**

a. The Secretary of MDH may appoint members of the Board and the Board Chairperson.

b. The term of a Board member is four (4) years.

c. The Chairperson shall serve no more than two (2) consecutive terms

d. The Secretary may reappoint a Board member - for an unlimited number of terms.

e. The Chairperson of the IRB shall appoint a Vice Chairperson from among the IRB members, who shall act in the place of the Chairperson in circumstances requiring the Chairperson's withdrawal from participation, or in the absence of the Chairperson.

f. The Secretary may remove a member whom the Secretary finds has been absent from three successive meetings without adequate reason.

5. **Appointment of Alternates.**

a. The Secretary shall appoint alternates to the Board to act on behalf of a member when a member cannot attend a scheduled or special meeting of the Board or is not available to perform expedited reviews.

b. The IRB Chairperson, with the consent of a majority of the other Board members, shall recommend alternates to the Secretary. The alternates should have the same diverse array of backgrounds and expertise as the Board itself (i.e., scientific, nonscientific, not affiliated with MDH, etc.).

c. The Secretary may appoint Board alternates from recommendations submitted by the Chairperson, reject any recommendation and request that a new name be submitted, or appoint an alternate as the Secretary finds appropriate.

d. An approved alternate shall attend a scheduled or special meeting of the IRB or review expedited protocols when an appointed board member cannot be available.

e. Alternates, when acting on behalf of a regular board member, shall have all the privileges and voting rights of the regular board member.

6. **Outside Expertise.**

The IRB may invite individuals with competence in special areas to assist in the review of complex issues that require expertise beyond or in addition to that available on the Board. These individuals may not vote with the IRB.

D. BOARD QUORUMS AND MEETINGS, STAFF AND COMPENSATION.

1. The Chairperson of the IRB shall schedule meetings of the IRB, as necessary, but no fewer than six times per year.

2. The first meeting of each year shall be held in January and every other month thereafter.

3. At the January meeting, the Chairperson shall inform the Board in writing of the date, time, and place of the other meetings for the year.

4. A scheduled meeting may be canceled by the Chairperson of the IRB if:

a. There is no business for the IRB to transact; or

b. There is an emergency.

5. A majority of members of the IRB shall constitute a quorum. A quorum may be achieved with one or more members participating by telephone conferencing.

6. At least one member who has experience, training, or expertise in a nonscientific area shall be present for the IRB to review proposed research, annual reviews or research modifications unless the research is subject to expedited review.

7. In accordance with the State budget, the Department shall employ the staff necessary to serve the Board and carry out the mandates of this policy.

8. A member of the Board may not receive compensation but may, in accordance with the State budget, be reimbursed for expenses at a rate determined by the Secretary.

E. GENERAL DUTIES AND RESPONSIBILITIES OF THE BOARD.

1. The Board is responsible for determining what constitutes "research" in accordance with 45 CFR 46.102 (l). When making this determination the Board considers the purpose of the research. Many quality improvement activities are not considered research, however in some cases quality improvement activities are designed to accomplish a research purpose as well as the purpose of improving the quality of care, and in these cases the Board may determine that the activity is research. The following activities are not considered research, but determination is responsibility of the Board:

   a. Quality improvement activities conducted by one or more institutions whose purposes are limited to (i) implementing a practice to improve the quality of patient care or client services; and (ii) collecting patients, clients, or provider data regarding the implementation of the practice for clinical practical or administrative purposes; and

   b. Quality improvement activities conducted by one or more institutions who purposes are limited to: (i) implementing a practice to improve the quality of patient care or client services; and (ii) measuring and reporting provider performance data for clinical, practical, or administrative uses.

2. The Board shall review proposed research projects to assure that the rights, safety and dignity of individuals who participate in research are protected.

3. A Board member may not participate in an initial or continuing review of a research project in which the member has a conflicting interest, except to provide information requested by the IRB.

4. The IRB may suspend or terminate approval of any research that the IRB finds is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects.

5. The Board shall maintain a record of its activities in accordance with Part III, Section L. of this policy.

6. The Board may conduct on-site reviews of the use of approved consent form, measures, surveys or questionnaires and confidentiality procedures of any research project to ensure the continued rights, safety and dignity of the human subjects and adherence to State and federal law and regulations.

