DEPARTMENT OF HEALTH

Institutional Review Board Policies and Procedures

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Institutional Review Board Policies and Procedures for the Minnesota Department of Health Institutional Review Board (IRB)

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Preface

To protect the privacy, well-being, and rights of Minnesotans who are subjects of research, the Minnesota Department of Health (MDH) established an institutional review board (IRB) in 2000. This board, which operates under Title 45, part 46 of the Code of Federal Regulations and applicable state law (e.g., Minnesota Government Data Practices Act), reviews and approves department-sponsored research using its prescribed process.

MDH created this board as the initial part of a long-range plan for addressing the issues related to human subjects—appropriately classifying and properly protecting data (i.e., information and biospecimens) gathered by the department. The IRB revises these Policies and Procedures as it continues its work to ensure consistency between state and federal protections, especially privacy protections, for human research subjects.

Additional information on the Minnesota Department of Health Institutional Review Board may be found at: Minnesota Department of Health: Institutional Review Board (https://www.health.state.mn.us/data/irb).

I. Statement of principles and policies

A. Ethical principles

The Minnesota Department of Health (MDH) is guided by the ethical principles for research involving human subjects stated in the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research report entitled "Ethical Principles and Guidelines for the Protection of Human Subjects in Research" (the Belmont Report) [see Section IV. List of authorities in this document]. MDH specifically recognizes the Belmont Report principles of respect for persons, beneficence (including minimization of harms and maximization of benefits), and justice and applies these principles in all research covered by these policies and procedures.

In addition, all MDH-funded or conducted research must meet the requirements stated in Title 45, Part 46 of the Code of Federal Regulations (45 CFR 46) [see Section IV. List of authorities in this document]. Any research involving products regulated by the U. S. Food and Drug Administration (FDA) must meet the requirements of 45 CFR 46 and FDA regulations for protecting human subjects, 21 CFR 50 and 56.

B. Institutional policies

The following policies guide all IRB activities and procedures outlined in this document.

- MDH acknowledges and accepts its responsibility for protecting the rights and welfare of human subjects participating in our research.
- MDH acknowledges that it and especially its investigators bear full responsibility for ethically performing all research covered by these policies and procedures and complying with federal, state, and local laws as they apply to such research.
- MDH assures that it and its investigators have satisfied the following requirements before involving human subjects:
    - Risks to participants are minimized by using procedures that are consistent with sound research design and do not unnecessarily expose participants to risks or duplicate procedures that are already being performed on participants for prevention, diagnostic, or treatment purposes.
    - Risks to participants are reasonable compared to the knowledge that might reasonably be expected to result.
    - Participant selection is equitable.
    - The principal investigator (PI) will acquire informed consent appropriate to the project from each prospective participant or the participant's legally authorized representative, unless otherwise exempted by state or federal law.
    - When required, the principal investigator will appropriately document informed consent and will retain it in a secure manner such as a locked file cabinet or protected computer server.
    - The research plan ensures participant safety.
    - Each research project will have adequate provisions to protect individual participant's privacy and maintain data confidentiality.

- MDH recognizes that for those who are likely to be especially vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capabilities, or economically or educationally disadvantaged persons, the research plan needs appropriate additional safeguards.
- MDH encourages and promotes constructive communication among its administrators, research supervisors, research investigators, and all other relevant parties to maintain a high level of awareness for safeguarding research subjects' rights and welfare.
- MDH oversees higher-risk projects by reviewing each open project at least annually to assure that investigators are effectively applying its practices and procedures designed for the protection of the rights and welfare of human subjects.
- MDH requires that principal investigators and other key project staff be trained in the rights and protection of human subjects.

C. Focus

The purpose of MDH's research and other research that this IRB reviews is to advance public health. "Public health research" seeks to understand population health. Consequently, the risks for subjects are generally data- and privacy-driven, and are therefore considerably less risky to individuals' physical health than experimental treatments or clinical trials. The IRB holds itself to very high ethical standards but evaluates risk to subjects according to specific risks posed by research of this nature.

II. Operating procedures

A. Institutional Review Board

1. Purpose, scope, and authority

To implement these principles and policies, MDH has established an institutional review board (IRB) under Title 45 of the Code of Federal Regulations, Part 46 Protection of Human Subjects and relevant state laws. MDH has registered its IRB with the Office for Human Research Protections (OHRP) (MDH IRB #: IRB 00000945), The IRB has Federal-Wide Assurance (FWA) approved by OHRP (# FWA 00000072). The IRB is charged with reviewing, and has authority to approve, require modification in, or disapprove all research activities involving human subjects conducted or funded by the Department. IRB approval does not preclude further review by other MDH officials for programmatic relevance, priority for funding, etc. Those officials may not, however, approve research unless the IRB has approved it.

The scope and authority of the IRB are as follows:

- All new MDH studies that meet the federal definition of research require MDH IRB approval regardless of funding source. MDH's public health practice and surveillance activities are not research [see Section II.B.2. Public health practice and surveillance in this document]. The IRB will review all studies submitted by MDH staff.
- MDH staff engaged in cooperative research that has been or will be reviewed by another IRB must submit an application to the MDH IRB for review. In the application, the PI may request that the MDH IRB defer review to the other IRB involved.
- Upon request, the IRB will review research projects conducted by an agency or organization with close links to MDH (e.g., local public health agencies, ClearWay Minnesota, Blue Cross and Blue Shield of Minnesota, or MDH grant recipients) that does not have another IRB available.
- Projects not affiliated with MDH or its closely related partners are out of the IRB's scope.

2. Staffing and other support

MDH provides both meeting space and staff to support IRB review and record-keeping duties, including a designated IRB Administrator and IRB Coordinator. MDH also funds IRB training and travel expenses.

Non-MDH members whose service on the board is not part of their regular job assignment are eligible for reimbursement for expenses incurred in attending meetings (e.g., mileage, lodging, meals, etc.).

3. Organizational placement and reporting

The IRB Administrator and IRB Coordinator are located organizationally in the Center for Health Statistics. The board reports to the Commissioner, Deputy Commissioner, or other Commissioner's delegate to assure high-level oversight of its actions and activities.

Each January the board submits an annual summary of its actions to the Commissioner. The board also notifies the Commissioner immediately of any serious adverse events, approval suspensions or terminations, or serious or continuing investigator non-compliance.

4. Members

a. Appointment of members

The Commissioner of Health appoints IRB members for staggered two-year terms. Before term expiration, the IRB recommends candidate members to the Commissioner for consideration. Members of the IRB are appointed from MDH staff, academic institutions, public or private health organizations, and from the community at large. The Commissioner may reappoint members for subsequent two-year terms.

b. Board composition

The IRB must have at least 10 members with sufficiently diverse race, gender, and cultural backgrounds to promote adequate review. Collectively, the IRB shall possess the competence, experience, and diversity of its members' backgrounds necessary to: 1) review research activities from the point of view of the subjects as well as the investigators; and 2) discern whether proposed research is consistent with MDH's mission, standards for professional conduct, and applicable law, regulations, and policies. Consistent with these goals and the federal regulations (45 CFR 46.107), the composition of the IRB must be:

- At least one physician (M.D., D.O.), who has training and experience in a medical field sufficient to assess medical risks.
- At least one person with advanced training and experience in conducting scientific investigations.
- At least one person whose primary work is not in the area of scientific investigations.
- At least one person who is not, and whose immediate family are not, affiliated with MDH. In addition, at least 20 percent of members must be non-MDH members.
- At least one person with expertise in agency data privacy rules is desired but not required.

c. Criteria for members

Individuals whose professional and cultural backgrounds satisfy the IRB composition requirements and complement the expertise and backgrounds of the existing members are eligible to serve on the IRB. Candidates must also possess excellent communication and critical thinking skills to effectively apply the complex regulations and guidance for safeguarding the rights and welfare of human subjects. In addition, members are expected to be responsive, timely, and participate regularly. Members must have an email address to receive IRB communications. Individuals who have been sanctioned for ethics violations or who are under investigation for ethics violations may not serve on the board.

