

THE DANBURY HOSPITAL
Danbury, Connecticut

**INSTITUTIONAL REVIEW BOARD
POLICIES AND PROCEDURES**

I. AUTHORITY AND PURPOSE

1. The Institutional Review Board is appointed by and responsible to the Danbury Hospital Board of Directors to assure compliance with the Federal Food, Drug and Cosmetic Act, the regulations promulgated by the Federal Food and Drug Administration and the regulations of the U.S. Department of Health and Human Services for the protection of the rights and welfare of human subjects involved in clinical investigations.
 1. "IRB/DH" is used as an abbreviation of Institutional Review Board/Danbury Hospital in these policies and procedures.
 2. The terms used in these policies and procedures are intended to have the same meaning as those defined in 21CFR50.3, 21CFR56.102, and 45CFR46.102
2. The purpose of the IRB/DH is to approve the initiation of, and to conduct periodic review of biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of human subjects.
3. The principles that govern IRB/DH are to assure that the rights and welfare of human subjects are adequately protected, that they are not exposed to unnecessary risks, and that they are provided with enough information about a study so that they may give effective informed consent.

II. SCOPE OF AUTHORITY

- A. IRB/DH shall review, have authority to approve, require modifications in (to secure approval) or disapprove all research activities within its authority.
- B. IRB/DH requires that information given to subjects as part of informed consent is in accordance with legal requirements and, when in the IRB/DH's judgment additional information would meaningfully add to the protection of the rights and welfare of subjects, such additional information is also given to subjects.
- C. IRB/DH requires documentation of **informed consent** in accordance with legal requirements, except that the IRB/DH may, for some or all subjects, waive the requirement that the subject or the subject's legally authorized representative sign a written consent form if it finds 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 the research context. In cases where the documentation requirement is waived, the IRB/DH may require the investigator to provide subjects with a written statement regarding the research.

Danbury Hospital

D. IRB/DH may suspend or terminate approval of research that is not being conducted in accordance with the IRB/DH requirements or that has been associated with unexpected serious harm to subjects. The IRB/DH may also place restrictions on research activity. Any suspension, termination of approval, or added restrictions shall include a statement of the reasons for the action and shall be reported promptly to the investigator, and if appropriate, institutional officials and the Food and Drug Administration and/or other regulatory bodies.

E. IRB/DH authority applies to the following situations:

1. When the investigational study is to utilize human subjects who are patients, both inpatients and outpatients, of Danbury Hospital or DOPS (Danbury Office of Physician Services);
2. When the investigational study is to be conducted by an individual employed by Danbury Hospital or DOPS;
3. If an investigator conducting clinical research outside Danbury Hospital requests review by the IRB/DH. However, the IRB/DH may decline such review if it so chooses.

F. Exemptions from IRB Review

1. IRB/DH review is not required for **life threatening emergency** use of a test article, provided that such emergency use is reported to the IRB/DH within 5 working days. Any subsequent use of the test article at the institution is subject to IRB/DH review. Emergency use of a test article on a human subject without prior IRB/DH approval is sanctioned only for those rare instances of a life-threatening situation in which no other acceptable treatment is available and in which there is not sufficient time to obtain prior FDA waiver. If the patient or his/her representative cannot give proper informed consent, the investigator must have another physician who is not involved in the care of that patient or in an investigation of that test article, certify in writing that the human subject is:
 - a. confronted by a life-threatening situation necessitating the use of test article;
 - b. informed consent cannot be obtained because of inability to communicate with, or obtain legally effective consent from the subject;
 - c. time is not sufficient to obtain consent from the subject's legal representative;
 - d. no alternative method of approved or generally recognized therapy is available that provides equal or greater likelihood of saving the life of the patient.
2. For waiver of IRB/DH review, the sponsor or the sponsor/investigator may apply to the FDA to waive any of the requirements contained in the FDA regulations, including the requirements for IRB/DH review.

F. Exemptions from IRB Review (continued):

3. Commercially available drugs, devices and biologics in a study protocol used for an indication not previously approved by FDA require review by IRB/DH.
4. The ultimate decision to review or not review a clinical trial rests with the IRB/DH (see Investigational Use of Marketed Products).