7. The IRB shall comply with all applicable State and federal law and regulations.

8. The IRB may require the following individuals to complete training in the responsible conduct of research at least every three (3) years:

a. Principal investigators and research staff;

b. Board members; and

c. Other Departmental employees engaged in human subject research.

F. RESEARCH SUBJECT TO OR EXEMPT FROM BOARD REVIEW.

1. The following research is subject to Board review:

a. Research involving human subjects that is funded with federal, State, or other funds available from or through MDH;

b. Research involving human subjects who are patients or clients of MDH;

c. Research involving human subjects that is directed or carried out by employees of MDH or students in a residency program at MDH if it is carried out as a function of the employee's or student's employment or training;

d. Research involving data that is held or compiled by or for the Department, except that, in collaboration with the appropriate Departmental unit, the Board may devise a plan for release of data in a manner that need not be individually reviewed by the Board.

2. In accordance with 45 CFR 46.104(d), the IRB may exempt the following types of research from review:

a. Research conducted in established or commonly accepted educational settings specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

b. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

1) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

2) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability, or be damaging to the subjects' financial standing, employability, or reputation; or

3) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can be readily ascertained, directly or through identifiers linked to the subjects, and the IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7).

c. Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

1) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

2) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

3) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and the IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7).

d. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

1) The identifiable private information or identifiable biospecimens are publicly available;

2) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

3) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes as describes under 45 CFR 164.512(b); or

4) The research is conducted by, or on behalf of, a federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44U.S. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5U.S.C. 552a, and if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

e. Research and demonstration projects that are conducted or supported by a federal department or agency or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs. Such projects include but are not limited to, internal studies by federal employees, and studies under contracts or consulting arrangements, cooperative agreement or grants. Exempt projects also include waivers of otherwise mandatory requirement using authorities such as section 1115 and 1115A of the Social Security Act, as amended.

Each federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible federal website or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

f. Taste and food quality evaluation and consumer acceptance studies:

1) If wholesome foods without additives are consumed, or

2) If a food is consumed that contains a food ingredient at or below the level 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.

g. Storage or maintenance for secondary research for which broad consent is required; Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if the IRB conducts a limited IRB review and makes the determinations required by 45 CFR 46.111(a)(8).

h. Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

1) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with 45 CFR 46.116(a)(1) through (4), (a)(6), and (d);

2) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with 45 CFR 46.117;

3) The IRB conducted a limited IRB review and makes the determination required by 45 CFR 46.111(a)(7) and makes the determination that the research conducted is within the scope of the broad consent referenced in (h)(1) of this section; and

4) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by a legal requirement to return individual research.

i. Research involving children in survey or interview procedures or observations of public behavior are not exempt from IRB review except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.

G. PROTOCOL SUBMISSION PROCEDURES, APPROVAL CRITERIA, AND BOARD DECISIONS.

1. If a project is research involving human subjects, the principal investigator shall apply to the Board for approval before beginning work on the project, including beginning any data collection.

2. If a research project is undertaken without the intention of involving human subjects but later proposes to involve human subjects, the principal investigator shall first obtain the approval of the Board

3. The principal investigator shall apply in the manner and on a form required by the Board. For new research projects, the principal investigator shall submit to the Board 10 days prior to the next scheduled meeting:

a. A completed application form (MDH Form 2124 or MDH Form 4804);

b. A research protocol (not required for MDH Form 4804);

c. An abstract summary of the research plan clearly describing the details of the study design including specific procedures for safeguarding the rights of human subjects;

d. If the research is to be conducted in collaboration with another institution, a copy of the approval granted by that institution's IRB;

e. A copy of all forms applicable to the protocol (e.g. disclosure statements, consent forms, recruitment flyers, interview scripts, questionnaires, data collection forms);

f. Proof of approval from the applicable MDH Program Director(s); and

g. Any other documentation requested by the Board that will assist the Board in making a reasoned decision.

4. The Chair of the IRB or the Chair's designee shall review each proposal received and may:

a. Subject the proposal to a full Board review; or

b. Send the proposal for expedited review or limited review.

