MINNESOTA DEPARTMENT OF HEALTH

POLICIES AND PROCEDURES GOVERNING

RESEARCH INVOLVING HUMAN SUBJECTS

September 2010
| PREFACE | ................................................................. | 3 |
| I. STATEMENT OF PRINCIPLES AND POLICIES | ................................................................. | 4 |
| A. ETHICAL PRINCIPLES | ................................................................. | 4 |
| B. INSTITUTIONAL POLICIES | ................................................................. | 4 |
| C. FOCUS | ................................................................. | 5 |
| II. OPERATING PROCEDURES | ................................................................. | 5 |
| A. INSTITUTIONAL REVIEW BOARD | ................................................................. | 5 |
| 1. Purpose, Scope, and Authority | ................................................................. | 5 |
| 2. Membership | ................................................................. | 6 |
| a. Appointment | ................................................................. | 6 |
| b. Composition | ................................................................. | 6 |
| c. Criteria for Members | ................................................................. | 6 |
| d. Leadership | ................................................................. | 7 |
| e. Responsibilities | ................................................................. | 7 |
| (i) Review | ................................................................. | 7 |
| (ii) Deliberate | ................................................................. | 7 |
| (iii) Attend | ................................................................. | 7 |
| 3. Meetings | ................................................................. | 8 |
| a. Timing | ................................................................. | 8 |
| b. Conduct | ................................................................. | 8 |
| c. Quorum | ................................................................. | 8 |
| d. Action by Electronic Means | ................................................................. | 8 |
| 4. Records | ................................................................. | 10 |
| 5. Conflict of Interest Policies and Procedures | ................................................................. | 10 |
| 6. Training and Orientation | ................................................................. | 11 |
| 7. Staffing and Other Support | ................................................................. | 11 |
| 8. Organizational Placement and Reporting | ................................................................. | 11 |
| B. SCOPE OF RESEARCH ACTIVITIES SUBJECT TO IRB REVIEW | ................................................................. | 11 |
| 1. Research defined | ................................................................. | 11 |
| 2. Exempt Research | ................................................................. | 12 |
| 3. Public Health Considerations | ................................................................. | 12 |
| C. REVIEW AND APPROVAL PROCESS | ................................................................. | 12 |
| 1. Types of Review | ................................................................. | 12 |
| a. Full Board Review | ................................................................. | 12 |
| 2. Expedited Review | ................................................................. | 14 |
| 3. Exemption from IRB Review | ................................................................. | 16 |
| 4. Continuing Review | ................................................................. | 17 |
| 5. Review Criteria | ................................................................. | 18 |
| 6. Informed Consent | ................................................................. | 19 |
| 7. Participant incentives | ................................................................. | 22 |
| 8. Research Participant Privacy | ................................................................. | 22 |
| 9. Review Procedures | ................................................................. | 22 |
| D. APPLICATION PROCEDURES | ................................................................. | 23 |
| E. APPEAL PROCEDURES | ................................................................. | 23 |
| F. RESPONSIBILITIES OF INVESTIGATORS | ................................................................. | 23 |
| G. NON-COMPLIANCE | ................................................................. | 24 |
| H. List of Appendices in Revised Policies and Procedures and Appendices | ................................................................. | 25 |
PREFACE

To protect the privacy, well-being, and other 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 gathered by the department. MDH also created it to provide discretionary IRB oversight to the greater research community. The IRB will revise these Policies and Procedures further 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’s Institutional Review Board may be found at: http://www.health.state.mn.us/irb/index.html.
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 of Research (the Belmont Report) [See Appendix A]. MDH specifically recognizes the Belmont Report’s 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 Appendix B]. 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

1. MDH acknowledges and accepts its responsibility for protecting the rights and welfare of human research subjects.

2. MDH acknowledges that it and especially its investigators bear full responsibility for performing all research covered by these policies and procedures, including complying with federal, state, and local laws as they apply to such research.

3. MDH assures that it and its investigators will satisfy the following requirements before involving human subjects:

   a. Risks to participants are minimized:
      (i) by using procedures that are consistent with sound research design but do not unnecessarily expose participants to risks, and
      (ii) whenever appropriate, researchers do not duplicate procedures that are already being performed on participants for prevention, diagnostic, or treatment purposes.

   b. Risks to participants are reasonable compared to the knowledge that might reasonably be expected to result.

   c. Participant selection is equitable.

   d. The principal investigator 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.
e. 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.

f. The research plan ensures participant safety.

g. Each research project will have adequate provisions to protect individual participant’s privacy and maintain data confidentiality.

4. MDH recognizes that for those who 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, the research plan needs appropriate additional safeguards.

5. 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.

6. MDH oversees 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.

7. MDH posts this statement of ethical principles and policy on its Web page as a separate document.

8. MDH requires that principal investigators and other key project staff be trained in the rights and welfare of human subjects.

C. FOCUS

The nature of MDH’s research and other research that this IRB reviews is public health. “Public health research” measures population health. Consequently, the risks for subjects are 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. The MDH has registered its IRB with the Office of Human Research Protections (OHRP) (MDH IRB #: IRB 00000945). The IRB has Federal-Wide Assurance (FWA) approved by OHRP (# FWA 00000072). A copy of this FWA is attached as Appendix C. 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 MDH IRB are as follows:
All new MDH research projects require IRB approval regardless of funding source. If a project does not receive funding and is discontinued, the IRB’s findings and recommendations may be used by MDH research staff to strengthen procedures for protecting human subjects, if necessary or by MDH management for other decisions regarding the research.

If a project has a principal investigator outside of MDH, has been approved by another IRB, and includes MDH staff as co-investigators or in support roles, the MDH IRB will review the project.

The MDH IRB may also review research projects conducted by an agency or organization with close links to MDH (e.g., local public health agencies, ClearWay Minnesota, Blue Cross/Blue Shield, or MDH grant recipients) that does not have another IRB available.

2. Membership

a. Appointment: The Commissioner of Health consults with current IRB members and staff to appoint new IRB members for staggered two-year terms. Members are chosen so that the IRB possesses the competence and experience to review specific research activities from the point of view of the subjects as well as the researchers. The IRB members must also be able to discern whether proposed research meets proper standards for Department commitments and complies with applicable law, professional conduct, and ethical standards. The Commissioner may reappoint members for subsequent two-year terms.

b. Composition: The IRB must have at least 10 members with varying backgrounds to promote complete and adequate review of MDH-sponsored or conducted research. Membership will include the following, as required by federal regulations [Federal Policy (Common Rule) for the Protection of Human Subjects and Department of Health and Human Services (HHS) regulations at 45 CFR 46.107]):

(i) At least one physician (M.D.), who has training and experience in a medical field sufficient to assess medical risks;

(ii) At least one person with advanced training and experience in conducting scientific investigations;

(iii) At least one person whose primary work is not in the area of scientific investigations;

(iv) A legal professional who has experience with the types of issues that MDH confronts, especially privacy issues; and

(v) At least one person who is not, and whose immediate family are not, affiliated with MDH.

c. Criteria for Members: Members of the IRB will be chosen from MDH staff; faculty members from the University of Minnesota or other academic institutions; public or private health organizations; and from the community at large. The Board must reflect race, gender, and cultural diversity.
Considerations for IRB members include research, professional or administrative expertise, community experience, availability to serve, and an e-mail address. At least 20 percent of members must be non-MDH members.

Ad hoc members with knowledge of special populations (e.g., prisoners, the elderly, the mentally ill, various ethnic subpopulations, pregnant women, and children) may also be appointed. Ad hoc members are non-voting members.

The IRB will draw its non-MDH members from those who are especially knowledgeable about their own local communities and are willing to review proposed research from that perspective. Ministers, teachers, attorneys, businesspersons, client advocates, or homemakers are possible candidates. Consideration will be given to the community from which the research institution will draw its research subjects.

d. **Leadership:** The IRB members will elect a Chair and Vice-Chair from the IRB membership.

e. **Responsibilities:**

(i) **Review:**
- 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 to report to the boards in detail, and lead the board’s deliberations about the project’s use of human research subjects. Primary reviewers must:
  - Conduct initial review and report at regularly scheduled meetings;
  - Follow up on stipulations as needed;
  - Examine re-review forms for compliance with IRB requirements and make recommendations whether to extend continued approval; and
  - Examine proposed revisions to the study and make recommendations.

(ii) **Deliberate**
- IRB members evaluate and discuss research proposals and re-reviews presented at meetings.
- IRB members discuss and set IRB policies as needed.

(iii) **Attend**
- IRB members are expected to attend meetings as their busy professional schedules allow.
- Members who miss at least four consecutive meetings will be asked to explain their absences and reconsider their time commitments to the IRB.
- The IRB Chair has the discretion to remove non-attending members.
3. Meetings

a. **Timing:** The IRB schedules monthly meetings to ensure timely review of proposals. If there is insufficient business, the Chair will cancel the meeting. The IRB Coordinator distributes meeting agendas and other materials to members 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 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:** Full Board actions require the presence of a quorum of the voting members. The “quorum” refers to the number of such members present, not to the number actually voting on a particular question. A “quorum” is 50% plus one of the members, which must include a nonscientist. A “nonscientist” is a member who has not had substantive training or experience in either a scientific discipline or in the scientific method. A majority of those present voting “aye” is required for approval of a motion. The quorum must be maintained. If enough member(s) leave so that the quorum is lost, no voting can take place. While the Chair is charged with conducting the meeting in an impartial manner so that all may participate and contribute freely, the Chair is a member of the Board for quorum and voting purposes.

d. **Action by Electronic Means:** The IRB may hold meetings solely by means of remote communication and act by written action or electronic means 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.

When to call meetings solely by means of remote communication is for the Chair’s discretion based on whether the agenda is appropriate for such a meeting. The key to such criteria is whether there are no issues that are likely to be controversial. Also, presentations of 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

---

1 Robert’s Rules of Order, Newly Revised, page 334, lines 5–7
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 meeting of members held solely by means of remote communication or in any meeting of members held at a designated place in which one or more members participate by means of remote communication:

(i) the IRB must verify the identity of each member. The IRB may rely on e-mail from the address provided by the member; and

(ii) 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 of the meeting substantially concurrently with those proceedings;
- have the member’s remarks heard or read by other participants in the meeting substantially concurrently with the making of those remarks; and
- vote on matters submitted to the members.

The IRB must announce the use of an e-meeting at least five business days before voting. Members must have at least four hours’ opportunity to register their votes on the day of meeting:

(i) Any notice to members by a form of electronic communication is effective when given by either:

- facsimile communication, when directed to a telephone number that the member has designated to receive notice; or
- electronic mail, when directed to an electronic mail address at which the member has consented to receive notice.

(ii) The IRB will not post notice or otherwise communicate IRB business on an electronic network or social networking site such as Facebook. The Chair may approve the use of another form of electronic communication only if the form meets MDH’s security standards, as determined by MDH’s security officer.

The IRB may, however, follow up on issues from duly called Board meetings by electronic means without calling an e-meeting. The chair may announce at a meeting that a follow-up decision will be made by e-mail. Members in attendance at the meeting may vote electronically 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 e-mail account that the IRB has on record for it and must also use the “reply to all” feature. The IRB Coordinator will document the vote by saving the messages until the outcome is written into the minutes. As soon as the IRB approves the minutes that include the electronic action, the IRB Coordinator will discard the messages.

4. Records

The IRB prepares and maintains documentation of its activities as required by federal regulation and in accordance with the IRB’s record retention schedule, Appendix D. In addition to written IRB procedures and membership lists, such documentation includes copies of all research proposals reviewed, minutes of all IRB meetings, records of continuing review activities, copies of all correspondence between the IRB and investigators, and statements of significant new findings provided to subjects. The IRB Coordinator maintains the IRB’s official records.

The IRB will keep minutes of IRB meetings in sufficient detail to record the following information: attendance at each meeting; 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 broken.

The IRB retains records for at least three (3) years. Records for research that is conducted are retained for three (3) years after the study is closed. After the study has been closed for three years, the PIs must remove identifiers and notify the IRB that it has done so, unless the PI presents sufficient reasons for keeping the identifiers. PIs will be notified via letter that all consent forms must be kept for 3 years following the project’s closure. The IRB Coordinator will ensure that all records will be 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 its file it will notify MDH PIs by letter that the PIs must keep any consent forms in accordance with the records retention schedule for the PI’s division. It will notify non-MDH PIs by letter that they must keep all consent forms for a minimum of 3 years following the project’s closure. Closing letters will state that if the research is re-opened, the PI must bring the project back to the IRB for another review.

5. Conflict of Interest Policies and Procedures

The IRB will not allow a member to participate in the IRB’s initial or continuing review of any research in which the member has a conflict of interest, 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 interest 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.
6. Training and Orientation

The IRB will assure that all members are trained about the federal regulations governing the protection of human research subjects. The IRB will also orient its members to this document, the *Minnesota Department of Health’s Policies and Procedures Governing Research Involving Human Subjects*. Information on other training resources (e.g., workshops, videos, books, computerized training) that might benefit the members will also be made available. The IRB budget will fund IRB training.

7. Staffing and Other Support

The Minnesota Department of Health provides both meeting space and adequate staff to support the IRB’s review and record-keeping duties, including a designated IRB Administrator and clerical support. 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.)

8. 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.

The board will submit an annual summary of Board actions to the Commissioner. The board will also notify the Commissioner immediately of any serious adverse events, approval suspensions or terminations, or serious or continuing investigator non-compliance.

B. SCOPE OF RESEARCH ACTIVITIES SUBJECT TO IRB REVIEW

1. **Research defined.** The federal regulations define “research” as “a systematic investigation . . . designed to develop or contribute to generalizeable knowledge”.

   **Human Subjects** are defined as “living individual(s) about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information”.

   Research involving human subjects is not limited to deliberate experimentation with human beings. It also includes the performance of any procedures not performed for the sole benefit of the person involved, and any procedures in which either a primary or secondary purpose, or objective, is the collection of data for research analysis.

   The scope of research involving human beings covered by these regulations not only involves physical, chemical, electrical, or psychological stimulation of responses within the human body, but also includes interviews, observation of behavior, administration of tests, or other measurement techniques.

2. **Exempt research.** Some research that involves human subjects is exempt from the regulations requiring IRB review. For example, educational testing and survey procedures where no identifying information will be recorded that can link subjects to the data. This example also means that 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. Research that involves the use of existing data, documents, or specimens, where no identifying information will
be recorded that can link subjects to the data is also exempt. Appendix E lists the federal criteria for exemption from IRB review.

Research involving human subjects does not cover data obtained as part of teaching or training individuals to perform therapeutic procedures for the direct and sole benefit of the person involved, or for any area of investigation of individuals as part performing professional services.

3. Public health considerations. The practice of public health poses several challenges in implementing 45 CFR 46. Although some public health activities can unambiguously be classified as either research or non-research, for other activities the classification is more difficult. The difficulty stems either from traditionally held views about what constitutes public health practice or from the fact that 45 CFR 46 does not directly address many public health activities. In addition, the regulations do not recognize the statutory authority of state and local health departments to conduct public health activities using methods similar to those used by researchers. The regulations thus do not lend themselves to ready interpretation for human-subject protection for activities that occur at the boundary between public health non-research and public health research.

The Centers for Disease Control and Prevention (CDC) has provided “Guidelines for Defining Public Health Research and Public Health Non-Research,” which have proven useful in determining which MDH projects are subject to IRB review. See Appendix F for a copy of these Guidelines.

Researchers should consult with the IRB Chair, Vice Chair or Administrator if there is any question as to whether their proposed project is considered to be research or non-research.

C. REVIEW AND APPROVAL PROCESS

The IRB Coordinator first reviews Applications for Approval of Research with Human Subjects upon receipt. The Coordinator checks the consents and letters to participants for appropriate reading levels and recommends changes, if necessary. The Coordinator also recommends the type of review. The Application then goes to the IRB Administrator, who will review it and recommend the type of review to the Chair and Vice-Chair, who will make the final determination.

1. Types of Review

a. Full Board Review

Each proposed research project must be submitted on the application form provided in Appendix G and include:

(i) A description of the Principal Investigator’s training about using human subjects in research from a recognized institution, such as the University of Minnesota or the Mayo Clinic. One of the on-line courses from the NIH or CDC can serve this purpose at a minimum.

(ii) A description of the training that anyone having access to identifiable data will have about using human subjects in research. (The IRB strongly recommends that any such people take an on-line course from the NIH or CDC. The Protecting Human Research Participants’ course from the NIH Office of Extramural Research, developed in July 2008 for academic researchers, meets this

(iii) A detailed description of the research design and procedures as they affect human subjects;

(iv) A list of precautions taken to safeguard the subjects’ welfare;

(v) A precise description of the research’s subject population;

(vi) A description of the Informed Consent process and copies of all recruitment materials and consent forms to be used; and

(vii) Methods to be used to protect data confidentiality and subject privacy.

The board will review proposals at regularly scheduled IRB meetings. The board will use the criteria outlined in this section to assign one of the following status types to the proposal:

(i) Approval

(ii) Approval Pending Stipulations

(iii) Deferral

(iv) Disapproval

A majority vote determines the proposal’s status. The vote must include the presence of a non-scientist member. A quorum must be present for 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. Investigators will receive written notification of the proposal’s status, approximately one week after the meeting. The notice will include a detailed description of stipulations that must be met before the IRB will grant approval. Approval status can be granted only after receipt and approval of the investigator’s written response to the IRB. The IRB will notify the PI that all stipulations have been reviewed and approved. Researchers may not begin data collection until the IRB Administrator and primary reviewer have reviewed and approved all stipulations and other requested materials.

In addition to formal “stipulations”, which must be met before starting data collection, the IRB may also make “suggestions” and “comments” in reviewing protocols, defined as follows:

Stipulations: approval with conditions that are mandatory (must be met) before final IRB approval and the beginning of research. The IRB will state these in its letter to the principal investigator and in the minutes of the meeting where the proposal was reviewed.

Suggestions: these are recommendations to the researcher, but are not mandatory for IRB final approval. These too will be stated in the letter to the principal investigator and in the minutes of the meeting where the proposal was reviewed.

Comments: these may or may not be included in the letter (depending on importance) and will not be recorded in the minutes unless related to a stipulation or suggestion.
2. Expedited Review

The IRB will use an expedited review process for research that involves no more than minimal risk, and for which the human subjects’ involvement falls into one of the categories listed below. The IRB may also use the expedited review process to review minor changes in previously approved research.