G. Expedited Review: The IRB/DH Chair or alternate(s) designated by IRB/DH from among IRB/DH members has authority to review research approved by the FDA for expedited review. Such research involves no more than minimal risk, and must be on the FDA Approved List for studies that can be expedited (Appendix A). Expedited review may also be used in situations involving minor changes in approved research.

1. The reviewer may exercise all of the authority of the IRB/DH except that the reviewer may not disapprove the research. Disapproval can be made only through the regular review procedures of the IRB/DH.
2. The decision of the reviewer of each expedited review and circumstances are to be reported to the IRB/DH at its next meeting.

H. IRB/DH will notify investigators in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB/DH approval. The completed revisions must be reviewed and approved by the IRB before the investigator is notified the study may begin. If the revisions are made by the IRB and all that is required of the investigator is concurrence and formal revision of the documents, the IRB Chair or other designated IRB member may approve the revisions and allow the study to begin. The minutes of the next meeting will inform the membership of these actions. If the revisions require substantial changes to the protocol by the investigator, the acceptability of the changes should be determined at a convened meeting of the IRB membership. In the case of IRB/DH disapproval, 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.

I. The investigator must submit written progress reports at least once per year or at other shorter intervals specified by the IRB/DH appropriate to the degree of risk. The interval for submission of progress reports will be specified when the study is initially approved. Review of submitted progress reports will be documented, at which time the IRB will decide if the research should be amended, terminated or allowed to continue as originally approved and if the review frequency should be maintained as originally approved.

J. Investigators must report promptly to the IRB/DH any changes in a research activity, or unanticipated problems involving risks or injury to subjects or others during the period for which IRB/DH approval has already been given.

K. Investigators must comply with all legal requirements of informed consent for biomedical research involving human subjects, including the responsibility to provide subjects with information of significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation.

Danbury Hospital

L. Medical Devices

Studies that propose to evaluate a **significant risk device** must be conducted under an Investigational Device Exemption (IDE) granted by the FDA. The determination that an IDE is necessary is generally made by the sponsor of the study. **Non-significant risk devices** may be studied without the need for an IDE. Whenever the IRB reviews an application for a study involving a medical device for which the sponsor/investigator has not obtained an IDE, the IRB will carefully evaluate the claim that the device is a non-significant risk device. The application should include a description of the device, a picture of the device and a report of prior investigations with the device. In addition, the IRB will evaluate the potential harm that may arise in the context of the actual use of the device, taking account of the risks associated with any surgical procedures that may need to be performed. The IRB will conduct its review in compliance with published guidance from the FDA concerning the evaluation of experimental medical devices. Guidance regarding device regulations can be found at: <http://www.fda.gov/oc/ohrt/irbs/devices.html>.

M. Research Misconduct

Danbury Health Systems is committed to fostering an environment in which research is conducted in accordance with the highest professional, ethical and legal standards. Misconduct of any nature in research undermines the fundamental concepts of scientific research, and the public's trust and confidence in our organization. Our Misconduct in Research policy outlines the process of reporting, inquiry and investigation of alleged misconduct in research (see Appendix B for complete policy). Annual assurances are filed with the Office of Research Integrity of the Department of Health and Human Services.

N. Special Classes of Subjects

Special consideration must be given by all researchers to protect the welfare of particularly vulnerable subjects, such as children, pregnant women, mentally disabled persons, or economically disadvantaged persons [45 CFR 46.111]. Federal regulations set forth specific provisions on research involving pregnant women, human fetuses and neonates (of uncertain viability or nonviable neonates), and children. Please refer to Appendix C for requirements related to these special classes. (Research related to prisoners also has special considerations. However, at this time the IRB/DH does not review and approve research involving prisoners since the composition of its membership is not suitable to do so.)

III. RELATIONSHIP TO OTHER DEPARTMENTS

The Danbury Hospital Board of Directors constitutes the authority for appointing members of the IRB/DH and is responsible for IRB/DH's actions.

Danbury Hospital

1. Minutes of the IRB/DH shall be sent to the Board of Directors of Danbury Hospital and the Chief Executive Officer. These minutes shall indicate all actions and decisions of IRB/DH.
2. The Board of Directors may overrule IRB/DH's approvals but may not overrule disapproval by the IRB/DH.
3. These Policies and Procedures and subsequent revisions thereof are approved by the Board of Directors of Danbury Hospital.