5. If a proposal is subject to review by the full Board, and all documentation is submitted to the Board by 10 days prior to the next scheduled meeting, the Board staff shall:

a. Place the research project on the Board agenda for the upcoming meeting.

b. Notify the principal investigator in writing prior to the scheduled meeting to review their protocol and invite the principal investigator to attend.

6. **Assigning a Proposal to a Board Member.**

a. In a full Board review, Board staff shall assign a proposal to a Board member who will act as the primary reviewer.

b. Board staff shall consider the following criteria when assigning a proposal to a Board member:

1) The Board member's training, experience and expertise;

2) The number of research projects assigned to the Board member; and

3) Any other federal or State requirements.

7. **Criteria for Approval.**

In order to approve a new research proposal, the IRB shall determine that all of the requirements in 45 CFR 46 and this policy, and if applicable 21 CFR 50 and 21 CFR 56 are satisfied. The IRB shall determine that:

a. Risks to subjects are minimized:

1) By using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk; and

2) Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

b. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

c. Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

d. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116.

e. Informed consent will be appropriately documented or appropriately waived in accordance with 45 CFR 46.117.

f. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

g. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

8. **BOARD DECISIONS.**

The staff of the IRB shall notify the principal investigator within 10 days after the convened meeting with the Board's decision.

a. After review, the Board shall make one of the following determinations for all research activities (including exempt research activities under 45 CFR 46.104 for which limited IRB review is a condition of exemption (under 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(c) and (d)(7), and (8):

1) Approve the proposal as submitted;

2) Conditionally (require changes and or additional information to secure approval) approve the proposal;

3) Table the proposal; or

4) Disapprove the proposal as submitted.

b. Conditional Approval.

The Board may require specific changes to the research protocol or consent document(s), confirm specific assumptions or understandings on how the research will be conducted or require the principal investigator to submit additional documents for protocol approval. The approval of the protocol is contingent on the receipt and review of the conditions. The principal investigator will receive written details of the requirements for approval within 5 days after the review. If the Board conditionally approves a proposal, the principal investigator has 60 days from the date of the contingency letter to meet the conditions or to request in writing, additional time. If the conditions are not met or additional time is not requested within the 60 days, the principal investigator will have to re-apply for approval of the proposal. The research may not proceed until the IRB reviews and approve the submitted documents.

c. Tabled.

When the Board is unable to approve a research protocol at a convened meeting because they are unable to make determinations required for approval. The Board will require changes to the protocol or consent document(s), or clarifications or additional documents to be submitted 10 days prior to the next scheduled IRB meeting. The research may not proceed until the IRB reviews and approves the revised protocol at a convened meeting.

d. Disapproval.

1) If the Board does not approve a proposal as submitted, the principal investigator may:

i. Request reconsideration of the proposal or question a recommendation, in writing; or

ii. Request a special meeting at which additional information or supporting testimony of others may be presented.

2) If the principal investigator requests a special meeting the Chairperson shall convene a special meeting of either the full IRB or subcommittee within 90 days.

H. MODIFICATIONS AND CONTINUING REVIEW.

1. A modification to a research project is:

a. Any change to the research design plan;

b. Any change to any documents used in the study;

c. Any change in the type of study subject sought;

d. Any change that alters the risk-benefit balance; and

e. Any other change affecting any of the human subjects.

2. Before a research project is modified, a principal investigator shall:

a. Complete MDH Form 4664;

b. Notify the appropriate MDH Program Director and the IRB; and

c. Obtain the approval of the Administration Director and the IRB.

3. The Chairperson or his or her designee may send the request for modification to either the full Board or for expedited review.

4. Any modification(s) to a protocol that has been deemed exempt by the Board shall be submitted and reviewed by the IRB to determine if the modification changes the exempt status of the protocol.

