

Massachusetts Executive Office of
Health and Human Services

Department of Public Health



Department of Public Health

CONDUCT OF HUMAN SUBJECT RESEARCH

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Section 1.0 Introduction

- 1.1 Assurance Statement**
- 1.2 Applicability**
- 1.3 Ethical Principles**
- 1.4 Policy**

1.1 Assurance Statement

- .1 The Massachusetts Department of Public Health, hereinafter known as “MDPH,” hereby gives assurance that it will comply with the U.S. Department of Health and Human Services (DHHS) regulations for the protection of human research subjects, 45 CFR Part 46, and U.S. Food and Drug Administration (FDA) regulations for the protection of human subjects, 21 CFR Part 50 and 56, as amended. This policy applies to all research conducted under the terms of MDPH’s Federalwide Assurance established with DHHS. Under this policy, all research involving human subjects under the jurisdiction of MDPH shall be reviewed and approved by MDPH’s Institutional Review Board, hereinafter referred to as the IRB, or by another institutional review board with whom an IRB Authorization Agreement has been executed.
- .2 This document describes the procedures at MDPH to fulfill the requirements of the DHHS Office for Human Research Protections (OHRP) specified in 45 CFR Part 46, the Food and Drug Administration (FDA) regulations in 21 CFR Part 50 and Part 56, and the requirements of Chapter 94C of the Massachusetts General Laws. H3 Sub-Paragraph

1.2 Applicability

- .1 Except for research in which the only involvement of humans is in one or more of the categories exempted under Section 46.101(b)(1-6) or waived under 46.101(i) of Title 45, this policy applies to all research involving human subjects in which an MDPH employee or agent is engaged, consistent with guidance from OHRP. Engagement may include one or more of the following:
 - a) The research is funded by MDPH; or
 - b) The research is conducted by or under the direction of any employee or agent of MDPH in connection with his or her job responsibilities; or
 - c) An employee or agent of MDPH is collaborating on a research project being conducted by a non-MDPH investigator; or
 - d) The research is conducted pursuant to a direct federal award received by MDPH to conduct human subject research, even where all activities involving human subjects are carried out by a subcontractor or collaborator.

When, for purposes of the research, MDPH employees or agents carry out the following activities, the MDPH is engaged:

- Intervene by performing invasive or noninvasive procedures or manipulating the environment (e.g., drawing blood, providing counseling, orchestrating environmental events);

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- Interact with any human subject of the research (e.g., interviews, questionnaires);
- Obtain data about the subjects of the research through intervention or interaction with them;
- Obtain identifiable private information about the subjects of the research;
- Obtain identifiable biological specimens from any source; or
- Obtain the informed consent of human subjects for the research.

In these situations, the employees or agents are individuals acting on behalf of the institution (MDPH), exercising institutional authority or responsibility, or performing institutionally designated activities.

- .2 MDPH would NOT be engaged if the role of MDPH employees or agents is limited to:

- Informing prospective subjects about the availability of the research;
- Providing prospective subjects with information about the research (i.e., informed consent document or other IRB-approved materials) or about contacting investigators for information or enrollment;
- Seeking or obtaining the prospective subjects' permission for investigators to contact them;
- Authorship of a paper, journal article or presentation describing a human subjects research study;
- Use of MDPH facilities for intervention or interaction with subjects by investigators from another institution;
- Release, to investigators from another institution, identifiable private information or biological specimens pertaining to the subjects of the research;
- Accessing or reviewing identifiable private information for purposes of study auditing; or
- Receipt of identifiable private information for purposes of satisfying US FDA reporting requirements.

In other situations where the IRB considers MDPH's participation so limited or marginal that considering the Department to be engaged would not meaningfully add to protection of the human subjects in research, OHRP will be consulted directly for guidance.

1.3 Ethical Principles

- .1 MDPH is guided by the ethical principles regarding human subject research set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research entitled Ethical Principles and Guidelines for the Protection of Human Subjects of Research [the "Belmont Report"], regardless of whether the research is subject to Federal regulation.
- .2 MDPH is guided by the following essential principles of the Belmont Report:

- a) Respect for Persons: This principle acknowledges individual autonomy, and protects persons with diminished autonomy.
- b) Beneficence: This principle requires that the benefits from the research project are maximized, while the harm to any human subject is minimized.
- c) Justice: This principle requires a fair distribution of the benefits and burdens of research.

1.4 Policy

- .1 MDPH is responsible for safeguarding the rights and welfare of persons who serve as human subjects in research sponsored or conducted by MDPH. Research procedures must comply with federal regulations for the protection of human subjects (45 CFR Part 46, and 21 CFR Part 50 and 56), relevant requirements of M.G.L. c. 94C, and applicable state laws relating to the use and disclosure of confidential records.
- .2 Research involving human subjects includes all activities that are “research,” and involve, “human subjects” according to 45 CFR Part 46, and to include all activities that are “research” according to 21 CFR Part 50 and 56. “Research” is a systematic investigation, including clinical investigations, research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. “Human Subjects” are living individuals about whom the investigator conducting research obtains:
 - a) data through intervention or interaction with the individual, or
 - b) identifiable private information (45 CFR Part 46).
- .3 According to FDA regulations, “research” is any experiment that involves:
 - a) a drug other than the use of an approved drug in the course of medical practice,
 - b) a medical device being evaluated for safety or effectiveness, or
 - c) any article subject to regulation by the Food, Drug, and Cosmetic Act where the results of the research are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit; and where one or more individuals are either recipients of the article or controls.
- .4 FDA regulations define a human subject as an individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient [21 CFR 50.3(g), 21 CFR 56.102(e)]. A human subject includes an individual on whose specimen a medical device is used [21 CFR 812.3(p)].
- .5 No MDPH employee or agent shall permit, or shall engage in, the conduct of human subject research until the plans or protocols for such activities have been reviewed and approved by the IRB, or by another institutional review board with whom an IRB Authorization Agreement has been executed, unless the research has been specifically exempted from this review requirement by this policy.
- .6 Federal (all departments and agencies bound by the Federal Policy) funds may not be expended for research involving human subjects unless the requirements of this Assurance have been satisfied.

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- .7** No MDPH official shall override a decision of the IRB to deny approval for a human subject research study subject to this policy.
- .8** Review of research and related activities by the IRB shall determine that:
 - a)** Subjects give their informed consent or a waiver of informed consent has been justified;
 - b)** The rights and welfare of human subjects are adequately protected;
 - c)** Risks to individuals are minimized, are not unreasonable, and are outweighed by the potential benefits to them or by the knowledge to be gained;
 - d)** The proposed project design and methods are adequate and appropriate in the light of stated project purposes; and
 - e)** The study protocol demonstrates adequate confidentiality and security measures to protect research data from unauthorized disclosure.

Section 2.0 Institutional Review Board

- 2.1 General IRB Policies**
 - 2.2 Research Determinations**
 - 2.3 IRB Membership**
 - 2.4 Conflict of Interest**
 - 2.5 Training of IRB Members**
 - 2.6 Undue Influence**
 - 2.7 Meetings**
 - 2.8 IRB Minutes**
 - 2.9 Approval Timeframes**
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 - 2.11 Consultants**
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2.1 General IRB Policies

- .1** Safeguarding the rights and welfare of subjects at risk in any research activity conducted or sponsored by MDPH, regardless of the source of any supporting funds, is primarily the responsibility of MDPH. In order to provide for the adequate discharge of MDPH's responsibility, no research activity involving human subjects may be undertaken by any MDPH staff, agents or contractors unless the IRB has reviewed and approved the research prior to commencing the research activity or it has delegated review to another institution's IRB by written agreement.
- .2** The IRB review must determine whether the subjects will be placed at risk and, if risk is involved, that:
 - a)** Risks to participants are minimized by using procedures consistent with sound research design;
 - b)** Risks to participants are minimized whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes;
 - c)** Risks to participants are reasonable in relation to anticipated benefits, if any, to participants, and the importance of the knowledge that may reasonably be expected to result;
 - d)** Selection of participants is equitable;
 - e)** Informed consent will be sought from each prospective participant or the participant's legally authorized representative, in accordance with, and to the extent required by the regulations;
 - f)** Informed consent will be appropriately documented, in accordance with, and to the extent required by the regulations;
 - g)** When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants;
 - h)** When appropriate, there are adequate provisions to protect the privacy of participants;

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- i) When appropriate, there are adequate provisions to maintain the confidentiality of data;
 - j) When some or all of the participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these participants; and
 - k) The conduct of the activity will be reviewed at intervals determined by the IRB, but not less than annually.
- .3 The determination of when an individual is at risk is a matter of the application of sound professional judgment as relates to the circumstances of the research activity in question.
- .4 The IRB will carefully weigh the relative risks and benefits of the research procedures to be applied to the subject as follows.
 - a) Research activities designed to yield fruitful results for the benefit of individual subjects or society in general may incur risks to the subjects provided such risks are outweighed by the benefit to be derived from activities;
 - b) The degree of risk involved in any activity should never exceed the humanitarian importance of the problems to be solved by that activity. Likewise, compensation to volunteers should never be such as to constitute an undue inducement to the subject;
 - c) There is a wide range of medical, social and behavioral research projects and activities in which no immediate physical risk to the subject is involved; e.g., those utilizing personality inventories, interviews, questionnaires, or the use of observation, photographs, taped records, or stored data. However, some of these procedures may involve varying degrees of discomfort, harassment, stigma, or invasion of privacy;
 - d) There may also be projects that involve tissues, body fluids, and other materials obtained from human subjects. The use of these materials generally involves minimal risk to the subject. However, their use for research, training, and service purposes may present psychological, sociological, or legal risks to the subjects. In these instances, application of the policy requires IRB review to determine that the circumstances under which the materials are to be procured are appropriate and, if the subject is deemed to be at risk, that adequate and appropriate consent will or can be obtained for the use of these materials for research purposes;
 - e) Similarly, some studies depend upon stored data or information that was often obtained for quite different purposes. Here, the IRB will determine whether the use of these materials is within the scope of the original consent, or whether consent should be obtained or waived.

2.2 Research Determinations

- .1 MDPH employees or agents seeking guidance regarding whether an activity is human subject research should consult the IRB Administrator and, if requested, submit a Preliminary Study Assessment form, available on HealthNet (MDPH Internal Intranet). The IRB Chair or Vice Chair, in consultation with other staff when appropriate, will review the project description and make a decision about whether the project is human subject research. Determinations are based upon the definition

of “human subject research” (see glossary) and the purpose of the investigation. The IRB Chair, Vice Chair or Administrator will issue a written decision to the investigator identified on the Preliminary Study Assessment form.

- .2 If research involves the use of a food, biologic, nutritional, or food supplement that might fit the FDA definition of a “drug,” the IRB Chair or Vice Chair, in consultation with legal advisors when appropriate, will review the definitions in the Federal Food, Drug, and Cosmetic Act, Section 201(g)(1), to determine whether the research involves the use of a drug. If the research involves a drug, the Chair or Vice Chair, in consultation with legal advisors when appropriate, will review the FDA regulations at 21 CFR 312.2(b) to determine whether the drug is exempt from the requirement for an Investigational New Drug (IND). If an IND is required, the IRB will not review the research and will return the protocol to the investigator with a written explanation.

2.3 IRB Membership

- .1 The IRB oversees human subject research conducted by the Massachusetts Department of Public Health and other institutions or agencies for which it serves as designated institutional review board, including the Department of Corrections.
- .2 The IRB shall have at least five members who shall be appointed by the Commissioner. The members shall have varying backgrounds to promote complete and adequate review of research activities commonly conducted within the jurisdiction of MDPH. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of its members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. The IRB maintains a roster of more than the minimum required number of members to ensure adequate and efficient review.
- .3 In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas as well as persons who are knowledgeable about and experienced in working with vulnerable populations such as children, prisoners, pregnant women, and handicapped or mentally disabled persons.
- .4 The IRB shall not consist entirely of men or entirely of women, nor shall it consist entirely of members of one profession. The IRB shall include at least one member in attendance whose primary concerns are in scientific areas, and at least one member in attendance whose primary concerns are in nonscientific areas. The IRB shall include at least one “community” member in attendance who is not otherwise affiliated with MDPH, and who is not part of the immediate family of a person who is affiliated with MDPH. Where applicable, membership shall include individuals with expertise concerning vulnerable populations or experience representing vulnerable populations (eg. prisoners, mentally disabled), as defined by OHRP.
- .5 IRB members serve three year terms, but may be re-appointed by the Commissioner for successive three year terms.
- .6 The IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the Committee. These individuals may not vote on any matter before the IRB.