The IRB Administrator will recommend and the Chair and Vice-Chair will determine whether a new protocol is eligible for expedited review. The Administrator determines whether expedited review is appropriate for amendments and continuation requests. The IRB Chair has delegated the responsibility to the Administrator to seek one or more members to conduct the expedited review. If the reviewer or reviewers find that the protocol should be disapproved, the protocol must go to the full board for a vote.

At every IRB meeting each member will be provided with a written report of any protocols handled through expedited review since the last meeting.

**Expedited Review**

*(Full text of the federal regulation appears in Appendix M.)*

1. The IRB may review through the expedited review procedure research activities that:
   a. present no more than minimal risk to human subjects, and
   b. involve only procedures listed in one or more of the following research categories (1 through 9).

2. The categories in this list apply regardless of the age of subjects, except as noted.

3. For studies where identifying the subjects or their responses would place them at reasonable risk of criminal or civil liability or damage the subjects’ financial or personal interests, the IRB may use the expedited review procedure only if the researchers implement reasonable and appropriate protections to reduce risks from invasion of privacy and breach of confidentiality so they are minimal.

4. The expedited review procedure may not be used for classified research involving human subjects.

5. The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—used by the IRB.

6. Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

**Research Categories (in abridged form)**

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, nonpregnant 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, researchers may not draw more that the lesser of 50 ml or 3 ml per kg in an eight-week period.

Researchers may not collect samples more than twice per week for either (a) or (b).

(c) Prospective collection of biological specimens for research purposes by noninvasive means.

* * *

(d) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.

* * *

(e) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

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

(g) Research on individual or group characteristics or behavior or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

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

(i) where
(ii) the research is permanently closed to the enrollment of new subjects;
(iii) all subjects have completed all research-related interventions; and
(iv) where no subjects have been enrolled and no additional risks have been identified; or
(v) where the remaining research activities are limited to data analysis.

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

3. Exemption from IRB Review

Research that meets the federal exemption criteria listed below is exempt from IRB review. The IRB Administrator will recommend and the Chair and Vice-Chair will determine whether research is exempt. Documentation of the exemption must include the specific category in the federal regulations justifying the exemption. The IRB must track exempt research projects and review them on an annual basis to make sure that they continue to meet the exemption criteria. (See Appendix E for review form.)

The exemption criteria do not apply to research involving prisoners, pregnant women, fetuses, or in-vitro fertilization.
### Table 1

**Exemption Criteria**

*(Abridged form - full text of the federal regulation appears in the appendix.)*

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
</table>
| 1. | Research conducted in educational settings, using normal educational practices, such as:
  (i) research on regular and special education instructional strategies, or
  (ii) research on instructional techniques, curricula, or classroom management methods. |
| 2. | Research using educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, *unless*:
  (i) information obtained is recorded in such a manner that subjects can be identified, directly or through identifiers linked to the subjects; and
  (ii) any disclosure of human subjects’ responses outside the research could reasonably place the subjects at risk of criminal or civil liability or damage to the subjects’ financial or personal interests. (This exemption does not apply to research with children except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.) |
| 3. | Research using educational tests, survey procedures, interview procedures or observation of public behavior that is not exempt under paragraph (2) if:
  (i) the human subjects are elected or appointed public officials or candidates for public office; or
  (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter. |
| 4. | Research using the collection or study of publicly available existing data, documents, records, pathological specimens, or diagnostic specimens, or if the investigator records the information so that subjects cannot be identified, directly or through identifiers linked to the subjects. |
| 5. | Research and demonstration projects which federal department or agency heads either conduct or approve, and which study:
  (i) public benefit or service programs;
  (ii) procedures for obtaining benefits or services under those programs;
  (iii) possible changes in or alternatives to those programs or procedures; or
  (iv) possible changes in methods or levels or payment for benefits or services under those programs. |
| 6. | Taste and food quality evaluation and consumer acceptance studies,
  (i) if the subjects consume wholesome foods without additives or
  (ii) if the subjects consume a food that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. |

### 4. Continuing Review

An IRB must review a research project until the PI notifies the IRB that the study is complete. “Completion of a study” is defined as when all analyses have been conducted. Approval for a research project is valid for no more than one year. The federal regulations require IRBs to conduct continuing reviews of research at intervals appropriate to the degree of risk, but not less than once a year. The principal investigator must...
submit a timely continuation application to the IRB that previously reviewed the protocol. Research protocols that required full IRB review initially and that have not completed data collection require full IRB review for continuation. The review must take place at a convened meeting of the IRB and action on the project must be approved by a majority of the members present. The researcher must meet the IRB’s stipulations, if any, before approval for continuation is granted. The IRB will assign a primary reviewer to review the full application, usually the person who reviewed the initial application.

The IRB focuses on research related to public health, which carries a lower level of risk to human subjects than clinical trials or drug and medical device studies. Therefore, an annual re-review is sufficient unless, in the IRB’s discretion, there are adverse events or other evidence to warrant more frequent or closer scrutiny. The IRB has the authority to observe or have a third party observe the consent process and the research. In full board reviews, the board will determine whether the risk is sufficient to require monitoring and what is needed to address the risk. The IRB will implement a monitoring plan when one is warranted.

Research protocols that initially required full IRB review, have completed collecting data, and are in the process of analyzing data may be reviewed using the expedited process. Research protocols that were reviewed initially using the expedited process may be re-reviewed using the expedited process as long as the degree of risk associated with the study has not changed.

A continuation request must include all of the following:

1. Re-Review of Previously Approved Research form or Re-Review of Exempt Research form (found in Appendix H & I); and

2. A brief report on the status of the project including the protocol’s progress to date, plans for the next approval period, a description of any adverse events or unanticipated problems involving risks to participants or others, withdrawal of participants from the research or complaints about the research, a summary of any recent literature, modifications to the research since the last review, and an expected completion date of the project.

5. Review Criteria

The primary role of the IRB is to protect the rights and welfare of human beings who are participants in research. In accordance with federal regulations, the IRB may approve research only after it has determined that all of the following requirements are satisfied:

a. 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, researchers are employing procedures that are being performed on participants for prevention, diagnosis, or treatment purposes.

b. Risks to participants are reasonable relative to anticipated benefits, if any, to participants and the importance of the knowledge that might reasonably be expected to result. In evaluating risks and benefits, the IRB should 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).

c. 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, pregnant women, fetuses, prisoners, mentally disabled persons, 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.

d. Informed consent will be sought from each prospective participant or the participant’s legally authorized representative, unless exempted by state or federal law.

e. Informed consent will be appropriately documented.

f. The research plan makes adequate provision for ensuring the safety of participants.

g. There are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data.

h. Applications from MDH’s student workers, temporary employees, or interns must include a permanent MDH employee as co-PI.

6. Informed Consent

The ethical principle of respect for persons (from the Belmont Report) requires that persons who participate in research have the opportunity to choose what will or will not happen to them. The IRB must judge whether three conditions are met:

a. Disclosure of information (participant has been provided full information regarding the research);

b. Comprehension (participant fully understands all ramifications of the research); and

c. Voluntariness (participant understands that she or he has the right to volunteer or refuse, free of coercion or undue influence).

Informed consent is not a single event or just a form to be signed — rather it is an educational process that takes place between the investigator and the prospective subject.

There are also state requirements related to collecting data on individuals (Minnesota Statutes, section 13.04, subdivision 2). These requirements, also known as the “Tennessen Warning”, appear in Appendix J. Research projects undertaken in Minnesota must comply with both the federal requirements on informed consent and the Tennessen requirements.

One frequent pertinent issue is how to obtain meaningful informed consent from non-English speaking participants. Minnesota’s population is becoming increasingly diverse with groups that use languages such as the following: Spanish, Hmong, Vietnamese, Laotian, Cambodian, Somali, or Russian. MDH has several resources to help investigators in translating materials into these and other languages, including information on Master Contracts maintained by the Department of Administration for these services. Information on these resources may be found on the MDH intranet under “Directory”. Choose the “Communicating” link and scroll down to “Translations/Interpretation.” [http://fyi.health.state.mn.us/polcomm/language/]

The IRB will approve protocols that contain the following informed-consent information:
Elements of Informed Consent

1. 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.

2. A description of any reasonably foreseeable risks or discomforts to the participant.

3. A description of any benefits to the participant or to others that may reasonably be expected from the research.

4. A disclosure of appropriate alternative procedures or courses of treatment if any that might be advantageous to the participant.

5. A statement describing the extent, if any, that confidentiality of records identifying the participant will be maintained.

6. 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.

7. 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.

8. 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.

When appropriate, one or more of the following elements of information must also be provided to each participant:

1. 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.

2. Anticipated circumstances under which the subject’s participation might be terminated by the investigator without regard to the participant’s consent.

3. Any additional costs to the participant that might result from participation in the research.

4. The consequences of a participant’s decision to withdraw from the research and procedures for orderly termination of participation by the subject.

5. 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.

6. The approximate number of participants involved in the study.

An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent stated above, or waive the requirements to obtain informed consent provided the IRB finds and documents that (45CFR46.116(d)):
1. The research involves no more than minimal risk to the participants;

2. The waiver or alteration will not adversely affect the rights and welfare of the participants;

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

4. Whenever appropriate, the participants will be provided with additional pertinent information after participation.

All four criteria must be met in order to alter some or all of the consent process.

The informed consent process must be documented by the use of a written consent form approved by the IRB and signed by the participant or the participant’s legally authorized representative. A copy will be given to the person signing the form. 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.

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 from the 8th grade, the investigator must justify his or her use of the higher reading level.

The investigator may, as an alternative, give the participant or the representative a short written consent form that documents that the elements of the informed consent were presented orally to the participant or representative. The participant or representative signs the short written consent form. When this method is used, a witness should observe the oral presentation and a written summary of what is to be said to the participant or representative should be used. The witness should sign the short written consent form and the summary. The person actually obtaining consent should sign the summary. A copy of the summary should be given to the participant or the representative, in addition to a copy of the short written consent form.

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)):

1. 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

2. 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.

[Placeholder – our current policy about participation by minors in research and parental consent-minor needs to be written out and added. Appendix K addresses it but the underlying principles are implicit rather than explicit.]

Appendix K contains an Informed Consent Checklist.
7. Participant incentives

[Placeholder – our policy about compensating subjects and proper level of incentives goes here.]

8. Research Participant Privacy

The issues of privacy and confidentiality are complex for several reasons: There are a number of both state and federal laws and regulations applicable to these issues. The IRB’s role in compliance with these various provisions is not always clear. The terminology used in state and federal law is not always consistent or the same as common usage.

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 IRB events and report to the IRB on the required follow-up activities under ARRA, including risk assessments. Appendix L 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 form (Section V). MDH’s Legal Unit can supply technical assistance on privacy issues, including HIPAA and the Minnesota Government Data Practices Act.

9. Review Procedures

The IRB uses a primary-reviewer system to review new protocols, amendments, and continuation requests, unless the study is exempt. The IRB Administrator seeks one or more IRB members to serve as the primary reviewer. Members are expected to give serious consideration to requests to serve as primary reviewer, but may decline. 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 primary reviewer is expected to continue with the study as long as he or she remains on the board, reviewing amendments, continuation requests, adverse events and other matters as they arise.

For new protocols being heard by the full board, the primary reviewer is responsible for making a presentation describing the research and highlighting any important human-subject-protection issues. The primary reviewer also presents recommendations regarding amendments and continuation requests that are before the full board. For each study that warrants a full board review, the Primary Reviewer will propose a monitoring schedule specific to the study, which the IRB will note on the IRB application form at the time of IRB approval.

For an expedited review, the primary reviewer submits a summary of human subjects concerns and recommendations for stipulations and suggestions to the IRB Administrator. The Administrator prepares a review letter to the primary investigator, and the Coordinator ensures that action taken by expedited review is communicated to the full board, usually through the Chair’s report.

D. APPLICATION PROCEDURES

PIs must submit a completed Application for Approval of Research with Human Subjects, found in Appendix G, with each new research proposal.

Previously approved projects may use the Re-Review of Previously Approved Research form, found in Appendix K, for their continuation review. Re-review and re-approval of research will occur on or before the one-year anniversary of the initial IRB approval date, unless the degree of risk, complaints about the research, or investigator non-compliance necessitates more frequent re-review. Projects previously found
to be exempt will be notified annually and should submit a *Re-Review of Exempt Research form*, found in Appendix I.

In general, action on all proposals will be taken within one month after submission. Investigators will be notified in writing of Board’s decisions within one week of Board action. Decisions to disapprove will be accompanied by reasons for the decision.

E. **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 accomplish any reconsideration in the same manner as an initial review. After the IRB reexamines and reconsiders its actions, the IRB’s decision is final.

F. **RESPONSIBILITIES OF INVESTIGATORS**

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.

Research investigators who intend to involve human subjects do not make the final determination of whether applicable federal regulations for the protection of human subjects apply. Researchers must consult a member of the IRB or the IRB Administrator to determine if their proposed project involves “human subjects” and “research” as defined in the federal regulations (45 CFR 46.102). If it is not clear that the research meets this definition, the IRB member or Administrator will seek assistance from the Chair to make this determination. Researchers shall also consult the IRB to determine whether their proposed research is exempt from review under 45 CFR 46.101. The IRB Chair shall make the final determination whether the research is exempt.

The investigator must submit an application giving a complete description of the proposed research according to the procedures. The application must describe provisions for adequately protecting the rights and welfare of prospective research subjects and ensure that pertinent laws and regulations are observed. Researchers must include samples of proposed consent forms with the application.

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

1. Any reports requested by the Board, including continuing review information;
2. Any changes in the project’s protocol;
3. Any adverse events associated with the project; and
4. Any stipulations required by the Board.

Any proposed changes in previously approved projects must be approved by the Board and cannot be implemented before being approved. Review of changes will be accomplished in the manner described for initial review of applications.

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. Following review by the IRB, the IRB Chair will determine whether the situation warrants notifying the Deputy Commissioner of the Minnesota Department of Health, who will notify the appropriate federal agencies in writing of the incident and the corrective actions taken.
Research investigators are responsible for complying with all IRB decisions, conditions, and requirements. If the IRB does not receive information to comply 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.

G. NON-COMPLIANCE

Common lapses in investigator compliance include:

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

Problems such as these are often caused by communication difficulties. If the investigator operates in good faith, these cases can usually be resolved by the IRB without jeopardizing the research participants’ welfare. Occasionally, an investigator will either avoid or ignore an IRB review. Such cases present a more serious challenge to the IRB and to the Department. 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 subject 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.
List of Appendices in Revised Policies and Procedures


C. MDH's updated Federalwide Assurance (FWA)

D. IRB Record Retention Schedule

E. Criteria for Exemption from IRB Review


G. Application for Approval of Research with Human Subjects (Form)

H. Re-review of Previously Reviewed Research (Form)

I. Re-review of Exempt Research (Form)

J. Tennessen Warning


L. Data Privacy Information

M. Criteria for Expedited Review.
The Belmont Report

Office of the Secretary

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

April 18, 1979

AGENCY: Department of Health, Education, and Welfare.

ACTION: Notice of Report for Public Comment.

SUMMARY: On July 12, 1974, the National Research Act (Pub. L. 93-348) was signed into law, thereby creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider: (i) the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine, (ii) the role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects, (iii) appropriate guidelines for the selection of human subjects for participation in such research and (iv) the nature and definition of informed consent in various research settings.

The Belmont Report attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. It is the outgrowth of an intensive four-day period of discussions that were held in February 1976 at the Smithsonian Institution's Belmont Conference Center supplemented by the monthly deliberations of the Commission that were held over a period of nearly four years. It is a statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects. By publishing the Report in the Federal Register, and providing reprints upon request, the Secretary intends that it may be made readily available to scientists, members of Institutional Review Boards, and Federal employees. The two-volume Appendix, containing the lengthy reports of experts and specialists who assisted the Commission in fulfilling this part of its charge, is available as DHEW Publication No. (OS) 78-0013 and No. (OS) 78-0014, for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

Unlike most other reports of the Commission, the Belmont Report does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare. Rather, the Commission recommended that the Belmont Report be adopted in its entirety, as a statement of the Department's policy. The Department requests public comment on this recommendation.

http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm

Appendix A

10/26/2010
National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

Members of the Commission

Kenneth John Ryan, M.D., Chairman, Chief of Staff, Boston Hospital for Women.
Joseph V. Brady, Ph.D., Professor of Behavioral Biology, Johns Hopkins University.
Robert E. Cooke, M.D., President, Medical College of Pennsylvania.
Dorothy I. Height, President, National Council of Negro Women, Inc.
Albert R. Jansen, Ph.D., Associate Professor of Bioethics, University of California at San Francisco.
Patricia King, J.D., Associate Professor of Law, Georgetown University Law Center.
Karen Lebacqz, Ph.D., Associate Professor of Christian Ethics, Pacific School of Religion.
David W. Louisell, J.D., Professor of Law, University of California at Berkeley.
Donald W. Seldin, M.D., Professor and Chairman, Department of Internal Medicine, University of Texas at Dallas.
Eliot Stellar, Ph.D., Provost of the University and Professor of Physiological Psychology, University of Pennsylvania.

*** Deceased.

Table of Contents

Ethical Principles and Guidelines for Research Involving Human Subjects

A. Boundaries Between Practice and Research

B. Basic Ethical Principles

1. Respect for Persons
2. Beneficence
3. Justice

C. Applications

1. Informed Consent
2. Assessment of Risk and Benefits
3. Selection of Subjects

Ethical Principles & Guidelines for Research Involving Human Subjects

Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the Nuremberg code was drafted as a set of standards for judging physicians and scientists who...
had conducted biomedical experiments on concentration camp prisoners. This code became the prototype of many later codes(1) intended to assure that research involving human subjects would be carried out in an ethical manner.

The codes consist of rules, some general, others specific, that guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted.

Three principles, or general prescriptive judgments, that are relevant to research involving human subjects are identified in this statement. Other principles may also be relevant. These three are comprehensive, however, and are stated at a level of generalization that should assist scientists, subjects, reviewers and interested citizens to understand the ethical issues inherent in research involving human subjects. These principles cannot always be applied so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects.

This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

[RETURN TO TABLE OF CONTENTS]

Part A: Boundaries Between Practice & Research

A. Boundaries Between Practice and Research

It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred partly because both often occur together (as in research designed to evaluate a therapy) and partly because notable departures from standard practice are often called "experimental" when the terms "experimental" and "research" are not carefully defined.

For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals.(2) By contrast, the term "research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental," in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.(3)
Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

Part B: Basic Ethical Principles

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions. Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect of persons, beneficence and justice.

1. Respect for Persons. -- Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

An autonomous person is an individual capable of deliberation about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny an individual the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequence. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.
2. Beneficence. -- Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment." Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psychotherapeutic, and social procedures.