5. **Continuing Review**.

a. Each research project shall be reviewed at least once each year before the expiration date of the prior years' IRB approval. Unless the IRB determines otherwise, continuing review is not required in the following circumstances:

1) Research eligible for expedited review in accordance with 45 CFR 46.110;

2) Research reviewed by the IRB in accordance with the limited IRB review described in 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8); or

3) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

i) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

ii) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

b. For continuing review, the principal investigator shall submit to the Board 45 days prior to the expiration of the prior approval date:

1) A completed renewal form (MDH form 2125);

2) A summary describing the current status of the project, including any activities proposed to be conducted the following 12 months;

3) A description of any proposed changes to the research design or procedure; and

4) Proof of continued approval of any other applicable IRB.

I. EXPEDITED REVIEW.

1. The Chairperson of the IRB may conduct or authorize another member(s) to use an expedited review procedure in accordance with 45 CFR 46.110 and 21 CFR 56.110 to review the following:

a. Some or all of the research procedures listed in paragraph 5 of this section, unless the reviewer determines that the study involves more than minimal risk;

b. Minor changes in previously approved research during the period for which approval is authorized; or

c. Research for which limited IRB review is a condition of exemption under 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7) and (8). The Chairperson of the IRB may conduct or authorize another member(s) to use a limited review procedure. The IRB need not make the determinations at section G(8) of this policy. The following determinations shall be made during limited review:

1) Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is:

i) Obtained in accordance with the requirement of 45 CFR 46.116(a)(1)-(4), (a)(6), and (d); and

ii) Appropriately documented, or waiver of documentation is appropriate, in accordance with 45 CFR 46.117;

2) If a change is made for research purposes in the way the identifiable private information or identifiable private biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data; and

3) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

2. Under an expedited review procedure, the reviewers may exercise all of the authorities of the IRB except the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with 45 CFR 46.108(b).

3. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risk related to invasion of privacy and breach of confidentiality are no greater than minimal.

4. The standard requirements for informed consent (or its waiver or alternation) apply.

5. At the discretion of the Board, the following categories of research may be subject to expedited review. Categories a. through i. pertain to both initial and continuing IRB review.

a. Clinical studies of drugs and medical devices only when the following is met.

1) Research on drugs for which an investigational new drug application (21CFR 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.)

2) Research on medical devices for which

i. an investigational device exemption application (21CFR 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.

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

1) From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or

2) 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 8-week period and collection may not occur more frequently than 2 times per week.

c. Prospective collection of biological specimens for research purposes by noninvasive means. Examples include:

1) Hair and nail clippings in a non-disfiguring manner;

2) Deciduous teeth at time of exfoliation, or if routine patient care indicates a need for extraction;

3) Permanent teeth if routine patient care indicates a need for extraction;

4) Excreta and external secretions (including sweat);

5) 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;

6) Placenta removed at delivery;

7) Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;

8) 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;

9) Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; and

10) Sputum collected after saline mist nebulization,

d. 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 include:

1) 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;

2) Weighing or testing sensory acuity;

3) Magnetic resonance imaging;

4) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; and

5) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

e. 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).

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

g. 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 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

h. Continuing review of research previously approved by the convened IRB as follows:

1) Where the research is permanently closed to the enrollment of new subjects, all subjects have completed all research-related interventions, and 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.

i. Continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories a. through h. 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.

6. When a proposal is sent for expedited review, it shall be reviewed by at least two Board members who must agree on the disposition of the proposal, except that a proposal may not be disapproved by expedited review.

7. If the proposal is not approved by both reviewers, or if a reviewer requests that the proposal be deferred to the full Board, the proposal will be referred for convened IRB review.

8. Board members will receive monthly reports of all protocols or modifications to protocols approved through an expedited review process via email.

J. ADVERSE EVENTS, UNANTICIPATED PROBLEMS, TERMINATIONS AND SUSPENSIONS.

1. The principal investigator shall promptly report to the IRB, and any others required by law or regulation, any information regarding adverse events or unanticipated problems involving risk to human subjects.

2. The Chair of the Board shall report to the appropriate Administration Director, the Secretary, and if federal funding is involved, the appropriate federal agency, an adverse event or unanticipated problems involving risk to human subjects.