IV. Regulatory Compliance

Research sponsors and investigators are responsible for compliance with all applicable regulations of the Federal Food and Drug Administration, the U.S. Department of Health and Human Services, any applicable State or local laws and the Policies and Procedures of the IRB/DH.

V. MEMBERSHIP

A. Number

No fewer than 9 individuals with varying backgrounds shall be appointed to the IRB/DH by the Board of Directors of Danbury Hospital from nominations made and voted on by the IRB Committee itself. The Board of Directors may also appoint IRB members with Alternate status. It will be clearly identified in whose place the Alternate may serve. Alternates must file with the IRB/DH the same biographical information as regular members.

B. Terms

The Board of Directors will stagger reappointment of members to assure overlapping terms of 3 years beginning January 1 annually. Initial appointments to the IRB/DH may take place as needed.

C. Compensation

Members will serve without monetary compensation other than reimbursement for necessary expenses, if funds are available.

D. IRB Chair

The IRB Chair shall be elected for continuous 3-year terms from among members who have served on the IRB/DH for at least 1 year, except when this requirement is waived by the IRB/DH itself by majority vote. A Vice-Chair may serve in similar terms, if needed.

Danbury Hospital

E. Qualifications of Members

1. Members shall have varying backgrounds to promote complete and adequate review of research activities conducted by the institution. The IRB/DH shall be sufficiently qualified through the experience and expertise of its members and the diversity of the members' backgrounds including consideration of the racial and cultural backgrounds of members and sensitivity to the 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, IRB/DH members 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.
2. Both men and women will be selected for membership.
3. Members may not all be entirely of one profession.
4. At least one member shall have primary concerns in non-scientific areas, for example, educator, lawyer, ethicist, and clergy.
5. At least one member must not otherwise be affiliated with Danbury Hospital and is not part of the immediate family of a person who is affiliated with Danbury Hospital.
6. No member may participate in the initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by IRB/DH.

F. Consultants

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

G. Orientation and Continuing Education of Members

Each new member shall be supplied with a copy of the approved Policies and Procedures, an IRB Educational notebook, the IRB Member Handbook and other helpful materials. All members shall be notified of changes, updates, or revisions in regulations promulgated by the FDA or other applicable regulatory bodies, and other pertinent information received by the IRB Chair.

VI. IRB/DH FUNCTIONS AND OPERATIONS

A. Meetings

IRB/DH shall hold regular meetings the third Monday of alternate months. Exceptions may be made at the discretion of the IRB Chair, depending on the volume and urgency of material requiring review, and quorum considerations.

Danbury Hospital

B. Quorum

A quorum shall consist of a majority of the official membership. Empowered alternates are members for quorum purposes. No quorum shall be constituted, regardless of numbers present, unless at least one voting member, whose primary concerns are in non-scientific areas, is present. Also, no research that includes drug administration may be approved unless at least one scientific member is present during discussion and votes on the protocol.

A quorum is required to transact business with the exception of expedited review, emergency use, and waivers as defined elsewhere.

C. Voting Requirements

1. A majority of a quorum must vote in the affirmative in order to approve a research project.
2. No member may participate in the IRB/DH's initial or continuing review of any project in which the member has a conflicting interest except to provide information requested by IRB/DH.
3. Only members or empowered alternates may vote.
4. Proxy votes will not be considered.

D. Agenda

Agendas for all meetings shall be prepared and distributed by the IRB Administrator to all attending members at least 5 days prior to the meeting, whenever possible. Copies of materials to be reviewed will accompany the Agenda. Empowered Alternates will receive the same materials as other voting members.

E. Minutes of Meetings

Minutes of all meetings shall be written and maintained accessible in files. They shall contain: names of those present and voting; names of guests; records of discussion on controversial issues and their resolution; actions taken, numbers voting for, against, and abstaining; and any basis for requiring changes in or disapproving research. A copy of the approved Minutes is posted on the Board of Director's confidential website for the Board's Review.