The IRB seeks members with knowledge of the populations commonly included in MDH research, particularly if these populations include groups who may be vulnerable to coercion or undue influence, such as children or persons disadvantaged educationally or economically.

The IRB seeks non-MDH members who are especially knowledgeable about their own local communities and are willing to review proposed research from that perspective. For example, ministers, teachers, attorneys, businesspersons, client advocates, or homemakers are possible candidates. The IRB considers the communities from which MDH will draw its research subjects when recruiting non-MDH members for the board.

Alternate members

The IRB may use designated alternate members either episodically or regularly: episodic alternate members serve in place of primary members who are temporarily unavailable; regular alternates share

their role with another alternate, trading responsibility for IRB activities to reduce individual burden. Whether episodic or regular, alternate members must have characteristics comparable to the substituted IRB member (e.g., both are unaffiliated members or both are physicians). Alternate members bear the same responsibilities as primary members to review, attend, and deliberate as described in this manual. Alternate members are counted for quorum only when present, and regular alternate pairs count as one member toward the minimum number of IRB members. Episodic alternates do not count toward the minimum number of IRB members.

Non-member experts

When the IRB requires specific expertise that its members lack, such as knowledge or experience in working with a study's population, methodology, or techniques, it may invite experts with the necessary competence to supplement the IRB's experience and assist with review.

Observers

MDH staff may attend convened meetings to observe. Others may observe at the IRB Chair's discretion. Individuals participating in the MDH student worker program are encouraged to observe IRB activities to enhance their learning experience at MDH. The Chair may ask observers to leave during deliberations.

d. Board leaders

Chair and Vice-Chair

IRB members will elect a Chair and Vice-Chair from the IRB membership when those positions are vacant. IRB members will nominate or self-nominate members for Chair and Vice-Chair and elect members for these positions by an affirmative vote from two-thirds of the members. The Chair leads full board meetings, determines in consultation with the Administrator which level of review is appropriate for new studies, and reports adverse events and investigator noncompliance to the Deputy Commissioner. The Chair reports IRB actions to the board. The Vice-Chair fulfills the duties of the Chair when the Chair is unavailable.

Administrator

The Administrator oversees the flow of IRB work including: reading new applications and recommending an appropriate level of review to the Chair, assigning and assisting primary reviewers, and communicating with Principal Investigators. The Administrator also responds to inquiries from MDH staff, provides training opportunities for IRB members, monitors changes in federal regulations or guidance, and leads revisions of the IRB's Policy and Procedures manual. The Administrator also prepares an annual report to the Commissioner on IRB activities, reports to the board on IRB activities quarterly (the Chair Report), and oversees the work of the IRB Coordinator.

Coordinator

The IRB Coordinator supports the timely flow of IRB work and maintains IRB records. Specifically, the IRB Coordinator prepares materials and minutes for IRB meetings, tracks incoming applications and their status, facilitates continuing review, and maintains a calendar for important IRB deadlines.

e. Member responsibilities

IRB members are expected to be familiar with the Belmont Report and the federal regulations that govern the board and human subjects protections, in general. Specific responsibilities include:

Training

Following their appointment and before serving as reviewers, IRB members must review the following materials about human subjects protections:

- The Belmont Report
- The MDH IRB Policies and Procedures Manual
- Complete at least one online training course on human subjects protections from a recognized institution such as:
  - The Office for Human Research Protections (OHRP) Human Research Protection Foundational Training (https://www.hhs.gov/ohrp/education-and-outreach/human-research-protection-training/human-research-protection-foundational-training/index.html): Lesson 1: Parts 1 and 2 only. Lessons 3 and 4: All sections. Submit certificates for Lessons 3 and 4 to the IRB Administrator.
  - Protecting Human Research Participants (PHRP) Online Training and Certification (https://phrptraining.com/): Submit certificate to the IRB Administrator.

When their schedules and workloads permit, members must participate in trainings offered at least every other year by the IRB Administrator on IRB topics.

Reviewing

IRB members review research projects primarily to assess human subjects' burdens to ensure that their rights and safety are properly protected. IRB members are appointed as "Primary Reviewers" from time to time to thoroughly analyze research projects and report in detail. For studies that qualify for expedited review, Primary Reviewers report on and recommend approval and any stipulations to the IRB Administrator. For studies that require full board review, Primary Reviewers lead the board's deliberations about the project's use of human research subjects. In addition, Primary Reviewers must:

- Follow up on stipulations, as needed.
- Examine re-review forms for compliance with IRB requirements and make recommendations whether to extend continued approval.
- Examine proposed revisions to the study and make recommendations.

Deliberating

IRB members evaluate and discuss research proposals and re-reviews presented at meetings.

Attending

IRB members are expected to attend meetings as their busy professional schedules allow. The IRB Administrator will ask members who miss at least four consecutive meetings to explain their absences and reconsider their time commitments to the IRB. The IRB Chair has the discretion to remove non-attending members.

f. Member list

The IRB maintains a current list of the IRB members identified by name, earned degrees, and representative capacity (e.g., scientist, nonscientist, unaffiliated).

5. Meetings

a. Timing

The IRB schedules monthly meetings to ensure timely review of proposals. If there is insufficient business, the Administrator, after consulting with the Chair, will cancel the meeting. The IRB Coordinator distributes meeting agendas and other materials to members at least one week before the meeting.

b. Conduct

The Chair conducts meetings in accordance with Robert's Rules of Order, Newly Revised, which governs meetings in all cases, unless the board has adopted special rules that control in a particular situation. The Vice-Chair or a senior member of the IRB conducts meetings if the Chair is not present. Meetings follow a predetermined agenda, which includes approving the minutes of prior meetings. All official actions require a motion, a second, discussion, and a vote by voice or show of hands by those present.

c. Quorum and voting

Full board actions require a quorum of the members eligible to vote. More than half of the members eligible to vote must be present for a quorum. A quorum must include a nonscientist. A nonscientist is a member who has not worked professionally in either a scientific discipline or position. Any member who is not physically present at a convened meeting may participate electronically by video or audio when the member has received a copy of the meeting documents. Such members may vote and are counted toward the quorum. The IRB Administrator, IRB Coordinator, and non-member experts do not vote or count toward quorum. Alternate members may vote and count toward quorum, if present.