- .7 Each voting member of the IRB may have an appointed alternate member from his or her Bureau or another similar discipline. The IRB roster shall list the alternate, who must serve in the same role as the primary member they represent, and the alternate may serve in place of a primary member who is not available to attend the meeting. Alternate membership requirements are the same as for regular voting membership and alternates are evaluated by the same process and criteria. Alternate members have voting rights and are counted as part of the quorum only when they replace their respective regular members.
- .8 The IRB Administrator shall report any IRB membership changes to OHRP. Administrative staff at MDPH may attend meetings as non-voting attendees. A non-voting attendee cannot be counted in the quorum and may not vote, but may participate in discussions and deliberations.
- .9 The IRB shall have a Chair and a Vice Chair appointed by the Commissioner. The Chair and Vice Chair are committee members who are knowledgeable in human subject research, including federal and state regulations, and ethics relevant to such research. The Chair and Vice Chair each serve two year terms, but may be re-appointed by the Commissioner for successive two year terms. Whenever the Chair is not available, the Vice Chair will assume the responsibilities of the Chair during the period of his or her absence.

2.4 Conflict of Interest

IRB members may not participate in the initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the Chair. Conflicts of interest may arise for either financial or personal reasons. IRB members shall disclose any potential conflicts of interest they may have to the Chair prior to discussion of a research proposal. Conflict of interest is further discussed in Section 3.5 of this policy.

2.5 Training of IRB Members

All IRB members and alternates must complete training in human subject protection every three years. In addition, the IRB staff will conduct periodic trainings in human subject protection issues at regular full board meetings.

2.6 Undue Influence

In cases in which an IRB member or staff person experiences either direct or indirect undue influence or coercion to make a ruling for a specific research study or investigator, the IRB member or staff person should document the issues related to the case and notify the Office of the General Counsel. That office will review the information and may convene a meeting and/or otherwise obtain additional information as necessary. The Commissioner's Office will subsequently inform the Chair of the findings and may take corrective action in consultation with the Chair.

2.7 Meetings

- .1 The IRB shall hold at least quarterly full board meetings and any additional meetings as necessary, at a time and place to be pre-determined and posted on the MDPH Internet site. Materials for review are made available to committee members at least one week in advance of a meeting. Full board research protocols (all protocols other than exempt or expedited) shall be reviewed only at meetings of the IRB at which a quorum has been established, and including at least one community member. A quorum is achieved when at least 50% of the members of the IRB roster are

participating in the meeting. To be approved, a protocol must receive a majority of affirmative votes of members participating in the meeting. If a quorum fails during a meeting, such as due to a lack of a majority of committee members participating or an absence of a community member, including because members are absent due to a conflicting interest, the IRB will not take further actions or votes until the quorum is restored. Remote participation is allowed, subject to the discretion of the Chair, as long as materials are made available in advance of the meeting.

- .2 Prior to each full board meeting, the IRB Administrator and Chair will review the agenda of protocols and will assign a primary reviewer who is knowledgeable about or experienced in working with the subject area or the population being recruited or studied. Should such experience within the IRB membership not be available, relevant consultation will be obtained. In most cases, a secondary reviewer without specific subject area expertise will also be assigned.

2.8 IRB Minutes

Minutes of each IRB meeting shall be recorded in writing. Minutes are distributed to all IRB members in advance of a full committee meeting. At the next full board meeting, comments or changes are requested and then the committee votes on approving the minutes from the last meeting. Members who were not in attendance at the meeting described in the minutes abstain from the vote.

Minutes shall include:

- .1 Attendance at the meeting (designating any advocates for vulnerable populations that are present, and alternate members replacing primary members):
 - a) Documentation of quorum/Loss of quorum and suspension of IRB activity
 - b) "Members present" documents the names of IRB members present at any time during the meeting and specifies voting members for each action.
 - c) "Members absent" documents the names of IRB members who never attended the meeting at any time.
 - d) Entry/Exit/Recusal
- .2 A list of all studies reviewed during the meeting with the respective information.
- .3 Actions taken and decisions made by the Committee:
 - a) Votes will record the number of members voting for, against, and abstaining, and the names of IRB members listed under "Members Present" who were absent from the vote. If a member was absent due to a conflicting interest, the notation "absent due to a conflicting interest," will appear next to the name.
 - b) In order for a protocol to be approved, it must receive the approval of a majority of members present at the meeting.
 - c) Basis for requiring modifications to the research proposal or consent documents or for disapproving the research proposals;
 - d) A summary of the discussion of controversial issues and their resolution;
 - e) A summary of discussion of issues pertinent to the protocol;
 - f) Minutes will also document determinations required by OHRP rules, including those for waiver or alteration of consent, waiver of consent documentation, research involving children, prisoners, pregnant women, fetuses, and neonates.

- a) Justification for any deletion or substantive modification of information concerning risks or alternative procedures contained in the informed consent document.
 - b) Approval by the committee chairperson.
 - c) The date of approval.
 - d) Signature of the chairperson.
 - e) For continuing review, the expiration date.
 - f) For initial and continuing review, the approval period.
- .4 A list of all actions that were taken administratively since the last full board meeting. IRB minutes should document all activity conducted by the Chair or Vice Chair since the last full board meeting, and be presented to the full committee. The report will include all protocols that were approved by expedited process, renewed, or amended, as well as any adverse events or unanticipated problems, and suspensions or terminations. The minutes should also document any discussion by the full committee regarding activities and decisions by the Chair or Vice Chair.
- .5 When educational sessions have been presented, the minutes should include a summary of the presentation and any follow-up discussion.

2.9 Approval Timeframes

- .1** The term of approval for studies approved by the full board or expedited process is no more than one year, but may be shorter. The expiration date is calculated from the date of study approval. Protocols that have not undergone continuing review will expire on the expiration date. Research activities may not continue after the expiration date. A shorter interval would indicate a degree of risk greater than minimal and, if this is the case, the research does not qualify for expedited review.
- .2** Continuing review approval periods are one year from the day of formal re-approval, unless otherwise stated.

2.10 Expiration and Inactive Notices

1. The IRBNet system sends investigators email notices 60 and 30 days prior to the study expiration date. Notices list the study title, IRB protocol number, expiration date, and continuing review and closure instructions. Principal Investigators (PIs) must submit a closure report and Affidavit of Data Destruction, when applicable, if a study is not expected to continue beyond the expiration date. PIs desiring to continue research beyond the study approval period must submit a continuing review application between 30 and 60 days prior to the expiration date. If a continuing review report is not received, the IRBNet system sends an expiration notice on the expiration date, informing the PI that all study activities must stop.
2. The PI has a 30-day grace period from the expiration date to submit a continuing review or closure report. However, this is an administrative grace period only and the expiration notice clearly states that all research must immediately cease on the expiration date if no continuing review approval has been issued. When an investigator does not provide continuing review information to the IRB or the IRB has not approved a protocol by the expiration date, interventions and interactions with current participants may continue ONLY when the IRB finds an over-riding safety concern or ethical issue involved such that it is in the best interests of individual participants. If the PI does not request a continuation or closure within the 30-day grace period, then the Administrator emails the PI a formal notice stating the protocol is no longer approved, study activities must cease, and confidential study data must be destroyed, if appropriate.

2.11 Consultants

- .1 Any time the Chair or Vice Chair determines that the IRB does not have the necessary scholarly or scientific expertise for sound review, they may request assistance from ad hoc consultants. Consultants are independent of the IRB and are selected according to scholarly and scientific expertise. Prior to counsel, consultants must disclose any conflicts of interest. The person requesting consultation must confirm the consultant does not have any conflict of interest, report this to the Chair, and document this in the study file.
- .2 Consultants may be called upon to judge the scientific soundness of a research protocol, make a fair and accurate determination of the risk-benefit ratio, review the cultural appropriateness of the informed consent process, and offer additional and unique expert advice. However, consultants cannot make any review determinations and may not vote with the IRB; they may only provide counsel. Consultants are required to either attend meetings to present their comments or to provide their comments to the IRB in a written report. If consultants attend a meeting, a summary of their findings will be described in the minutes. If consultants provide a written report, a copy of the report will become part of the study file.

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Section 3.0 General Research Procedures

- 3.1 Scientific Merit**
 - 3.2 Confidentiality and Privacy**
 - 3.3 Protecting Participants' Health Information**
 - 3.4 Investigator and Staff Training**
 - 3.5 Conflict of Interest**
 - 3.6 Records Retention Requirements**
 - 3.7 Guidelines on Compensation for Research Participants**
 - 3.8 Guidelines for Research Advertisement Content**
 - 3.9 Equitable Recruitment**
 - 3.10 Suspension and Termination Policy**
 - 3.11 Noncompliance with IRB Policies, Procedures, or Decisions**
 - 3.12 Delegating Review**
 - 3.13 Emergency Use of a Test Article**
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3.1 Scientific Merit

It is not the charge of the IRB to comment upon the scientific merit of proposals submitted for review, where scientific merit refers to the value of the research proposal relative to other research proposals. The IRB is responsible to evaluate the scientific or scholarly validity of the research (using its own expertise or the expertise of consultants) so that the IRB can determine whether the research design is sound enough to reasonably expect the research to answer its hypotheses, and whether the importance of the knowledge expected to result from this research outweighs any risk to subjects.

3.2 Confidentiality and Privacy

- .1** All research project members (investigators, directors, analysts, programmers, transcribers, students, and other staff) shall demonstrate to the satisfaction of the IRB that they will take appropriate measures to prevent accidental and intentional breaches of confidentiality. Confidentiality measures shall include, but not be limited to, substituting codes for identifiers, removing survey cover sheets that contain names and addresses, limiting access to identified data, and/or storing research records in locked cabinets. All measures used to assure confidentiality of data need to be understood by all research staff before research is initiated, outlined in the proposal, and followed once research is initiated. Confidentiality procedures must be described in research applications presented to the IRB. PIs must ensure that all staff recognize that the assurance of confidentiality includes protecting the identity of participants and restricting confidential information to the minimum necessary to accomplish the research. Confidentiality is best maintained by anonymous data collection whenever possible. PIs proposing projects that will address sensitive or stigmatizing topics, must explicitly outline the steps they will take to assure any information linking participants to the study is maintained in confidence. Consideration re electronic data should include encryption, data destruction, and cell size. The requirement of signed consent forms may be waived in sensitive studies if the consent document is the only written record linking participants to the project and a breach of confidentiality presents the principal risk of harm anticipated in that research.

- .2 The informed consent process must disclose any risks to privacy and describe how investigators specifically plan to protect privacy. Investigators are required to follow the privacy protections outlined in the approval documents. The IRB reviews studies to ensure adequate privacy protections and to prevent unnecessary invasions of privacy. Privacy is best protected by making sure the research is designed so that participants will be comfortable with the way investigators interact or intervene with them. Investigators must maintain the confidentiality of all private and identifiable information unless disclosure is mandated according to federal, state, or local law.
- .3 If a PI is compelled, through a subpoena, discovery request, court order or any other form of compulsory legal process, to provide any information or copies of any documents, records or other materials obtained during the course of an approved study, the PI must immediately notify the IRB Administrator and comply with MDPH's requirements related to compulsory legal process.

3.3 Protecting Participants' Health Information

When a research study seeks to access Protected Health Information (PHI) from a HIPAA-covered entity, an authorization from the study subject is required. This is in addition to informed consent. This requirement may be waived only when all criteria cited in Section 5.8 of this Policy are met.