3. **Suspension or Termination of Approval**

a. The IRB may suspend or terminate its approval of research that:

1) Is not being conducted in accordance with the IRB's requirements;

2) Is not being conducted in accordance with State or federal law or regulation; or

3) Has been associated with an adverse event or unexpected harm to subjects.

b. If the IRB suspends or terminates approval of a research project, the IRB shall:

1) Promptly notify the principal investigator, the Secretary, the appropriate Administration Director, and, if federal funding is involved, the federal funding agency; and

2) Include a written statement of the reasons for the IRB's action in the notification.

K. COOPERATIVE RESEARCH PROJECTS.

1. In a Cooperative Research Project, the MDH IRB may:

a. Enter into a joint review arrangement with another institution's IRB;

b. Rely upon the review of another qualified IRB; or

c. Make any other similar arrangement to avoid duplication of effort.

2. The IRB's decision to defer review of a Cooperative Research Project to a cooperating institution will be determined by the federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the federal department or agency supporting the research.

3. When a proposed research project is reviewed by a cooperating institution's review board the principal investigator shall submit to the MDH IRB, a copy of the cooperating institution's IRB initial approval and any continuing approval, any request for modification, and notification of any serious adverse event.

4. Under 45 CFR 46.114, when the Department relies on the review of a cooperating institution's IRB, the Department retains responsibility for safeguarding the rights, safety, and dignity of the human subjects.

L. RECORDS.

1. **Records Kept by the IRB.**

a. The IRB shall prepare and maintain adequate documentation of its activities, including the following:

1) A copy of each research proposal reviewed; if applicable, a scientific evaluation of the proposal; if applicable, an approved consent form for each proposal; any progress report submitted by an investigator for a proposal; and, each report of a serious adverse event;

2) Minutes of IRB meetings, in sufficient detail to show attendance at the meeting; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; the discussion in summary form of controversial issues and their resolution; reasons for waiving documented informed consent; reasons for waiving any part or all of informed consent as stated in Section M of this policy;

3) Records of continuing review activities, including rationale for conducting continuing review of research that otherwise would not require continuing review as described in 45 CFR 46.109(f)(1);

4) Copies of all correspondence between the Board and the investigator;

5) A list of IRB members in the detail set forth in 45 CFR 46.108(a)(2);

6) Written procedures for the IRB in the detail set forth in 45 CFR 46.108(a)(3) and (4); and

7) Rationale for an expedited reviewer's determination under 45 CFR 46.110(b)(1)(i) that research appearing on the expedited review list described in 45 CFR 46.110(a) is more than minimal risk.

b. The IRB shall retain the records required by this policy for at least 3 years after completion of the research.

c. The IRB shall ensure that its records are accessible for inspection and copying by authorized representatives of the federal government at reasonable times and in a reasonable manner.

2. **Records Kept by the Principal Investigator.**

a. Except when required by State or federal law or regulation, research records with personal identifiers may not be retained beyond the period of time specified in the proposal, consented to by the subjects, and approved by the Board.

b. When a study has been completed, the principal investigator shall dispose of records that include personal identifiers in a manner approved by the Board.

c. The principal investigator shall provide an annual summary on confidentiality measures for all research data with personal identifiers that is retained after the completion of the study until the data is destroyed.

d. A principal investigator may not use Departmental data or research records with personal identifiers approved for use in one study for any other reason or in any other manner not specified in the proposal.

e. A principal investigator shall ensure that records are accessible for inspection and copying by an authorized representative of the Board at any reasonable time and in a reasonable manner.

M. INFORMED CONSENT.

1. **General Requirements of Informed Consent.**

General requirements for informed consent, whether written or oral, are set forth in this paragraph and apply to consent obtained in accordance with the requirements set forth in paragraphs (2) through (4) of this section. Broad consent may be obtained in lieu of informed consent obtained in accordance with paragraphs (2) and (3) of this section only with respect to the storage, maintenance, and secondary research uses of identifiable private information and identifiable biospecimens. Waiver or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of State or local

officials is described in paragraph (5) of this section. General waiver or alteration of informed consent is described in paragraph 6 of this section. Except as provided elsewhere in this policy:

a. Before involving a human subject in research covered by this policy, an investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative.

b. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.

c. The information that is given to the subject or the legally authorized representative shall be in language (including sign language or alternative learning format) understandable to the subject or the legally authorized representative.