A majority (greater than 50%) of those present voting "aye" is required to approve a motion. The quorum must be maintained. If the quorum is lost by members leaving, the board may not vote. Members who abstain from voting count toward the quorum and the denominator of the voting percentage. While the Chair conducts the meeting in an impartial manner so that all may participate and contribute freely, the Chair counts toward quorum and may vote.

d. Action by electronic means

The IRB may meet and act by electronic means or written action in lieu of a meeting. The IRB may take an action required or permitted to be taken at a board meeting by written action signed, or consented to by authenticated electronic communication, by the number of members that would be required to take that action at an IRB meeting where all members were present.

The written action is effective when signed, or consented to by authenticated electronic communication, by the required number of members, unless a different effective time is provided in the written action.

The Chair has discretion to determine when to call meetings solely by means of remote communication, based on whether the agenda contains issues that are likely to be controversial. New research proposals requiring full board review are not appropriate for this process. Proposals previously discussed that require final approval or re-reviews are appropriate.

If controversy arises during deliberations, the Chair may cancel the electronic meeting and call for the IRB to meet in person. In addition, members may request that the e-meeting be suspended and that the Chair call a full meeting. The concurrence of three voting members requires the Chair to suspend the e-meeting and call a full IRB meeting. The IRB may hold no more than two consecutive e-meetings before holding a full board meeting.

Participants in e-meetings must disclose conflicts or affirmatively state that no conflicts exist.

In any electronic meeting or in any in-person meeting in which one or more members participate electronically:

- The IRB must verify the identity of each member. The IRB may rely on email from the address provided by the member.
- The IRB must use reasonable measures so that each member participating by means of remote communication has a reasonable opportunity to participate in the meeting, including the ability to:
    - Read or hear the proceedings substantially concurrently with those proceedings.
    - Have the members' remarks heard or read by other participants substantially concurrently with the making of those remarks.
    - Vote on matters submitted to the members.

The IRB must notify members of an electronic meeting at least five business days before voting. The IRB will notify members via the email address on record for the member. The IRB will not post notice or otherwise communicate IRB business on an electronic network or social networking site, such as Facebook. Members must have at least four hours to register their votes on the day of the meeting. The Chair may approve the use of another form of electronic communication only if the form meets MDH's security standards, as determined by the MDH security officer.

The IRB may, however, follow up on issues from in-person board meetings by electronic means without calling an electronic meeting. The Chair may announce at a meeting that a follow-up decision will be made by email. Only members who were in attendance at the in-person meeting may vote by email on this issue. Approval requires the same number of votes as it would have required if the vote had been taken at the meeting where the issue was discussed.

Members voting electronically must use the email accounts that the IRB has on record for them and must also use the "reply to all" feature. The IRB Coordinator will document the vote by saving the emails until the outcome is written into the minutes. After the IRB approves the minutes that include the electronic action, the IRB Coordinator may discard the emails.

6. Records

The IRB documents its activities and maintains records as required by federal regulation and in accordance with the IRB's record retention schedule. In addition to written IRB procedures and membership lists, such documentation includes copies of research proposals reviewed, minutes of IRB meetings, records of continuing review activities, copies of correspondence between the IRB and investigators, and statements of significant new findings provided to subjects that may affect participants' willingness to continue in the study (e.g., unexpected adverse events or a data breach).

The IRB will keep meeting minutes that record the following information: attendance; actions taken by the IRB; the vote on actions taken (including the number of members voting for, against, and abstaining); the basis for requiring changes in or disapproving research; and a written summary of the discussion of controversial issues and their resolution. The minutes must also reflect the time members leave and return to the meeting, and when quorum is lost.

The IRB retains records consistent with the MDH records retention schedule for the IRB. The IRB Coordinator will maintain records and ensure that they are accessible for inspection and copying at reasonable times and in a reasonable manner, consistent with state and federal law. Board members have no individual responsibility for keeping IRB records.

When the IRB closes a study file it will notify MDH PIs that the PIs must keep any consent forms in accordance with the records retention schedule for his or her division. It will notify non-MDH PIs that they must keep all consent forms for a minimum of 3 years following the project's closure.

7. Conflicts of interest

A member who has a conflict of interest may not participate in the IRB's initial or continuing review, except to provide information requested by the IRB. A "conflict of interest" is any interest in the research that might compromise a member's ability to review a protocol for protection of human subjects objectively, according to applicable state or federal regulation. Types of interests that might cause a conflict are financial interest; special or unusual knowledge specific to the research project; direct involvement in the research; supervision of any of the research investigators by the member; supervision of the member by the research investigators; or and other considerations that would provoke bias or the appearance of impropriety.

Each IRB member must sign a conflict-of-interest form at the beginning of each IRB meeting, stating whether he or she has a conflicting interest with any item on the agenda. The IRB must keep the completed forms on file. During the discussion of an agenda item that might be a conflict for the member, the member must leave the meeting room and may not participate in the discussion or vote on that item. A quorum is not lost by a member's absence for this reason.

8. Member training and orientation

The IRB will ensure and document that all members are adequately trained. Members will be aware of the federal regulations governing the protection of human research subjects and the *Minnesota Department of Health Institutional Review Board Policies and Procedures*. At least every other year, the IRB will deliver training or offer other training resources (e.g., workshops, videos, books, computerized training) on IRB-related topics, such as informed consent, vulnerable populations, or protecting participant privacy and autonomy. The IRB budget will fund IRB training. The IRB Administrator will train members on changes to the federal regulations or IRB policies and procedures, as needed.

9. Changes to policies and procedures

The policies and procedures in this manual are revised, as needed, to accommodate changes to federal regulations and guidance concerning the protection of human subjects. Major revisions of the manual are reviewed with and approved by the board. After the changes to the manual are approved by the board, the Commissioner is informed of the changes and provided a copy of the revised manual. The IRB website is updated with the new manual and MDH staff are informed of the changes, as appropriate.

B. Scope of research activities subject to IRB review

MDH gathers and uses data to carry out its mission. This activity meets the definition of research when any part is designed to contribute to generalizable knowledge. Contributing to generalizable knowledge means the primary intent of gathering and using the data or biospecimens is to learn beyond what MDH needs to: a) prevent or control disease or injury and improve the health of Minnesotans or b) improve a

public health program or service provided to Minnesotans. If the Principal Investigator (PI) has any doubt whether an activity involves research with human subjects, the PI must submit a Preliminary Review form or the full IRB application. All MDH staff who are PIs conducting human subjects research must receive IRB approval before collecting or analyzing data for the project. Consistent with OHRP recommendations, the IRB reserves the authority to determine whether a study qualifies as human subjects research.

1. Definition of human subjects research

The board uses the definitions listed in 45 CFR 46.102 to determine whether a proposed study meets the criteria for human subjects research. The federal regulations define **research** as a systematic investigation designed to develop or contribute to generalizable knowledge. **Human subjects** are living individual(s) about whom an investigator obtains (1) information or biospecimens through intervention or interaction with the individual, or (2) identifiable private information or identifiable biospecimens. **Intervention** means both physical procedures by which information or biospecimens are gathered and manipulations of the subject or the subject's environment. **Interaction** means communication or interpersonal contact between investigator and subject.