3.4 Investigator and Staff Training

The Principal Investigator of a study and all other individuals working in any manner related to the study who will have access to identifiable or potentially identifiable information must demonstrate completion of an adequate human subject protection training program. Proof of compliance shall be submitted with the application for approval.

3.5 Conflict of Interest

- .1 All investigators, consultants, and/or IRB members are required to disclose any conflicts of interest.
- .2 Consultants found to have a conflict of interest cannot serve as consultants for the study under review.
- .3 For Principal Investigators, conflicts of interests that might affect the protection of participants are prohibited unless a management plan is in place that prevents the conflict of interests from affecting the protection of participants.
- .4 Management plans that may be considered include: partial or complete divestment, limiting involvement of the conflicted individual, additional oversight or disclosure. Disclosure alone cannot be used to manage conflicts of interests that might affect the protection of participants. If required, the IRB Chair or Vice Chair will request that the investigator/researcher prepare a conflict of interest management plan. When finalized, the management plan will be submitted to the IRB for review and final approval. Under no circumstances shall research be approved until the IRB has reviewed and approved the management plan.
- .5 If an IRB member declares involvement in any way in a research protocol under review by the IRB, for example, as an investigator, consultant, or study participant, or state a conflict of interest with the research protocol, then the member is excluded from discussion and voting except to provide information requested by the IRB, must leave the meeting room for voting and is not counted towards quorum.

3.6 Records Retention Requirements

- .1 The IRB shall collect, prepare and maintain adequate documentation of IRB activities. All records shall be accessible for inspection and copying by authorized representatives of OHRP, DHHS, FDA, MDPH, sponsors, and internal auditors at reasonable times and in a reasonable manner.
- .2 The IRB shall keep all submitted electronic or paper study files for a minimum of three years after study closure, unless a longer period of time is required by state records retention rules.
- .3 Minutes and IRB membership/rosters shall be kept for a minimum of ten years, unless a longer period of time is required by state records retention rules.
- .4 Other than minutes, IRB records not related to a specific research activity (i.e., records that are not relevant to a specific protocol file) shall be kept for a minimum of three years unless a longer period of time is required by state records retention rules.
- .5 The principal investigator or project director shall maintain, in a designated location, all records relating to research for at least three years after completion of the research. All records must be accessible for inspection and copying by authorized representatives at reasonable times and in a reasonable manner. Records must be made available to representatives of MDPH, OHRP, the FDA (as appropriate), and other regulatory agencies and/or sponsors as applicable. Should a principal investigator or project director leave the sponsoring institution prior to the completion of the research protocol, the investigator is responsible for notifying the IRB and seeking approval to transfer the study to a new location or to a new PI.

3.7 Guidelines on Compensation for Research Participants

- .1 The guidelines outlined below are meant to assist investigators in determining a reasonable amount of compensation that can be given to research participants and also place some boundaries on what is and is not “reasonable.” The “reasonableness” of a particular sum of money or other form of payment should be based upon the time involved, the inconvenience to the subject, reimbursement for expenses incurred while participating, and should not be so large as to constitute a form of undue influence or coercion.
- .2 During the initial review of a research protocol, the IRB is required to review both the amount of compensation proposed and the method and timing of disbursement to assure that neither are coercive or present undue influence. The following are some additional guidelines:
 - a) Any compensation should not be contingent upon the subject completing the study, but should accrue as the study progresses.
 - b) Compensation given as a “bonus” or incentive for completing the study is acceptable provided that the amount is not coercive. The IRB is responsible for determining if the incentive amount is so large as to be coercive or represent undue influence.
 - c) The amount and type of compensation (gift card, etc.) along with how and when it will be provided should be clearly set forth in the informed consent document.
 - d) Compensation to children should be appropriate for their age.

3.8 Guidelines for Research Advertisement Content

- .1 The IRB must review and approve all advertisements that will be used to recruit subjects to a specific research study. Generally, advertisements used to recruit research subjects should be limited to information that a potential subject would need to determine if they are eligible and interested in participating. More specifically, the ads should include information such as:
 - a) Name and address of the research facility;
 - b) Organization funding the research, if different;
 - c) The condition or disease that will be the focus of the research;
 - d) Purpose of the research with reference to the fact that the study is investigational;
 - e) Summary of criteria for eligibility to participate;
 - f) Time and other commitments that will be required of the subject;
 - g) Location of the study and the office to contact for further information.
- .2 The ads should not:
 - a) Contain explicit or implicit claims of safety and efficacy or equivalency or superiority to approved procedures or treatments;
 - b) Emphasize the amount of reimbursement that subjects will receive. The ads may state that reimbursement for time, travel, etc. will be given;
 - c) Promise a favorable outcome or benefits;
 - d) Include exculpatory language;
 - e) Promise “free treatment” when the intent was only to say participants would not be charged for taking part in the investigation;
 - f) For FDA-regulated research, advertisements should not:
 - Make claims, either explicitly or implicitly, about the drug, biologic or device under investigation that were inconsistent with FDA labeling;
 - Use terms, such as “new treatment,” “new medication” or “new drug” without explaining that the test article was investigational;
 - Allow compensation for participation in a trial offered by a sponsor to include a coupon for a discount on the purchase price of the product once it had been approved for marketing
- .3 Advertisements conforming to the above guidelines may be approved for any advertising format, e.g., posted flyers, newspapers, internet advertisements, radio/television. However, the IRB must review the final copy of advertisements prior to publication.

3.9 Equitable Recruitment

The IRB shall only approve studies demonstrating equitable subject recruitment, taking into account the purposes of the research and the setting in which it will be conducted. The IRB evaluates all research applications to verify that investigators have demonstrated equitable selection and recruitment of all research subjects and have made every effort to ensure diversity of subject selection. In particular, the IRB evaluates any special concerns with proposed research involving vulnerable populations, such as children, prisoners,

pregnant women, cognitively-impaired individuals, and economically or educationally disadvantaged persons. The IRB must ensure that proposed sampling efforts do not favor some classes of participants solely due to ease of availability, compromised positions, or manipulability. The IRB must also ensure that PIs make every effort to include women and members of minority groups, if appropriate, as research subjects.

3.10 Suspension and Termination Policy

- .1 Suspension means a temporary withdrawal of approval of some or all research, or a permanent withdrawal of approval of some research activities. A suspended protocol requires continuing review before it can proceed again. Termination means a permanent withdrawal of approval of all research activities. The IRB has the authority to suspend or terminate approval of a research protocol that has been determined to not be conducted according to MDPH human subjects research policies and procedures, including failure to comply with administrative requirements, or in cases in which there has been unexpected serious adverse events or harm to participants.
- .2 While the IRB Chair has the right to suspend a study that poses an immediate risk to participants, generally suspensions will be determined by a vote of the full IRB. Suspensions ordered by the IRB Chair or Vice Chair must be placed on the agenda of the next full board meeting for consideration of 1) reversal of the suspension, 2) continuation or 3) termination of the study. Should a study be suspended or terminated so that interventions or interactions with current participants will stop or change, the IRB will communicate to the PI in its letter that the PI must inform current participants that the study has been suspended or terminated along with the reasons for such suspension or termination. Such a letter must be submitted to the IRB Chair or Vice Chair for formal approval prior to use. Before suspending or terminating research, the Chair or Vice Chair or full board must consider whether the action might adversely affect the rights or welfare of current participants. In such cases, the IRB will require explicit conditions for participant withdrawal. The IRB will consider whether follow-up of participants for safety reasons is necessary and if so, the IRB will require that the PI notify participants of this and require the PI to continue to report unanticipated problems. Such information must be submitted to the IRB Chair or Vice Chair for review and approval. Where appropriate, the IRB will report the suspension or termination, including the reasons for the action, to the appropriate federal regulatory agency or agencies, including, but not limited to, the OHRP and the FDA.

3.11 Noncompliance with IRB Policies, Procedures, or Decisions

- .1 Human subject research that deviates from the policies, procedures, stipulations, or approval conditions of the IRB or that violates state or federal law is non-compliant and subject to further inquiry by the IRB and other federal or state oversight officials. All reports and complaints of non-compliance should be directed to the IRB Administrator via email, phone, mail, or in person. The IRB Chair or Vice Chair will immediately investigate all allegations of non-compliance. If necessary, the IRB Administrator or Chair will send the investigator(s) in question a notice requiring the immediate suspension of all specified research activities while the issue of non-compliance is reviewed, consistent with this policy and federal regulations (45 CFR Part 46.113). This initial notice will also include a statement detailing the rationale for the action.
- .2 All non-compliance allegations shall be brought to the attention of the IRB Chair or Vice Chair. If the 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 lost consent forms). Otherwise, the Chair will refer allegations to the Office of the Commissioner for further review. After complete investigation, the Chair shall present findings to the full IRB as soon as possible for a vote on whether the non-compliance was serious or continuing and whether to: suspend or terminate an approval; require the investigator to notify subjects; or impose additional conditions.

- .3 The IRB may request any appropriate additional consultation and expertise to resolve non-compliance. Deliberations and determinations of the IRB must be fully documented in the minutes. All cases of non-compliance which the IRB determines to be serious or continuing noncompliance will be reported according to the reporting requirements in section 6.3 of this policy.

3.12 Delegating Review

- .1 The IRB may delegate review to another institution's IRB when the Department's involvement with the study is only in a supportive role and when the IRB Chair or Vice Chair determines that the study involves only minimal risk to participants and/or risk considerations have been determined to be adequately addressed by the PI. The IRB must execute an IRB Authorization Agreement with the IRB of the institution providing review.
- .2 The IRB must determine that the review performed by the designated IRB will meet the human subject protection requirements of the MDPH's OHRP-approved FWA. The IRB at the institution providing review must follow written procedures for reporting its findings and actions to appropriate officials at the MDPH IRB. Relevant minutes of IRB meetings of the institution providing review must be made available to the MDPH IRB upon request. The MDPH IRB remains responsible for ensuring compliance with its OHRP-approved FWA. The IRB must retain a copy of the IRB Authorization Agreement and provide a copy to OHRP upon request. The MDPH IRB will retain the right to retract the delegated IRB authority at any time. The MDPH IRB may conduct review on behalf of another institution if that institution has a federally approved FWA and agrees to execute an IRB Authorization Agreement with the MDPH IRB.

3.13 Emergency Use of a Test Article

Pursuant to 21 CFR §56.104(c), emergency use of an FDA-regulated test article is not subject to IRB review, provided that such emergency use is reported to the IRB within five working days. Any subsequent use of the test article at the institution is subject to IRB review.

Section 4.0 Initial IRB Review

- 4.1 Requirements for Initial IRB Review**
 - 4.2 Submission Schedule Requirements**
 - 4.3 Initial Evaluation of Submitted Projects**
 - 4.4 Exempt Research Review Process**
 - 4.5 Expedited Research Review Process**
 - 4.6 Full Committee Reviews**
 - 4.7 Administrative Approval of Decisions Made by the IRB**
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4.1 Requirements for Initial IRB Review

Any employee or agent of MDPH who proposes to engage in any research activity involving human subjects, including the use of their confidential information, must submit an application to the IRB Administrator through IRBNet. The applicant must complete the initial overview form, core application, any required appendices, and any required attachments (e.g., consent forms, contact letters and scripts, other recruitment materials, questionnaires or other survey instruments, grant applications, and training verification).

4.2 Submission Schedule Requirements

Electronic applications must be submitted through IRBNet a minimum of three weeks prior to a meeting date to be considered for the agenda of that meeting. Every effort will be made to review applications at the next full board meeting for clear and complete applications submitted in a timely manner, but review may be delayed if the study requires clarification or additional information before it is considered ready for review or if the meeting agenda is already full.

After submission, each new protocol is given an IRB specific number for tracking purposes. IRB members have complete access to documents provided by the investigator through IRBNet.