The principle of beneficence often occupies a well-defined justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children -- even when individual research subjects are not direct beneficiaries. Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that on closer investigation turn out to be dangerous. But the role of the principle of beneficence is not always so unambiguous. A difficult ethical problem remains, for example, about research that presents more than minimal risk without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out that this limit would rule out much research promising great benefit to children in the future. Here again, as with all hard cases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices.

3. Justice. -- Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are (1) to each person an equal share, (2) to each person according to individual need, (3) to each person according to individual effort, (4) to each person according to societal contribution, and (5) to each person according to merit.

http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm
Questions of justice have long been associated with social practices such as punishment, taxation and political representation. Until recently these questions have not generally been associated with scientific research. However, they are foreshadowed even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries the burdens of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly flagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

Part C: Applications

C. Applications

Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects of research.

1. Informed Consent. -- Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied.

While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

Information. Most codes of research establish specific items for disclosure intended to assure that subjects are given sufficient information. These items generally include: the research procedure, their purposes, risks and anticipated benefits, alternative procedures (where therapy is involved), and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Additional items have been proposed, including how subjects are selected, the person responsible for the research, etc.

However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate since research takes place precisely when a common understanding does not exist.
Another standard, currently popular in malpractice law, requires the practitioner to reveal the information that reasonable persons would wish to know in order to make a decision regarding their care. This, too, seems insufficient since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care. It may be that a standard of "the reasonable volunteer" should be proposed: the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified only if it is clear that (1) incomplete disclosure is truly necessary to accomplish the goals of the research, (2) there are no undisclosed risks to subjects that are more than minimal, and (3) there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply inconvenience the investigator.

Comprehension. The manner and context in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration or curtailing opportunities for questioning, all may adversely affect a subject's ability to make an informed choice.

Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. On occasion, it may be suitable to give some oral or written tests of comprehension.

Special provision may need to be made when comprehension is severely limited -- for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disable patients, the terminally ill and the comatose) should be considered on its own terms. Even for these persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in research. The objections of these subjects to involvement should be honored, unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm. Such persons are thus respected both by acknowledging their own wishes and by the use of third parties to protect them from harm.

The third parties chosen should be those who are most likely to understand the incompetent subject's situation and to act in that person's best interest. The person authorized to act on behalf of the subject should be given an opportunity to observe the research as it proceeds in order to be able to withdraw the subject from the research, if such action appears in the subject's best interest.

Voluntariness. An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence.

http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm
Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable.

Unjustifiable pressures usually occur when persons in positions of authority or commanding influence -- especially where possible sanctions are involved -- urge a course of action for a subject. A continuum of such influencing factors exists, however, and it is impossible to state precisely where justifiable persuasion ends and undue influence begins. But undue influence would include actions such as manipulating a person's choice through the controlling influence of a close relative and threatening to withdraw health services to which an individual would otherwise be entitled.

2. Assessment of Risks and Benefits. -- The assessment of risks and benefits requires a careful array of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.

The Nature and Scope of Risks and Benefits. The requirement that research be justified on the basis of a favorable risk/benefit assessment bears a close relation to the principle of beneficence, just as the moral requirement that informed consent be obtained is derived primarily from the principle of respect for persons. The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm.

The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike, "risk," "benefit" is not a term that expresses probabilities. Risk is properly contrasted to probability of benefits, and benefits are properly contrasted with harms rather than risks of harm. Accordingly, so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harm and anticipated benefits. Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.

Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society). Previous codes and Federal regulations have required that risks to subjects be outweighed by the sum of both the anticipated benefit to the subject, if any, and the anticipated benefit to society in the form of knowledge to be gained from the research. In balancing these different elements, the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interests other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been protected. Beneficence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of the substantial benefits that might be gained from research.

The Systematic Assessment of Risks and Benefits. It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws
attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, nonarbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less subject to misinterpretation, misinformation and conflicting judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

Finally, assessment of the justifiability of research should reflect at least the following considerations: (i) Brutal or inhumane treatment of human subjects is never morally justified. (ii) Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. (iii) When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject -- or, in some rare cases, to the manifest voluntariness of the participation). (iv) When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits. (v) Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process.

3. Selection of Subjects. -- Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects.

Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. Thus, it can be considered a matter of social justice that there is an order of preference in the selection of classes of subjects (e.g., adults before children) and that some classes of potential subjects (e.g., the institutionalized mentally infirm or prisoners) may be involved as research subjects, if at all, only on certain conditions.

Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators and treated fairly in the course of research. Thus injustice arises from social, racial, sexual and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if IRBs are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and benefits of research. Although individual institutions or investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects.
Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept these risks of research, except where the research is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same directions as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects if more advantaged populations are likely to be the recipients of the benefits.

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.

(1) Since 1945, various codes for the proper and responsible conduct of human experimentation in medical research have been adopted by different organizations. The best known of these codes are the Nuremberg Code of 1947, the Helsinki Declaration of 1964 (revised in 1975), and the 1971 Guidelines (codified into Federal Regulations in 1974) issued by the U.S. Department of Health, Education, and Welfare Codes for the conduct of social and behavioral research have also been adopted, the best known being that of the American Psychological Association, published in 1973.

(2) Although practice usually involves interventions designed solely to enhance the well-being of a particular individual, interventions are sometimes applied to one individual for the enhancement of the well-being of another (e.g., blood donation, skin grafts, organ transplants) or an intervention may have the dual purpose of enhancing the well-being of a particular individual, and, at the same time, providing some benefit to others (e.g., vaccination, which protects both the person who is vaccinated and society generally). The fact that some forms of practice have elements other than immediate benefit to the individual receiving an intervention, however, should not confuse the general distinction between research and practice. Even when a procedure applied in practice may benefit some other person, it remains an intervention designed to enhance the well-being of a particular individual or groups of individuals; thus, it is practice and need not be reviewed as research.

(3) Because the problems related to social experimentation may differ substantially from those of biomedical and behavioral research, the Commission specifically declines to make any policy determination regarding such research at this time. Rather, the Commission believes that the problem ought to be addressed by one of its successor bodies.

http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm
Appendix B

Code of Federal Regulations

TITLE 45
PUBLIC WELFARE

Department of Health and Human Services

PART 46
PROTECTION OF HUMAN SUBJECTS

***

Revised January 15, 2009
Effective July 14, 2009

SUBPART A—
Basic HHS Policy for Protection of Human Research Subjects

Sec.
46.101 To what does this policy apply?
46.102 Definitions.
46.103 Assuring compliance with this policy—research conducted or supported by any Federal Department or Agency.
46.104- [Reserved]
46.106
46.107 IRB membership.
46.108 IRB functions and operations.
46.109 IRB review of research.
46.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.
46.111 Criteria for IRB approval of research.
46.112 Review by institution.
46.113 Suspension or termination of IRB approval of research.
46.114 Cooperative research.
46.115 IRB records.
46.116 General requirements for informed consent.
46.117 Documentation of informed consent.
46.118 Applications and proposals lacking definite plans for involvement of human subjects.
46.119 Research undertaken without the intention of involving human subjects.
46.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.
46.121 [Reserved]
46.122 Use of Federal funds.
46.123 Early termination of research support: Evaluation of applications and proposals.
46.124 Conditions.

SUBPART B—
Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research

Sec.
46.201 To what do these regulations apply?
46.202 Definitions.
46.203 Duties of IRBs in connection with research involving pregnant women, fetuses, and neonates.
46.204 Research involving pregnant women or fetuses.
46.205 Research involving neonates.
46.206 Research involving, after delivery, the placenta, the dead fetus or fetal material.
46.207 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.

Appendix B
SUBPART C—
Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects

Sec.
46.301 Applicability.
46.302 Purpose.
46.303 Definitions.
46.304 Composition of Institutional Review Boards where prisoners are involved.
46.305 Additional duties of the Institutional Review Boards where prisoners are involved.
46.306 Permitted research involving prisoners.

SUBPART D—
Additional Protections for Children Involved as Subjects in Research

Sec.
46.401 To what do these regulations apply?
46.402 Definitions.
46.403 IRB duties.
46.404 Research not involving greater than minimal risk.
46.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.
46.406 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.
46.407 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.
46.408 Requirements for permission by parents or guardians and for assent by children.
46.409 Wards.

SUBPART E—
Registration of Institutional Review Boards

Sec.
46.501 What IRBs must be registered?
46.502 What information must be provided when registering an IRB?
46.503 When must an IRB be registered?
46.504 How must an IRB be registered?
46.505 When must IRB registration information be renewed or updated?

Editorial Note: The Department of Health and Human Services issued a notice of waiver regarding the requirements set forth in part 46, relating to protection of human subjects, as they pertain to demonstration projects, approved under section 1115 of the Social Security Act, which test the use of cost-sharing, such as deductibles, copayment and coinsurance, in the Medicaid program. For further information see 47 FR 9208, Mar. 4, 1982.
SUBPART A
Basic Human Policy for Protection of Human Research Subjects

Authority: 5 U.S.C. 301; 42 U.S.C. 289;
42 U.S.C. 300v-1(b).

Source: 56 FR 28012, 28022, June 18, 1991,
unless otherwise noted.

§46.101 To what does this policy apply?
(a) Except as provided in paragraph (b) of
this section, this policy applies to all research
involving human subjects conducted, sup­
ported or otherwise subject to regulation by
any federal department or agency which
takes appropriate administrative action to
make the policy applicable to such research.
This includes research conducted by federal
civilian employees or military personnel,
except that each department or agency head
can adopt such procedural modifications as
may be appropriate from an administrative
standpoint. It also includes research con­
ducted, supported, or otherwise subject to
regulation by the federal government outside
the United States.

(1) Research that is conducted or sup­
ported by a federal department or agency,
whether or not it is regulated as defined in
§46.102(e), must comply with all sections of
this policy.

(2) Research that is neither conducted nor
supported by a federal department or
agency but is subject to regulation as de­
defined in §46.102(e) must be reviewed and
approved, in compliance with §46.101,
§46.102, and §46.107 through §46.117 of
this policy, by an institutional review
board (IRB) that operates in accordance
with the pertinent requirements of this
policy.

(b) Unless otherwise required by department
or agency heads, research activities in which
the only involvement of human subjects will
be in one or more of the following cat­
cegories are exempt from this policy:

(1) Research conducted in established or
commonly accepted educational settings,
involving normal educational practices,
such as (i) research on regular and special
education instructional strategies, or (ii)
research on the effectiveness of or the
comparison among instructional tech­
niques, curricula, or classroom manage­
ment methods.

(2) Research involving the use of educa­
tional tests (cognitive, diagnostic, aptitude,
achievement), survey procedures, inter­
view procedures or observation of public
behavior, unless: (i) information obtained
is recorded in such manner that human
subjects can be identified, directly or
through identifiers linked to the subjects;
and (ii) any disclosure of the human sub­
jects' responses outside the research could
reasonably place the subjects at risk of
criminal or civil liability or be damaging to
the subjects' financial standing, employ­
ability, or reputation.

(3) Research involving the use of educa­
tional tests (cognitive, diagnostic, aptitude,
achievement), survey procedures, inter­
view procedures, or observation of public
behavior that is not exempt under para­
graph (b)(2) of this section, if:
(i) the human subjects are elected or
appointed public officials or candidates for
public office; or (ii) federal statute(s) re­
quire(s) without exception that the confi­
dentiality of the personally identifiable
information will be maintained through­
out the research and thereafter.

(4) Research involving the collection or
study of existing data, documents, records,
pathological specimens, or diagnostic
specimens, if these sources are publicly
available or if the information is recorded
by the investigator in such a manner that
subjects cannot be identified, directly or
through identifiers linked to the subjects.

(5) Research and demonstration projects
which are conducted by or subject to the
approval of department or agency heads,
which are designed to study, evaluate,
or otherwise examine:(i) Public benefit or
service programs; (ii) procedures for
obtaining benefits or services under those
programs; (iii) possible changes in or alter­
 natives to those programs or procedures;
or (iv) possible changes in methods or
levels of payment for benefits or services
under those programs.

(6) Taste and food quality evaluation and
consumer acceptance studies, if whole­
some foods without additives are con­
sumed or if a food is consumed that
contains a food ingredient at or below the
level and for a use found to be safe, or
agricultural chemical or environmental
contaminant at or below the level found
to be safe, by the Food and Drug Admini­
stration or approved by the Environ­
mental Protection Agency or the Food

Safety and Inspection Service of the U.S.
Department of Agriculture.

(c) Department or agency heads retain final
judgment as to whether a particular activity
is covered by this policy.

(d) Department or agency heads may require
that specific research activities or classes of
research activities conducted, supported, or
otherwise subject to regulation by the de­
partment or agency but not otherwise cov­
ered by this policy, comply with some or all
of the requirements of this policy.

(e) Compliance with this policy requires
compliance with pertinent federal laws or
regulations which provide additional protec­
tions for human subjects.

(f) This policy does not affect any state or
local laws or regulations which may other­
wise be applicable and which provide addi­
tional protections for human subjects.

(g) This policy does not affect any foreign
laws or regulations which may otherwise be
applicable and which provide additional
 protections to human subjects of research.

(h) When research covered by this policy
takes place in foreign countries, procedures
normally followed in the foreign countries
to protect human subjects may differ from
those set forth in this policy. [An example is
a foreign institution which requires with
guidelines consistent with the World Medi­
cal Assembly Declaration (Declaration of
Helsinki amended 1989) issued either by
sovereign states or by an organization whose
function for the protection of human re­
search subjects is internationally recognized.]
In these circumstances, if a department or
agency head determines that the procedures
prescribed by the institution afford protec­
tions that are at least equivalent to those
provided in this policy, the department or
agency head may approve the substitution of
the foreign procedures in lieu of the proce­
dural requirements provided in this policy.
Except when otherwise required by statute,
Executive Order, or the department or
agency head, notices of these actions as they
occur will be published in the FEDERAL
REGISTER or will be otherwise published
as provided in department or agency proce­
dures.
(j) Unless otherwise required by law, department or agency heads may waive the applicability of some or all of the provisions of this policy to specific research activities or classes of research activities otherwise covered by this policy. Except when otherwise required by statute or Executive Order, the department or agency head shall forward advance notices of these actions to the Office for Human Research Protections, Department of Health and Human Services (HHS), or any successor office, and shall also publish them in the FEDERAL REGISTER or in such other manner as provided in department or agency procedures.1

§46.102 Definitions.

(a) Department or agency head means the head of any federal department or agency and any other officer or employee of any department or agency to whom authority has been delegated.

(b) Institution means any public or private entity or agency (including federal, state, and other agencies).

(c) Legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research.

(d) 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 service programs may include research activities.

(e) Research subject to regulation, and similar terms are intended to encompass those research activities for which a federal department or agency has specific responsibility for regulating as a research activity (for example, Investigational New Drug requirements administered by the Food and Drug Administration). It does not include research activities which are incidentally regulated by a federal department or agency solely as part of the department’s or agency’s broader responsibility to regulate certain types of activities whether research or non-research in nature (for example, Wage and Hour requirements administered by the Department of Labor).

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

1 Data through intervention or interaction with the individual, or

(2) Identifiable private information.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

(g) IRB means an institutional review board established in accord with and for the purposes expressed in this policy.

(h) IRB approval means the determination of the IRB that the research has been reviewed and may be conducted at an institution

Within the constraints set forth by the IRB and other institutional and federal requirements.

(i) 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.

(b) When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. An example is a foreign institution which complies with guidelines consistent with the World Medical Assembly Declaration (Declaration of Helsinki amended 1989) issued either by sovereign states or by an organization whose function for the protection of human research subjects is internationally recognized. In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy. Except when otherwise required by statute, Executive Order, or the department or agency head, notices of these actions as they occur will be published in the FEDERAL REGISTER or will be otherwise published as provided in department or agency procedures.

1Institutions with HHS-approved assurances on file will abide by provisions of Title 45 CFR part 46 subparts A-D. Some of the other departments and agencies have incorporated all provisions of Title 45 CFR part 46 into their policies and procedures as well. However, the exceptions at 45 CFR 46.101(b) do not apply to research involving prisoners, subpart C. The exception at 45 CFR 46.101(b)(2), for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, subpart D, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.
§46.103 Assuring compliance with this policy -- research conducted or supported by any Federal Department or Agency.

(a) Each institution engaged in research which is covered by this policy and which is conducted or supported by a federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in this policy. In lieu of requiring submission of an assurance, individual department or agency heads shall accept the existence of a current assurance, appropriate for the research in question, on file with the Office for Human Research Protections, HHS, or any successor office, and approved for federalwide use by that office. When the existence of an HHS-approved assurance is accepted in lieu of requiring submission of an assurance, reports (except certification) required by this policy to be made to department and agency heads shall also be made to the Office for Human Research Protections, HHS, or any successor office.

(b) Departments and agencies will conduct or support research covered by this policy only if the institution has an assurance approved as provided in this section, and only if the institution has certified to the department or agency head that the research has been reviewed and approved by an IRB provided for in the assurance, and will be subject to continuing review by the IRB. Assurances applicable to federally supported or conducted research shall, at a minimum, include:

1. A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution, regardless of whether the research is subject to Federal regulation. This may include an appropriate existing code, declaration, or statement of ethical principles, or a statement formulated by the institution itself. This requirement does not preclude provisions of this policy applicable to department- or agency-supported or regulated research and need not be applicable to any research exempted or waived under §46.101(b) or (f).

2. Designation of one or more IRBs established in accordance with the requirements of this policy, and for which provisions are made for meeting space and sufficient staff to support the IRB's review and recordkeeping duties.

3. A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant. Changes in IRB membership shall be reported to the department or agency head, unless in accord with §46.103(b) of this policy, the existence of an HHS-approved assurance is accepted. In this case, change in IRB membership shall be reported to the Office for Human Research Protections, HHS, or any successor office.

4. Written procedures which the IRB will follow (i) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (ii) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and (iii) for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

5. Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing non-compliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval.

(c) The assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this policy and shall be filed in such form and manner as the department or agency head prescribes.

(d) The department or agency head will evaluate all assurances submitted in accordance with this policy through such officers and employees of the department or agency and such experts or consultants engaged for this purpose as the department or agency head determines to be appropriate. The department or agency head's evaluation will take into consideration the adequacy of the proposed IRB in light of the anticipated scope of the institution's research activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution.