Private information means information that an individual has provided for specific purposes under the reasonable expectation that: a) the party receiving the information is not recording either the information or an observation of it; or b) the information will not be made public (e.g., a medical record).

Anonymous data or biospecimens are collected in such a way that subjects' identities are never associated with the data or biospecimens. Information or biospecimens are **identifiable** if the subject's identity is associated with the information or biospecimen or if the investigator may readily ascertain the subject's identity. Identifiable data become **de-identified** when direct personal identifiers are removed from the data or biospecimens before the data are analyzed for research purposes. If the data analyst or laboratory analyst maintains a key that can link the data or biospecimens back to the subjects and has direct access to the identifiers, the IRB considers these data or biospecimens identifiable.

2. Public health practice and surveillance

Public health practice and surveillance activities conducted by a public health authority do not meet the federal definition of research. MDH or its grantees or contractors are examples of public health authorities. The IRB relies on *Distinguishing Public Health Research and Public Health Nonresearch* (https://stacks.cdc.gov/pdfjs/web/viewer.html?file=https://stacks.cdc.gov/view/cdc/24235/cdc_24235_DS1.pdf), written by the Centers for Disease Control and Prevention (CDC), to determine whether a study is public health practice and surveillance or public health research. Public health practice and surveillance activities are not subject to IRB review, continuing review, or annual monitoring.

Public health practice and surveillance activities include collecting and testing information or biospecimens to monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including injury resulting from consumer products). In contrast, studies that are public health research are designed to contribute to generalized knowledge to improve public health practice, and intended benefits of the project extent beyond the study participants, and the data collected exceed what are needed to provide services to the study population. A public health study is deemed human subjects research and is subject to review if all or part of it will generate generalizable knowledge that can be applied to populations outside of Minnesota.

To maximize the protection of human participants in investigations, the board encourages MDH staff who are leading public health practice or surveillance studies to contact the MDH IRB for consultation when targeting vulnerable populations or obtaining sensitive information. When the IRB determines a study does not meet the definition of human subjects research but involves vulnerable populations or obtains sensitive information, the IRB nevertheless will consult with the PI about safeguarding subjects' privacy and safety.

C. Application and review process

1. Application for approval of research with human subjects

PIs must submit a completed *Application for Approval of Research with Human Subjects* with each new study proposal, available at: Minnesota Department of Health: IRB Forms and Applications (https://www.health.state.mn.us/data/irb/forms.html). The application requires:

- A detailed description of the research design and procedures as they affect human subjects.
- A list of precautions taken to safeguard the subjects' welfare.
- A precise description of the research's subject population.
- A description of the Informed Consent process and copies of all recruitment materials and consent forms to be used.
- Methods to be used to protect data confidentiality and subject privacy.
- A description of the training the PI(s) and anyone having access to identifiable data will have about using human subjects in research.

The IRB acts on all applications within one month after submission. The IRB notifies investigators in writing of board's decisions within one week of board action. Decisions to disapprove are accompanied by reasons for the decision.

a. Applications for secondary analysis of existing data

IRB approval authorizes the PI and co-PIs, with or without others, to analyze and publish on the data collected under an IRB-approved protocol. The PI and co-PIs may continue to analyze and publish using the same data as long as the analysis theme is generally consistent with the intent of the data collection that was originally presented to the IRB. Secondary analysis of existing data requires an IRB application when none of the investigators doing the analysis is the original PI or co-PIs or their successors, or the investigator will address an entirely different research question with the data and the data are identifiable and not publicly available.

b. Preliminary review application

PIs who believe their study does not meet the federal definition of human subjects research may submit an *Application for Preliminary Review*, which is briefer than the full application form, available at: Minnesota Department of Health: IRB Forms and Applications (https://www.health.state.mn.us/data/irb/forms.html). The IRB Administrator will determine whether the study is human subjects research. If the IRB Administrator determines that the study is not human

subjects research, the IRB will send the PI a formal letter with this determination. If the IRB Administrator determines all or part of the study is research with human subjects, the investigator must complete the full application unless the IRB Administrator determines the study meets the criteria for exemption. An Application for Preliminary Review may be emailed to the IRB Coordinator at any time. The IRB typically responds with a determination within two to three (2-3) business days.

2. Request for deferral to another IRB

MDH staff engaged in cooperative research that has been or will be reviewed by another IRB must submit an application to the MDH IRB for review. Cooperative research involves MDH staff obtaining access to data or biospecimens through one or more cooperative institutions, or when PIs from cooperating institutions obtain access to data or biospecimens from MDH. If a funder requires single IRB review, the PI shall request that the MDH IRB defer review to another IRB involved. PIs request a deferral by checking "yes" for the corresponding question in the IRB review application.

When the MDH IRB receives a request to defer to another IRB, the Administrator, after consulting with the Chair, will determine whether to defer review. The MDH IRB shall defer to another IRB when the funding entity requires using an external IRB; when federal regulations, state laws, or local policies require using a specific IRB; or when the study is low risk. In all other cases involving a request to defer review to an external IRB, the IRB Administrator will determine the level of review required and assign a primary reviewer, if applicable. Either the Administrator or the Primary Reviewer will review the application and make a recommendation to the board. Before deciding whether to defer, the board will assess whether the reviewing IRB will uphold comparable standards. Included in this assessment is whether the reviewing IRB maintains an active FWA, AAHRPP accreditation, engaged in a quality self-evaluation, or has prompted concerns in the past. If the board chooses to defer, it may notify the reviewing IRB of human subject concerns. If the board declines to defer, the IRB will provide the PI with written explanation of its reasons for not deferring.

When relying on an external IRB the MDH IRB will prepare or sign a reliance agreement and will work with investigators to prepare materials requested by reviewing IRBs, such as local context information forms. Reliance agreements will document the following responsibilities, at minimum:

- Initial and continuing review of research;
- Review of unanticipated problems involving risk to subjects or others;
- Review of serious or continuing noncompliance;
- Preparation, review, and submission of reports to federal agencies;
- Conflict of interest review;
- Post-approval monitoring and access to research records, including complying with the Minnesota Government Data Practices Act; and
- Maintenance of IRB records.

Once the MDH IRB has ceded review to another IRB, Principal Investigators must comply with the policies and procedures of the reviewing IRB.

3. Intake and initial determination

The IRB Coordinator first reviews both Applications for Preliminary Review and Applications for Approval of Research with Human Subjects upon receipt. The Coordinator verifies the application is complete,

records the necessary information in the IRB database, generates an electronic study folder in which to store materials, and notifies the Administrator an application has been received. The IRB Administrator reviews the Applications for Preliminary Review according to section 2 above. The IRB Administrator also reviews the Applications for Approval of Research with Human Subjects and makes a preliminary determination whether the study meets the definition. If the study meets the definition, the Administrator further assesses whether the study meets the criteria for exempt or expedited review, and recommends the type of review to the Chair or Vice-Chair, who will make the final determination. The Administrator notifies the PI what level of review (exempt, expedited or full board) is required.

4. Overview of primary reviewer role

The IRB appoints a Primary Reviewer who reviews new applications, amendments to approved research, and annual reviews. In selecting members for the role of Primary Reviewer, the IRB Administrator considers special expertise the member might bring to the proposed study, fair distribution of the IRB workload, and potential conflicts of interest. The IRB Administrator may seek an additional IRB member to serve jointly with a non-affiliated member who is serving as the Primary Reviewer. The Primary Reviewer continues with the study as long as he or she remains on the board to review changes to approved research, annual reviews, adverse events, and other matters as they arise.