4.3 Initial Evaluation of Submitted Projects

Upon receipt of a new application, the IRB Chair, Vice Chair or Administrator will assign reviewer(s), as appropriate. Whenever possible, this will be a member of the IRB, but may also be a consultant to the IRB membership. The primary reviewer conducts a preliminary review and identifies any omissions or need for clarification. The primary reviewer completes the IRB Application Review Worksheet and submits a completed copy to the IRB Administrator. The primary reviewer consults with the IRB Chair, Vice Chair or Administrator with any questions about the appropriate review level, jurisdiction of IRB, or otherwise relating to necessity of review. The IRB Administrator, in consultation with the Chair or Vice Chair and the primary reviewer, may correspond with the investigator(s) to resolve any questions.

When the primary reviewer deems an application ready for review, the IRB Administrator assigns the review to the IRB Chair or Vice Chair for expedited reviews or to the next full committee meeting for full committee reviews.

4.4 Exempt Research Review Process

Federal regulations identify specific categories of research activities that are exempt from the federal regulations on the protection of human subjects in research (45 CFR 46.101(b)). The Chair, Vice-Chair, or Administrator shall make exemption determinations for MDPH employee or agent conducted studies.

The IRB Chair or Vice Chair will review the study materials and make the determination. The determination requires that the research activity meets the criteria for exempt status and meets the criteria for protection of research participants in exempt research. When a study is determined to be exempt, the IRB will issue a letter of exempt designation to the investigator.

While a project may be exempt from the regulations, the ethical principles of conducting research with humans still apply. The investigator is responsible for knowing and adhering to the ethical principles of human subject research. The investigator is also responsible for informing the IRB Chair, Vice Chair or Administrator immediately of any adverse or unexpected events that would alter the exempt status.

1. Limitations on exempting research involving children or prisoners

The regulations require additional protections for research involving children. The only Exempt Category that applies to children as research subjects is Exempt Category (2). This category applies to research involving children as subjects only under specific conditions as specified in 45 CFR 46.401(b).

Research involving children **cannot be classified as exempt** if the research involves:

- a) Surveys;
- b) Interview procedures; or
- c) Observations of public behavior when the investigator participates in the activities being observed.

Research involving children can only be classified as exempt if the research involves only educational tests and observation of public behavior where the investigator does not participate in the activities being observed and meets the other conditions of 45 CFR 46.101(b)(2).

The federal regulations on exemptions do not apply to research involving prisoners. Research involving prisoners as subjects is never exempt from the regulations.

2. Principal Investigator Assurance Statement

Research that is determined to be exempt from IRB oversight is not exempt from protection of the human subjects. The following criteria to protect human subjects must be met:

- a) The investigator assures that all investigators and co-investigators are trained in the ethical principles, relevant Federal Regulations and institutional policies governing human subject research;
- b) The investigator assures that human subjects will voluntarily consent to participate in the research when appropriate (e.g. surveys, interviews) and will provide subjects with pertinent information, e.g. risks and benefits, contact information for investigators and IRB Chair, etc.;
- c) The investigator assures that human subjects will be selected equitably, so that the risks and benefits of the research are justly distributed.

- d) The investigator assures that the IRB will be immediately informed of any information, unanticipated problems that would increase the risk to the human subjects and cause the category of review to be upgraded to Expedited or Full Review;
- e) The investigator assures that the IRB will be immediately informed of any complaints from participants regarding their risks and benefits; and
- f) The investigator assures that confidentiality and privacy of the subjects and the research data will be maintained appropriately to ensure minimal risk to subjects.

4.5 Expedited Research Review Process

.1 Initial Review

Protocols determined to be minimal risk but not falling into any exempt category, may be considered for expedited review. The IRB Chair or Vice Chair, in consultation with the primary reviewer, determines whether a study qualifies for expedited review and conducts the review when considered appropriate. If the IRB Chair or Vice Chair and primary reviewer believe the protocol should be disapproved, the protocol is scheduled for review by the full IRB. All expedited items (new proposals, amendments, continuing reviews, unanticipated problems, closures, terminations) must be listed in a monthly agenda and corresponding minutes, as a method of informing IRB members.

Expedited review may be considered under the following circumstances:

- a) Research activities that:
 - present no more than minimal risk to human subjects, and
 - involve only procedures listed in one or more of the categories in 45 CFR 46.110 and 21 CFR 56.110.

The activities listed in the federal rules should not be deemed to be of minimal risk simply because they are included on the list. Inclusion on the list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

- b) 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 subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented, so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- c) Standard requirements for informed consent (or its waiver, amendment, or exception) apply, regardless of the type of review utilized by the IRB.

.2 Continuing Review

For minimal risk studies, continuing review may be conducted under expedited procedures by the IRB Chair or designee when:

- a) The research was eligible for initial review by an expedited procedure as specified in 45 CFR 46.110 and 21 CFR 56.110;
- b) The research was previously approved by the full board if:

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- the protocol is permanently closed to the enrollment of new participants, all participants have completed all research-related interventions, and the research remains active only for long-term follow-up of participants; or
 - no further participant enrollment is taking place and no additional risks have been identified; or
 - the remaining research activities are limited to data analysis.
- c) Studies that initially required full board approval can later become eligible for expedited continuing review under the following conditions:
- they are not conducted under IND or IDE; and
 - at a convened meeting, the IRB has determined that the research involves no greater than minimal risk to the subjects; and
 - no additional risks have been identified.
- .3 Amendments

Amendment requests may be expedited by the MDPH Chair, Vice Chair or designee if the amendment request is considered minor. Minor amendments are changes that do not pose any additional risk to study subjects and do not affect the rights or welfare of study subjects. This includes, but is not limited to, changes in staffing, minor changes in the protocol or procedures, minor changes in contact materials, or modifications to data storage or security procedures.

4.6 Full Committee Reviews

- .1 All submissions for initial review, continuing review, or review of modifications to previously approved research determined by the IRB Chair or Vice Chair to not be eligible for exemption or review by expedited procedures must be reviewed and approved at a full board meeting. The IRB adheres to the following process to facilitate the thorough review of each protocol according to Federal regulations.
- .2 Materials submitted by the PI relating to a study and any relevant internal correspondence relating to that study will be made available to all members of the IRB via IRBNet at least one week prior to the meeting. Effort will be made to provide more lead review time whenever possible.
- .3 The protocols undergoing initial review as well as those undergoing continuing review are presented and discussed individually at a full committee meeting. The primary reviewer presents each new study to the IRB and raises any additional points for discussion. The Principal Investigator may be asked to attend or call in to a meeting after the initial discussion period to answer additional questions. After discussion is completed, each protocol is voted upon, with one of four possible dispositions:
 - **Approved** – Accepted and endorsed as written with no conditions except standard conditions.
 - **Approved with Explicit Conditions** – Accepted and endorsed with explicit minor changes or simple concurrence of the principal investigator. All explicit conditions requested of the PI must be completed and documented prior to beginning the research. For these conditions, the IRB Chair or Vice Chair can, upon reviewing the PI's response(s) to stipulations, approve the research on behalf of the IRB.
 - **Tabled** – Decision deferred due to clarifications, explanations, and justifications of the protocol, consent form, or other application materials.

This generally occurs when the protocol, consent form, or other materials have deficiencies that prevent accurate determination of risks and benefits or require significant clarifications, modifications or conditions that, when met or addressed, require full IRB review and approval of the PI's responses and revisions. The deficiencies will be specified to the PI.

- **Disapproved** – The protocol describes a research activity that is deemed to have risks which outweigh potential benefits or the protocol is significantly deficient in several major areas. A principal investigator has the right to request that the decision be reconsidered. To request reconsideration, investigators must submit a written response to the IRB for a protocol that is disapproved or tabled. The written response will be reviewed by the IRB. The IRB will invite the investigator to the IRB meeting if the IRB has additional questions for the investigator. The IRB will reconsider its decision based on the written response and additional information provided by the investigator in-person or in writing. The IRB's second decision is final.

Protocols requesting significant modifications or of special interest to the IRB are discussed in detail, and voted upon by the IRB. If a study is approved, an approval letter is provided to the PI.

- .4 There are times when the risks associated with a particular protocol are such that continuing review should take place more frequently than annually (e.g., prior cases of non-compliance, significant risks to human subjects, etc.). In these cases, the IRB will specify that the PI report to the IRB either at a shorter time interval or after a specified number of subjects (e.g., after each subject or after 3 subjects) are enrolled. The PI's reports must describe the observed effects of the research activities and/or how the subject(s) responded to the research interventions. The determination will be recorded in the IRB minutes and reports forwarded to the IRB members.
- .5 The full committee will also be presented with the following:
 - a) A listing of unanticipated problems reported;
 - b) A listing of those protocols, amendments and continuing reviews approved through expedited review procedures; and
 - c) Other information relating to ongoing research activities are reported to the IRB.

4.7 Administrative Approval of Decisions Made by the IRB

Approvals, favorable actions, and recommendations made by the IRB are subject to review and further restriction by MDPH administration. For example, protocols could be approved by the IRB on a scientific and ethical basis, but be restricted or disapproved by MDPH administration due to the potential for fiscal impacts or adverse public/community reaction. Protocol disapproval, restrictions or conditions imposed by the IRB upon any activity involving human subjects cannot be rescinded or removed except by subsequent action of the IRB.

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Section 5.0 Informed Consent of Research Participants

- 5.1 Informed Consent**
 - 5.2 Elements of Informed Consent/Assent Forms**
 - 5.3 Additional Consent Information for Different Types of Studies**
 - 5.4 Obtaining and Documenting Informed Consent**
 - 5.5 Waiver of Documentation of Informed Consent**
 - 5.6 Waiver of Informed Consent**
 - 5.7 Elements of a Consent/Authorization Using Protected Health Information**
 - 5.8 Waiver of Authorization For Use and Disclosure of Protected Health Information**
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5.1 Informed Consent

- .1** Except as described in **Sections 5.6** and **5.7** below, investigators may not enroll or involve human subjects in non-exempt research unless they have obtained the legally effective, written, informed consent of the subject or the subject's legally authorized representative, prior to enrollment of the subject in the research. Investigators are responsible for ensuring that the subjects, or their representatives, are given sufficient opportunity to consider whether or not to participate and must seek to avoid coercion or undue influence. The IRB is responsible for evaluating the informed consent process. Information given to potential subjects or their representatives must be in a language and at an appropriate reading level that is understandable to the subject or representative. No process of obtaining consent may include exculpatory language through which subjects waive any of their legal rights or release or appear to release the investigator, sponsor, or institution or its agents from liability for negligence. The consent process must provide sufficient opportunity to consider whether to participate.
- .2** Occasionally, the setting in which the consent is sought will pose the possibility of coercion or undue influence. Conducting research at institutions that provide services to subjects may be perceived as implying that continued service is dependent upon participation in the research. Students in the educational setting may be concerned that refusal to participate will affect their grades. Prisoners may anticipate that participation will impact parole considerations. These institutional pressures should be addressed in the research design. The protocol must adequately preserve the right to refuse participation.
- .3** There are many other examples of possible sources of undue influence on subjects. It may not be possible to remove all sources of undue influence, but in the development of the protocol for obtaining informed consent, the principal investigator must make every effort to minimize coercion and other undue influences. The requirement to obtain informed consent should be seen as not only a legal obligation, but also as an ethical obligation. The research design must adequately address how informed consent will be obtained and what information will be given to prospective subjects. The IRB must look at the issues of coercion and undue influence in each proposal and insist on protocols where the circumstances of the consent process minimize the possibility of coercion and undue influence to participate.

- .4 For research studies involving non-English speaking participants the investigator will be required to submit translated consent forms as an explicit condition for approval.