(e) On the basis of this evaluation, the department or agency head may approve or disapprove the assurance, or enter into negotiations to develop an approvable one. The department or agency head may limit the period during which any particular approved assurance or class of approved assurances shall remain effective or otherwise condition or restrict approval. (f) Certification is required when the research is supported by a federal department or agency and not otherwise exempted or waived under §46.101(b) or (f). An institution with an approved assurance shall certify that each application or proposal for research covered by the assurance and by §46.103 of this Policy has been reviewed and approved by the IRB. Such certification must be submitted with the application or proposal or by such later date as may be prescribed by the department or agency to which the application or proposal is submitted. Under no condition shall research covered by §46.103 of the Policy be supported prior to receipt of the certification that the research has been reviewed and approved by the IRB. Institutions without an approved assurance covering the research shall certify within 30 days after receipt of a request for such a certification from the department or agency, that the application or proposal has been approved by the IRB. If the certification is not submitted within these time limits, the application or proposal may be returned to the institution.

(Approved by the Office of Management and Budget under Control Number 0990-0260.)

§46.107 IRB membership.

(a) Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the 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. 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. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

(b) Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of members of one profession.

(c) Each IRB shall include at least one member whose primary concern is in scientific areas and at least one member whose primary concern is in nonscientific areas.

(d) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

(e) No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

(f) An 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 IRB. These individuals may not vote with the IRB.

§46.108 IRB functions and operations.

In order to fulfill the requirements of this policy each IRB shall:

(a) Follow written procedures in the same detail as described in §46.103(b)(4) and, to the extent required by, §46.103(b)(5).

(b) Except when an expedited review procedure is used (see §46.109), review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting.

§46.109 IRB review of research.

(a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy.

(b) An IRB shall require that information given to subjects as part of informed consent is in accordance with §46.116. The IRB may require that information, in addition to that specifically mentioned in §46.116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.

(c) An IRB shall require documentation of informed consent or may waive documentation in accordance with §46.117.

(d) An IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

(e) An IRB shall conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

(Adopted by the Office of Management and Budget under Control Number 0990-0260.)

§46.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

(a) The Secretary, HHS, has established, and published as a Notice in the FEDERAL REGISTER, a list of categories of research that may be reviewed by the IRB through an expedited review procedure. The list will be amended, as appropriate, after consultation with other departments and agencies, through periodic republication by the Secretary, HHS, in the FEDERAL REGISTER. A copy of the list is available from the Office for Human Research Protections, HHS, or any successor office.

(b) An IRB may use the expedited review procedure to review either or both of the following:

(1) Some or all of the research appearing on the list and found by the reviewer(s) to involve no more than minimal risk,

(2) Minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

Under an expedited review procedure, the review may be carried out by the IRB chair-person or by one or more experienced reviewers designated by the chairperson from among members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in §46.108(b).

(c) Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure.

(d) The department or agency head may restrict, suspend, terminate, or choose not to authorize an institution's or IRB's use of the expedited review procedure.

§46.111 Criteria for IRB approval of research.

(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized; (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject’s legally authorized representative, in accordance with, and to the extent required by §46.116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117.

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

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

(b) When some or all of the subjects 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 subjects.

§46.113 Suspension or termination of IRB approval of research.

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB’s requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB’s action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.

(Approved by the Office of Management and Budget under Control Number 0990-0260.)

§46.114 Cooperative research.

Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the department or agency head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

§46.115 IRB records.

(a) An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:

(1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.

(2) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

(3) Records of continuing review activities.

(4) Copies of all correspondence between the IRB and the investigators.

(5) A list of IRB members in the same detail as described in §46.103(b)(3).

(6) Written procedures for the IRB in the same detail as described in §46.103(b)(4) and §46.103(b)(5).

(7) Statements of significant new findings provided to subjects, as required by §46.116(b)(5).

(b) The records required by this policy shall be retained for at least 3 years, and records relating to research which is conducted shall be retained for at least 3 years after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the department or agency at reasonable times and in a reasonable manner.

(Approved by the Office of Management and Budget under Control Number 0990-0260.)

§46.116 General requirements for informed consent.

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(a) Basic elements of informed consent.

Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

(1) 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;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) A listing, whether oral or written, of any benefits to the subject; and

(7) A description of alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

(Approved by the Office of Management and Budget under Control Number 0990-0260.)
Appendix B

(6) 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;

(7) 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

(8) 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.

(b) Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

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

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(3) Any additional costs to the subject that may result from participation in the research;

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

(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

(6) The approximate number of subjects involved in the study.

(c) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

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

(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

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

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

(3) The research could not practically be carried out without the waiver or alteration; and

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

(e) 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.

(f) Nothing in this policy is intended to limit, exclude, or alter any rights or requirements under federal, state, or local law.

§46.117 Documentation of informed consent.

(a) Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.

(b) Except as provided in paragraph (c) of this section, the consent form may be either of the following:

1) A written consent document that embodies the elements of informed consent required by §46.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or

2) A short form written consent document stating that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative.

Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.

(c) An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

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

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

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

(Approved by the Office of Management and Budget under Control Number 0990-0260)

56 FR 28012, 28022, June 18, 1991, as amended at 70 FR 39328, June 23, 2005

§46.118 Applications and proposals lacking definite plans for involvement of human subjects.

Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants when selection of specific projects is the institution's responsibility; research training grants in which the activities involving subjects remain to be selected; and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under §46.101(b) or (f), no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted, by the institution, to the department or agency.
§46.119 Research undertaken without the intention of involving human subjects.

In the event research is undertaken without the intention of involving human subjects, but it is later proposed to involve human subjects in the research, the research shall first be reviewed and approved by an IRB, as provided in this policy, a certification submitted, by the institution, to the department or agency, and final approval given to the proposed change by the department or agency.

§46.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.

(a) The department or agency head will evaluate all applications and proposals involving human subjects submitted to the department or agency through such officers and employees of the department or agency and such experts and consultants as the department or agency head determines to be appropriate. This evaluation will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained.

(b) On the basis of this evaluation, the department or agency head may approve or disapprove the application or proposal, or enter into negotiations to develop an approved one.

§46.121[Reserved]

§46.122 Use of Federal funds.

Federal funds administered by a department or agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.

§46.123 Early termination of research support: Evaluation of applications and proposals.

(a) The department or agency head may require that department or agency support for any project be terminated or suspended in the manner prescribed in applicable program requirements, when the department or agency head finds an institution has materially failed to comply with the terms of this policy.

(b) In making decisions about supporting or approving applications or proposals covered by this policy the department or agency head may take into account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant has been subject to a termination or suspension under paragraph (a) of this section and whether the applicant or the person or persons who would direct or have directed the scientific and technical aspects of an activity has/have, in the judgment of the department or agency head, materially failed to discharge responsibility for the protection of the rights and welfare of human subjects (whether or not the research was subject to federal regulation).

§46.124 Conditions.

With respect to any research project or any class of research projects the department or agency head may impose additional conditions prior to or at the time of approval when in the judgment of the department or agency head additional conditions are necessary for the protection of human subjects.

Subpart B

Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research

Source: 66 FR 56778, Nov. 13, 2001, unless otherwise noted.

§46.201 To what do these regulations apply?

(a) Except as provided in paragraph (b) of this section, this subpart applies to all research involving pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates conducted or supported by the Department of Health and Human Services (DHHS). This includes all research conducted in DHHS facilities by any person and all research conducted in any facility by DHHS employees.

(b) The exemptions at §46.101(b)(1) through (6) are applicable to this subpart.

(c) The provisions of §46.101(c) through (f) are applicable to this subpart. Reference to State or local laws in this subpart and in §46.101(f) is intended to include the laws of federally recognized American Indian and Alaska Native Tribal Governments.

(d) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

§46.202 Definitions.

The definitions in §46.102 shall be applicable to this subpart as well. In addition, as used in this subpart:

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

(b) Delivery means complete separation of the fetus from the woman by expulsion or extraction or any other means.

(c) Fetus means the product of conception from implantation until delivery.

(d) Neonate means a newborn.

(e) Nonviable neonate means a neonate after delivery that, although living, is not viable.

(f) Pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menstrual periods, until the results of a pregnancy test are negative or until delivery.

(g) Secretary means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

(h) Viable, as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the FEDERAL REGISTER guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of subparts A and D of this part.

§46.203 Duties of IRBs in connection with research involving pregnant women, fetuses, and neonates.

In addition to other responsibilities assigned to IRBs under this part, each IRB shall review research covered by this subpart and approve only research which satisfies the conditions of all applicable sections of this subpart and the other subparts of this part.

§46.204 Research involving pregnant women or fetuses.

Pregnant women or fetuses may be involved in research if all of the following conditions are met:

(a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
(b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;

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

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

e) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman, the fetus's, or both the pregnant woman and the fetus if both the pregnant woman and the fetus are involved in research and the research is the development of important biomedical knowledge cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of subpart A of this part, except that the consent of the father 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 paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

(g) For children as defined in §46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;

(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; and

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

§46.205 Research involving neonates.

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

(1) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

(2) Each individual providing consent under paragraph (b)(2) or (c)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

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

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

(b) Neonates of uncertain viability. Until its viability has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following additional conditions have been met:

(1) The IRB determines that:

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

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

(2) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

(c) Neonates of certain viability. Neonates of uncertain viability that have been ascertained whether or not a neonate is viable, and until the following additional conditions have been met:

(1) The IRB determines that:

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

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

(2) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

(d) Neonates of certain viability. Neonates of uncertain viability that have been ascertained whether or not a neonate is viable, and until the following additional conditions have been met:

(1) The IRB determines that:

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

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

(e) The IRB finds that the research presents
§46.302

Inasmuch as prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research, it is the purpose of this subpart to provide additional safeguards for the protection of prisoners involved in activities to which this subpart is applicable.

§46.303 Definitions.

As used in this subpart:

(a) Secretary means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

(b) DHHS means the Department of Health and Human Services.

(c) Prisoner means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statute or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending assignment, trial, or sentencing.

(d) Minimal risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

§46.304 Composition of Institutional Review Boards where prisoners are involved.

In addition to satisfying the requirements in §46.107 of this part, an Institutional Review Board, carrying out responsibilities under this part with respect to research covered by this subpart, shall also meet the following specific requirements:

(a) A majority of the Board (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the Board.

(b) At least one member of the Board shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one Board only one Board need satisfy this requirement.

Appendix B
Appendix B

§46.306 Permitted research involving prisoners.

(a) Biomedical or behavioral research conducted or supported by DHHS may involve prisoners as subjects only if:

(1) The institution responsible for the conduct of the research has certified to the Secretary that the Institutional Review Board has approved the research under §46.305 of this subpart; and

(2) In the judgment of the Secretary the proposed research involves solely the following:

(i) 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;

(ii) 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;

(iii) 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 has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of his intent to approve such research; or

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

(b) Except as provided in paragraph (a) of this section, biomedical or behavioral research conducted or supported by DHHS shall not involve prisoners as subjects.

Subpart D

Additional Protections for Children Involved as Subjects in Research

Source: 48 FR 9818, March 8, 1983, unless otherwise noted.

§46.401 To what do these regulations apply?

(a) This subpart applies to all research involving children as subjects, conducted or supported by the Department of Health and Human Services.

(1) This includes research conducted by Department employees, except that each head of an Operating Division of the Department may adopt such nonsubstantive, procedural modifications as may be appropriate from an administrative standpoint.

(2) It also includes research conducted or supported by the Department of Health and Human Services outside the United States, but in appropriate circumstances, the Secretary may, under paragraph (i) of §46.101 of subpart A, waive the applicability of some or all of the requirements of these regulations for research of this type.

(b) Exemptions at §46.101(b)(1) and (b)(3) through (b)(6) are applicable to this subpart. The exemption at §46.101(b)(2) regarding educational tests is also applicable to this subpart. However, the exemption at §46.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the investigator does not participate in the activities being observed.

(c) The exceptions, additions, and provisions for waiver as they appear in paragraphs (c) through (f) of §46.101 of subpart A are applicable to this subpart.

§46.402 Definitions.

The definitions in §46.102 of subpart A shall be applicable to this subpart as well. In addition, as used in this subpart:

(a) Children are persons who have not attained the legal age for consent to treatment or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

(b) Assent means a child's affirmative agreement to participate in research. Merely to object should not, absent affirmative agreement, be construed as assent.

(c) Permission means the agreement of parent (s) or guardian to the participation of their child or ward in research.

(d) Parent means a child's biological or adoptive parent.

(e) Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

§46.403 IRB duties.

In addition to other responsibilities assigned to IRBs under this part, each IRB shall review research covered by this subpart and approve only research which satisfies the conditions of all applicable sections of this subpart.

§46.404 Research not involving greater than minimal risk.

HHS will conduct or fund research in which the IRB finds that no greater than minimal risk to children is presented, only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in §46.408.

§46.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.

HHS will conduct or fund research in which 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, only if the IRB finds that:

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

(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 their parents or guardians, as set forth in §46.408.
§46.406 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.

HHS will conduct or fund research in which 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, only if the IRB finds that:

(a) the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

(b) the research will be conducted in accordance with sound ethical principles;

(c) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in §46.408.

§46.408 Requirements for permission by parents or guardians and for assent by children.

(a) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with §46.116 of Subpart A.

(b) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine in accordance with and to the extent that consent is required by §46.116 of Subpart A, that adequate provisions are made for soliciting the permission of each child’s parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 or §46.405. Where research is covered by §§46.406 and 46.407 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

(c) In addition to the provisions for waiver contained in §46.116 of subpart A, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in Subpart A of this part and paragraph (b) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

(d) Permission by parents or guardians shall be documented in accordance with and to the extent required by §46.117 of subpart A.

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

§46.409 Wards.

(a) Children who are wards of the state or any other agency, institution, or entity can be included in research approved under §46.406 or §46.407 only if such research is:

(1) Related to their status as wards; or

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

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

Source: 74 FR 2399, January 15, 2009, unless otherwise noted.

§46.501 What IRBs must be registered?
Each IRB that is designated by an institution under an assurance of compliance approved for federalwide use by the Office for Human Research Protections (OHRP) under §46.103(a) and that reviews research involving human subjects conducted or supported by the Department of Health and Human Services (HHS) must be registered with HHS. An individual authorized to act on behalf of the institution or organization operating the IRB must submit the registration information.

§46.502 What information must be provided when registering an IRB?
The following information must be provided to HHS when registering an IRB:
(a) The name, mailing address, and street address (if different from the mailing address) of the institution or organization operating the IRB(s); and the name, mailing address, phone number, facsimile number, and electronic mail address of the senior officer or head official of that institution or organization who is responsible for overseeing activities performed by the IRB.
(b) The name, mailing address, phone number, facsimile number, and electronic mail address of the contact person providing the registration information.
(c) The name, if any, assigned to the IRB by the institution or organization, and the IRB's mailing address, street address (if different from the mailing address), phone number, facsimile number, and electronic mail address.
(d) The name, phone number, and electronic mail address of the IRB chairperson.
(e)(1) The approximate numbers of:
(i) All active protocols; and
(ii) Active protocols conducted or supported by HHS.
(ii) For purpose of this regulation, an "active protocol" is any protocol for which the IRB conducted an initial review or a continuing review at a convened meeting or under an expedited review procedure during the preceding twelve months.
(f) The approximate number of full-time equivalent positions devoted to the IRB's administrative activities.

§46.503 When must an IRB be registered?
An IRB must be registered before it can be designated under an assurance approved for federalwide use by OHRP under §46.103(a). IRB registration becomes effective when reviewed and accepted by OHRP.
The registration will be effective for 3 years.

§46.504 How must an IRB be registered?
Each IRB must be registered electronically through http://ohrp.nih.gov/efile unless an institution or organization lacks the ability to register its IRB(s) electronically. If an institution or organization lacks the ability to register an IRB electronically, it must send its IRB registration information in writing to OHRP.

§46.505 When must IRB registration information be renewed or updated?
(a) Each IRB must renew its registration every 3 years.
(b) The registration information for an IRB must be updated within 90 days after changes occur regarding the contact person who provided the IRB registration information or the IRB chairperson. The updated registration information must be submitted in accordance with §46.504.
(c) Any renewal or update that is submitted to, and accepted by, OHRP begins a new 3-year effective period.
(d) An institution's or organization's decision to disband a registered IRB which it is operating also must be reported to OHRP in writing within 30 days after permanent cessation of the IRB's review of HHS-conducted or -supported research.
1. Institution Filing Assurance

Legal Name: Minnesota Department of Health

City: St. Paul State: MN 55164

DHHS Institution Profile File (IPF) code, if known:

Federal Entity Identification Number (EIN), if known: 41-6007162

If this Assurance replaces an MPA or CPA, please provide the “M” or “T” number:

2. Institutional Components

List below all components over which the Institution has legal authority that operate under a different name. Also list with an asterisk (*) any alternate names under which the Institution operates. The Institution should have available for review by the Office for Human Research Protections (OHRP) upon request a brief description and line diagram explaining the interrelationships among the Assurance Signatory Official, the Institutional Review Board (IRB), IRB support staff, and investigators in these various components.

NOTE: The Signatory Official signing this Assurance must be legally authorized to represent the Institution providing this Assurance and all components listed below. Entities that the Signatory Official is not legally authorized to represent may not be listed here without the prior approval of OHRP.

☐ Please check here if there are no additional components or alternate names.

<table>
<thead>
<tr>
<th>Name of Component or Alternate Names Used</th>
<th>City</th>
<th>State (or Country if Outside U.S.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. Statement of Principles

This Institution assures that all of its activities related to human subject research, regardless of funding source, will be guided by the ethical principles in the following document(s). (indicate below)

☐ The Belmont Report

☐ Other (please submit copy to OHRP with this Assurance)

4. Applicability

☐ Other (please submit copy to OHRP with this Assurance)

(a) This Institution assures that all of its activities related to federally-conducted or -supported human subject research will comply with the Terms of Assurance for Protection of Human Subjects for
Institutions Within the United States. NOTE: The Terms of Assurance are contained in a separate document on the OHRP website.

(b) Optional: This Institution elects to apply the following to all of its human subject research regardless of source of support:

☐ 45 CFR 46 and all of its subparts (A,B,C,D)
☒ Common Rule (e.g., 45 CFR 46, subpart A)

5. Designation of Institutional Review Boards (IRBs)

This Institution designates the following IRB(s) for review of research under this Assurance (if the IRB is not previously registered with DHHS or has not provided a membership roster to DHHS, please attach the appropriate IRB registration materials available on the OHRP website).

NOTE: Reliance on another institution's IRB or an independent IRB must be documented by a written agreement that is available for review by OHRP upon request. OHRP's sample IRB Authorization Agreement may be used for this purpose, or the institutions involved may develop their own agreement. Future designation of other IRBs requires update of the FWA.