The Primary Reviewer presents a summary of the research application and highlights any important human subjects-protection issues to the full board. The Primary Reviewer makes recommendations about amendments and annual reviews to the full board. For an expedited review, the Primary Reviewer summarizes the human subjects concerns and makes recommendations for stipulations and suggestions to the IRB Administrator who reviews the Primary Reviewer's recommendations and communicates them to the PI. The Primary Reviewer also reviews and approves protocol changes and continuing review requests. In the rare cases when the investigator falls within the definition of a covered entity under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 (P.L.104-191), as modified by the American Recovery and Reinvestment Act (ARRA), the Primary Reviewer must review the authorization or privacy notice to assure that it is HIPAA-compliant [see Section II.E.3. Research participant privacy in this document].

5. Full board review

The board reviews proposals at regularly scheduled IRB meetings, using the criteria outlined in this section to assign the proper determination:

- Approved
- Approved pending stipulations
- Postponed pending further review
- Disapproved

The IRB makes it decision by majority vote. A quorum must be present for the vote. A non-scientist member must take part in the vote. The IRB must record the number voting for, against, and abstaining. It must also record all stipulations, recommendations, and comments (as defined below), or reasons for disapproval. The IRB will notify investigators in writing of the determination approximately one week after the meeting. The notice will include any stipulations that must be met before the IRB will grant approval. The IRB can approve research with stipulations only after the IRB receives and the IRB Administrator and the Primary Reviewer approve the investigator's written response. The IRB notifies

the PI when it has reviewed and approved all response to stipulations. Investigators may not begin data collection until the IRB notifies the investigator of final approval.

- **Stipulations**: Approval with conditions that are mandatory (must be met) before final IRB approval and the beginning of research.
- **Suggestions**: These are recommendations to the investigator, but are not mandatory for IRB final approval.
- **Comments**: These are statements from IRB members recorded in the minutes that the Chair or Administrator may deem helpful to the PI.

6. Expedited review

The IRB uses expedited review for research that involves no more than minimal risk and involves only procedures listed in one or more of the expedited categories listed in the regulations. The IRB also uses expedited review for minor changes in previously approved research.

The IRB Administrator recommends and the Chair determines whether a new protocol is eligible for expedited review. When an expedited review is necessary, the Administrator seeks one or more members to conduct it. If the Primary Reviewer(s) recommends that the protocol be disapproved, the protocol must go to the full board for a vote.

a. Categories of research eligible for expedited review

The IRB will review research activities that present no more than minimal risk to human subjects by expedited review. Expedited review is limited to procedures listed in one or more of the following research categories:

1. Clinical studies of drugs and medical devices that are minimal risk and meet specific additional requirements;
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
    a. From healthy, non-pregnant adults who weigh at least 110 pounds. The amounts drawn may not exceed 550 ml in an eight-week period or
    b. From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, investigators may not draw more that the lesser of 50 ml or 3 ml per kg in an eight-week period.
    c. Investigators may not collect samples more than twice per week for either (a) or (b).
3. Prospective collection of biological specimens for research purposes by noninvasive means.
4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.
5. Research involving materials (data, documents, records, or biospecimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).
6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. Research on individual or group characteristics or behavior or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

8. Using the expedited review is limited when studies either 1) identify the subjects or 2) seek responses that pose foreseeable risk of harm for the subjects. Such risk comes from responses that might lead to criminal liability, civil liability, or damage to the subjects' financial or personal interests. The IRB may then use expedited review only if the investigators minimize risk from invasion of privacy and breach of confidentiality by implementing reasonable and appropriate protections.
9. The expedited review procedure may not be used for classified research involving human subjects. The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or full board--used by the IRB. Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

b. IRB responsibilities for expedited research

The IRB Administrator distributes a quarterly written report to each IRB member about any protocols handled through expedited review. Studies reviewed using expedited procedures are subject to annual monitoring.

7. Exemption from IRB Review

Research that meets the federal exemption criteria listed in section 45 CFR 46.104 is exempt from IRB review. For example, research that involves in-person interviews with adults on non-sensitive topics where no identifying information will be recorded that can link subjects to the data is exempt. Research that uses existing data, documents, or biospecimens, where no identifying information will be recorded that can link subjects to the data is also exempt. If identifiers are collected, some research is exempt if disclosure of the data could not reasonably place the subject at risk of civil or criminal liability or be damaging to the subject's financial standing, employability, or reputation.

The IRB Administrator will recommend and the Chair will determine whether research is exempt. Documentation of the exemption must include the specific category in the federal regulations justifying the exemption. In some cases, exempt status is conditional upon limited review to ensure there are adequate provisions to safeguard the data and the subjects' privacy.

a. Exemption criteria

The research categories eligible for exemption are:

1. Research conducted in educational settings, using normal educational practices that are unlikely to adversely affect either students' opportunity to learn required content or the assessment of instructors.
2. Research using educational tests, survey procedures, interview procedures, or observation of public behavior, if at least one of the following is true: a) the data are anonymous; b) the data are non-sensitive; or c) the IRB conducts a limited review.
3. Research involving benign behavioral interventions (brief, painless, unlikely to have significant lasting adverse effects, and the subjects are unlikely to find the intervention offensive or embarrassing) with consenting adult subjects and at least one of the following is true: a) the data are anonymous; b) the data are non-sensitive; or c) the IRB conducts a limited review.
4. Secondary research (research using existing data, documents, records, pathological specimens, or diagnostic specimens) for which consent is not required. Secondary research is exempt when using identifiable data or biospecimens, if at least one of the following is true:
    a. the data are publicly available;

b. the information is recorded by the investigator so that the identity of the subjects cannot be readily ascertained directly or through identifiers linked to the subjects, and the investigator does not contact or attempt to re-identify the subjects;

c. the research involves only collecting health information when that use is regulated under 45 CFR 160 and 45 CFR 164 and deemed "health care operations" or "research" or "public health activities and purposes;" or

d. the research is conducted by or on behalf of a federal entity using data collected for non-research purposes, if i) the data are maintained on technology in compliance with the E-Government Act of 2002, ii) all data will be maintained on systems of record subject to the Privacy Act of 1974, and iii) the data were collected subject to the Paperwork Reduction Act of 1995.

5. Research and demonstration projects that federal department or agency heads either conduct or approve and are designed to study, evaluate, or improve public benefit or service programs.
6. Some taste and food quality evaluation and consumer acceptance studies.
7. Storage or maintenance for secondary research for which broad consent is required.
8. Secondary research for which broad consent is required if broad consent was obtained, documentation of informed consent was obtained (or its waiver), the IRB conducts a limited review, and the investigator does not return research results to subjects unless legally required to do so.

B. IRB responsibilities for exempt research

Human subjects research deemed exempt by the IRB is not subject to further review or any stipulations or conditions specified by the IRB. At its discretion, the IRB may review the submitted documentation and make suggestions to strengthen the protections of human subjects. The IRB will annually monitor studies exempt from IRB review.