F. Records

Records shall be maintained to provide adequate documentation of IRB/DH activities. Records shall include the following:

1. The written Policies and Procedures of the IRB/DH;
2. A list of IRB/DH members identified by name, earned degrees, representative

Danbury Hospital

capacity, indications or experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB/DH deliberations; and any employment or other relationship between each member and the institution, for example: unaffiliated, staff member, full-time employee, part-time employee, a member of governing board, paid or unpaid consultant;

3. Minutes of meetings, as defined above;
4. 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;
5. Records of continuing review activities;
6. Copies of all correspondence between IRB/DH and investigators; and,
7. Statements of significant new findings provided to subjects.

The records shall be retained for at least 3 years after completion of the research, and the records shall be accessible for inspection and copying by authorized representatives of the Food and Drug Administration at reasonable times and in a reasonable manner.

G. Operations of the IRB/DH review process include:

1. IRB members have access to all materials maintained in the IRB Administrator's office, including complete records, and are encouraged to review them in entirety.
 - a. Entire protocols are sent with agenda more than 5 days prior to meetings, when feasible.
 - b. In case of great volume or complexity of materials, summaries of primary materials only may be mailed to all members.
2. When protocols are lengthy or complex, the IRB/DH Chair may:
 - a. Summarize part or all of the protocol to supplement material mailed;
 - b. Request review and report by a subcommittee of the IRB/DH;
 - c. Request that one or more primary reviewers review entire protocol, report to IRB/DH and lead the discussion.
3. Emergency use/studies information will be reported to IRB/DH members for their review at their next scheduled meeting and documented in IRB/DH records.
4. Expedited reviews and decisions by the IRB Chair or designated alternates will be reported to the IRB/DH members at the next scheduled meeting and documented in IRB/DH records.
5. Policies and procedures of the IRB/DH will be reviewed and changes made as necessary.

Danbury Hospital

H. IRB/DH Functions Regarding the Review Process

1. IRB/DH will review and act upon research within its scope of authority as outlined in Parts I and II of these Policies and Procedures.
2. IRB/DH review may take place before, during, or after FDA review, but must take place before initiation of research in human subjects in the Danbury Hospital.
3. IRB/DH will follow written procedures which have been approved by the Board of Directors of Danbury Hospital, as follows:
 - a. conduct of its initial and continuing review of research and for reporting its findings and actions to the investigators and to the Board of Directors of Danbury Hospital;
 - b. determination of projects which require review more often than annually, and which projects require verification from sources other than the investigators that nonmaterial changes have occurred since previous review;
 - c. IRB/DH 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 approval of the research activity. If the IRB/DH 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;
 - d. IRB/DH shall determine and conduct continuing review of research at intervals appropriate to the degree of risk, but not less often than once per year, and shall have authority to observe or have a third party observe the informed consent process and the research.
4. IRB/DH shall be responsible for reporting to the appropriate Hospital officials and the FDA, any serious or continuing non-compliance by investigators with the requirements and determinations of IRB/DH.
5. Principal investigators are responsible for full compliance with the applicable regulations of the FDA, HHS, any applicable State or local laws, the Danbury Hospital, and these Policies and Procedures.
 - e. Information to be provided the IRB/DH by the investigator shall include at least the following:
 1. Professional qualifications to do the research (including a description of necessary support services and facilities);
 2. Title of the study;
 3. Purpose of the study (including the benefit obtained by doing the study);

Information to be provided by the investigator (continued)

4. Sponsor of the study;
5. Description of any funding by sponsor;
6. A copy of the investigator's brochure, when available, or a summary of the results of previous animal and human research using the proposed test article if appropriate;
7. Subject selection criteria:
8. Subject exclusion criteria;
9. Justification for use of special subject populations (for example, the mentally retarded, children, etc.);
10. Study design (including as needed a discussion of the appropriateness of research methods);
11. Description of procedures to be performed;
12. Provisions for managing adverse reactions;
13. Any involvements of the investigator with any other department or personnel in Danbury Hospital and include approvals granted by them;
14. Any costs to subjects;
15. A subject informed consent form using language clear to a layperson including the following (as per FDA guidelines)
 - a. statement that the study involves research;
 - b. an explanation of the purposes of the research and the expected duration of the subject's participation;
 - c. a description of the procedures to be followed and identification of any procedures that are experimental;
 - d. a description of any reasonable foreseeable risks or discomforts to the subject;
 - e. a description of any benefits to the subject or to others which may reasonably be expected from the research;
 - f. a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

Subject informed consent form (continued)