d. The prospective subject or the legally authorized representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.

e. Except for broad consent obtained in accordance with paragraph (4) of this section:

1) Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension; and

2) Informed consent as a whole must present information in sufficient detail relating to the research and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.

f. No informed consent may include any exculpatory language through which the subject or the legal authorized representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

2. **Basic Elements of Informed Consent.**

Except as provided in paragraph (4), (5) or (6) of this section, in seeking informed consent the following shall be proved to each subject or the legally authorized representative:

a. A statement that the study involves research;

b. An explanation of the purposes of the research and the expected duration of the subject's participation;

c. A description of the procedures to be followed;

d. Identification of any procedures that are experimental;

e. A description of any reasonably foreseeable risks or discomforts to the subject;

f. A description of any benefits to the subject or to others that may reasonably be expected from the research;

g. Disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

h. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

i. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

j. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;

k. A statement 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; and

l. One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

1) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or

2) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

3. **Additional Elements of Informed Consent.**

Except as provided in paragraph (4), (5), or (6) of this section, one or more of the following elements of information when appropriate shall also be provided to each subject or the legally authorized representative:

a. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable;

b. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or the legally authorized representative's consent;

c. Any additional costs to the subject that may result from participation in the research;

d. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

e. A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject;

f. The approximate number of subjects involved in the study;

g. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;

h. A statement regarding whether clinically relevant research results including individual research will be disclosed to subjects and if so under what conditions; and

i. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e. sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

4. Elements of broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens. Broad consent for the storage maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or nonresearch purposes) is permitted as an alternative to the informed consent requirements in paragraphs (2) and (3) of this section. If the subject or the legally authorized representative

is asked to provide broad consent, the following shall be provided to each subject or the subject's legally authorized representative:

a. The information required in paragraphs (2)(e), (2)(f), and (2)(h) and when appropriate, (3)(g) and (3)(i) of this section;

b. A general description of the type of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted;

c. A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens;

d. A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite);

e. Unless the subject or legally authorized representative will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies;

f. Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject; and

g. An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.

5. **Waiver or Alteration of Consent in Research Involving Public Benefit and Service Programs Conducted by or Subject to the Approval of State, or Local Officials.**

a. Waiver. The IRB may waive the requirement to obtain informed consent for research under paragraphs (1) through (3) of this section, provided the IRB satisfies the requirements of paragraph (5)(c) of this section. If an individual was asked to provide broad consent for the

storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at paragraph (4) of this section and refused to consent, The IRB cannot waive consent for the storage, maintenance or secondary research use of the identifiable private information or identifiable biospecimens.

b. An Alteration. The IRB may approve a consent procedure that omits some or alters some or all of the elements of informed consent set forth in paragraphs (2) and (3) of this section provided the IRB satisfies the requirements of paragraph (6)(c) of this section. The IRB may not omit or alter any of the requirements described in paragraph (1) of this section. If a broad consent procedure is used, the IRB may not omit or alter any of the elements required under (4) of this section.

c. Requirements for Waiver and Alteration. In order for the IRB to waive or alter consent as described in this subsection, the IRB must find and document that:

1) 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

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

6. **General Waiver or Alteration of Consent.**

a. Waiver. The IRB may waive the requirements to obtain informed consent for research under paragraphs (1) through (3) of this section, provided the IRB satisfies the requirements of paragraph (6)(c) of this section. If an individual was asked to provide broad consent for the storage maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at paragraph (4) of this section, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

b. Alteration. The IRB may also approve a consent procedure that omits some or alters some or all of the elements of informed consent set

forth in paragraphs (2) and (3) of this section, provided the IRB satisfies the requirements of paragraph (6)(c) of this section. The IRB may not omit or alter any of the requirements described in paragraph (1) of this section. If a broad consent procedure is used, the IRB may not omit or alter any of the elements required under paragraph (4) of this section.

c. Requirements for Waiver and alteration. In order for the IRB to waive or alter consent as described in this subsection, the IRB must find and document that:

1) The research involves no more than minimal risk to the subjects;