8. Approval criteria

The IRB's primary role is protecting the rights and welfare of human beings who participate in research. In accordance with federal regulations (45 CFR 46.111), the IRB may approve research only after it has determined that all of the following requirements are met:

- Risks to participants are minimized: 1) by using procedures that are consistent with sound research design, and that do not unnecessarily expose participants to risks, and 2) whenever appropriate, investigators employ procedures for prevention, diagnosis, or treatment purposes.
- Risks to participants are reasonable compared to anticipated benefits, if any, to participants and the importance of the knowledge that might reasonably be expected to be gained. In evaluating risks and benefits, the IRB will consider only those risks and benefits that might result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research).
- Selection of participants is equitable. In making this assessment the IRB must take into account the purpose of the research and the setting in which it will be conducted. The IRB must be particularly attentive to the special problems that might arise when research involves vulnerable populations, such as children, prisoners, individuals with impaired decision-making capabilities, or economically or educationally disadvantaged persons. If any of the participants are likely to be susceptible to undue influence or coercion, the IRB may require additional safeguards in the study to protect such participants.

- Investigators must seek informed consent from each prospective participant or the participant's legally authorized representative [see Section II.E.1.b. Elements of informed consent in this document], unless exempted by state or federal law.
- Investigators must document informed consent.
- The research plan ensures participants' safety.
- The research plan protects participants' privacy and maintains data confidentiality.

In addition, PIs and anyone who has access to human subjects or identifiable private information must have sufficient training in human subjects protections. IRB applications from MDH student workers, temporary employees, or interns must include a permanent MDH employee as co-PI.

9. Determination notification

After the board makes a determination, the Administrator prepares a determination letter and the Coordinator emails it to the primary investigator within 5 business days of the determination. The determination letter reflects the board's determination and includes any stipulations and recommendations. In addition, the Coordinator communicates determinations for expedited reviews to the full board through the Chair's quarterly report.

10. Appeal procedures

By federal regulation, institutional officials may not approve research that has been disapproved by the IRB. There is no mechanism for an appeal of IRB decisions to other departments. The IRB is an autonomous entity that issues binding decisions. Principal investigators may request the IRB to reconsider a decision regarding a research protocol by a written request that includes any pertinent information. The IRB will reconsider the protocol in the same manner as an initial review. After the IRB reconsiders its actions, the IRB's decision is final.

D. Post approval

1. Continuing review

Consistent with the federal regulations, the IRB reviews at least annually full-board approved research until the study is closed. The IRB reviews research at intervals appropriate to the degree of risk. The IRB oversees research related to public health, which typically carries a lower level of risk to human subjects than most clinical trials or drug and medical device studies. Therefore, an annual re-review is sufficient unless, the IRB determines that the degree of risk, adverse events, complaints about the research, or investigator non-compliance necessitates more frequent re-review.

The PI must respond to the IRB's request for continuing review. Approximately 30 days before the expiration of the study's approval, the IRB coordinator will send a continuing review form to the PI. Using the form, the PI must provide: 1) A brief report on the status of the project, including the protocol's progress to date; 2) plans for the next approval period; 3) a description of any adverse events or unanticipated problems involving risks to participants or others; 4) withdrawal of participants from the research or complaints about the research; 5) a summary of any recent literature; 6) modifications to the research since the last review, and 7) the expected study completion date.

A Primary Reviewer (usually the person who reviewed the initial application) will review the submitted continuing review form, present a summary to the board at a duly called or electronic IRB meeting, and make a recommendation. Action on the project must be approved by a majority of the members present. The investigator must meet the IRB's stipulations, if any, before approval for continuation is granted.

2. Annual monitoring

Continuing review is not required for studies that were determined to be exempt, exempt with limited review, or eligible for expedited review. These studies are monitored annually until the study is closed. Sixty to 30 days before the anniversary of the initial IRB approval date, the IRB Coordinator will ask the PI whether there have been any changes to the study protocol that might increase the risk to participants, whether there have been any adverse events, and whether the study is collecting data or enrolling participants.

The IRB may elect to continually review these lower risk studies but must document why doing so would enhance participant protections.

3. Transitioning studies to revised common rule

Transitioning a human subjects research study refers to the process of an IRB making the voluntary determination to re-review an ongoing study initiated before January 21, 2019 to ensure it complies with the 2018 Common Rule requirements [See: Office for Human Research Protections: The Revised Common Rule Compliance Dates and Transition Provision (45 CFR 46.101(l)) (https://www.hhs.gov/ohrp/regulations-and-policy/requests-for-comments/draft-guidance-revised-common-rule-compliance-dates-transition-provision-45-cfr-46-1011/index.html)]. Once the MDH IRB determines (documents and dates) that an ongoing study will transition, the study must comply in its entirety with the 2018 Common Rule Requirements. Once a study is transitioned to the 2018 Requirements, the decision cannot be reversed and the study cannot be transitioned back to the pre-2018 Requirements.

Policy for transitioning studies

The MDH IRB's policy for transitioning ongoing studies initiated before January 21, 2019:

- If there are no changes to the study protocol or study materials that require IRB review, the study will not be transitioned and will remain subject to the pre-2018 Requirements.
- If the principal investigator requests IRB review of changes to the study protocol or materials, the study will be transitioned in its entirety, including new determination of level of review.
- If the principal investigator submits a report of an adverse event or unanticipated problem involving risks to subjects or others, the study will be transitioned to the revised 2018 Common Rule requirements.

4. Study closure

The IRB closes studies when continuing review or annual monitoring is no longer required or the PI fails to respond to communications or requests by the deadline (typically one month from the date sent). Continuing review and annual monitoring are no longer required when the PI notifies the IRB that the study is no longer active, or data collection is complete or involves only accessing follow-up data from clinical care procedures. In cases of PI nonresponse, the IRB Coordinator notifies the PI in the study closing letter that collecting data or specimens on or after study closure is an ethics violation and may

be reported to the Office of Human Research Protections, National Institutes of Health, and Department of Health and Human Services. All closing letters will state that if the research will be re-opened, the PI must bring the project back to the IRB for another review.

5. Changes to protocol

Investigators must inform the IRB of changes to an approved study's protocol that could affect participants. Examples are changing the value of an incentive or linking the data with another data set. The Administrator determines whether the changes are substantial enough to require review by the Primary Reviewer. If the study is re-reviewed, the IRB Administrator may change the continuing review date to 12 months following re-approval.

6. Adverse events

Investigators must report any adverse events associated with the research to the IRB, including any injuries to participants, unanticipated problems, or breaches of privacy or protocol. The IRB reviews all such reports of adverse events. Following this review, the IRB Chair determines whether the situation is an unanticipated problem involving risks to subjects or others and, if so, notifies the MDH Deputy Commissioner. The Deputy Commission will notify the appropriate federal agencies in writing of the incident and the corrective actions taken. Any suspension or termination of IRB approval is similarly reported to the Deputy Commissioner and appropriate federal agencies.