- g. a statement describing the extent, if any to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the FDA may inspect the records;
 - h. explanation of whether compensation or medical treatment is available if injury occurs and, if so, what that consists of, and where further information may be obtained, if applicable;
 - i. an identification of who to contact (including phone number) for answers to pertinent questions about the research and research subject's rights, and who to contact (including phone number) in the event of a research-related injury;
 - j. a statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled;
 - k. a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable;
 - l. anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
 - m. any additional costs to the subject that may result from participation in the research;
 - n. the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
 - o. statement that significant new findings developed during the course of the research which may be related to the subject's willingness to continue participation will be provided to the subject;
 - p. the approximate number of subjects involved in the study.
- 16.** Report to the IRB/DH any serious adverse reactions that occur in subjects.
- 17.** The investigators will provide written progress reports as designated by the IRB/DH at the time of approval, but at least annually. The report should contain the number of subjects enrolled and withdrawn, a description of the subjects'

experiences (benefits/adverse reactions), preliminary observations and conclusions (if available), and plans for continuing study.

- a. If the requested update is not submitted, IRB/DH approval is automatically terminated.
 - b. Any protocol approved should be implemented within six months.
 - c. If the protocol is not implemented within that period of time, the investigator should explain why the protocol was not implemented and why the protocol should not be terminated.
- 18.** A final report should be submitted to the IRB/DH at the completion of the study. The final report should include a summary of pertinent findings, adverse reactions, number of subjects, enrolled and any other pertinent information. A copy of any resulting publication is to be submitted to IRB/DH.
- 19.** Investigators must:
- a. Insure prompt reporting of changes in research activity;
 - b. Insure that changes in approved research are not initiated without IRB/DH review and approval except where necessary to eliminate apparent immediate hazards to the human subjects;
 - c. Insure prompt reporting to the IRB/DH of unanticipated problems involving risks to subjects or others.
- 20.** All **advertising** requires IRB approval. The IRB will review the information contained in the advertisement, as well as the mode of its communication, to determine whether the procedure for recruiting subjects affords adequate protection. IRB review is necessary to ensure that the information is not misleading to potential research subjects.
- 21.** All **press releases or article about the research study** released to the public media also require IRB review/approval by the IRB Chair, IRB Administrator, or designated IRB member.

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Appendix A

RESEARCH ACTIVITIES THAT MAY BE REVIEWED THROUGH EXPEDITED REVIEW PROCESS

(Source: Federal Register, Vol. 63, No. 216, November 9, 1998)

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.

Research Activities Which May Be Reviewed Through Expedited Review Procedures (Continued)

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

Danbury Hospital

Research Activities Which May Be Reviewed Through Expedited Review Procedures (Continued)

- 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 Chair or by one or more experienced reviewers designated by the IRB Chair 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).

APPENDIX B

Administrative Policy

SUBJECT: Misconduct in Research – Process for Reporting and Investigating Allegations

PURPOSE:

Danbury Health Systems, Inc. (“DHS”) is committed to fostering an environment in which research is conducted in accordance with the highest professional, ethical and legal standards. Misconduct of any nature in research undermines the fundamental concepts of scientific research, and the public’s trust and confidence in our organization. This policy outlines the process of reporting, inquiry and investigation of alleged misconduct in research.

SCOPE:

All members of our research community, including physicians, medical staff, research assistants and coordinators, graduate students, postdoctoral fellows, technicians and administrative staff involved in the institution’s research program, have a shared responsibility to report incidents of suspected misconduct. Allegations should not be made capriciously, but evidence of fraud or misconduct must not be ignored.

DEFINITIONS – *What constitutes research misconduct?*

At DHS, research misconduct is defined as fabrication, falsification, or plagiarism that are a significant departure from those that are commonly accepted within the scientific community for proposing, performing, or reviewing research, or in reporting research results. It does not include honest error or honest differences in interpretations or judgments of data.

Some violations are more serious than others. Lesser offenses, such as carelessness or questionable research practices, should be handled through normal administrative channels. Other situations are sufficiently serious that they require review through an inquiry or formal investigation. The process outlined in this policy pertains to handling major offenses.