5.2 Elements of Informed Consent/Assent Forms

- .1 The following are the basic required elements of informed consent (extracted from 45 CFR Part 46.116):
- a) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
 - b) A description of any reasonably foreseeable risks or discomforts to the subject;
 - c) A description of any benefits to the subject or to persons that may reasonably be expected from the research;
 - d) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
 - e) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained; if the research is subject to FDA regulation, the statement also must note the possibility that the Food and Drug Administration will inspect the records.
 - f) 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;
 - g) 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; and
 - h) 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.
- .2 Whenever appropriate, one or more of the following elements of information shall also be provided to each subject:
- a) If the risks of any research procedure are not well known, for example because of limited experience in humans: A statement that the particular treatment or procedure may involve risks to the participant, which are currently unforeseeable;
 - b) If the research includes women of child bearing potential or pregnant women, and the effects of any research procedures on embryos and fetuses is not well known: A statement that the particular treatment or procedure may involve risks to the embryo or fetus, if the participant is or may become pregnant, which are currently unforeseeable.
 - c) If there are anticipated circumstances under which the participant's participation will be terminated by the investigator without regard to the participant's consent: Anticipated circumstances under which participation may be terminated by the investigator without the participant's consent.

- d) If there are costs to the participant that may result from participation in the research: Additional costs associated with study participation.
 - e) If there are adverse consequences (e.g., physical, social, economic, legal, or psychological) of a participant's decision to withdraw from the research: Consequences of a participant's decision to withdraw from the research and procedures for an orderly termination of participation.
 - f) If significant new findings during the course of the research that may relate to the participant's willingness to continue participation are possible: Statement that new findings developed during the course of the research that may relate to the participant's willingness to continue in the research study will be provided to the participant.
 - g) If the approximate number of participants involved in the study might be relevant to a decision to take part in the research: Approximate number of participants involved in the study.
- .3 The informed consent requirements in this policy are not intended to preempt any applicable Federal, State, or local laws which require additional information to be disclosed in order for informed consent to be legally effective. Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable Federal, State, or local law.
- .4 Obtaining informed consent for investigational in vitro diagnostic devices used to identify chemical, biological, radiological, or nuclear agents that would suggest a terrorism or other public health emergency will be deemed feasible unless, before use of the test article, both the investigator and a physician who is not otherwise participating in the clinical investigation make the determinations and later certify in writing all of the relevant requirements set forth in 21 CFR §50.23(e).
- .5 For studies involving children, child assent is required when the child is old enough to understand what participation in a research study means. Assent is the affirmative agreement by a child. Mere failure to object may not, absent affirmative agreement, be construed as assent. [45 CFR §46.402(b)] [21 CFR §50.3(n)]

5.3 Additional Consent Information for Different Types of Studies

- .1 Studies involving blood samples: The MDPH form, [Title of Biologics form?] must be completed and submitted to the IRB for studies involving the collection of blood samples. The consent form should contain a statement such as, "Blood samples will be obtained by venipuncture. This method involves inserting a needle into a vein in the arm and withdrawing a sample of blood. It is routinely used to obtain blood for physical examinations. Venipuncture is accompanied by minor discomfort at the site of the needle entry and may result in slight bruising and/or a feeling of faintness. In this study a trained technician will obtain a 30 ml (about 2 tablespoonfuls) sample of your blood that will be analyzed for..."
- .2 Studies involving blood, tissue or body fluid for possible genetic research: If the research involves the use of a subject's blood, tissue or body fluid, the MDPH form, "Research Involving Human Blood, Urine, or Tissue Collection for Analytical Testing and/or Storage", must be completed and submitted to the IRB. In addition, the researcher must include in the consent form information explaining the subjects' rights, including:
- a) whether or not the specimens will be maintained without identifiers,

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- b)** where the specimens will be stored,
 - c)** who will own the specimens,
 - d)** whether and how the specimens will be used in the future, including use for commercial purposes,
 - e)** whether a subject may request that specimens be destroyed and how to make such requests, and
 - f)** retention plans for specimens, including expected length of time.
- .3** Studies that involve drugs: The participants must be given a statement of known side effects, warned about possible drug interactions (including interactions with alcohol), and warned about activities that may be dangerous (such as driving with a drug that has a sedative effect).
- .4** Studies that involve sensitive topics: Participants should be told that some of the questions are of a personal or sensitive nature and should be given examples of the topics or questions. They should also be told whether they can skip a question if they do not wish to answer it. If questionnaires or interviews may generate reports of child physical or sexual abuse, the participant must be informed that the researcher is legally required to report this information to appropriate authorities. If the questionnaire or interview may generate reports that the participant plans to harm him or herself or others, the participant must be told that the investigator is ethically required to report that information to the local police department. This information about the legal obligations to report abuse and threats of harm to oneself or others may be omitted if the responses cannot be linked to an individual subject.
- .5** Studies that involve audio or video recordings: Participants must be told:
 - a)** that the interviews or sessions will be audio or videotaped;
 - b)** that they may request that they not be audio or videotaped;
 - c)** that any physical tapes will be coded so that no personally identifying information is visible on them;
 - d)** that the recordings will be kept in a secure place (e.g., a locked file cabinet in the investigator's office);
 - e)** that recordings will be heard or viewed only for research purposes by the investigator and his or her associates;
 - f)** that recordings will be erased after they are transcribed or coded; and
 - g)** whether or not participants can request that the recording be deleted at any time.
 - h)** If the researcher wishes to keep the recordings because of the requirements of his/her professional organization with respect to data or because the researcher may wish to review them for additional analyses at a later time, the statement about erasing them should be omitted and replaced with a statement that recordings will be retained for possible future analysis.
- .6** Studies that involve monetary or other compensation: The amount and type of the stipends or other compensations and the requirements to earn them must be clearly specified. If the study extends over a period of time, it is acceptable to reward a participant with a bonus if he or she completes all the interim components of the study. However, the participant must be paid for each component, and the bonus should not be greater than 50% of the total compensation.

- .7 Device Clinical Trials and Drug Clinical Trials Other than Phase I Investigations: When seeking informed consent for applicable clinical trials, as defined in 42 U.S.C. 282(j)(1)(A), the following statement shall be provided to each clinical trial subject in informed consent documents and processes. This will notify the clinical trial subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank under paragraph (j) of section 402 of the Public Health Service Act. The statement is “A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.”

5.4 Obtaining and Documenting Informed Consent

Federal regulations governing the use of human subjects in research activities require written documentation of informed consent unless the research meets the criteria for Waiver of Documentation of Consent. The participant and investigator (or their designee) should sign and date the IRB approved consent form. The following are the acceptable methods for documentation of informed consent of human research subjects:

- .1 The IRB must be made aware of the person(s) who will be conducting the consent interviews. These individuals should be listed in the IRB application and research proposal, and, unless indicated otherwise, are the only personnel allowed to obtain consent.
- .2 Each subject (or their legally authorized representative) must be provided adequate time to read and review the consent form, in addition to being advised of the procedures, risks, potential benefit, alternatives to participation, etc. This is frequently accomplished using the consent form as an outline for the discussion process.
- .3 After completing the consent discussion and assuring that the subject (or their representative) has no further questions and agrees to participate in the research activity, the research team member should instruct the subject (or their representative) to sign and date the consent form in the appropriate spaces.
- .4 The person conducting the consent discussion must then sign and date the consent form in the appropriate spaces (PI or designee). It is assumed that in most cases, all persons signing the consent form will do so at the conclusion of the consent discussion.
- .5 Each subject (or their representative) must be given a copy of the signed consent form. The original consent form should be filed in such a manner as to ensure immediate retrieval when required by auditing entities, e.g., FDA, IRB, or sponsor monitors.
- .6 Written documentation of informed consent is required, unless waived. Therefore, obtaining consent from an authorized third party via the telephone is not acceptable unless the IRB waives the requirement to document the informed consent process.
- .7 The regulations include provisions for approval of a waiver or amendment of part or all of the consent process, except when FDA regulated products are being studied. The IRB will consider written requests for waiver or amendment of the process when accompanied by sufficient justification.
- .8 Obtaining informed consent from subjects must be accomplished prior to performing the research activity and using only an IRB approved consent form. Written requests for amendments to an existing consent form must be approved prior to implementation, at which time the IRB office will provide a formal approval letter of the amendment to the consent form.

- .9 Upon receipt of an IRB approved consent form, all old versions should be discarded to prevent inadvertent use of an outdated consent form. Copies of the most recently approved consent form may be made and should be used until replaced by an amended consent form. The consent form must be reviewed at least annually as part of the continuing review process.

5.5 Waiver of Documentation of Informed Consent

The IRB can waive the requirement that the consent process include a signed consent form. Investigators desiring to not have a signed consent form must still provide participants with a consent document or information sheet disclosing all the required elements necessary for informed consent. In such cases, the IRB encourages investigators to use a written consent form and remove the signature section. According to 45 CFR 46.117 and / or 21 CFR 56.109(c)(1) an IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds:

- The research presents no more than minimal risk; **and**
- The research involves procedures that do not require written consent when performed outside of a research setting 45 CFR 46.117; 21 CFR 56.109(c)(1)

Or,

- The principle risks are those associated with a breach of confidentiality concerning the subject's participation in the research; **and**
- The consent document is the only record linking the subject with the research (45 CFR 46.117); **and**
- The study is not FDA regulated

Fact sheets, brochures, or preambles in survey instruments may be used in lieu of consent forms for some categories of minimal-risk research with adults, such as survey or questionnaire research on non-sensitive topics. The document should state the purpose of the survey, the expected number of respondents, a description of the topic of the survey and the general focus of the questions on the survey, a statement about confidentiality or anonymity, and a statement about how the participant may obtain additional information about the study. The document should also state that participation is voluntary and a decision not to participate will not affect the person's rights with respect to the institution or other benefits to which the person may be eligible. The participant should be provided a copy, whenever feasible. He or she need not sign it when the IRB has determined that responding to the survey indicates a willingness to participate in the study.

5.6 Waiver of Informed Consent

The IRB may waive the requirements for obtaining informed consent or approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent listed in 5.1, provided that all of the following five conditions are met:

- .1 The research involves no more than minimal risk to the subjects;
- .2 The waiver or amendment will not adversely effect the rights and welfare of the subjects;
- .3 The research could not practicably be carried out without the waiver or amendment;
- .4 Whenever appropriate, the subjects will be provided with additional pertinent information after participation; and

- .5 The study is not FDA regulated.

5.7 Elements of a Consent/Authorization Using Protected Health Information

Where a research project will be using or creating protected health information (PHI) subject to the HIPAA Privacy Rule, the subject must authorize the use or disclosure of his or her information by the HIPAA covered entity or the researcher must obtain a waiver of authorization from the IRB (see below). A separate authorization may accompany the informed consent documentation or they may be combined into a single document. If the investigator elects to use a separate authorization form, he must assure the IRB that it is HIPAA-compliant; the IRB need not review the form. If the authorization and informed consent are combined, the IRB must review the entire form.

- .1 Required Information. A valid authorization for release of PHI must set out the specific information stipulated in the Privacy rule:
 - a) A description of the information to be used or disclosed that identifies the information in a specific and meaningful fashion.
 - b) The name or other specific identification of the person(s), or class of persons, authorized to make the requested use or disclosure.
 - c) The name or other specific identification of the person(s), or class of persons, to whom the covered entity may make the requested use or disclosure.
 - d) A description of each purpose of the requested use or disclosure. The statement, "at the request of the individual" is a sufficient description of the purpose when an individual initiates the authorization and does not, or elects not to, provide a statement of the purpose.
 - e) An expiration date or an expiration event that relates to the individual or the purpose of the use or disclosure. A statement of the individual's right to revoke the authorization in writing and the exceptions to the right to revoke, together with a description of how the individual may revoke the authorization. The statement, "end of the research study," "none," or similar language is sufficient if the authorization is for a use or disclosure of protected health information for research, including for the creation and maintenance of a research database or research repository.
 - f) Signature of the individual and date. If the authorization is signed by a personal representative of the individual, a description of such representative's authority to act for the individual must also be provided.
- .2 Required Statements. In addition to the core elements, the authorization must contain statements adequate to place the individual on notice of all of the following:
 - a) The individual's right to revoke the authorization in writing, and either:
 - The exceptions to the right to revoke and a description of how the individual may revoke the authorization; or
 - To the extent that the information in (A) of this section is included in the notice required by 45 CFR §164.520, a reference to the covered entity's notice.
 - b) The ability or inability to condition treatment, payment, enrollment or eligibility for benefits on the authorization, by stating either:

- The covered entity may not condition treatment, payment, enrollment or eligibility for benefits on whether the individual signs the authorization when the prohibition on conditioning of authorizations applies; or
 - The consequences to the individual of a refusal to sign the authorization, the covered entity can condition treatment, enrollment in the health plan, or eligibility for benefits on failure to obtain such authorization.
- c) The potential for information disclosed pursuant to the authorization to be subject to redisclosure by the recipient and no longer be protected by this subpart.
- .3 Plain Language Requirement. As with the Consent element of the form, the authorization must be written in plain language.
- .4 Copy to the Individual. If a covered entity seeks an authorization from an individual for a use or disclosure of protected health information, the covered entity must provide the individual with a copy of the signed authorization.