7. Non-compliance

The IRB Administrator assesses the seriousness of investigator noncompliance. If the Administrator determines that the investigator is operating in good faith, the Administrator may resolve the issue as long as the noncompliance does not jeopardize the research participant's welfare. Such relatively minor lapses can include:

- Unreported changes in protocols,
- Misuse or nonuse of the informed consent document,
- Failure to submit protocols to the IRB in a timely fashion,
- Failure to respond to stipulations,
- Failure to submit a Re-review form, and
- Failure to report adverse events, breaches of confidentiality, breaches of protocol promptly to IRB.

Occasionally, an investigator will either avoid or ignore an IRB review. Such cases present more serious noncompliance. In these cases, the Administrator will involve the Chair who will determine appropriate action. Regardless of investigator intent, unapproved research involving human participants places those participants at an unacceptable risk. When unapproved research is discovered, the IRB and MDH will act promptly to halt the research, assure remedial action is taken regarding any breach of regulatory or institutional human subject protection requirements, and address the question of the investigator's fitness to conduct human subjects research. In addition, the IRB will report any serious or continuing non-compliance with the federal regulations to the Office for Human Research Protections (OHRP), National Institutes of Health, and Department of Health and Human Services.

E. Ethical considerations

1. Informed consent

The ethical principle of respect for persons requires that persons who participate in research have the opportunity to choose what will or will not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied. When assessing the adequacy of an applicant's informed consent procedures, the IRB will judge whether three objectives are met:

- Disclosure of information (participant will be provided full information regarding the research).
- Comprehension (participant will fully understand all ramifications of the research).
- Voluntariness (participant will understand that she or he has the right to volunteer or refuse, free of coercion or undue influence).

The IRB will approve protocols that meet these objectives and also conform to federal and state requirements.

a. Federal regulations affecting informed consent

The federal regulations specifically require that informed consent documents: a) contain specific content (i.e., basic and additional elements of informed consent); b) present a summary of key information first; and c) use plain language. The informed consent requirements in this policy are not intended to preempt any applicable Federal, state, or local laws (including tribal laws) that require additional information to be disclosed in order for informed consent to be legally effective (45 CFR 46.116).

b. Elements of informed consent

The federal regulations list basic elements of informed consent that must be conveyed to potential research participants or their legally authorized representatives (45CFR46.116(b)). A legally authorized representative is an individual authorized under applicable law or designated by a court or other body having jurisdiction to designate authority to consent on behalf of the prospective participant. If no one holds such a designation, the IRB recognizes the authority of the prospective participant's primary caregiver to consent (45 CFR 46.102(i)). The following are the basic elements of informed consent:

- A statement that the study involves research, an explanation of the research's purposes and the expected duration of the participant's participation, a description of the procedures to be followed, and identification of any procedures that are experimental.
- A description of any reasonably foreseeable risks or discomforts to the participant.
- A description of any benefits to the participant or to others that may reasonably be expected from the research.
- A disclosure of appropriate alternative procedures or courses of treatment if any that might be advantageous to the participant.
- A statement describing the extent, if any, that confidentiality of records identifying the participant will be maintained.
- For research involving more than minimal risk, an explanation about the following: whether any compensation for the injury is available; whether any medical treatments are available if injury occurs and, if so, what they consist of; or where further information may be obtained.

- An explanation of whom to contact for answers to pertinent questions about the research and research participants' rights, and whom to contact in the event of a research-related injury to the participant.
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.
- One of the following statements about any research that involves the collection of identifiable information or identifiable specimens:
- A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or
- A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

When appropriate, one or more of the following additional elements of information must also be provided to each participant (45CFR46.116(c)):

- A statement that the particular treatment or procedure might involve risks to the participant (or to the embryo or fetus, if the participant is or might become pregnant) that are currently unforeseeable.
- Anticipated circumstances under which the subject's participation might be terminated by the investigator without regard to the participant's consent.
- Any additional costs to the participant that might result from participation in the research.
- The consequences of a participant's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
- A statement that significant new findings developed during the course of the research that might relate to the participant's willingness to continue participation will be provided to the participant.
- The approximate number of participants involved in the study.
- A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.
- A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and
- For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

An IRB may approve a consent procedure that does not include or alters the elements of informed consent stated above, or the IRB may waive the requirement to obtain informed consent if the IRB finds and documents that each of the following criteria is true (45CFR46.116(e)):

- The research involves no more than minimal risk to the participants.
- The waiver or alteration will not adversely affect the rights and welfare of the participants.
- The research could not practicably be carried out without the waiver or alteration.
- Whenever appropriate, the participants will be provided with additional pertinent information after participation.

No informed consent may include any exculpatory language through which the subject or the legally authorized representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability or negligence (45CFR46.116(a)(6)).

c. Summary of key information

Consistent with the Federal regulations, the IRB requires that the written informed consent form (or oral presentation) must begin with a concise and focused presentation of key information that is most likely to assist a prospective research participant with understanding the reasons why one might or might not want to participate in the research. This key summary must be organized in a way that facilitates comprehension (45CFR46.116(a)(5)). In general, the IRB expects the key summary to include:

- The fact that consent is being sought for research and participation is voluntary.
- The purposes of the research, the expected duration of the subject's participation, and the procedures to be followed in the research.
- The most likely risks involved with participation.
- The benefits to the person or others that may reasonably be expected from participation.

In addition, the key summary should be a narrative not a collection of isolated facts. The consent form need not duplicate information presented in the key summary.

d. Plain language

A consent form must be written at a level that is understandable to the study population. For most populations, the reading level of the consent form should be at the 8th grade level. Investigators must include the reading level of the consent form in its application. If the reading level is at a higher level, the investigator must justify using the higher reading level.

One frequent pertinent issue is how to obtain meaningful informed consent from non-English speaking participants. Minnesota's increasingly diverse population uses many languages, such as Spanish, Hmong, Vietnamese, Laotian, Cambodian, Somali, or Russian. To ensure all potential participants fully understand the information, the IRB encourages translation of informed consent documents whenever non-English speakers are expected to be asked to participate. There are several resources to help investigators to translate materials into these and other languages, including information on Master Contracts maintained by the Department of Administration for these services.

e. Documentation of informed consent

The investigator must document informed consent by using a written consent form approved by the IRB and signed (including in an electronic format) by the participant or the participant's legally authorized representative. The investigator must provide a copy of the form to the participant. The written consent form may be read to the participant or the participant's legally authorized representative (45CFR46.117), but the investigator must give the participant or the representative adequate opportunity to read it before signing it.

The investigator may, as an alternative, orally present informed consent information to the participant or the participant's legally authorized representative. When this method is used, a witness must observe the oral presentation, and the investigator must prepare two documents: 1) a short form stating that the elements of informed consent were presented orally and the key summary information was presented first; and 2) a written summary approved by the IRB of what was said. The participant and

witness must sign the short form. The witness and the person obtaining consent must sign the written summary. The investigator will provide copies of each document to the participant.

An IRB may waive the requirement for the investigator to obtain a signed consent form from some or all participants under one of two conditions (45CFR46.117(c)):

- The only record linking the participant and the research would be the consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each participant will be asked whether the participant wants documentation linking the participant with the research, and the participant's wishes will govern; or
- The research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside the research context.