<table>
<thead>
<tr>
<th>DHHS IRB Registration Number</th>
<th>Name of IRB As Registered with DHHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRB00000183</td>
<td>Centers for Disease Control &amp; Prevention IRB #1 – A</td>
</tr>
<tr>
<td>IRB00000184</td>
<td>Centers for Disease Control &amp; Prevention IRB #2 – B</td>
</tr>
<tr>
<td>IRB00000185</td>
<td>Centers for Disease Control &amp; Prevention IRB #3 – C</td>
</tr>
<tr>
<td>IRB00000186</td>
<td>Centers for Disease Control &amp; Prevention IRB #4 - NIOSH</td>
</tr>
<tr>
<td>IRB00000187</td>
<td>Centers for Disease Control &amp; Prevention IRB #5 - NCHS</td>
</tr>
<tr>
<td>IRB00000188</td>
<td>Centers for Disease Control &amp; Prevention IRB #6 - G</td>
</tr>
<tr>
<td>IRB00000945</td>
<td>Minnesota Department of Health IRB #1</td>
</tr>
<tr>
<td>IRB00002724</td>
<td>Centers for Disease Control &amp; Prevention IRB #7 - S</td>
</tr>
</tbody>
</table>

6. Human Protections Administrator (e.g., Human Subjects Administrator or Human Subjects Contact Person)

First Name: Peter Middle Initial: . Last Name: Rode

Degrees or Suffix (e.g., MD, PhD): MA Institutional Title: IRB Administrator

Institution: Minnesota Department of Health

Telephone: 651/201-5942 FAX: 651/201-5179 E-Mail: peter.rode@state.mn.us

Address: 85 East Seventh Place, Suite 300, P.O. Box 64882

City: St. Paul State: MN Zip Code: 55164-0882
7. Signatory Official (i.e., Official Legally Authorized to Represent the Institution -- cannot be IRB Chairperson or IRB member)

I understand that the Assurance Training Modules on the OHRP website describe the responsibilities of the Signatory Official, the IRB Chair(s), and the Human Protections Administrator under this Assurance. Additionally, I recognize that providing all research investigators, IRB members and staff, and other relevant personnel with appropriate initial and continuing education about human subject protections will help ensure that the requirements of this Assurance are satisfied.

Acting officially in an authorized capacity on behalf of this Institution and with an understanding of the Institution's responsibilities under this Assurance, I assure protections for human subjects as specified above. The IRB(s) designated above are to provide oversight for all research conducted under this Assurance. These IRB(s) will comply with the Terms of Assurance and possess appropriate knowledge of the local context in which this Institution's research will be conducted. I understand that all collaborating institutions engaged in federally-conducted or -supported human subject research must submit their own Assurance.

All information provided with this Assurance is up to date and accurate. I am aware that false statements could be cause for invalidating this Assurance and may lead to other administrative or legal action.

Signature: Jeanne Danaher Date: 10/09/05

First Name: Jeanne Middle Initial: Jeanne
Last Name: Danaher

Degrees or Suffix (e.g., MD, PhD): JD

Institutional Title: Deputy Commissioner

Telephone: 651/201-4872 FAX: 651/201-4986

E-Mail: Jeanne.danaher@state.mn.us

Address: Freeman Building, 5C, 625 Robert Street North, P.O. Box 64975

City: St. Paul State: MN Zip Code: 55164-0975

NOTE: Facilities operated by the U.S. Government may require Department or Agency clearance. Please contact the relevant Department or Agency Human Protections Officer before forwarding this Assurance to OHRP.

8. DHHS Approval

The Federalwide Assurance of Protection for Human Subjects submitted to DHHS by the above Institution is hereby approved.

Assurance Number: Expiration Date:

Signature of DHHS Approving Official: Date:
(d) The following information is required for IRBs designated under OHRP Assurances. This information is optional for other IRBs.

<table>
<thead>
<tr>
<th>Last Name</th>
<th>First Name &amp; Middle Initial</th>
<th>Gender</th>
<th>Affiliated*</th>
<th>Status**</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRB Chairperson</td>
<td>Richard N.</td>
<td>Male</td>
<td>Yes</td>
<td>OS</td>
</tr>
<tr>
<td>Danila</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voting Members</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Belgea, J.D.</td>
<td>Lynn</td>
<td>Female</td>
<td>Yes</td>
<td>NS</td>
</tr>
<tr>
<td>Griffith</td>
<td>Jayne</td>
<td>Female</td>
<td>Yes</td>
<td>OS</td>
</tr>
<tr>
<td>Messing, Vice Chair</td>
<td>Rita B.</td>
<td>Female</td>
<td>Yes</td>
<td>OS</td>
</tr>
<tr>
<td>Lynfield</td>
<td>Ruth L.</td>
<td>Female</td>
<td>Yes</td>
<td>PS</td>
</tr>
<tr>
<td>Pierce</td>
<td>Alexandra R.</td>
<td>Female</td>
<td>No</td>
<td>SS</td>
</tr>
<tr>
<td>Desai</td>
<td>Jay R</td>
<td>Male</td>
<td>Yes</td>
<td>OS</td>
</tr>
<tr>
<td>Farah</td>
<td>Huda</td>
<td>Female</td>
<td>No</td>
<td>OS</td>
</tr>
<tr>
<td>Fried</td>
<td>Brett</td>
<td>Male</td>
<td>Yes</td>
<td>SS</td>
</tr>
<tr>
<td>Winget</td>
<td>Patricia</td>
<td>Female</td>
<td>Yes</td>
<td>NS</td>
</tr>
<tr>
<td>Liao</td>
<td>Louise</td>
<td>Female</td>
<td>Yes</td>
<td>OS</td>
</tr>
<tr>
<td>Tsai</td>
<td>Albert</td>
<td>Male</td>
<td>Yes</td>
<td>OS</td>
</tr>
<tr>
<td>Zabel</td>
<td>Erik</td>
<td>Male</td>
<td>Yes</td>
<td>OS</td>
</tr>
<tr>
<td>Johnson</td>
<td>David</td>
<td>Male</td>
<td>No</td>
<td>OS</td>
</tr>
<tr>
<td>Winnett</td>
<td>Mary</td>
<td>Female</td>
<td>No</td>
<td>PS</td>
</tr>
<tr>
<td>Hatcher</td>
<td>Penny</td>
<td>Female</td>
<td>Yes</td>
<td>OS</td>
</tr>
<tr>
<td>York</td>
<td>Pamela</td>
<td>Female</td>
<td>Yes</td>
<td>OS</td>
</tr>
<tr>
<td>Clark</td>
<td>Julie</td>
<td>Female</td>
<td>No</td>
<td>NS</td>
</tr>
<tr>
<td>Gutierrez</td>
<td>Rodolfo</td>
<td>Male</td>
<td>No</td>
<td>SS</td>
</tr>
<tr>
<td>Pomplun</td>
<td>Nancy</td>
<td>Female</td>
<td>No</td>
<td>NS</td>
</tr>
<tr>
<td>Ad Hoc Members***</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jaede</td>
<td>Ann C</td>
<td>Female</td>
<td>No</td>
<td>NS</td>
</tr>
<tr>
<td>Wyss</td>
<td>William</td>
<td>Male</td>
<td>No</td>
<td>SS</td>
</tr>
<tr>
<td>Vang</td>
<td>Kou</td>
<td>Male</td>
<td>No</td>
<td>OS</td>
</tr>
<tr>
<td>Gervais</td>
<td>Karen</td>
<td>Female</td>
<td>No</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Affiliated: Please indicate whether or not each individual is affiliated (other than as an IRB member) with the entity conducting the research or operating the IRB.
Yes = The IRB member is affiliated with the entity conducting the research or operating the IRB
No = Other than as an IRB member, the individual is not affiliated with the entity conducting the research or operating the IRB.

** Status: Choose one of the following for each member or alternate:
PS = Physician-Scientist
OS = Other Scientist
NS = Non-Scientist
SS = Social Behavioral Scientist

NOTE: Any individual who has had substantive training or experience in a scientific discipline or in the scientific method should be considered a scientist. In addition, the IRB must have members with sufficient knowledge of the specific scientific discipline(s) relevant to the research that it reviews.
<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Schedule Number</td>
<td>Date</td>
<td>2. X New Revision of</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Agency</td>
<td>Health</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Page</td>
<td>1</td>
<td>of</td>
<td>3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MINNESOTA RECORDS RETENTION SCHEDULE**

**AUTHORIZATION:** under the authority of M.S. 138.17, it is hereby ordered that the records listed on this application be disposed per approved schedule. 

**NOTICE:** This retention schedule has been reviewed by the state records disposition panel in accordance with Minnesota Statutes 138.17. The records listed on this schedule have been reviewed for their historical, fiscal and legal value. This schedule’s compliance with the Minnesota Government Data Practices Act (Minnesota Statutes Chapter 13) has not been verified by the records disposition panel.

8. Agency Records Management Officer | Date | 11. Minnesota Historical Society | Date |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>9. Type RMO Name / Phone</td>
<td></td>
<td>12. Legislative Auditor</td>
<td>Date</td>
</tr>
<tr>
<td>James L. Mack, CRM</td>
<td>651-201-5005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Agency Head or Designee</td>
<td>Date</td>
<td>13. Attorney General</td>
<td>Date</td>
</tr>
</tbody>
</table>

DRAFT

1/15/2010
This new records retention schedule covers the records of the Institutional Review Board (IRB) for the Minnesota Department of Health created under 45 CFR 46.115 – Protection of Human Research Subjects.

<table>
<thead>
<tr>
<th>Item No.</th>
<th>Record Class TITLE and Description</th>
<th>Retention Instructions</th>
<th>SM*</th>
<th>Statute</th>
<th>Vital</th>
<th>Archival?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RESEARCH / STUDIES REVIEWED.</td>
<td>Retention based on</td>
<td>P/E</td>
<td>Confidential.</td>
<td>M.S. 144.053.</td>
<td>Yes. (Duplicate copy stored off site.)</td>
</tr>
<tr>
<td></td>
<td>This records series includes copies of all research proposals reviewed, scientific evaluations that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, reports of injuries to subjects, and correspondence between the IRB and investigators.</td>
<td>disposition of the application – see 1A, 1B, and 1C below:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1A</td>
<td>RESEARCH APPROVED AND COMPLETED.</td>
<td>3 years after completion.</td>
<td>No (Important)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Includes proposals that required modification before approval and records of the annual review of continuing studies.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1B</td>
<td>RESEARCH APPROVED BUT NOT COMPLETED.</td>
<td>3 years after decision to terminate research.</td>
<td>No (Important)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1C</td>
<td>RESEARCH DISAPPROVED.</td>
<td>3 years after disapproval.</td>
<td>No (Useful)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>APPROVED STATEMENTS ON CONSENT FORMS.</td>
<td>3 years.</td>
<td>P</td>
<td>No (Important)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Information given to research subjects about the reporting of significant new findings developed during the course of research that relate to the subject's willingness to continue to participate.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>MINUTES OF BOARD MEETINGS.</td>
<td>20 years. Electronic recordings cannot be used for long term storage.</td>
<td>P/E</td>
<td>Yes. (Duplicate copy stored off site.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Item No.</td>
<td>Record Class</td>
<td>TITLE and Description</td>
<td>Retention Instructions</td>
<td>Statute</td>
<td>Vital</td>
<td>Archival?</td>
</tr>
<tr>
<td>---------</td>
<td>--------------</td>
<td>-----------------------</td>
<td>------------------------</td>
<td>---------</td>
<td>-------</td>
<td>----------</td>
</tr>
<tr>
<td>4.</td>
<td></td>
<td>MEETING AGENDAS AND SUPPORTING DOCUMENTS.</td>
<td>3 months after minutes of the meeting are approved.</td>
<td>P/E</td>
<td></td>
<td>No (Nonessential)</td>
</tr>
<tr>
<td>5.</td>
<td></td>
<td>MEMBERSHIP LIST. A list of IRB members identified by name, earned degrees, representative capacity, and experience sufficient to describe each member's chief anticipated contributions to IRB deliberations.</td>
<td>20 years.</td>
<td>P/E Private M.S. 13.43</td>
<td></td>
<td>No (Useful)</td>
</tr>
<tr>
<td>6.</td>
<td></td>
<td>PROCEDURES, PROTOCOLS, GUIDELINES. Written procedures that the IRB will follow for conducting its review of research, reporting actions and findings, determining which projects require additional reviews, which projects need verification, and reporting proposed changes in research activity, risks to subjects, noncompliance, or termination of IRB approval.</td>
<td>3 years after superseded.</td>
<td>P/E</td>
<td></td>
<td>No (Important)</td>
</tr>
<tr>
<td>7.</td>
<td></td>
<td>CORRESPONDENCE AND MESSAGES. Transitory records, letters, memos or electronic messages of short-term interest and that are considered incidental and not vital to the business of the IRB.</td>
<td>Until action taken or decision made that no action is required.</td>
<td>P/E</td>
<td></td>
<td>No (Nonessential)</td>
</tr>
</tbody>
</table>

*SM: P = paper; M = microfilm/microfiche; C = computer output microfilm; E = electronic (including discs, tapes, DVD); A = other.

DRAFT
§46.101(b) [Exemption Criteria]

(1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
   (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

(3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:
   (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

(4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

(5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:
   (i) Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

(6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.
CDC's Policy for Distinguishing Public Health Research and Public Health Non-Research

Revised October 4, 1999

Purpose

The Centers for Disease Control and Prevention (CDC) is committed to preventing disease and improving health for all Americans. CDC is also committed to protecting individuals who participate in all public health activities. In the conduct of public health research, CDC follows the Code of Federal Regulations, Title 45, Part 46, The Public Health Service Act as amended by the Health Research Extension Act of 1985, Public Law 99-158, which sets forth regulations for the protection of human subjects.

This document, Defining Public Health Research and Public Health Non-Research, sets forth CDC guidelines on the definition of public health research conducted by CDC staff irrespective of the funding source (i.e., provided by CDC or by another entity). Under Federal regulations (45 CFR 46), the final determination of what is research and whether the Federal regulations are applicable lies with CDC and, ultimately, with the Office for Protection from Research Risks (OPRR). Thus, this document is intended to provide guidance to state and local health departments and other institutions that conduct collaborative research with CDC staff or that are recipients of CDC funds. The guidelines are intended to ensure both the protection of human subjects and the effective practice of public health.

Background

In 1974, the Department of Health and Human Services (formerly the Department of Health, Education and Welfare) developed regulations to assure the protection of human subjects from research risks. These regulations were developed to address ethical issues raised in connection with biomedical or behavioral research involving human subjects. Because most biomedical research is funded by the National Institutes of Health (NIH), the regulations were developed to deal specifically with the types of research funded by NIH. The regulations have been revised several times; currently the Department is operating under Title 45 Code of Federal Regulations Part 46, 1991 revision. The regulations will be referred to as 45 CFR 46.

The practice of public health poses several challenges in implementing 45 CFR 46. Although some public health activities can unambiguously be classified as either research or non-research, for other activities the classification is more difficult. The difficulty in classifying some public health activities as research or non-research stems either from traditionally held views about what constitutes public health practice or from the fact that 45 CFR 46 does not directly address many public health activities. In addition, the statutory authority of state and local health departments to conduct public health activities using methods similar to those used by researchers is not recognized in the regulations. Human subject protections applicable for activities occurring at the boundary between public health non-research and public health research are not readily interpretable from the regulations.

The regulations state that "research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." Obtaining and analyzing data are essential to the usual practice of public health. For many public health activities, data are systematically collected and analyzed, blurring the distinction between research and non-research. Scientific methodology is used both in non-research and research activities that comprise the practice of public health. Because scientific principles and methodology are applied to both non-research and research activities, knowledge is generated in both cases. Furthermore, at times the extent to which knowledge is generalizable may not differ greatly in research and non-research. Thus, non-research and research activities cannot be easily defined by the methods they employ. Three public health activities - surveillance, emergency responses, and evaluation - are particularly susceptible to the quandary over whether the activity is research or non-research.

The key word in the regulations' definition of research for the purpose of classifying public health activities as either research or non-research is "designed." The major difference between research and non-research lies in the primary intent of the activity. The primary intent of research is to generate or contribute to generalizable knowledge. The primary intent of non-research in public health is to prevent or control disease or injury and improve health, or to improve a public health program or service. Knowledge may be gained

http://www.cdc.gov/od/science/integrity/hrpo/researchDefinition.htm

Appendix F

10/26/2010
in any public health endeavor designed to prevent disease or injury or improve a program or service. In some cases, that knowledge may be generalizable, but the primary intention of the endeavor is to benefit clients participating in a public health program or a population by controlling a health problem in the population from which the information is gathered.

Classifying an activity as research does not automatically lead to review by an institutional review board (IRB) for the protection of human subjects. Once an activity is classified as research, two additional determinations must be made: (1) does the research involve human subjects and, if so, (2) does the research meet the criteria for exemption from IRB review. This policy deals only with the first determination of whether a public health activity is research or non-research.

---

**Definitions**

**Research** - As defined in 45 CFR 46, research means "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

**Human Subjects** - As defined in 45 CFR 46, a human subject means "a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information. Intervention includes both physical procedures by which data are gathered and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects."

**Surveillance** - The ongoing, systematic collection, analysis, and interpretation of outcome-specific data, closely integrated with the timely dissemination of these data to those responsible for preventing and controlling disease or injury (Thacker and Berkelman, 1988).

**Emergency Response** - A public health activity undertaken in an urgent or emergency situation, usually because of an identified or suspected imminent health threat to the population, but sometimes because the public and/or government authorities perceive an imminent threat that demands immediate action. The primary purpose of the activity is to document the existence and magnitude of a public health problem in the community and to implement appropriate measures to address the problem (Langmuir, 1980).

**Program Evaluation** - An essential organizational practice in public health using a systematic approach to improve and account for public health actions (Centers for Disease Control and Prevention, 1999)

**Evaluation** - The systematic application of scientific and statistical procedures for measuring program conceptualization, design, implementation, and utility; making comparisons based on these measurements; and the use of the resulting information to optimize program outcomes (Rossi and Freeman, 1993; Fink, 1993).

---

**Policy**

CDC is required to and has an ethical obligation to ensure that individuals are protected in all public health research activities it conducts. All CDC activities must be reviewed to determine whether they are research involving human subjects. When an activity is classified as research involving human subjects, CDC and its collaborators will comply with 45 CFR 46 in protecting human research subjects.