5.8 Waiver of Authorization for Use and Disclosure of Protected Health Information

A HIPAA covered entity may use or disclose PHI for research without an authorization by the research subject only where an IRB waives the requirement or where the subjects are deceased.

The IRB may waive subject authorization in the following circumstances:

- .1 Waiver of Authorization Preparatory to Research:
- a) To request a waiver of authorization for activities preparatory to research the researcher must submit a request stating:
 - b) That the research is only for purposes of preparing a research protocol or similar uses preparatory to research;
 - c) That he or she will not remove any PHI from the covered entity; and
 - d) That the PHI is necessary for the research purpose.

- .2 Waiver of Authorization for Research Activities:

A PI may request a waiver of the research participants' authorizations for use/disclosure of PHI. This provision may be used, for example, to conduct records research, when PIs are unable to use de-identified information.

The DPH IRB may waive authorization for research purposes if it finds the use or disclosure of protected health information involves no more than minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:

- a) an adequate plan to protect the identifiers from improper use and disclosure;
- b) an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers, or such retention is otherwise required by law; and
- c) adequate written assurances that the protected health information will not be re-used or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by the Privacy rule

- d)** The research could not practicably be conducted without access to, and use of, the protected health information
 - e)** Documentation of the amendment or waiver of authorization must be signed by the Chair or other member, as designated by the Chair of the IRB, as applicable.
- .3** Permission to Use or Disclose PHI of Decedents.
 - a)** To use or disclose PHI of decedents, the researcher must represent that the use or disclosure of PHI is:
 - b)** Solely for research on the PHI of decedents,
 - c)** Necessary for the research, and
 - d)** Documentation of the death of the individuals about whom PHI is sought and provided.

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Section 6.0 Continuing Review, Amendments, and Reporting Requirements

- 6.1 Continuing Review Procedure**
 - 6.2 Greater than Annual Continuing Review**
 - 6.3 Amendments to Protocols**
 - 6.4 Investigator Identification and Reporting of Unanticipated Problems and Noncompliance**
 - 6.5 IRB Reporting of Unanticipated Problems and Noncompliance**
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6.1 Continuing Review Procedure

- .1** Any research activity involving the participation of human subjects or the use of their personal data that has received initial review and approval by the IRB (including expedited and full board) is subject to continuing review and approval. Time intervals for such reviews shall be made at the discretion of the IRB but shall occur no less than annually.
- .2** Request for approval for continuing review should be submitted to the IRB via IRBNet.com. Investigators must submit a continuing review when: research is ongoing, the remaining research activities are limited to data collection, the research remains active for long-term follow-up of participants despite the protocol being permanently closed to the enrollment of new participants and all participants having completed all research related interventions, or for the analysis of identifiable data. A continuing review may stop only when:
 - a)** The research is permanently closed to the enrollment of new participants;
 - b)** All participants have completed all research-related interventions; and
 - c)** Collection and analysis of private information has been completed.
- .3** Full board and expedited studies require the following be submitted for continuing review: an Annual Renewal or Amendment form, a current copy of the consent form, and any additional documents and materials, including questionnaires, recruitment materials, and scripts, which have changed since the prior approval. Any revisions to the previously approved consent process, the protocol, recruitment, enrollment, or other study related activity prior to the renewal date must be submitted to the IRB as an amendment request. All changes should be clearly indicated in a tracked change or highlighted format.
- .4** For studies that received full committee review at the time of initial application, continuing review shall be approved by the full board unless it meets criteria for expedited review. Continuing reviews for expedited studies are reviewed and approved by the IRB Chair, Vice Chair or designee without a vote of the full committee. A summary of studies approved by expedited review shall be presented at the next full committee meeting. No research protocol may continue until final approval for continuation is granted.
- .5** Continuing review approval periods are one year from the day of formal re-approval, unless otherwise necessitated (see below). Only continuing reviews received and approved within 30 days prior to the expiration date will be issued a concurrent approval date. Continuing reviews submitted prior to their expiration date but not formally reviewed and approved by the expiration date are expired and all research and research related activity must cease until formal IRB re-approval. The IRB

provides PIs a 30-day grace period after the expiration date to submit a continuing review. However, during this time all research and research related activities must may be ordered to cease.

- .6 The IRB has the authority to observe or appoint a third-party to observe research conduct, including consent procedures. It may also consider whether a study requires independent verification from sources other than the PI to ensure that no material changes have occurred since the last IRB approval. The IRB will require verification of the information provided for continuing review when:
 - a) continuing review materials appear inconsistent or inaccurate compared to prior applications or records and discrepancies cannot be resolved via communication with the PI, or
 - b) the IRB determines that such actions are useful as part of a corrective action plan for any unanticipated problem or event.
- .7 If the findings of such investigations during the continuing review process warrant corrective actions, the IRB may suspend or terminate a research project to ensure the quality of research.

6.2 Greater than Annual Continuing Review

The IRB may require certain protocols be reviewed more frequently than annually. Any study requiring more than annual review will have a limited set approval time period. The frequency of continuing review is to be determined by the IRB appropriate to the protocol under review.

The IRB may require more than annual review because of any of the following:

- a) Noncompliance history by PI or co-PI
- b) Marginal Risk / Benefit Ratio
- c) As necessitated by protocol
- d) Based on complaints, unanticipated problems, or adverse events

6.3 Amendments to Protocols

- .1 All amendments, modifications, or changes to protocols, consent forms, or other materials must be requested by a PI by submitting a Renewal or Amendment form to the IRB via IRBNet. Requests must describe what modifications are desired, why the changes are required, and if the changes pose any additional risks to the subjects. PIs are required to submit complete and updated research materials and indicate all changes in tracked change or highlighted format.
- .2 The amendment request will be reviewed by the IRB Administrator and/or the IRB Chair or Vice Chair and either approved if amendments are minor, or referred to the full board, as appropriate. Minor changes are defined as changes that involve minimal risk procedures and/or do not increase the risk or decrease the potential benefit to subjects. Typical changes include changes in key personnel, non-significant changes in sample size, an addition of a questionnaire that does not include sensitive or controversial questions, etc.
- .3 When amendments, modifications, or changes are reviewed by the full board, all IRB members will be provided with a copy of all documents submitted by the investigator. At the discretion of the IRB Chair or Vice Chair, the amendment may be reviewed by the full board. Changes considered to be more than minor must be reviewed at a full board meeting.

6.4 Investigator Identification and Reporting of Unanticipated Problems and Noncompliance

Required reporting: PIs are required to promptly report the following to the IRB:

.1 Any unanticipated problem involving risks to subjects or others.

An unanticipated problem involving risks to participants or others means an event that was (1) unforeseen, (2) related to the research procedures, and (3) either caused harm to participants or others, or placed them at increased risk of harm.

Examples of an unanticipated problem involving risks to subjects include, but are not limited to:

- a)** An actual unforeseen harmful or unfavorable occurrence to participants or others that relates to the research protocol (injuries, side effects, deaths);
- b)** An unforeseen development that potentially increases the likelihood of harm to participants or others in the future;
- c)** A problem involving data collection, data storage, privacy, or confidentiality;
- d)** A participant complaint about IRB approved research procedures;
- e)** New information about a research study (e.g., a publication in the literature, interim findings, safety information released by the sponsor or regulatory agency, or safety monitoring report) that indicates a possible increase in the risks of the research;
- f)** Changes in approved research initiated without IRB review and approval to eliminate apparent immediate hazards to the participant; or
- g)** Incarceration of a subject.

.2 Any serious or continuing noncompliance.

Any serious or continuing noncompliance includes noncompliance with this policy, the federal rules for the protection of human research subjects, or requirements and conditions of the IRB.

“Noncompliance” means any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with either the research plan as approved by a designated IRB, or federal regulations or institutional policies governing such research. Noncompliance may range from minor to serious, be unintentional or willful, and may occur once or several times. Noncompliance may result from the action of the participant, investigator, or staff, and may or may not affect the rights and welfare of research participants or others or the integrity of the study. Complaints or reports of noncompliance from someone other than the research investigator are handled as allegations of noncompliance until such time that the report is validated or dismissed.

Serious noncompliance is any behavior, action or omission in the conduct or oversight of human research that has been determined to:

- a)** Affect the rights and welfare of participants and others;
- b)** Increase risks to participants and others, decrease potential benefits or otherwise unfavorably alter the risk/benefit ratio;
- c)** Compromise the integrity or validity of the research; or
- d)** Result from the willful or knowing misconduct on the part of the investigator(s) or study staff.

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Examples of serious noncompliance include, but are not limited to:

- Conducting non-exempt research that requires direct interaction or interventions with human subjects without first obtaining IRB approval;
- Enrolling subjects who fail to meet the inclusion or exclusion criteria in a protocol that involves greater than minimal risk and that in the opinion of the IRB Chair, designee, or full board, places the participant(s) at greater risk;
- Deviating from or violating the provisions of an IRB-approved protocol;
- Continuing to conduct a study after IRB approval has lapsed; or
- Failure to report adverse events, unanticipated problems, or substantive changes to the proposed protocol to the IRB as required by this policy.

Continuing noncompliance is a pattern of noncompliance that indicates an unwillingness to comply or a lack of knowledge that may lead to an adverse effect on the rights and welfare of participants, may place participants at greater risk of harm, or may adversely affect the scientific integrity of the study.

Examples of continuing noncompliance include, but are not limited to:

- Repeated instances of allowing a study to expire before it is re-approved;
- Repeated failure to respond to IRB inquiries or requests for documentation;
- Repeated failure to respond to and resolve any study contingencies; or
- Repeated instances of failures to follow conditions of approval, requirements of this policy, or federal regulations.

.3 Any suspension or termination of an IRB approval.

Whenever an IRB Chair or institution suspends or terminates an ongoing research study that has been approved by the IRB, the suspension or termination must be reported to the full IRB.

.4 Reporting responsibilities of the PI to the IRB: Within 3 days of knowledge of the unanticipated problem or noncompliance related to the study, the PI shall submit an Unanticipated Problem or Noncompliance form (available at www.mass.gov/dph/research) to the IRB office.

.5 Reporting responsibilities of the PI to other officials: The PI is responsible for complying with any other reporting requirements from his/her institution, grant sponsors, or government oversight agencies, including, but not limited to, OHRP and the FDA.

.6 Review responsibilities of the IRB:

- a) The IRB Chair or Vice Chair will review the details of the reported event and determine whether the event constitutes: (1) an unanticipated problem involving risks to subjects or others; (2) minor noncompliance that does not present a risk to subjects; (3) serious noncompliance; or (4) a pattern of continuing noncompliance.
- b) Based on this decision, the IRB Chair or Vice Chair will determine whether the incident meets reporting requirements to OHRP or FDA based on whether the event was (1) unforeseen, more likely than not related to the research, and caused harm to participants or others, or placed them at an increased risk of

harm, or (2) involved noncompliance with this policy, federal human subject protection rules, or conditions of approval by the IRB. The IRB Chair or Vice Chair will work with the PI to resolve any ongoing issues or concerns related to the study. If the event is determined to be a serious unanticipated problem, it will be referred to the full IRB for review. The IRB may vote to take one or more of the following actions:

- Accept the actions taken by the PI to report and resolve the incident;
 - Require the PI to notify current participants when information about the unanticipated problem might affect their willingness to continue to take part in the research;
 - Alter the continuing review schedule
 - Require peer review monitoring
 - Require explicit changes to the protocol:
 - Require notification of previous subjects;
 - Require modification of consent and/or protocol;
 - Suspend some or all research activities
 - Approve the study for a shorter period of time (e.g. 6 months versus 12 months);
 - Terminate the study for cause.
- c) Deliberations and determinations of the IRB will be fully documented in the minutes.