Examples of serious misconduct include:

1. ***Fabrication of data:*** dishonesty in recording or reporting results, ranging from fabrication of data, improper adjustment of results, and gross negligence in collecting or analyzing data to selective reporting or omission of conflicting data for deceptive purposes;

Danbury Hospital

2. **Falsification in research:** manipulating research materials, equipment, or processes, or changing or omitting data or results such that research is not accurately represented in the research record.
3. **Plagiarism:** taking credit for someone else's work or ideas, stealing others' results or methods, copying the writing of others without proper acknowledgment, or otherwise falsely taking credit for the work or ideas of another; plagiarism does not include disputes about authorship or credit among collaborators;
4. **Abuse of confidentiality:** taking or releasing the ideas or data of others which were shared with the legitimate expectation of confidentiality, e.g., stealing ideas from others' grant proposals, award applications, or manuscripts for publication when one is a reviewer for granting agencies or journals;
5. **Dishonesty in publication:** knowingly publishing material that will mislead readers, e.g., misrepresenting data, particularly its originality, misrepresenting research progress, or adding the names of other authors without permission;
6. **Deliberate violation of regulations:** flagrant and repeated failure to adhere to or to receive the approval required for work under Federal, State, or local research regulations;
7. **Property violations:** stealing or destroying the property of others, such as research papers, supplies, equipment, or products of research or scholarship;
8. **Failure to report observed major offenses:** covering up or otherwise failing to report major offenses or breaches of research ethics by others that one has observed; or,
9. **Retaliation:** taking punitive action against an individual for having reported alleged major offenses (refer to DHS administrative policy titled "Compliance – Non-Retaliation for Reports").

OVERVIEW OF PROCESS:

The process of addressing allegations of research misconduct can be outlined in four categories: (1) Making/receiving reports of research misconduct; (2) initiating and conducting an "Inquiry", or preliminary fact-finding to determine if the allegation has substance to warrant an investigation; (3) conducting an "investigation" which is a thorough review and analysis of all relevant facts to reach a conclusion as to whether research misconduct has occurred, who was responsible, and how serious any misconduct was; and (4) determining sanctions, if misconduct is confirmed, and final notification of the appropriate regulatory parties.

REPORTING: Individuals should report allegations of research misconduct by:

1. contacting the Institutional Review Board (IRB) Administrator at (203) 739-7608; or
2. calling the Patient Safety Management Office at (203) 739-7064; or
3. calling the Corporate Compliance Officer at (203) 739-7110; or
4. calling the Compliance HelpLine at (203) 737-7676.

Danbury Hospital

Upon receipt of a report of misconduct, the recipient will, in a timely manner:

- explain the rights of the individual(s) wishing to make the report;
- notify the individual(s) that if the report has not been made in written form, it will be put in writing by the recipient, encouraging these individual(s) to provide as much detail as possible in this initial allegation;
- inform the individual(s) that the report may be submitted anonymously, but that complete confidentiality cannot be guaranteed in that their identity may be revealed on a need to know basis (or may be inferred) during the investigation; and,
- that in accordance with federal policies on research misconduct, the individual(s) who report a possible case of research misconduct should not participate in the fact-finding phase, or in any other aspect of the determination of misconduct, other than as a witness.

INQUIRY AND INVESTIGATION PROCEDURES / PROCESS:

The Chief Medical Officer (CMO) is responsible for receiving the allegation and/or evidence, coordinating and conducting the inquiry and, if applicable, conducting the investigation and preparing the necessary reports. The Corporate Compliance Officer will be notified of any reported allegations and updated during the process.

Although the following procedure for reviewing, investigating and reporting allegations of research misconduct is specific to research and research training activities funded by the Public Health Service (PHS), the same process pertains to research with other types of funding. The exception is that proper notification to the appropriate agencies, such as the Food & Drug Administration or the Office of Human Research Protections (OHRP) in addition to or instead of the Office of Research Integrity (ORI) will be made.