Some surveillance projects, emergency responses, and evaluations are research involving human subjects; others are not. Each project must be reviewed on a case-by-case basis. Although general guidance can be given to assist in classifying these activities as either research or non-research, no one criterion can be applied universally. The ultimate decision regarding classification lies in the intent of the project. If the primary intent is to generate generalizable knowledge, the project is research. If the primary intent is to prevent or control disease or injury or to improve a public health program, and no research is intended at the present time, the project is non-research. If the primary intent changes to generating generalizable knowledge, then the project becomes research.
Guidance for Compliance

I. General

The Human Subjects Contact (HSC) in each Center, Institute, or Office (CIO) determines whether the project constitutes research. If the HSC is unclear about classifying a project, the HSC should consult with the CDC's Deputy Associate Director for Science. This determination is made by examining the intent of the project. What is the primary purpose for which the project was designed?

General Attributes of Public Health Research - Intent of the project is to generate generalizable knowledge to improve public health practice; intended benefits of the project may or may not include study participants, but always extend beyond the study participants, usually to society; and data collected exceed requirements for care of the study participants or extend beyond the scope of the activity. Generalizable knowledge means new information that has relevance beyond the population or program from which it was collected, or information that is added to the scientific literature. Knowledge that can be generalized is collected under systematic procedures that reduce bias, allowing the knowledge to be applied to populations and settings different from the ones from which it was collected. Generalizable, for purposes of defining research, does not refer to the statistical concept of population estimation or to the traditional public health method of collecting information from a sample to understand health in the population from which the sample came. Holding public health activities to a standard of studying every case in order to classify an activity as non-research is not practical or reasonable.

General Attributes of Non-Research - Intent of the project is to identify and control a health problem or improve a public health program or service; intended benefits of the project are primarily or exclusively for the participants (or clients) or the participants' community; data collected are needed to assess and/or improve the program or service, the health of the participants or the participants' community; knowledge that is generated does not extend beyond the scope of the activity; and project activities are not experimental.

Other attributes, such as publication of findings, statutory authority (see discussion in next section), methodological design, selection of subjects, and hypothesis testing/generating, do not necessarily differentiate research from non-research because these types of attributes can be shared by both research and non-research projects.

A non-research project may generate generalizable knowledge after the project is undertaken even though generating this knowledge was not part of the original, primary intent. In this case, since the primary intent was not to generate or contribute to generalizable knowledge, the project is not classified as research at the outset. However, if subsequent analysis of identifiable private information is undertaken to generate or contribute to generalizable knowledge, the analysis constitutes human subjects research that requires IRB review.

If a project includes multiple components and at least one of those components is designed to generate generalizable knowledge, then the entire project is classified as research unless the components are separable.

II. Specific

A. Surveillance - Surveillance is a term describing a method for public health data collection. Surveillance systems may be either research or non-research. Surveillance systems are likely to be non-research when they involve the regular, ongoing collection and analysis of health-related data conducted to monitor the frequency of occurrence and distribution of disease or a health condition in the population. Data generated by these systems are used to manage public health programs. They have in place the ability to invoke public health mechanisms to prevent or control disease or injury in response to an event. Thus, the primary intent of these surveillance systems is to prevent or control disease or injury in a defined population by producing information about the population from which the data were collected. These attributes of surveillance that is non-research are generally found in state statute or regulation where the intent of the activity, its purposes, and uses of the data are specified. Surveillance systems that most easily fit into this category are ones in which the data are limited to describing the occurrence of a health-related problem (disease reporting) and systems in which no analytic (etiologic) analyses can be conducted. Subjects are rarely selected according to a design; rather, all cases are entered into the surveillance system because they are passive reporting systems. Hypothesis testing is not part of the system.

Surveillance systems are likely to be research when they involve the collection and analysis of health-related data conducted either to generate knowledge that is applicable to other populations and settings than the ones from which the data were collected or to contribute to new knowledge about the health condition. The information gained from the data collection system may or may not be used to invoke public health mechanisms to prevent or control disease or injury,
but this is not a primary intent of the project. Thus, the primary intent of these surveillance systems is to generate generalizable knowledge. Characteristics of surveillance systems that most easily fit into this category are: longitudinal data collection systems (e.g., follow-up surveys and registries) that allow for hypothesis testing; the scope of the data is broad and includes more information than occurrence of a health-related problem; analytic analyses can be conducted; and cases may be identified to be included in subsequent studies.

In general, lawful state disease reporting, monitoring requirements and other data collection activities conducted under state statute or under recognized public health authority are non-research. Disease reporting activities are not research. Disease reporting, for these purposes, is defined narrowly to include the reporting of the specific health condition or disease, demographic information; and accepted, known risk factors as specified in state statutes or regulations. When reporting systems collect data beyond standard reporting information, the reporting activity is not automatically considered to be non-research. Collection of data that would allow etiologic analysis is likely to be research.

If other activities are added to a surveillance project with the specific intent of generating new or generalizable knowledge, these additional activities are considered to be research. It becomes important to distinguish between disease reporting activities that are non-research and uses of the reported data that may be either non-research or research.

Sometimes, CDC funds state and local health departments to establish surveillance systems with dual intentions on the part of CDC: to build state capacity in disease reporting and for CDC to generate new knowledge. Disease reporting activities conducted at the state level are generally non-research. However, if CDC uses the data collected through such reporting to generate new knowledge, CDC would be engaged in research. CDC may consider state health departments to be engaged in the research depending upon their role. If state health departments are participating beyond merely providing the data, they may be considered as engaged in the research. Institutions providing information to state health departments would not be considered engaged in the research (see OPRR memorandum dated 1/26/99).

Some surveillance projects do not fit easily into the categories described above. For these projects, the primary intent and elements of the project must be examined carefully.

B. Emergency Responses - Most emergency responses tend to be non-research because these projects are undertaken to identify, characterize, and solve an immediate health problem and the knowledge gained will directly benefit those participants involved in the investigation or their communities. However, an emergency response may have a research component if: 1) samples are stored for future use intended to generate generalizable knowledge or 2) additional analyses are conducted beyond those needed to solve the immediate health problem. When investigational new drugs are used or drugs are used off-label, the emergency response is almost always research. The same applies to medical devices. For emergency responses, whenever a systematic investigation of a non-standard intervention or a systematic comparison of standard interventions occurs, the activity is research.

C. Evaluation - The terms "evaluation" and "program evaluation" are used interchangeably. Yet, there are subtle differences between the two terms (see definitions and reference provided above). Evaluation is a term, broad in meaning, that refers to the systematic use of scientific methods to measure efficacy, implementation, utility, and so on of a program in its entirety or its components. Evaluations may or may not be research. Program evaluations are a subset of evaluations. As defined here program evaluations are almost never research.

When the purpose of an evaluation is to test a new, modified, or previously untested intervention, service, or program to determine whether it is effective, the evaluation is research. The systematic comparison of standard or non-standard interventions in an experimental-type design is research. In these cases, the knowledge gained is applicable beyond the individual, specific program. Thus, the primary intent is to generate new knowledge or contribute to the knowledge in the scientific literature. Further, it is intended to apply the knowledge to other sites or populations.

When the purpose is to assess the success of an established program in achieving its objectives in a specific population and the information gained from the evaluation will be used to provide feedback to that program, the evaluation, referred to as program evaluation, is non-research. In the non-research scenario, the evaluation is used as a management tool to monitor and improve the program. The evaluation activity is often a component of the regular, ongoing program. Information learned from the evaluation has immediate benefit for the program and/or the clients receiving the services or interventions. The information is often not generalizable beyond the individual program. Interventions and services that are evaluated are never experimental or new; they are known (either from empirical data or through consensus) to be effective.

Sometimes, the term "formative evaluation" is used to describe data collection activities that occur prior to the implementation of an intervention, service, or program. Whether the "formative evaluation" is research or non-research depends upon its intent. If the evaluation is conducted prior to implementing a new, modified, or previously untested
intervention, the evaluation is part of the overall research project. If the evaluation is conducted to provide information on how to tailor a proven-effective intervention, service, or program in a specific setting or context, the evaluation is not research.

Evaluations of CDC's national programs, i.e., programs that CDC funds to all state health departments and in which evaluation is one component, are not research. These evaluation activities are on-going and involve generally the collection of minimal, standard data elements across all sites. The data are generally used at the local level as a management tool as well as at the national level for the same purpose. Sometimes, data from these evaluation activities will be aggregated at CDC and used for other purposes. When this occurs, subsequent use of the data may be research.

In some cases, program activities and evaluation activities are separable. For example, interventions or services are being provided; they have a history of being provided and there is an intention to continue to provide them. An evaluation is conducted to determine the efficacy of these program activities. In another example, a public health department, under its public health authority, may provide an untested intervention in an outbreak situation. An evaluation component is added. In both of these examples, because the intervention and evaluation activities are undertaken with different intentions and are separable, the intervention activities are not research but the evaluation activities are research.

Appendix

Examples of CDC surveillance, emergency responses, and evaluation activities that are non-research and research.

Surveillance:

Non-research -

**National Notifiable Diseases Surveillance System (NNDSS)** - States and territories have asked CDC to act as a common data collection point for data on nationally notifiable diseases. A notifiable disease is considered by the Council of State and Territorial Epidemiologists to be a condition for which regular, frequent, and timely information about individual cases is necessary at the national level for the prevention and control of disease. NNDSS data are collected and published weekly in the Morbidity and Mortality Weekly Report and annually in the Summary of Notifiable Diseases, United States. The NNDSS is essential to the day to day practice of public health. The primary intent of the surveillance system is to provide CDC and state and local health officials with information to detect and control outbreaks of disease. The NNDSS is also used to measure the impact of programs such as immunization. The intended benefits resulting from the NNDSS are for the residents of the states and local areas who contribute data to the system.

**Diabetes Surveillance Report** - Using public use data from several national surveys, a national diabetes surveillance system is produced. Data from the surveillance system are used to describe the burden of diabetes and its complications on a national and state level. The primary intent of the surveillance system is to provide information for the development of national and state public health priorities and policies regarding the prevention and control of diabetes. The intended benefits are for those who have diabetes or those who are at risk of developing diabetes.

Research -

**A Sentinel Surveillance System for Lassa Fever In the Republic of Guinea** - Four study sites were selected to identify and describe cases of Lassa fever. Cases were identified from hospital and outpatient admissions. The purpose of the project was to generate baseline information on the Lassa virus and human clinical Lassa fever in the Republic of Guinea. No public health interventions were planned as part of this project; there was no direct benefits for study participants. Thus, the primary intent was to contribute to the knowledge of Lassa fever.

**Developmental Disabilities in Very Low Birthweight Children: Linkage of the Georgia Very Low Birthweight Study and the Metropolitan Atlanta Developmental Disabilities Surveillance Program** - The Metropolitan Atlanta Developmental Disabilities Surveillance Program, an ongoing CDC surveillance program to monitor trends in the occurrence of selected developmental disabilities in children living in the metropolitan area.
Atlanta area, and the Georgia Very Low Birthweight Study, conducted in the 1980s to investigate the environmental and other risk factors for very low birthweight were linked for specific investigations of adverse developmental outcomes. Linkage of these primary files provides a unique opportunity to assist efforts to assess the occurrence of selected developmental disabilities in metropolitan Atlanta children and to identify causes of these conditions without the additional time and resource expenditure of additional field data collection. For these investigations involving secondary analyses of the linked primary data sets, no individuals were contacted; only information available from the linkage were used. The purpose of the project was to estimate the prevalence of cerebral palsy, mental retardation, and hearing and visual impairments and to identify pre- and perinatal medical and sociodemographic risk factors for these disabilities in a population-based cohort of very low birthweight children in Atlanta. The primary intent was to generate generalizable knowledge about developmental disabilities.

Emergency Responses:

Non-research -

Outbreak of Gastroenteritis - Three days after a cruise ship left Los Angeles, California for several ports in Mexico, CDC was notified that 24 of 1,899 passengers and 6 of 670 crew had presented to the ship’s infirmary with gastrointestinal illness. The purpose of the investigation was to determine the cause and extent of the outbreak and to prevent and control gastrointestinal illness among the ships passengers and crew. Although this type of investigation is often undertaken after the outbreak has occurred and therefore information gained is likely to benefit the ship’s next set of cruise passengers and crew, the primary intent of the investigation is to assist in controlling the current disease outbreak.

Recall of Six Lots of Influenza Vaccine - One of the pharmaceutical companies who manufactures influenza vaccine instituted a voluntary recall of six lots of influenza vaccine. The lots were recalled due to decreased potency of the A/Nanchang/933/95 (H3N2) component of the vaccine. CDC was notified by a state health department that a nursing home had vaccinated its residents with the recalled vaccine. The purpose of the investigation was to determine whether residents of this nursing home who received the vaccine had a suboptimal immune response and required revaccination. The primary intent of this investigation was to prevent the occurrence of influenza among the participants if they demonstrated a suboptimal immune response; there was a potential for participants to receive a direct benefit in the form of revaccination if they participated.

Research -

Childhood Exposure to Nicotine-Containing Products in Rhode Island - Between January 1, 1995 and June 30, 1996, 90 cases of nicotine-containing products were reported to the Rhode Island Poison Control Center. No known population-based investigation has been conducted to determine risk factors associated with nicotine-containing products poisoning. The purpose of the Epi-Aid was to determine risk factors associated with childhood exposure to nicotine-containing products, and to develop appropriate control measures. Although there may be some benefit to the 90 children exposed in Rhode Island, the benefits from this study extend beyond the study participants to the population of children who are at risk of exposure to nicotine-containing products. In addition, there was no immediate health problem to be controlled. Thus, the primary intent of the investigation was to generate generalizable knowledge about the risk factors associated with childhood exposure to nicotine-containing products.

Azithromycin Used as Prophylaxis Against the Spread of Illness Due to Mycoplasma Pneumoniae in the Setting of an Outbreak - During the first week of freshman entering a post high school academic institution, a cluster of respiratory illness was recognized by the infirmary staff. Early serologic testing suggest Mycoplasma pneumoniae as the etiologic agent. About four weeks later 42% of the freshman and 17% of the upperclassmen reported a respiratory illness; 50% of those tested had serologic evidence of Mycoplasma pneumoniae infection. The lower attack rate among upperclassmen was likely a consequence of them returning to campus 15 days after the freshmen arrived. A trial of chemoprophylaxis with azithromycin was proposed. Highly effective control measures in the setting of an outbreak have not been described. There is limited information about the role of antimicrobials in controlling an epidemic of Mycoplasma pneumoniae. Thus, the primary intent of the investigation was to generate generalizable knowledge about the efficacy of azithromycin to prevent the spread of Mycoplasma pneumoniae in an outbreak situation.

Program Evaluation:

Non-research -
Evaluation of School-based HIV Prevention Program - As part of the evaluation of the school-based HIV prevention program in Denver public schools, principals, teachers, student contact staff, students, and parents were interviewed. HIV program efforts in policy awareness, staff development, curriculum implementation, and status of students receiving HIV prevention education were assessed.

The purpose (primary intent) of the program evaluation was to provide information to Denver public schools that will be used to improve their school-based HIV prevention programs. The results from the evaluation were used to assess the success of the interventions in a specific population (Denver public school children) and to refine the interventions in that population.

IMPACT Progress Reports - The Office on Smoking and Health awarded 32 states and the District of Columbia health departments cooperative agreements to build capacity to conduct tobacco use prevention and control programs. These cooperative agreements are part of CDC’s Initiatives to Mobilize for the Prevention and Control of Tobacco Use (IMPACT), which is a nationwide effort to establish comprehensive, coordinated tobacco use prevention programs. Evaluation of IMPACT is comprised of awardees submitting semi-annual progress reports. Information in the evaluation includes staffing, coalition composition and efforts, status of a state tobacco control plan, development of a resource center, training efforts, community outreach and mobilization, and participation in CDC national campaigns.

The primary intent of these state tobacco control program evaluations is to assess the success of the intervention activities within each state. The information gained from the evaluation is used to refine the interventions in that state. In addition, the information is used nationally to evaluate the success of the IMPACT program.

Research -

Evaluation of Community Based Organization Intervention to Reduce Sexually Transmitted Disease (STD) Rates Among STD Patients in Miami - Male STD Patients were randomized to either the standard HIV prevention counseling or intensive counseling comprised of four sessions of HIV counseling from a community based organization. STD clinic records were reviewed to determine whether there was a difference in return rates with new STDs between the groups. The objective of intervention and evaluation is to determine whether intensive counseling reduces the acquisition of new STDs among high risk people attending a STD clinic. The purpose of the project was to evaluate a new intervention for reducing the transmission of STDs. Knowledge gained from this evaluation would be used to generalize to other sites.

A Comprehensive Evaluation for Project DIRECT (Diabetes Intervention: Reaching and Educating Communities Together) - Project DIRECT is a community diabetes demonstration project targeting African American adults residing in Raleigh, North Carolina. The project is three-tiered and addresses diabetes care, community screening for persons at high risk for developing diabetes, and population based approaches to increase physical activity and reduce dietary fat intake (two risk factors for diabetes). The goals of the community project are to reduce preventable complications of diabetes via a health systems approach, increase the proportion of persons at risk for diabetes who are screened, and increase the proportion who participate in regular vigorous physical activity and eat a reduced fat diet. Baseline and follow-up population-based surveys are planned to evaluate the community intervention. The purpose of this project is to evaluate new and innovative interventions to prevent diabetes and its complications. Knowledge gained from this project will be used to develop similar intervention projects in other communities.

References


Application for Approval of Research with Human Subjects

INSTRUCTIONS

☐ The attached Application for Approval of Research with Human Subjects must be completed, signed, and sent a minimum of two (2) weeks prior to the IRB meeting date to ensure review by the IRB. (IRB meetings are held the second Wednesday of every month.)

☐ Three (3) unbound, signed copies of the application and all appropriate forms and instruments should be sent to: Ann Kowski, MDH, Institutional Review Board, P.O. Box 64882, St. Paul, MN 55164-0882. (Interoffice address: Institutional Review Board, 300 GRB) Unsigned and incomplete applications will be returned to principal investigator for completion prior to any IRB review.

☐ The Principal Investigator (PI) (or an alternate) may be expected to be at the meeting to present a brief overview of the project and answer questions. They will be notified if this is necessary.

☐ If you have questions about the MDH IRB review process or need technical assistance, please contact Peter Rode by writing to the address listed above, by telephone 651.201-5942, or by e-mail peter.rode@state.mn.us.

☐ Copies of this application form are also available to MDH employees on the MDH intranet at http://fyi.health.state.mn.us/

☐ More information on the MDH IRB may be found at the following website: http://www.health.state.mn.us/irb/index.html

☐ Links to training resources on the protection of human subjects in research can also be found on the IRB website: http://www.health.state.mn.us/irb/index.html

☐ In addition to all sections of the application form, the Principal Investigator MUST fill out the HIPAA checklist at the end of the application.