6.5 IRB Reporting of Unanticipated Problems and Noncompliance

- .1 The IRB Chair, Vice Chair, or Administrator must issue a written report when one or more of the following occurs:
- a) The Chair or Vice Chair determines that there has been an unanticipated problem involving risks to participants or others, as described in Section 6.4 above; or
 - b) The IRB Chair or Vice Chair makes a determination of serious or continuing non-compliance with the federal regulations, MDPH human subject protection policies and procedures, or conditions of IRB approval, as described in Section 6.4 above; or
 - c) The IRB Chair or Vice Chair or full IRB suspends or terminates a previously approved research protocol, as described in Section 6.4 above.

A copy of the report must be provided to:

- The Chair of the IRB and all IRB members;
 - The Office of the Commissioner;
 - The Principal Investigator; and
 - OHRP or the FDA, when reporting is required.
- .2 For unanticipated problems involving risks to subjects or others; the report shall contain:

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- a)** Name of the institution (e.g., university, hospital, foundation, school, etc) conducting the research;
 - b)** Title of the research project and/or grant proposal in which the problem occurred;
 - c)** Name of the principal investigator on the protocol;
 - d)** Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
 - e)** A detailed description of the problem; and
 - f)** Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.).
- .3** For serious or continuing noncompliance; the report shall contain:
 - a)** Name of the institution (e.g., university, hospital, foundation, school, etc) conducting the research;
 - b)** Title of the research project and/or grant proposal in which the noncompliance occurred, or, for IRB or institutional noncompliance, the IRB or institution involved;
 - c)** Name of the principal investigator on the protocol, if applicable;
 - d)** Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
 - e)** A detailed description of the noncompliance; and
 - f)** Actions the institution is taking or plans to take to address the noncompliance (e.g., educate the investigator, educate all research staff, educate the IRB or institutional official, develop or revise IRB written procedures, suspend the protocol, suspend the investigator, conduct random audits of the investigator or all investigators, etc.).
- .4** For suspension or termination; the report shall contain:
 - a)** Name of the institution (e.g., university, hospital, foundation, school, etc.) conducting the research;
 - b)** Title of the research project and/or grant proposal that was suspended or terminated;
 - c)** Name of the principal investigator on the protocol;
 - d)** Number of the research project assigned by the IRB that was suspended or terminated and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
 - e)** A detailed description of the reason for the suspension or termination; and
 - f)** The actions the institution is taking or plans to take to address the suspension or termination (e.g., investigate alleged noncompliance, educate the investigator, educate all research staff, require monitoring of the investigator or the research project, etc.).
- .5** Serious incidents must be reported within 3 days. Less serious incidents not involving risks to human subjects must be reported within 2 weeks. The IRB may

send an initial report and indicate that a follow-up or final report will follow when an investigation has been completed or a corrective action plan has been implemented.

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Section 7.0 Procedures for Research with Vulnerable Populations

- 7.1 Inclusion of Pregnant Women, Human Fetuses, and Neonates in Research**
 - 7.2 Inclusion of Prisoners in Research**
 - 7.3 Inclusion of Children in Research**
 - 7.4 Inclusion of Adults Who Lack Decision-Making Capacity in Research**
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For studies involving vulnerable populations, there are additional requirements on the researcher and the institutional review board. These additional requirements are described in this section.

7.1 Inclusion of Pregnant Women, Human Fetuses, and Neonates in Research

For studies involving pregnant women, human fetuses, and neonates, PIs and the IRB must follow the guidelines set forth in Subpart B of 45 CFR 46. Investigators must include in the research proposal the rationale and details for the inclusion of pregnant women, fetuses, or neonates in research activities. PIs shall ensure that the informed consent process adequately addresses the risk to the fetus or neonate and pregnant women. The IRB must review all guidelines as set forth in Subpart B of 45 CFR 46 and only approve those studies that the IRB has determined to fulfill all necessary regulatory requirements.

- .1** Pregnant women or fetuses may be involved in research if all of the following conditions are met (45 CFR 46.204):
 - 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, the woman's consent is obtained;
 - 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, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;
 - f)** Each individual providing consent under (4) or (5) above is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

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- g)** For minors who are pregnant, assent and permission are obtained in accord with Subpart D for studies involving children;
 - h)** No inducements, monetary or otherwise, will 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;
 - j)** Individuals engaged in the research will have no part in determining the viability of a neonate, and
 - k)** A data safety monitoring plan has been established to monitor participants.
- .2** Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met (45 CFR 46.205(a)):
 - a)** Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
 - b)** Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate;
 - c)** Individuals engaged in the research will have no part in determining the viability of a neonate; AND if the neonate is of uncertain viability (45 CFR 46.205(b)) until it has been ascertained whether or not a neonate is viable, the following additional conditions are met:
 - The IRB determines that 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 the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
 - 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 accord with Subpart A, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest. OR
- .3** According to 45 CFR 46.205(c) if the neonate is nonviable after delivery, all of the following additional conditions are met:
 - a)** Vital functions of the neonate will not be artificially maintained;
 - b)** The research will not terminate the heartbeat or respiration of the neonate;
 - c)** There will be no added risk to the neonate resulting from the research;
 - d)** The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
 - e)** The legally effective informed consent of both parents of the neonate is obtained, except that the waiver and alteration provisions of Subpart A do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy

resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirement of this paragraph.

- .4 According to 45 CFR 46.207(b) research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates will be sent to the Secretary of DHHS for review. The Secretary will determine the approvability of the research based on the conditions stated in 45 CFR 46.207(b).

7.2 Inclusion of Prisoners in Research

Special procedures are in place in the Federal Regulations that provide additional safeguards for the protection of prisoners involved in research activities. Investigators using prisoners as participants must provide specific detail and rationale in the research proposal. Investigators are also required to take extra measures to ensure appropriate informed consent from prisoners. Since prisoners may be influenced by their incarceration to participate in research, and, in order to assure that their decision to participate is not coerced, the IRB will adhere to Subpart C of 45 CFR 46. Prior to IRB approval, investigators are required to obtain and submit written confirmation from the prison that the parole boards will not take into account a prisoner's participation in the research when making decisions regarding parole. In the review of research involving prisoners the IRB will apply the prisoner specific definition of minimal risk as stated in 45 CFR 46.303(d). In reviewing prisoner research, the IRB will follow the requirements for IRB membership outlined in 45 CFR 46.107. If at some point while participating in a research project a participant becomes incarcerated, it is the responsibility of the PI to notify the IRB. The protocol will then be re-reviewed according to Subpart C or the participant-prisoner withdrawn from research. Subpart C of 45 CFR 46 provides four research categories that IRB may approve for prisoner research.

- .1 The DPH IRB will review the proposed research to ensure one of the following four categories is applicable:
 - a) 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 (45 CFR 46.306(a)(1)(A)).
 - b) 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 (45 CFR 46.306(a)(1)(B)).
 - c) 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 the study may proceed only after the Secretary of the Health and Human Services Department 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 (45 CFR 46.306(a)(1)(C)).
 - d) 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 of the Health and Human Services Department 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 (45 CFR 46.306(a)(1)(D)).

- .2 The IRB will then proceed to confirm that the following items are applicable 45 CFR 46.305(a):

IRB membership shall include a prisoner advocate

- a) Any possible advantages accruing to the prisoner through his/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/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;
- b) The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
- c) 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;
- d) The information is presented in language which is understandable to the subject population;
- e) 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;
- f) Where the Board finds there may be a need for follow-up examinations 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, and
- g) A data-safety monitoring plan has been established to monitor participants.

7.3 Inclusion of Children in Research

Special procedures are in place in the Federal Regulations that provide additional safeguards for the protection of children involved in research activities. The IRB will adhere to 45 CFR Part 46, Subpart D or 21 CFR Part 50, Subpart D. The exemptions listed in 45 CFR 46.101(b)(1) through b(6) are applicable for research involving children except for 45 CFR 46.101(b)(2) for research involving surveys, interview procedures, or interventions with children. Studies involving children require parental, guardian, or legally authorized representative consent and participant assent (unless waived). If there is any person other than the biological or adoptive parent who claims to be the child's guardian (grandparents, foster parents, etc.), the PI must verify documentation that the individual has the legal authority to make health care decisions on behalf of the child and therefore is the guardian as defined in federal regulations.

For studies involving children where the risk is greater than minimal, the IRB may approve only the categories of research listed below provided all applicable criteria are met:

- .3 Research not involving greater than minimal risk (45 CFR 46.404), if the IRB finds that no greater than minimal risk to children is presented, approval may be given only

if adequate provisions are made for soliciting the assent of the children and the permission of at least one (1) parent/guardian. Minimal risk means that the probability and magnitude of the 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 exams or tests.

- .4** Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (45 CFR 46.405), if the IRB finds that more than minimal risk to children 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, approval may be given only if the IRB finds that:

 - a)** the risk is justified by the anticipated benefit to the subjects, and
 - b)** 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
 - c)** adequate provisions are made for soliciting the assent of the children and permission of at least one (1) parent/guardian, and
 - d)** a data safety monitoring plan has been established to monitor participants.
- .5** 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 (45 CFR 46.406), if the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, approval may be given only if IRB finds that:

 - a)** the risk represents a minor increase over minimal risk, and
 - b)** the intervention/procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations, and
 - c)** the intervention/procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the subject's disorder or condition, and
 - d)** adequate provisions are made for soliciting assent of the child and permission of both parents/guardians, and
 - e)** a data safety monitoring plan has been established to monitor participants.
- .6** Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (45 CFR 46.407), if the IRB does not believe the research meets the requirement of 404, 405, or 406, approval may be given only if:

 - a)** The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, and
 - b)** The Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines and following opportunity for public review and comment has determined either (1) that the research in fact satisfies the conditions of 404, 405, or 406, or (2) the research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children and the research will be conducted in accordance

with sound ethical principles and adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, and

- c) A data safety monitoring plan has been established to monitor participants.

7.4 Requirements for Consent and Assent Involving Children

- .1 In accordance with 45 CFR 46.408(a), the IRB must determine that adequate provisions have been made for soliciting the assent of children, when in the judgment of the IRB the children are capable of providing assent. The IRB recommends that assent be sought for children ages eight and older, but may be appropriate for younger children depending on their aptitude. The IRB may determine that assent is not a necessary condition for proceeding with the research if:
 - a) The aptitude of some or all of the children is so limited that they cannot reasonably be assented (determinations of capacity to assent will be assessed by age, maturity, and psychological state; and may be made for one, some, or all children in the research).
 - b) The intervention or procedure involved 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 research; or
 - c) The research meets the required criteria for waiver of consent stated in 45 CFR 46.116(d).
- .2 When assent is required, the PI and the child will sign the assent form to document that the participant has been given an explanation of the proposed research, in language appropriate to the children's age and intellectual capacity.
- .3 In addition to the children's assent, the PI is required to solicit consent of each child's parents or adoptive parents. However, if there is any other person who claims to be the child's guardian (grandparents, foster parents, etc.) the PI must determine whether the individual has the legal authority to make health care decisions on behalf of the child and therefore is the guardian as defined in federal regulations. Parents must be consented following criteria in 45 CFR 46.116(a)(1-8) and any additional criteria specified by the IRB. One parent's signature is sufficient for research that is minimal risk or greater than minimal risk with the prospect of direct benefit to the participant (45 CFR 46.404 through 46.405). For research conducted under 45 CFR 56.406 (21 CFR 50.53) and 45 CFR 46.407 (21 CFR 50.54) consent is required from both parents unless: 1) one parent is deceased, unknown, incompetent, or not reasonably available; or 2) when only one parent has legal responsibility for the care and custody of the child. Parental consent must be documented according to 45 CFR 46.117.
- .4 The IRB may waive the requirement for obtaining consent from a parent or legal guardian if the research meets the provisions for waiver set forth in 45 CFR 46.116(d) (1-4), if the IRB determines that the research is designed for conditions or a population for which parental, guardian, or legally authorized representative is not a reasonable requirement to protect the participants (examples: homeless, neglected, abused children), the waiver is consistent with Federal, State, or local law, and the research is not subject to FDA regulations. The criteria for approving such a waiver are that the research is designed for: conditions for which parental, guardian, or legally authorized representative permission is not a reasonable requirement to protect the participants, or a participant population for which parental, guardian, or legally authorized representative permission is not a reasonable requirement to protect the participants. However, in such cases the IRB will substitute an

appropriate mechanism for protecting the children who will participate. The determination for an appropriate mechanism would depend upon the nature and purpose of the research, risks, benefits, age, maturity, and psychological condition of the participants.