1. Upon receiving a legitimate allegation of scientific misconduct or other evidence of possible misconduct, the CMO will appoint a subcommittee comprised of three experts who will be responsible for conducting an inquiry of the allegations or other evidence of possible research misconduct. In appointing investigators, precautions against real or apparent conflicts of interest on the part of those involved in the inquiry or investigation will be taken.
2. The inquiry must be completed within sixty (60) calendar days of its initiation, unless circumstances clearly warrant a longer period of review. A written report shall be prepared stating what evidence was reviewed, summarizing relevant interviews, and including conclusions of the inquiry. The individual(s) against whom the allegation was made shall be given a copy of the inquiry report. If the individual(s) comments on that report, the comments will be made part of the record. If the inquiry takes longer than sixty (60) days to complete, the record of the inquiry shall include documentation of the reasons for exceeding the sixty (60) day period.
3. DHS will protect, to the maximum extent possible, the privacy of those who in good faith report apparent misconduct in science.

Danbury Hospital

4. The individual(s) against whom the allegation was made shall be afforded confidential treatment to the maximum extent possible. The individual(s) shall also be afforded a prompt and thorough investigation, and an opportunity to access the evidence and to comment on allegations and findings of the inquiry and/or investigation.
5. The DHS will notify the Office of Research Integrity (ORI) at any stage of the inquiry or investigation if any of the following conditions exist:
 - a. there is an immediate health hazard involved;
 - b. there is an immediate need to protect federal funds or equipment;
 - c. there is an immediate need to protect the interests of the person(s) making the allegation or of the individual(s) who is the subject of the allegations as well as his/her co-investigators and associates, if any;
 - d. it is probable that the alleged incident is going to be reported publicly; or
 - e. the allegation involves a public health sensitive issue, e.g., a clinical trial.
6. DHS will notify the ORI within 24 hours of obtaining any reasonable indication of possible criminal violations, so that the ORI may then notify the Office of Inspector General (OIG) of the Department of Health and Human Services (DHHS).
7. Sufficient detailed documentation of inquiries will be maintained to permit a subsequent assessment of the reasons for determining that an investigation was not warranted, if necessary. These records will be maintained in a secure manner for a minimum period of seven (7) years after the termination of the inquiry, and shall be provided to authorized DHHS personnel, if requested.
8. If DHS plans to terminate an inquiry (or later, an investigation), for any reason without completing all relevant federal requirements, a report of such planned termination describing the reasons for doing so, shall be made to ORI.
9. The CMO will undertake an investigation within thirty (30) days of the completion of the inquiry, if findings from that inquiry provide sufficient basis for conducting an investigation. ORI will be notified on or before the date the investigation begins. The investigation normally will include examination of all documentation, including but not necessarily limited to, relevant research data and proposals, publications, correspondence, and memoranda of telephone calls. Whenever possible, interviews will be conducted of all individuals involved either in making the allegation or against whom the allegation is made, as well as other individuals who might have information regarding key aspects of the allegations. Complete summaries of these interviews, should be prepared, provided to the interviewed party for comment or revision, and included in the investigatory file. Also, the individual(s) against whom the allegation was made shall be given a copy of the investigation report. If the individual(s) comments on that report, the comments will be made part of the record.
10. The CMO will secure the necessary and appropriate expertise to conduct a thorough and authoritative evaluation of the relevant evidence in any inquiry or investigation.

Danbury Hospital

This may include a subcommittee comprised of those who handled the Inquiry, with additional experts or replacements added as may be needed.

11. Precautions will be taken against real or apparent conflicts of interest on the part of those involved in the inquiry or investigation.
12. DHS will take interim administrative actions, as appropriate, to protect federal funds and ensure that the purposes of the federal financial assistance are carried out.
13. DHS will keep the ORI apprised of any developments during the course of the investigation that disclose facts that may affect current or potential DHHS funding for the individual(s) under investigation or that the Public Health Service (PHS) needs to know to ensure appropriate use of federal funds and otherwise protect the public interest.

I. OUTCOMES AND FINAL REPORTING

1. The investigation will be completed and report submitted to ORI within 120 calendar days of initiation of the investigation. If the investigation and report cannot be completed within this time period, a request for an extension will be submitted to ORI and will include an explanation for the delay, an interim report on the progress to date, an outline of what remains to be done, and an estimated date of completion.
2. The final report to ORI will describe the policies and procedures under which the investigation was conducted, how and from whom information was obtained relevant to the investigation, the findings, and the basis for the findings, and include the actual text or an accurate summary of the views of any individual(s) found to have engaged in misconduct, as well as a description of any sanctions taken by the institution. The document shall be made available to the Director of the ORI, who will decide whether the office will either proceed with its own investigation or will act on the findings of DHS.
3. Sufficient detailed documentation of investigations will be maintained to permit a subsequent assessment of the reasons for determining that an investigation was not warranted, if necessary. These records will be maintained in a secure manner for a minimum period of seven (7) years after the termination of the inquiry, and shall be provided to authorized DHHS personnel, if requested.
4. DHS will undertake diligent efforts, as appropriate, to restore the reputations of persons alleged to have engaged in misconduct when allegations are not confirmed, and to protect the positions and reputations of those persons, who in good faith, make allegations.
5. DHS will impose appropriate sanctions on individuals when the allegation of misconduct has been substantiated.