More information on HIPAA (Health Insurance Portability and Accountability Act) may be found at www.hhs.gov/ocr/hipaa
Application for Approval of Research with Human Subjects

<table>
<thead>
<tr>
<th>Title of Research:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Principal Investigator Information:</th>
<th>Co-Principal Investigator Information:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name: ____________________________</td>
<td>Name: ______________________________</td>
</tr>
<tr>
<td>Title: ___________________________</td>
<td>Title: ______________________________</td>
</tr>
<tr>
<td>Address: _________________________</td>
<td>Address: ___________________________</td>
</tr>
<tr>
<td>City ___________________________ State Zip</td>
<td>City ___________________________ State Zip</td>
</tr>
<tr>
<td>E-Mail/Internet Address:</td>
<td>E-Mail/Internet Address:</td>
</tr>
<tr>
<td>Phone Number: _______________</td>
<td>Phone Number: _______________</td>
</tr>
<tr>
<td>Fax Number: _______________</td>
<td>Fax Number: _______________</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Funding Agency Information:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name: ________________________</td>
</tr>
<tr>
<td>Phone Number: _______________</td>
</tr>
<tr>
<td>Fax Number: _______________</td>
</tr>
<tr>
<td>Address: _____________________</td>
</tr>
<tr>
<td>City ___________________________ State Zip</td>
</tr>
<tr>
<td>E-Mail/Internet Address:</td>
</tr>
</tbody>
</table>

If known, Application or Proposal Identification Number: ____________________________

| Proposed Project Dates: From: _______________ To: _______________ |
|------------------------|------------------------|
| Month/Day/Year          | Month/Day/Year          |

Is this project being reviewed by any other IRB?  □ Yes  □ No

If yes, give name of IRB and name and phone number of IRB contact person:

<table>
<thead>
<tr>
<th>Name of IRB</th>
<th>Name of Contact Person</th>
<th>Phone Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>____________________________</td>
<td>____________________________</td>
<td>____________________________</td>
</tr>
</tbody>
</table>

Has this project been approved by another IRB?  □ Yes  □ No

If yes, give date of approval, name and phone number of IRB contact person:

<table>
<thead>
<tr>
<th>Name of IRB</th>
<th>Name of Contact Person</th>
<th>Phone Number</th>
<th>Date of Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>____________________________</td>
<td>____________________________</td>
<td>____________________________</td>
<td>____________________________</td>
</tr>
</tbody>
</table>

I CERTIFY THAT THE INFORMATION FURNISHED CONCERNING THE PROCEDURES TO BE TAKEN FOR THE PROTECTION OF HUMAN SUBJECTS IS CORRECT. I WILL SEEK AND OBTAIN PRIOR APPROVAL FROM THE IRB FOR ANY SUBSTANTIVE MODIFICATION IN THE PROPOSAL. I WILL PROMPTLY REPORT TO THE IRB ANY UNEXPECTED OR SIGNIFICANT ADVERSE EFFECTS (E.G., BREACHES OF CONFIDENTIALITY, BREACHES OF PROTOCOL, WITHDRAWAL OF STUDY SUBJECTS, AND COMPLAINTS ABOUT THE STUDY) IN THE COURSE OF THIS STUDY.

Signature of Principal Investigator ____________________________ Date ____________________________

Form #HE-01578-07  
Revised: June 16, 2011  
Appendix G
I. PURPOSE OF THE STUDY, INCLUDING THE RESEARCH QUESTION (S).

II. RESEARCH METHODS - Include the following:

A. Description of the subject population - number of subjects, age range, how subjects will be identified and selected;

B. Explanation of subject involvement in the research (the who, what, when, and how of subject involvement);

C. Summary of data analysis or statistical methods to be used in the study;

D. Specification of any inducements or rewards to be given subjects for their participation;

E. Specification of any research-related expenses to be charged to the subject or their third party payor.
III. RISKS Describe any reasonably foreseeable risks or discomforts to participants, including physical, emotional, economic, cultural or social factors. Delineate any steps taken to minimize risks, as well as care of subjects in the event of an accident or complication.

IV. BENEFITS Describe all reasonably foreseeable direct benefits to subjects as well as potential benefits to society.

V. CONFIDENTIALITY AND PRIVACY OF DATA Include the following:

A. An explanation of the procedures that will be implemented to safeguard data privacy, including how and where the data will be stored, in what form the data will be stored, how long the data will be stored, methods for destroying the data, and how the anonymity of the subjects will be insured. The classification of the data under the Minnesota Government Data Practices Act or other relevant statutes should also be submitted, as well as specific security measures to be used.

B. Identification of all persons who will have contact with private information, including research staff, clerical staff, network administrators, and computer staff. Describe how these persons will maintain confidentiality of the data.
VI.  TRAINING IN HUMAN SUBJECTS PROTECTION

A. Please describe the training that the Principal Investigator has received about using human subjects in research. Identify the institution (e.g. University of Minnesota) or on-line course providing the training. Include date (year) training was received. [NOTE: Links to training resources on the protection of human subjects in research can be found on the IRB web site at http://www.health.state.mn.us/irb/index.html.]

B. Describe the training in human subjects protection and data confidentiality received by all persons identified in section V.(B) above who will have access to private information.

VII.  INFORMED CONSENT

Please describe procedures for obtaining consent. Attach a copy of the proposed consent form(s).

NOTE: You must submit a consent form or letter that contains all of the elements of informed consent as outlined in the Informed Consent Checklist found near the end of this application.

VIII.  RESEARCH INSTRUMENTS

Attach copies of all instruments to be used (questionnaires, surveys, etc.)
Appendix G

Minnesota Department of Health
Institutional Review Board

Application for Approval of Research with Human Subjects

IX. VULNERABLE POPULATIONS CHECKLIST

Will your research involve any of the following? If yes, attach a list of additional safeguards you will use.

| A. Prisoners? | □ Yes | □ No |
| B. Pregnant Women? | □ Yes | □ No |
| C. Children? | □ Yes | □ No |
| D. Cognitively Impaired Persons? | □ Yes | □ No |
| E. Economically or Educationally Disadvantaged Persons? | □ Yes | □ No |
| F. Fetuses? | □ Yes | □ No |
| G. Human In-Vitro Fertilization? | □ Yes | □ No |
| H. HIV Antibody Testing? | □ Yes | □ No |
| I. Non-English Speaking Participants? | □ Yes | □ No |
| J. Other Vulnerable Populations? Please specify*: | □ Yes | □ No |

Additional Safeguards:

Attached additional sheets if necessary.

*Since these subjects, and others like them are particularly vulnerable to coercion and undue influence, investigators must incorporate safeguards in the research plan, and be certain to document fully their informed consent or the informed consent of their legal representatives.

PLEASE BE SURE TO SIGN PAGE 2 OF THIS APPLICATION
### Informed Consent Checklist

<table>
<thead>
<tr>
<th>Elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>A statement that the study involves research.</td>
</tr>
<tr>
<td>An explanation of the purposes of the research.</td>
</tr>
<tr>
<td>The expected duration of the subject's participation.</td>
</tr>
<tr>
<td>A description of the procedures to be followed.</td>
</tr>
<tr>
<td>Identification of any procedures that are experimental.</td>
</tr>
<tr>
<td>A description of any reasonably foreseeable risks or discomorts to the subject.</td>
</tr>
<tr>
<td>A description of any benefits to the subject or to others which may reasonably be expected from the research.</td>
</tr>
<tr>
<td>A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.</td>
</tr>
<tr>
<td>A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.</td>
</tr>
<tr>
<td>For research involving more than minimal risk, an explanation as to whether any compensation will be offered, 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.</td>
</tr>
</tbody>
</table>

| Research Qs | An explanation of whom to contact for answers to pertinent questions about the research (research study contact name and phone number) and research subjects' rights ("For questions about your rights as a participant in this research, contact Peter Rode, Administrator of the Minnesota Department of Health Institutional Review Board, at 651-201-5942.") and whom to contact in the event of a research-related injury to the subject (if the research is more than minimal risk). |
| Rights Qs    | A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is entitled. |
| Injury Qs    |                                                                                     |
# HIPAA Checklist

<table>
<thead>
<tr>
<th>Y YES</th>
<th>Y NO</th>
<th>Elements</th>
</tr>
</thead>
</table>
|       |      | 1. Will any of the information for the study be “protected health information” (PHI) that the study obtains directly from a HIPAA “covered entity”? (Exact definitions of “covered entity” and “PHI” are available at www.hhs.gov/ocr/hipaa For the most part, however, you can use the following definition):

- A HIPAA “covered entity” includes providers (hospitals, clinics, doctors, etc.), health plans (health insurers, HMOs), and health care clearinghouses (go-betweens for providers & plans). NOTE: MDH is not a covered entity under HIPAA and any health information that MDH has collected or received for public health purposes is not PHI in MDH's possession.

- PHI is individually identifiable health information that is held by a covered entity and that relates to the health condition of an individual, the provision of health care to an individual or the payment for the provision of health care.

*If you answered no to this question you do not have to complete the rest of the checklist.* |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2. Has the research been reviewed by a Privacy Board or another IRB for HIPAA purposes? If yes, specify which entity is doing this review and submit their review when available.</td>
</tr>
<tr>
<td>-------</td>
<td>------</td>
<td>----------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If no, are you requesting this IRB to review HIPAA requirements? If yes, you will be contacted by MDH staff for further information.</td>
</tr>
</tbody>
</table>
RE-REVIEW OF PREVIOUSLY APPROVED RESEARCH

<table>
<thead>
<tr>
<th>Title of Study or Project</th>
<th>IRB Identification Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Project Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date of Initial IRB Approval</th>
<th>Last Re-Review Date</th>
<th>Next Scheduled IRB Review</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

☐ Check if PI has changed

<table>
<thead>
<tr>
<th>Name of Principal Investigator</th>
<th>Phone Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Address (Street or P.O. Box)</th>
<th>City</th>
<th>State</th>
<th>Zip</th>
<th>E-Mail/Internet Address</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Complete EITHER Section I OR Section II

SECTION I  This study does NOT require re-review because:

☐ It is no longer in progress.
☐ It was never started. (Grant funding was denied, did not meet criteria, etc.)
☐ The MDH IRB has deferred to another IRB, which recently re-reviewed and approved the study on (date): _______/_____/_____
    By: ____________________________________________ (See Section III)
☐ Other
    (Specify): ____________________________________

SECTION II For studies that require re-review. NOTE: If any question in this section is answered yes, it is possible the proposal will need to go through a full IRB review.

1. How many subjects have been entered into the study? _________
SECTION III

1. Has this proposal been reviewed or approved by another IRB?

☐ Yes  ☐ No  If Yes, list name, organization, and phone number of IRB contact and date of review.

<table>
<thead>
<tr>
<th>Name and Organization of IRB Contact:</th>
<th>Phone Number of IRB Contact: (include area code)</th>
<th>Date of Review:</th>
</tr>
</thead>
</table>

Signature of Principal Investigator Date
1a. Is active recruitment of participants still occurring? □ YES □ NO

1b. What stage is the project in?
□ Finalizing design and procedures
□ Data collection
□ Data analysis
□ Report writing
□ Other (explain): _______________________

2. Briefly describe progress to date, plans for the next year, and any change in expected completion date for the study.

3. Have you received notice of or are you aware of any adverse events or unanticipated problems involving risks to subjects or others, including breach of confidentiality, withdrawal of study subjects, or complaints about the study?

□ Yes □ No
If Yes, please describe on an attached sheet.

4. Has there been any recent literature, findings, or other relevant information, especially information about risks associated with the research, which study subjects should be aware of since last reviewed by the IRB in ________?

□ Yes □ No
If Yes, describe on separate sheet.

If Yes, have study subjects been informed of these findings?

□ Yes □ No
If No, why not?

5. Have there been any changes in the informed consent form since the last review by the IRB in ________?

□ Yes □ No
If Yes, please submit 3 UNBOUND copies of the revised form. Use highlight or track changes to show revisions.

6. Have there been any significant changes from the original protocol or in previously reviewed instruments (e.g., questionnaires, surveys, etc.)?

□ Yes □ No
If Yes, please describe on an attached sheet and include 3 UNBOUND copies of the changed protocol or instruments. Use highlight or track changes to show revisions.
Instructions: Use this form when submitting a request for re-review of a protocol with exemption from 45 CFR 46. Please send the signed original to the IRB Administrative Office at the address listed above. Complete all applicable items and sign the form or it will be returned to you.

<table>
<thead>
<tr>
<th>Title of Study or Project</th>
<th>IRB Identification Number</th>
</tr>
</thead>
</table>

Project Description

<table>
<thead>
<tr>
<th>Date of Initial IRB Review/Exemption</th>
<th>Last Re-Review Date</th>
<th>Next Scheduled IRB Review</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

☐ Check if PI has changed

<table>
<thead>
<tr>
<th>Name of Principal Investigator</th>
<th>Phone Number</th>
<th>Fax Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Address (Street or P.O. Box)</th>
<th>City</th>
<th>State &amp; Zip</th>
<th>E-mail/Internet Address</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

List Below names of other MDH Employee Co-investigators:

- 
- 
- 
- 

1. Is the study or project still active? ☐ Yes ☐ No

1a. If still active: What stage is the project in?

☐ Finalizing design and procedures ☐ Data analysis
☐ Data collection ☐ Report writing
☐ Other (explain): ________________________________

ExemptRe-review5.doc
2. Have there been any changes in the study's objectives, methods, or subjects?
   □ Yes, If yes, please describe below and submit 3 unbound copies of the revised protocol.
   □ No

3. Have there been any changes in the study's informed consent process or forms?
   □ Yes, If yes, please describe below and submit 3 unbound copies of the current consent form(s).
   □ No

4. Have there been any adverse events or unanticipated problems involving risks to subjects or others, any withdrawal of subjects from the research, or complaints about the research?
   □ Yes, If yes, please describe below.
   □ No

4a. Have these events been reported to the IRB or other authorities?
   □ Yes, If yes, date reported: __________ reported to: ____________________________
   □ No

[Signature and Position Title] [Date]
The Tennessen Warning
Minnesota Statutes section 13.04, subdivision 2

| The Tennessen Warning must be given when: | 1. An individual  
|                                          | 2. Is asked to supply  
|                                          | 3. Private or confidential data  
|                                          | 4. Concerning himself or herself  

All four conditions must be present to trigger the requirement.

| The Tennessen Warning is not required if: | • the data subject is not an individual  
|                                          | • the individual offers information that has not been requested by the government entity  
|                                          | • the information requested from the individual is about someone else  
|                                          | • the government entity requests or receives information about the individual from someone else, or  
|                                          | • the information requested from the individual is public data about the individual.  

The individual must be informed:

| • Why the information is being collected from the individual and how the government entity intends to use the information;  
| • Whether the individual may refuse or is legally required to supply the information;  
| • Any consequences to the individual of either supplying or refusing to supply the information; and  
| • The identity of other persons or entities authorized by law to receive the information.  

Consequences of giving a proper Tennessen Warning are: Private and confidential data on the individual may be collected, stored, used, and released as described in the Tennessen Warning without liability to the government entity.

Consequences of giving an incomplete notice, or not giving the Tennessen Warning at all, are:

| Private and confidential data on the individual must not be collected, stored, used, or released for any purposes other than those stated, unless:  
| • The individual gives informed consent;  
| • The Commissioner of Administration gives approval; or  
| • A state or federal law or court order subsequently authorizes or requires a new use or a release.  

§46.116 - Informed Consent Checklist - Basic and Additional Elements

<table>
<thead>
<tr>
<th>Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>A statement that the study involves research</td>
</tr>
<tr>
<td>An explanation of the purposes of the research</td>
</tr>
<tr>
<td>The expected duration of the subject's participation</td>
</tr>
<tr>
<td>A description of the procedures to be followed</td>
</tr>
<tr>
<td>Identification of any procedures which are experimental</td>
</tr>
<tr>
<td>A description of any reasonably foreseeable risks or discomforts to the subject</td>
</tr>
<tr>
<td>A description of any benefits to the subject or to others which may reasonably be expected from the research</td>
</tr>
<tr>
<td>A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject</td>
</tr>
<tr>
<td>A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained</td>
</tr>
<tr>
<td>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</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Qs</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Qs</td>
<td>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</td>
</tr>
<tr>
<td>Rights Qs</td>
<td>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</td>
</tr>
</tbody>
</table>

Additional elements, as appropriate

<table>
<thead>
<tr>
<th>Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently unforeseeable</td>
</tr>
<tr>
<td>Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent</td>
</tr>
<tr>
<td>Any additional costs to the subject that may result from participation in the research</td>
</tr>
<tr>
<td>The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject</td>
</tr>
</tbody>
</table>
A statement that significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject.

The approximate number of subjects involved in the study

§46.117 Documentation of Informed Consent Checklist

<table>
<thead>
<tr>
<th>WRITTEN</th>
<th>The consent form may be either of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. A <strong>written consent</strong> document that embodies the elements of informed consent required by §46.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator should give either the subject or the representative adequate opportunity to read it before it is signed.</td>
<td></td>
</tr>
</tbody>
</table>

| DONE ORALLY | 2. A **short form written consent** document, stating that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a **written summary** of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form. |

<table>
<thead>
<tr>
<th>WAIVER of req't for signed form</th>
<th>c. An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects, if it finds either:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. That the only record linking the subject and the research would be the consent document, and the <strong>principal risk</strong> would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or</td>
<td></td>
</tr>
<tr>
<td>2. That the research presents <strong>no more than minimal risk</strong> of harm to subjects, and involves no procedures, for which written consent is normally required outside of the research context.</td>
<td></td>
</tr>
</tbody>
</table>

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

IRB Latitude to Approve a Consent Procedure that Alters or Waives some or all of the Elements of Consent
§ 46.116 - An IRB may approve a consent procedure, which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

C: 1. The research or demonstration project is to be conducted by, or subject to the approval of, state or local government officials, and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and

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

D: 1. The research involves no more than minimal risk to the subjects;

D: 2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;

D: 3. The research could not practicably be carried out without the waiver or alteration; and

D: 4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Special Requirements - 45 CFR 46 Subpart D - Additional DHHS Protections for Children Involved as Subjects in Research

Assent/ Waiver

The IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted, or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children, and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances, in which consent may be waived in accord with §46.116 of Subpart A.

Parents

The IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 or §46.405.

Where research is covered by §46.406 and §46.407, and permission is to be obtained from parents, both parents must give their permission, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

If the IRB determines that a research protocol is designed for conditions or for a subject population, for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in Subpart A of this part and paragraph (b) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with Federal,
09/30/98
13.02 DEFINITIONS.