- .5 Children who are wards of the State or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406 and 45 CFR 46.407 only if such research is: 1) related to their status as wards; or 2) conducted in school, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards. If the research meets the criteria above, the IRB requires the appointment of a participant advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or legally authorized representative. One individual may serve as an advocate for more than one child. The advocate must have necessary expertise and experience, and agree to act in the best interest of the child. Only those advocates without any conflicts of interest can be appointed as advocates.

7.5 Inclusion of Adults Who Lack Decision-Making Capacity in Research

- .1 Special procedures for IRB review and approval apply to research activities involving potential research subjects who, for a wide variety of reasons, are incapacitated to the extent that their decision-making capabilities are diminished or absent. Impaired capacity is not limited to individuals with neurological, psychiatric, or substance abuse problems. Conversely, individuals with these problems should not be presumed to be cognitively impaired.
- .2 Cognitively impaired research subjects may not understand the difference between research and treatment or the dual role of the researcher. Therefore, when appropriate, it is essential that the consent / assent process clearly indicate the differences between individualized treatment (e.g., special education in classroom settings) and research. PIs may want to consider using an independent expert to assess the participant's capacity to consent or assent. Consent from a legally authorized representative must be obtained if participants are unable to consent. The PI should evaluate whether participants unable to consent should be required to assent to participation. The IRB will only approve research involving adults that cannot consent provided the following criteria are met:
 - a) The research question cannot be answered by using adults able to consent;
 - b) The research is of minimal risk or more than minimal risk with the prospect of direct benefit to each individual participant;
 - c) The assent of the adult will be a requirement for participation unless the adult is incapable of providing assent;
 - d) When assent is obtained, the PI will document the assent by noting on the consent or assent form that the participant assented to participate in research.

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Appendix A: Definitions

Assent – means the child's affirmative agreement to participate in research or clinical investigation. Mere failure to object may not, absent affirmative agreement, be construed as assent.

Children – means persons who have not attained the legal age for consent to treatments or procedures involved in research or clinical investigations, under the applicable law of the jurisdiction in which the research or clinical investigation will occur. In Massachusetts, individuals under the age of 18 are children unless emancipated by filing a petition and meeting the statutory requirements, or they have been adjudicated to be an adult for the purpose of criminal prosecution.

Common Rule – means the federal regulation for the protection of human subjects. The rule is codified for the Department of Health and Human Services in Title 45 CFR Part 46.

Conflict of Interest – means situations in which financial or other personal considerations may compromise, or have the appearance of compromising, an investigator's judgment in conducting or reporting research. A conflict of interest in research exists when a principal investigator or co-investigator has interests in the outcome of the research that may lead to a personal advantage and that might therefore, in actuality or appearance, compromise the integrity of the research. **Consent/Permission** – means the agreement of participant or the parent(s) of or guardian to the participation of their child or ward in the research/clinical investigation.

Continuing Noncompliance – means a pattern of noncompliance that, in the judgment of the IRB Chair, designee, or a full board, indicates a lack of understanding or disregard for the regulations or institutional requirements that protect the rights and welfare of participants and others, compromises the scientific integrity of a study such that important conclusions can no longer be reached, suggests a likelihood that noncompliance will continue without intervention, or involves frequent instances of minor noncompliance. Continuing noncompliance may also include failure to respond to a request from the IRB to resolve an episode of noncompliance or a pattern of minor noncompliance.

Continuing Review – means the periodic review of a research study by an IRB to evaluate whether the study continues to meet organizational and regulatory requirements. Federal regulations stipulate that continuing review should be conducted at intervals appropriate to the level of risk involved in the study, and not less than once per year. [45 CFR §46.109 (e)] [21 CFR §56.109 (f)]

Disclosure – means the release, transfer, provision of access to, or divulging in any other manner of information outside the entity holding the information.

Emancipated Minor – means a minor who has been adjudicated by a court to be considered an adult.

Engaged in Research – means that an institution becomes “engaged” in human subjects research when its employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes [45 CFR 46.102(d),(f)].

FDA – means the Food and Drug Administration.

Federalwide Assurance (FWA) – means the written assurance of compliance with the federal regulations for the protection of human subjects which institutions must provide as a condition for the receipt of federal research funds.

Fetus – means the product of conception from implantation until delivery.

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Guardian – means a person who is appointed guardian of the person and/or the estate of an incapacitated person under a court order.

Health Information – means any information created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse that relates to the past, present, or future physical or mental health or condition of an individual, the provision of health care to an individual, or the past, present or future payment for the provision of health care to an individual.

HIPAA – means the Health Insurance and Portability and Accountability Act of 1996 (HIPAA) that protects the privacy of a research participant's health information.

Human Subject – means a living individual about whom a research investigator (whether a professional or a student) obtains data through intervention or interaction with the individual or from individually identifiable information.

A human subject is defined by FDA is an individual who is or becomes a participant in research, either as a recipient of a test article or as a control who may be either a healthy human or a patient. [21 CFR 50.3(g), 21 CFR 56.102(e)]. A human subject according to FDA includes an individual on whose specimen a medical device is used [21 CFR 812.3(p)].

Human Subject Research – means any activity that either:

Meets the DHHS definition of “Research” and involves “Human Subjects” as defined by DHHS; or

Meets the FDA definition of “Research” and involves “Human Subjects” as defined by FDA;

Individually Identifiable – means that a record contains information which reveals or can likely be associated with the identity of the person or persons to whom the information pertains.

Informed Consent – means the agreement to participate in research that is made voluntarily by an individual with legal and mental competence and the requisite decision-making capacity, after disclosure of all material information about the research. Informed Consent means the knowing consent of an individual or his legally authorized representative, so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion. Information conveyed in the informed consent/ authorization procedure must include all essential elements listed in Section 5 of this manual.

Interaction – means communication or interpersonal contact between investigator and subject.

Intervention – means 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.

Investigational Device Exemption (IDE) – means the exemption by which the FDA permits a device that otherwise would be required to comply with a performance standard or to have pre-market approval, to be shipped lawfully in interstate commerce for the purpose of conducting investigations of that device. (21 CFR part 812)

Investigational New Drug (IND) – means an investigational drug or biologic application by which the FDA allows testing in human beings of a substance having an effect in the body. (21 CFR part 312, subpart B)

IRB – means the MDPH review board that ensures compliance with human research subject protection requirements described in this policy and MDPH's Federalwide Assurance.

Legally Authorized Representative – means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to that subject's participation in the procedures involved in the research. [45 CFR §46.402(c)] [21 CFR §50.3(l)]. The individuals authorized to consent on behalf of a prospective participant to participation in the procedures involved in the research are the parent or legal guardian if the patient is a child, a legal guardian if the individual has been adjudicated incapacitated to manage the individual's personal affairs, an agent of the individual authorized under a durable power of attorney for health care, an attorney ad litem appointed for the individual, a guardian ad litem appointed for the individual, or an attorney retained by the individual.

MDPH – means the Massachusetts Department of Public Health.

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.

Minor Noncompliance – means any behavior, action or omission in the conduct or oversight of research involving human subjects that deviates from the approved research plan, federal regulations or institutional policies but, because of its nature, research project or subject population, does not:

- .1 place, or have the potential to place, participants and others at greater risk than previously anticipated;
- .2 have a substantive effect on the value of the data collected; and
- .3 result from willful or knowing misconduct on the part of the investigator(s) or study staff.

Examples of minor noncompliance may include, when such noncompliance does not create additional risks to subjects:

- .1 Changing study personnel without notifying the IRB;
- .2 Shortening the duration between planned study visits;
- .3 Implementing minor wording changes in study questionnaires without first obtaining IRB approval;
- .4 Routine lab missed at scheduled visit and re-drawn later.

Neonate – means a newborn.

Parent – means a child's biological or adoptive parent.

Permission – means the agreement of parent(s) or guardian to the participation of the child in the research or clinical investigation.

Personal Records – means any information obtained or maintained by a state agency which refers to a person and which is declared exempt from public disclosure, confidential, or privileged under state or federal law.

Pregnancy – means the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the presumptive signs of pregnancy, such as missed menses, until the results of pregnancy testing are negative or until delivery.

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Principal Investigator (PI) – means the researcher responsible for the design, conduct, or reporting of the research or other educational activity proposed for funding. In some cases, even graduate students and postdoctoral fellows may be responsible for the design, conduct, or reporting of research such that the graduate student or postdoctoral fellow is considered to be an Investigator under this policy and may be required to complete a financial disclosure statement. The principal investigator on each grant or contract should insure that all staff on the project are aware of and comply with this policy.

Private Information – means 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 in order for obtaining the information to constitute research involving human subjects.

Protected Health Information (PHI) – means individually identifiable health information created or received by a health care provider, health plan or health care clearinghouse that is transmitted or maintained in any form or medium.

Public Health Practice – means any activity which is intended to prevent disease or injury to the public and improve health. A project is generally considered public health practice if the intent of the project is to identify and control a health problem; the intended benefits of the project are primarily or exclusively for the study participants; data collected are needed to assess and/or improve the health of the participants; and the project activities are not experimental.

Quality Improvement – means periodic examination of organizational activities, policies, procedures and performance to identify best practices and target areas in need of improvement; includes implementation of corrective actions or policy changes where needed.

Research – means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and services programs may include research activities. In general, a project is research if it is intended to generate generalizable knowledge concerning public health; the intended benefits of the project may or may not include study participants but always extend beyond the study participants to the larger population; and data collected exceed the requirements for care of the study participants.

Research, as defined by FDA, means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. [21 CFR 50.3(c), 21 CFR 56.102(c)]

- “Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act” means any use of a drug other than the use of an approved drug in the course of medical practice. [21 CFR 312.3(b)]

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- “Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act” means any activity that evaluates the safety or effectiveness of a device. [21 CFR 812.2(a)]

Sponsor – means an entity who takes responsibility for and initiates research, but who may not conduct the investigation. A person other than an individual (e.g., corporation or agency) that uses one or more of its own employees to conduct research it has initiated is considered to be a sponsor, and the employees are considered to be investigators. [21 CFR §50.3(k)] [21 CFR §50.102(j)] [21 CFR §312.3]

Use – means, with respect to individually identifiable information, the sharing, employment, application, utilization, examination, or analysis of such information within the entity that maintains the information.

Vulnerable Subjects/Participants – means individuals who lack the capacity to provide informed consent or whose willingness to participate in research may be subject to undue influenced or coercion. Vulnerable subjects include, for example, children, prisoners, individuals with emotional or cognitive disorders/impairments, and economically or educationally disadvantaged persons. [45 CFR §56.107] [45 CFR §56.111(a)(3)] [45 CFR §56.111(b)] [21 CFR §56.107] [21 CFR §56.111(a)(3)] [21 CFR §56.111(b)]