2) The research could not practically be carried out without the requested waiver or alteration;

3) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;

4) The waiver or alteration will not adversely affect the rights and welfare of the subjects; and

5) Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

7. **Screening, Recruiting, or Determining Eligibility.** The IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

a. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or

b. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

8. **Posting of Clinical Trial Consent Form.**

a. For each clinical trial conducted or supported by a federal department or agency, one IRB approved informed consent form used to enroll subjects must be posted by the awardee or the federal department or agency component conducting the trial on a publicly available federal website that will be established as a repository for such informed consent forms.

b. If the federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a federal website (e.g. confidential commercial information), such federal department or agency may permit or require redactions to the information posted.

c. The informed consent form must be posted on the federal website after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

9. **Preemption.** The informed consent requirements in this policy are not intended to preempt any applicable federal, State or local laws (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe) that requires additional information to be disclosed in order for informed consent to be legally effective.

10. **Emergency Medical Care.** Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent that the physician is permitted to do so under applicable federal, State, or local law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe).

11. **Documentation of Informed Consent**

a. Unless documentation is waived under Section M12 of this policy, informed consent shall be documented by the use of a written informed consent form.

b. The form shall be approved by the IRB and signed (including in an electronic format) by the subject or the subject's legally authorized representative.

c. A written copy shall be given to the person signing the informed consent form.

d. The consent form may be either of the following formats:

1) A written informed consent form that meets the requirement of Section M of this policy. The investigator shall give either the subject or the representative adequate opportunity to read the informed consent form before it is signed; alternatively, this form may be read to the subject or the subject's legally authorized representative.

2) A short form written informed consent form stating that the elements of informed consent required by Section M of this policy have been presented orally to the subject or the subject's legally authorized representative and that the key information required by Section M (1)(e)(1) of this policy was presented first to the subject, before other information, if any was provided. The IRB shall approve a written summary of what is to be said to the subject or the legally authorized representative. When this method is used,

there shall be a witness to the oral presentation. The IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the subject's legally authorized representative, in addition to a copy of the short form.

e. The IRB's approval stamp must appear on all informed consent documents signed by subjects.

12. **Waiver of Documentation.**

a. The IRB may waive the requirement for the investigator to obtain a signed informed consent form for some or all subjects if it finds any of the following:

1) That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. In such cases, each subject (or legally authorized representative) shall be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern;

2) That 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; or

3) If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

b. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding the research.

N. ADDITIONAL PROTECTIONS FOR SPECIAL POPULATIONS.

1. **Pregnant Women and Fetuses.**

Pregnant women and fetuses may be involved in research if the following conditions are met:

a. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

b. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;

c. Any risk is the least possible for achieving the objectives of the research;

d. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accordance with the informed consent provisions of 45 CFR 46 subpart A;

e. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accordance with the informed consent provisions of 45 CFR 46 subpart A except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, temporary incapacity, or the pregnancy resulted from rape or incest;

f. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

g. For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accordance with the provisions of 45 CFR 46 subpart D;

h. No inducements, monetary or otherwise, may be offered to terminate a pregnancy;

i. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

j. Individuals engaged in the research will have no part in determining the viability of a neonate.

2. **Neonates.**

a. Neonates of uncertain viability and nonviable neonates may be involved in research if all the following conditions are met:

1) Studies have been conducted and provide data for assessing potential risks for neonates.

2) Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

3) Individuals engaged in the research will have no part in determining the viability of a neonate.

4) The requirements of subparagraph 2b or 2c of this paragraph have been met as applicable.

b. Until it has been ascertained whether a neonate is viable, a neonate may not be involved in research covered by this policy unless the following additional conditions are met:

1) The IRB determines that:

i) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective; or

ii) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

2) The legally effective informed consent of either parent of the neonate, or if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accordance with Section M of this policy, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

c. After delivery, a nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:

1) Vital functions of the neonate will not be artificially maintained;

2) The research will not terminate the heartbeat or respiration of the neonate;

3) There will be no added risk to the neonate resulting from the research;

4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

5) The legally effective informed consent of both parents is obtained in accordance with Section M of this policy, except that

the waiver and alteration provisions of §46.116(c) and (d) do not apply.

d. A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted and in accordance with the requirements of Part III, Sections A—M of this policy and subparagraph 5) above.