[This policy is based on 42 CFR Parts 50 and 93 (May 17, 2005).]

Danbury Hospital

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Appendix C Special Classes of Subjects

Additional Considerations for Approval of Research Involving Children

Children are defined by 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)]. In the State of Connecticut the minimum age for consent is 18, with certain exceptions for emancipated minors or for treatment of certain conditions such as AIDS.

1. The IRB may approve research involving children if it finds:
 - a. No greater than minimal risk is presented, and adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.
 - b. More than minimal risk 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, and:
 - (1) the risk is justified by the anticipated benefit to the subjects;
 - (2) the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
 - (3) adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.
 - c. More than minimal risk 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, and:
 - (1) the risk represents a minor increase over minimal risk;
 - (2) the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
 - (3) the intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
 - (4) adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.
 - d. The research does not meet the requirements of paragraphs a., b., or c., but presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.
2. Requirements for permission by parents or guardians and for assent by children:
 - a. In addition to the determinations required under other applicable sections, 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

Danbury Hospital

- 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.
- b. In addition to the determinations required under other applicable sections, the IRB shall determine, in accordance with and to the extent that consent is required, 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 paragraph 1.a. or b., above. Where research is covered by paragraph 1.c. or d., 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, 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 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 Documentation of Informed Consent.
 - e. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.
3. Wards
- a. Children who are wards of the State or any other agency, institution, or entity can be included in research approved under paragraph 1.c. or d. 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.

Additional Considerations for Approval of Research Involving Pregnant Women, Fetuses or Neonates or Fetal Material

Viable neonate is defined by regulations as a neonate after delivery that is able to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration [45 CFR 46.202(h)].

1. The IRB may approve research involving pregnant women or fetuses if it finds:
 - 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 section VIII;
 - e. If the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of section VIII, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
 - f. Each individual providing consent under 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 who are pregnant, assent and permission are obtained in accord with the provisions of section H;
 - h. No inducements, monetary or otherwise, will be offered to terminate a pregnancy; and
 - 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.
2. The IRB may approve research involving neonates of uncertain viability and nonviable neonates provided that:
 - a. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
 - b. Each individual providing consent under paragraph e.(2) or f.(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
 - c. Individuals engaged in the research will have no part in determining the viability of a neonate.

Danbury Hospital

- d. The requirements of paragraph e. or f. of this section have been met as applicable.
 - e. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met:
 - (1) The IRB determines that:
 - (a) 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
 - (b) 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) The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with section VIII, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.
 - f. After delivery, a nonviable neonate may be involved in research only if all of the following additional conditions are met:
 - (1) Vital functions of the neonate will not be artificially maintained;
 - (2) The research will not terminate the heartbeat or respiration of the neonate;
 - (3) There will be no added risk to the neonate resulting from the research;
 - (4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
 - (5) The legally effective informed consent of both parents of the neonate is obtained in accord with section VIII, except that the waiver and alteration provisions of section VIII.E.4. do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.
3. The IRB may approve research involving viable neonates only to the extent permitted by and in accord with the requirements pertaining to general human subjects (45 CFR 46 Subpart A) and as permitted by and in accord with the requirements pertaining to children (45 CFR 46 Subpart D).
 4. The research does not meet the requirements of paragraphs 1., 2., or 3., but 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 pregnant women, fetuses or neonates; and
 - b. informed consent will be obtained in accord with the informed consent provisions and other applicable parts of this section.
 5. Research involving, after delivery, the placenta, the dead fetus, macerated fetal material, or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities.

Danbury Hospital

If information associated with material described in the previous paragraph is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent parts of this section are applicable.

6/25/07jb