In either case, the IRB may require the investigator to provide participants with a written statement regarding the research.

f. State requirements

Minnesota law requires that the government provide certain disclosures when collecting data on individuals (Minn. Stat. § 13.04, subd. 2). These requirements are also known as the "Tennessen Warning" [see Section IV. List of authorities in this document]. Research projects undertaken in Minnesota must comply with both the federal requirements on informed consent and the Tennessen requirements.

2. Participant incentives

Study participants may be offered payment or a gift to encourage participation in studies when the benefit of study participation is very low. The amount of payment or the value of the gift should be reasonable, based on the burden of study participation. The amount of payment must not be based on the risk of study participation. The value of the incentive must not be coercive or present undue influence for initial or continued participation in the study. MDH staff who offer incentives must comply with MDH's incentive policy, currently policy number: PL501.01.

3. Research participant privacy

Data privacy issues are complex. Several state and federal laws and regulations apply. Also, the terminology used in state and federal law is not always consistent or the same as common usage. The IRB defines privacy, confidentiality, and security as follows:

Privacy refers to rights of people to control how information about them is collected, used, and disclosed.

Confidentiality refers to the obligations of people with access to personal information to respect the privacy interests of the subjects.

Security refers to technological, physical or administrative safeguards or tools designed to protect data, including health data, from unwarranted access or disclosure.

Federal regulations require IRBs to determine the adequacy of provisions to protect the privacy of subjects and to maintain the confidentiality and security of research data. To meet this requirement, the IRB requires investigators to collect or use data with subject identifiers only when necessary to carry out the research and describe a plan to protect the confidentiality and security of research data when using identifiable data.

a. Data security

All research activities result in some type of risk, and investigators must mitigate the risk of improper data disclosure. Depending on the type of data involved in the research, the IRB must: 1) assess potential risks to participants, and 2) evaluate the researchers' plan to minimize risks. To fulfill this responsibility, the IRB considers the following:

What is the risk to participants?

- Are the data identifiable, de-identified (coded), or anonymous?
- Is sensitive information being collected that, if improperly accessed, could result in harm to participants or an identifiable category of participants?
- If the data were improperly accessed, what harm could come to the participant or others?

What are the protections against anticipated threats or hazards (during data collection, transmission, storage)? For example, will investigators use the following data security techniques?

- Data encryption to mitigate risk if a device is lost or stolen;
- Use of secure data transmission channels to protect against data interception;
- Strong passwords to protect against unauthorized access;
- Data storage behind a secure firewall whenever possible; or
- Strong data security controls on all storage sites.

b. HIPAA

Occasionally, the IRB might review a new protocol for which the investigator falls within the definition of a covered entity under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 (P.L.104-191), as modified by the American Recovery and Reinvestment Act (ARRA). In that rare case, the Primary Reviewer must review the authorization or privacy notice to assure that it is HIPAA-compliant. The application must acknowledge the investigator's affirmative duty to disclose HIPAA breaches as adverse events and report to the IRB on the required follow-up activities under ARRA, including risk assessments. Data Privacy Information [see Section IV. List of authorities in this document] provides information on the relevant state and federal privacy and confidentiality statutes. Investigators should be familiar with which provisions apply to their proposed research and address how they will comply with them in their IRB application. The MDH General Counsel's Office can supply technical assistance on privacy issues, including HIPAA and the Minnesota Government Data Practices Act.

III. Responsibilities of investigators

A. Minimize risks

The investigator must design research projects in a way that minimizes risks to subjects and to continuously monitor the activities of their project to assure that the risks remain at a minimum. Investigators must collect information anonymously or de-identify information whenever possible.

B. Consult the IRB for determinations

MDH staff who intend to obtain information or specimens from living persons or analyze data for research purposes do not make the final determination of whether federal regulations for the protection of human subjects apply. MDH staff must consult the IRB Administrator to determine if their proposed project is research involving human subjects as defined in the federal regulations (45 CFR 46.102). Investigators shall also consult the IRB to determine whether their proposed human subjects research is exempt from review under 45 CFR 46.104.

PIs who believe their study does not meet the federal definition of human subjects research may submit a completed Preliminary Review Form to obtain an official determination from the IRB. Studies that do not meet the definition require no further involvement with the IRB. However, if the IRB determines that the study meets the definition, the PI is required to complete an application for approval to proceed. The IRB Administrator may waive the requirement for a full application if the research methods are eligible for exemption.

C. Report to the board

Once a project is approved, the investigator must submit to the board in writing:

- Any reports requested by the board, including continuing review information.
- Any changes in the project's protocol.
- Any adverse events associated with the project.
- Any stipulations required by the board.

Any proposed changes in previously approved projects must be reported to and approved by the board and cannot be implemented before being approved. Review of changes is accomplished in the manner described for initial review of applications, re-assigning the initial Primary Reviewer when possible.

The investigator must report any adverse events to the IRB. Examples of "adverse events" include: physical, psychological, and social injuries to participants; breaches of privacy (participant's private data revealed) or confidentiality (participant's data entrusted to the study revealed); unanticipated problems; and any breach in the protocol. The investigator must report serious events immediately. Other events must be reported in a timely fashion but no later than in the continuation request. The report must include a statement about the nature of the adverse event, impact on participants, and what has been done to correct the problem.

D. Compliance

Investigators are responsible for complying with all IRB decisions, conditions, and requirements. If the IRB does not receive information to verify that the PI has complied with board stipulations by one month before the project's start date, the IRB will send a reminder to the investigator and notify the Chair. Board approval is contingent upon compliance with all board stipulations and requirements.

E. Training

PIs and anyone who will have access to study data must have recent training (completed within three years of the application date) on human subjects protections from a recognized institution, such as the University of Minnesota or the Mayo Clinic. One of the following online training courses on human subjects protections would satisfy the requirement:

- The Office for Human Research Protections (OHRP) Human Research Protection Foundational Training (https://www.hhs.gov/ohrp/education-and-outreach/human-research-protection-training/human-research-protection-foundational-training/index.html): Lesson 1: Parts 1 and 2 only. Lessons 3 and 4: All sections. Submit certificates for Lessons 3 and 4 with your application.
- Protecting Human Research Participants (PHRP) Online Training and Certification (https://phrptraining.com/): Submit certificate with your application.

IV. List of authorities

The MDH IRB relies on the following authorities to govern and guide its policies, procedures, and determinations:

- U.S. Department of Health and Human Services: Office for Human Research Protections: The Belmont Report (https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html) (also known as Ethical Principles and Guidelines for the Protection of Human Subjects in Research)
- U.S. Department of Health and Human Services: Office for Human Research Protections: 2018 Requirements (2018 Common Rule) (https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html) (Code of Federal Regulations, Title 45, Part 46)
- Centers for Disease Control and Prevention: Distinguishing Public Health Research and Public Health Nonresearch (https://stacks.cdc.gov/pdfjs/web/viewer.html?file=https://stacks.cdc.gov/view/cdc/24235/cdc_24235_DS1.pdf)
- Minnesota Department of Administration: Tennessen Warning Notice (https://mn.gov/admin/data-practices/data/warnings/tennessen/) (Minn. Stat. § 13.04, Rights of subjects of data)
- Minnesota Department of Health IRB: Relevant Provisions of the Data Practices Act (https://www.health.state.mn.us/data/irb/docs/datapractices.pdf)