3. **Placenta, Dead Fetus or Fetal Material.**

a. Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accordance with any applicable federal, State, or local laws and regulations regarding such activity.

b. If information associated with material described above in subparagraph 3a. is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent portions of this policy are applicable.

4. **Prisoners**.

a. In addition to satisfying the requirements of Part II I, Sections. A—M this policy, the IRB shall also meet the following specific requirements when prisoners are involved:

1) Majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB; and

2) At least one member of the IRB shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by the MDH IRB and another IRB, only one IRB need satisfy this requirement;

b. The IRB may approve research involving prisoners only if it finds that:

1) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

2) The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;

3) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the

group of available prisoners who meet the characteristics needed for that particular research project;

4) The information is presented in language that is understandable to the subject population;

5) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

6) Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

c. Only the following categories of research may involve prisoners:

1) Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

2) Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

3) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that with respect to federally funded research the study may proceed only after the Secretary of DHHS has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research; or

4) Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research.

5. **Children**.

When children are involved, the IRB may approve research that satisfies the following conditions:

a. If the research does not involve greater than minimal risk, the IRB shall find that adequate provisions are made for soliciting assent of the children and the permission of the parents or guardians.

b. If the more than minimal risk to the child is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, before approving, the IRB shall find that:

1) The risk is justified by the anticipated benefit to the subjects;

2) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and

3) Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.

c. Requirements for permission by parents or guardians and for assent by children:

1) In addition to the determinations required under other applicable sections of this policy, the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accordance with Section M.5 of this policy.

2) In addition to the determinations required under other applicable sections of this policy, the IRB shall determine, in accordance with and to the extent that consent is required by Section M that adequate provisions are made for soliciting the permission of each child's parents or guardian. In addition to the provisions for waiver contained in, Section M.5 if the IRB

determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in this Policy provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, State, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

3) Permission by parents or guardians shall be documented in accordance with and to the extent required by Section M.

4) When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

5) If the IRB determines that a research protocol is designed for conditions or subject population for which parental or guardian permission is not a reasonable requirement (for example abused or neglected children), it may waive the requirements of permission provided that:

i) An appropriate mechanism for protecting child participants is substituted; and,

ii) The waiver is not inconsistent with federal, State, or local law;

6. **Wards.**

a. Children who are wards of the State or any other agency, institution, or entity may be included in research involving greater than minimal risk and no prospect of direct benefit to individual subjects but likely to yield generalizable knowledge about the subject's disorder or condition only if such research is:

1) Related to their status as wards; or

2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

b. If the research is approved under this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or *in loco parentis*. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

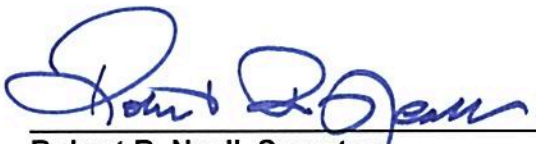
7. **Other Subject Categories**.

Where federal regulations do not cover a particular category of subject, it shall be the IRB's responsibility to ensure that the risk of harm is minimized and that informed consent has been obtained.

IV. REFERENCES

- **Code of Federal Regulations**
  - **Title 45, Public Welfare, Part 46 (45 CFR 46)**
    http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html
  - **Title 21, Protection of Human Subjects, Part 50 (21 CFR 50)**
    http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50
  - **Title 21, Institutional Review Boards, Part 56 (21 CFR 56)**
    http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56
- **Maryland Annotated Code**
  - **Health General Article §13-2001- Et seq.**
    http://mgaleg.maryland.gov/webmga/frmStatutesText.aspx?article=ghg&section=13-2001&ext=html&session=2019RS&tab=subject5
- **MDH OIG Institutional Review Board Web Site**
  http://www.health.maryland.gov/oig/irb
- **Department of Health and Human Services- Office for Human Research Protections**
  https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/quality-improvement-activities/index.html

Approved:



Robert R. Neall, Secretary

12/11/19

December 11, 2019