Subd. 3. **Confidential data on individuals.** "Confidential data on individuals" means data which is made not public by statute or federal law applicable to the data and is inaccessible to the individual subject of that data.

Subd. 7. **Government data.** "Government data" means all data collected, created, received, maintained or disseminated by any government entity regardless of its physical form, storage media or conditions of use.

Subd. 8. **Individual.** "Individual" means a natural person. In the case of a minor or an incapacitated person as defined in section 524.5-102, subdivision 6, "individual" includes a parent or guardian or an individual acting as a parent or guardian in the absence of a parent or guardian, except that the responsible authority shall withhold data from parents or guardians, or individuals acting as parents or guardians in the absence of parents or guardians, upon request by the minor if the responsible authority determines that withholding the data would be in the best interest of the minor.

Subd. 8a. **Not public data.** "Not public data" means any government data which is classified by statute, federal law, or temporary classification as confidential, private, nonpublic, or protected nonpublic.

Subd. 9. **Nonpublic data.** "Nonpublic data" means data not on individuals that is made by statute or federal law applicable to the data: (a) not accessible to the public; and (b) accessible to the subject, if any, of the data.

Subd. 12. **Private data on individuals.** "Private data on individuals" means data which is made by statute or federal law applicable to the data: (a) not public; and (b) accessible to the individual subject of that data.

Subd. 13. **Protected nonpublic data.** "Protected nonpublic data" means data not on individuals which is made by statute or federal law applicable to the data (a) not public and (b) not accessible to the subject of the data.

Subd. 15. **Public data on individuals.** "Public data on individuals" means data which is accessible to the public in accordance with the provisions of section 13.03.

Subd. 19. **Summary data.** "Summary data" means statistical records and reports derived from data on individuals but in which individuals are not identified and from which neither their identities nor any other characteristic that could uniquely identify an individual is ascertainable.
13.03 ACCESS TO GOVERNMENT DATA.

Subdivision 1. Public data. All government data collected, created, received, maintained or disseminated by a government entity shall be public unless classified by statute, or temporary classification pursuant to section 13.06, or federal law, as nonpublic or protected nonpublic, or with respect to data on individuals, as private or confidential.

Subd. 3. Request for access to data. (a) Upon request to a responsible authority or designee, a person shall be permitted to inspect and copy public government data at reasonable times and places, and, upon request, shall be informed of the data's meaning. If a person requests access for the purpose of inspection, the responsible authority may not assess a charge or require the requesting person to pay a fee to inspect data.

(f) If the responsible authority or designee determines that the requested data is classified so as to deny the requesting person access, the responsible authority or designee shall inform the requesting person of the determination either orally at the time of the request, or in writing as soon after that time as possible, and shall cite the specific statutory section, temporary classification, or specific provision of federal law on which the determination is based.

13.3805 PUBLIC HEALTH DATA.

Subdivision 1. Health data generally. (a) Definitions. As used in this subdivision:

(1) "Commissioner" means the commissioner of health.

(2) "Health data" means data on individuals created, collected, received, or maintained by the Department of Health, political subdivisions, or statewide systems relating to the identification, description, prevention, and control of disease or as part of an epidemiologic investigation the commissioner designates as necessary to analyze, describe, or protect the public health.

(b) Data on individuals. (1) Health data are private data on individuals. Notwithstanding section 13.05, subdivision 9, health data may not be disclosed except as provided in this subdivision and section 13.04.

(2) The commissioner or a local board of health as defined in section 145A.02, subdivision 2, may disclose health data to the data subject's physician as necessary to locate or identify a case, carrier, or suspect case, to establish a diagnosis, to provide treatment, to identify persons at risk of illness, or to conduct an epidemiologic investigation.

(3) With the approval of the commissioner, health data may be disclosed to the extent necessary to assist the commissioner to locate or identify a case, carrier, or suspect case, to alert persons who may be threatened by illness as evidenced by epidemiologic data, to control or prevent the spread of serious disease, or to diminish an imminent threat to the public health.
13.3806 PUBLIC HEALTH DATA CODED ELSEWHERE.

Subdivision 1. Scope. The sections referred to in this section are codified outside this chapter. Those sections classify data on public health as other than public, place restrictions on access to government data, or involve data sharing.

Subd. 1a. Death investigation data. Data gathered by the commissioner of health to identify the body of a person believed to have died due to a declared emergency as defined in section 12.03, subdivision 1e, the circumstances of death, and disposition of the body are classified in and may be released according to section 12.381, subdivision 2.

Subd. 2. Certain epidemiologic studies. Use of data collected by the commissioner of health under sections 176.234, 268.19, and 270B.14, subdivision 11, is governed by section 144.0525.

Subd. 3. Public health studies. Data held by the commissioner of health in connection with public health studies are classified under section 144.053.

Subd. 4. Vital statistics. (a) Parents’ Social Security number; birth record. Parents' Social Security numbers provided for a child's birth record are classified under section 144.215, subdivision 4.

(b) Foundling registration. The report of the finding of an infant of unknown parentage is classified under section 144.216, subdivision 2.

(c) New record of birth. In circumstances in which a new record of birth may be issued under section 144.218, the original record of birth is classified as provided in that section.

(d) Vital records. Physical access to vital records is governed by section 144.225, subdivision 1.

(e) Birth record of child of unmarried parents. Access to the birth record of a child whose parents were not married to each other when the child was conceived or born is governed by sections 144.225, subdivisions 2 and 4, and 257.73.

(f) Health data for birth registration. Health data collected for birth registration or fetal death reporting are classified under section 144.225, subdivision 2a.

(g) Birth record; sharing. Sharing of birth record data and data prepared under section 257.75, is governed by section 144.225, subdivision 2b.

(h) Group purchaser identity for birth registration. Classification of and access to the identity of a group purchaser collected in association with birth registration is governed by section 144.225, subdivision 6.

Subd. 4a. Birth defects information system. Information collected for the birth defects information system is governed by section 144.2217.
Subd. 5. School health records. (a) Student health data. Data collected for the health record of a school child are governed by section 144.29.

(b) Tuberculosis screening. Access to health records of persons enrolled in or employed by a school or school district for tuberculosis screening purposes is governed by section 144.441, subdivision 8.

Subd. 6. Health records. Access to health records is governed by section 144.291 to 144.298.

Subd. 7. Immunization data. Sharing of immunization data is governed by section 144.3351.

Subd. 8. Hepatitis B maternal carrier. Sharing of information regarding the hepatitis B infection status of a newborn's mother is governed by section 144.3352.

Subd. 9. Human leukocyte antigen type registry. Data identifying a person and the person's human leukocyte antigen type which is maintained by a government entity are classified under section 144.336, subdivision 1.

Subd. 10. Health threat procedures. Data in a health directive issued by the commissioner of health or a board of health are classified in section 144.4186.

Subd. 10a. Isolation or quarantine directive. Data in a directive issued by the commissioner of health under section 144.4195, subdivision 2, to isolate or quarantine a person or group of persons are classified in section 144.4195, subdivision 6.

Subd. 11. Tuberculosis health threat. Data collected by the commissioner of health in connection with a tuberculosis health threat are classified under section 144.4813.

Subd. 12. Epidemiologic data. Epidemiologic data that identify individuals are classified under section 144.6581.

Subd. 13. Traumatic injury. Data on individuals with a brain or spinal injury or who sustain major trauma that are collected by the commissioner of health are classified under sections 144.6071 and 144.665.

Subd. 14. Cancer surveillance system. Data on individuals collected by the cancer surveillance system are classified pursuant to section 144.69.

Subd. 15. Bloodborne pathogens. Data sharing between the emergency medical services agency and facilities is governed by section 144.7402, subdivision 3.

Subd. 16. Test information. Information concerning test results is governed by section 144.7411.
Subd. 17. **Lead exposure.** Data on individuals exposed to lead in their residences are classified under sections 144.9502, subdivision 9, and 144.9504, subdivision 2.

Subd. 18. **Terminated pregnancies.** Disclosure of reports of terminated pregnancies made to the commissioner of health is governed by section 145.413, subdivision 1.

Subd. 19a. **Maternal death.** Access to and classification of medical data and health records related to maternal death studies are governed by section 145.901.

Subd. 20. **Hazardous substance exposure.** Disclosure of data related to hazardous substance exposure is governed by section 145.94.

13.386 TREATMENT OF GENETIC INFORMATION HELD BY GOVERNMENT ENTITIES AND OTHER PERSONS.

Subdivision 1. **Definition.** (a) "Genetic information" means information about an identifiable individual derived from the presence, absence, alteration, or mutation of a gene, or the presence or absence of a specific DNA or RNA marker, which has been obtained from an analysis of:

1. the individual's biological information or specimen; or
2. the biological information or specimen of a person to whom the individual is related.

(b) "Genetic information" also means medical or biological information collected from an individual about a particular genetic condition that is or might be used to provide medical care to that individual or the individual's family members.

Subd. 2. **Private data.** Genetic information held by a government entity is private data on individuals as defined by section 13.02, subdivision 12.

Subd. 3. **Collection, storage, use, and dissemination of genetic information.** Unless otherwise expressly provided by law, genetic information about an individual:

1. may be collected by a government entity, as defined in section 13.02, subdivision 7a, or any other person only with the written informed consent of the individual;
2. may be used only for purposes to which the individual has given written informed consent;
3. may be stored only for a period of time to which the individual has given written informed consent; and
4. may be disseminated only:
   i. with the individual's written informed consent; or
(ii) if necessary in order to accomplish purposes described by clause (2). A consent to disseminate genetic information under item (i) must be signed and dated. Unless otherwise provided by law, such a consent is valid for one year or for a lesser period specified in the consent.

144.053 RESEARCH STUDIES CONFIDENTIAL.

Subdivision 1. Status of data collected by commissioner. All information, records of interviews, written reports, statements, notes, memoranda, or other data procured by the state commissioner of health, in connection with studies conducted by the state commissioner of health, or carried on by the said commissioner jointly with other persons, agencies or organizations, or procured by such other persons, agencies or organizations, for the purpose of reducing the morbidity or mortality from any cause or condition of health shall be confidential and shall be used solely for the purposes of medical or scientific research.

144.293 RELEASE OR DISCLOSURE OF HEALTH RECORDS

Subd. 2. Patient consent to release of records. A provider, or a person who receives health records from a provider, may not release a patient's health records to a person without:

1. a signed and dated consent from the patient or the patient's legally authorized representative authorizing the release;

2. specific authorization in law; or [emphasis added]

3. a representation from a provider that holds a signed and dated consent from the patient authorizing the release.

Subd. 7. Exception to consent. Subdivision 2 does not apply to the release of health records to the commissioner of health or the Health Data Institute under chapter 62J, provided that the commissioner encrypts the patient identifier upon receipt of the data.

144.295 DISCLOSURE OF HEALTH RECORDS FOR EXTERNAL RESEARCH

Subdivision 1. Methods of release. (a) Notwithstanding section 144.293, subdivisions 2 and 4, health records may be released to an external researcher solely for purposes of medical or scientific research only as follows:

1. health records generated before January 1, 1997, may be released if the patient has not objected or does not elect to object after that date;

2. for health records generated on or after January 1, 1997, the provider must:
(i) disclose in writing to patients currently being treated by the provider that health records, regardless of when generated, may be released and that the patient may object, in which case the records will not be released; and

(ii) use reasonable efforts to obtain the patient's written general authorization that describes the release of records in item (i), which does not expire but may be revoked or limited in writing at any time by the patient or the patient's authorized representative;

(3) the provider must advise the patient of the rights specified in clause (4); and

(4) the provider must, at the request of the patient, provide information on how the patient may contact an external researcher to whom the health record was released and the date it was released.

(b) Authorization may be established if an authorization is mailed at least two times to the patient's last known address with a postage prepaid return envelope and a conspicuous notice that the patient's medical records may be released if the patient does not object, and at least 60 days have expired since the second notice was sent.

Subd. 2. Duties of researcher. In making a release for research purposes, the provider shall make a reasonable effort to determine that:

(1) the use or disclosure does not violate any limitations under which the record was collected;

(2) the use or disclosure in individually identifiable form is necessary to accomplish the research or statistical purpose for which the use or disclosure is to be made;

(3) the recipient has established and maintains adequate safeguards to protect the records from unauthorized disclosure, including a procedure for removal or destruction of information that identifies the patient; and

(4) further use or release of the records in individually identifiable form to a person other than the patient without the patient's consent is prohibited.

**RELEVANT HIPAA PROVISIONS**
(citations are to 2010 CFR Title 45)

§164.512 Uses and disclosures for which consent, an authorization, or opportunity to agree or object is not required.

A covered entity may use or disclose protected health information without the written authorization of the individual, as described in § 164.508, or the opportunity for the individual to agree or object as described in § 164.510, in the situations covered by this section, subject to the applicable requirements of this section. When the covered entity is required by this section to
inform the individual of, or when the individual may agree to, a use or disclosure permitted by
this section, the covered entity’s information and the individual’s agreement may be given orally.

(a) **Standard: Uses and disclosures required by law.** (1) A covered entity may use or disclose
protected health information to the extent that such use or disclosure is required by law and the
use or disclosure complies with and is limited to the relevant requirements of such law.

(b) **Standard: uses and disclosures for public health activities.**--(1) **Permitted disclosures.** A
covered entity may disclose protected health information for the public health activities and
purposes described in this paragraph to:

(i) A public health authority that is authorized by law to collect or receive such information
for the purpose of preventing or controlling disease, injury, or disability, including, but not
limited to, the reporting of disease, injury, vital events such as birth or death, and the conduct of
public health surveillance, public health investigations, and public health interventions; or, at the
direction of a public health authority, to an official of a foreign government agency that is acting
in collaboration with a public health authority;

(iv) A person who may have been exposed to a communicable disease or may otherwise be at
risk of contracting or spreading a disease or condition, if the covered entity or public health
authority is authorized by law to notify such person as necessary in the conduct of a public health
intervention or investigation;

(i) **Standard: uses and disclosures for research purposes**--(1) **Permitted uses and disclosures.** A
covered entity may use or disclose protected health information for research, regardless of the
source of funding of the research, provided that:

(i) **Board approval of a waiver of authorization.** The covered entity obtains documentation
that an alteration to or waiver, in whole or in part, of the individual authorization required by
§164.508 for use or disclosure of protected health information has been approved by either:

(A) An Institutional Review Board (IRB), established in accordance with 7 CFR 1c.107, 10
CFR 745.107, 14 CFR 1230.107, 15 CFR 27.107, 16 CFR 1028.107, 21 CFR 56.107, 22 CFR
CFR 26.107, 45 CFR 46.107, 45 CFR 690.107, or 49 CFR 11.107;

(ii) **Reviews preparatory to research.** The covered entity obtains from the researcher
representations that:

(A) Use or disclosure is sought solely to review protected health information as necessary to
prepare a research protocol or for similar purposes preparatory to research;

(B) No protected health information is to be removed from the covered entity by the
researcher in the course of the review; and

(C) The protected health information for which use or access is sought is necessary for the
research purposes.

(iii) **Research on decedent’s information.** The covered entity obtains from the researcher:

(A) Representation that the use or disclosure is sought is solely for research on the protected
health information of decedents;

(B) Documentation, at the request of the covered entity, of the death of such individuals; and

(C) Representation that the protected health information for which use or disclosure is sought
is necessary for the research purposes.
(2) **Documentation of waiver approval.** For a use or disclosure to be permitted based on documentation of approval of an alteration or waiver, under paragraph (i)(1)(i) of this section, the documentation must include all of the following:

(i) **Identification and date of action.** A statement identifying the IRB or privacy board and the date on which the alteration or waiver of authorization was approved;

(ii) **Waiver criteria.** A statement that the IRB or privacy board has determined that the alteration or waiver, in whole or in part, of authorization satisfies the following criteria:

   (A) The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:

      (1) An adequate plan to protect the identifiers from improper use and disclosure;

      (2) 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

      (3) Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted by this subpart;

   (B) The research could not practicably be conducted without the waiver or alteration; and

   (C) The research could not practicably be conducted without access to and use of the protected health information.

(iii) **Protected health information needed.** A brief description of the protected health information for which use or access has been determined to be necessary by the IRB or privacy board has determined, pursuant to paragraph (i)(2)(ii)(C) of this section;

(iv) **Review and approval procedures.** A statement that the alteration or waiver of authorization has been reviewed and approved under either normal or expedited review procedures, as follows:


   . . .

(v) **Required signature.** The documentation of the alteration or waiver of authorization must be signed by the chair or other member, as designated by the chair, of the IRB or the privacy board, as applicable.
EXAMPLE FOR DATA PRACTICES WITHIN THE IRB APPLICATION

This is an example of a “Confidentiality and Privacy of Data” paragraph in the IRB application that covered:
- data classification under Minnesota Law;
- records retention; and
- specific security measures.

“. . . [A] permission and release of information form … that will be signed by the parent/guardian of all study participants prior to turning in the questionnaire [is included]. … Specific results will be stored in the Minnesota Blood Lead Surveillance database with a unique identifier for easy retrieval and analysis. Once the hard copy is entered into the database, the results [will be] stored in a locked cabinet when not under the physical control of an authorized employee. Record retention is consistent with the Record Retention Schedule for the EH unit [that is attached]. . . . Hard copy results [will be] stored and retained for a period of 1 to 2 years … Electronic data is backed up nightly/weekly and then copied onto an electric storage medium for duplication and permanent retention. Electronic records are “double locked” using a password for system access and a second password for file access. Access is restricted to those employees with a “need to know.” Blood lead test results are classified as private data by Minnesota statutes (Minn. Stat. § 144.9502).”
Appendix M

Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure

Applicability

(A) Research activities that
   (1) present no more than minimal risk to human subjects, and
   (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this 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 categories in this list apply regardless of the age of subjects, except as noted.

(C) 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.

(D) The expedited review procedure may not be used for classified research involving human subjects.

(E) IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.

(F) Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

Research Categories

(1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

   (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

   (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

(2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
(a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

(b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

(3) Prospective collection of biological specimens for research purposes by noninvasive means.

Examples: (a) hair and nail clippings in a non-disfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncanulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

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

Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)
(6) Collection of data from voice, video, digital, or image recordings made for research purposes.

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

(8) Continuing review of research previously approved by the convened IRB as follows:

   a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

   b) where no subjects have been enrolled and no additional risks have been identified; or

   c) where the remaining research activities are limited to data analysis.

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

---

1 An expedited review procedure consists of a review of research involving human subjects by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in 45 CFR 46.110.

2 Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." 45 CFR 46.402(a).

Source: 63 FR 60364-60367, November 9, 1998