(Revised 8/04)

**Introduction**

The National Naval Medical Center (NNMC) Clinical Investigation Department (CID), *Investigator's Manual* describes the policies and regulations governing research with human subjects and the requirements for submitting research proposals for review by the NNMC Institutional Review Board (IRB). The NNMC website.

Sections of the manual describe and explain the various aspects of the review process and regulatory requirements. Investigators should familiarize themselves with the contents of the manual. In addition, they should carefully review the sections of the manual that address their specific research activities before submitting proposals to the Clinical Investigation Department (CID). Interspersed throughout the text are web links, which are best, viewed with Microsoft Explorer.

This manual presents the most current information for reference by potential investigators and their staff. Since the field of human subject protection is constantly evolving, sections of the manual may be subject to change.

**The Foundation of 45 CFR 46: The Belmont Report**

In 1974, the passage of the National Research Act established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission published the *Belmont Report*, (website) which articulated the basic ethical principles that guide the conduct of research with human subjects and form the foundation of 45 CFR 46. Three principles were defined in the report as basic to the protection of human subjects: 1) respect, 2) beneficence, and 3) justice. The Commission also published a report on IRBs and a series of reports on research involving the human fetus, children, prisoners, and mentally impaired individuals ("those institutionalized as mentally infirm").

**Research Defined**

Virtually all federally funded research with human subjects is governed by federal regulations patterned on those of the Department of Health and Human Services (DDHS), found at Title 45 Code of Federal Regulations Part 46 (45 CFR 46). The DoD version of this regulation (i.e. the "Common Rule") is 32 CFR Part 219. (Http://www.access.gpo.gov/nara/cfr/waisidx_99/32cfr219_99.html) **Research** is defined in 32 CFR 219 as, *"a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."* **Human subjects** are defined by the regulations as *"living individual(s) 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 and manipulations of the subject or the subject's environment that are performed for research proposals. 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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associate with the information) in order for obtaining the information to constitute research involving human subjects.*

**Research: A Shared Responsibility**

The dignity and welfare of individuals who participate in research is a central concern of everyone involved with the protections of human subjects. Our primary goal is to develop a fair and explicit process in which subjects voluntarily decide to participate in a study based on an intelligent and knowledgeable assessment of the risk and benefits of the research.

The NNMC, investigators and their research staff, and the IRB, share the collective responsibility for the ethical conduct of research. This collaboration must exist in a culture of trust, complete openness, and honesty by upholding the highest ethical principles in the conduct of research. By upholding the highest standards, we build public support for the pursuit of greater knowledge in a safe research environment.

The review of research performed by staff, faculty, students, or employees of NNMC is conducted by the IRB. The IRB is comprised of faculty representatives from various academic disciplines at NNMC, including clinicians, researchers, non-scientific members, and some professionals who are not affiliated with NNMC. The IRB operates within the federal guidelines with respect to the review and approval of research protocols involving human subjects.

The IRB is charged with a twofold mission: 1) to determine and certify that all projects reviewed by the Board conform to the regulations and policies set forth by DoD and the DHHS regarding the health, welfare, safety, rights, and privileges of human subjects; and 2) assist investigators in conducting ethical research which complies with the DoD and DHHS regulations in a way that permits accomplishment of the research activity.

The mission is accomplished through an educational process of IRB review of protocols, negotiation between investigators and the IRB for approval of research, and IRB/CID outreach to the research community. The process serves to ensure the safe and ethical conduct of research that ultimately will protect the rights and welfare of human subjects.

Ethics and ethical review are a potentially dynamic and humanizing element in the search for knowledge. In preparing a protocol, the investigator is creating an ethical strategy that should reflect the norms and standards of the scientific community and the society served by the research. The process of creating a written protocol should enable the researcher to become a reviewer of his or her own research before submitting a project to the IRB.

## GUIDELINES FOR DEVELOPING A RESEARCH PROPOSAL

1. **Introduction and Purpose**. The purpose of this manual is to aid the investigator in the preparation, processing and conduction of human research studies. It includes policies implemented by Federal and Naval regulations to ensure protection of participants in human research studies. As a service to investigators, the CID Office keeps all forms on disks in Microsoft Word 6.0 format and on the NNMC website. We encourage investigators to meet with the CID staff to review and discuss protocol preparation and processing before final submission:

a. Role of the Clinical Investigation Department (CID). The CID acts as the focal point, advisor and coordinator of the Clinical Investigation Program. Clinical research is essential to achieving continuous improvement in the quality of patient care and in support of Graduate and Continuing Medical Education.

(1) The CID's mission is to:

(a) Encourage clinical investigation and maintain an atmosphere of inquiry consistent with the dynamic nature of the health sciences.

(b) Provide the Medical staff with experience in conducting research, which contributes to their professional career growth and academic excellence while supporting the Medical staff's mission.

(c) Administrative support for the NNMC Institutional Review Board.

(2) The CID staff is available to work with the investigator in the following ways:

(a) "Walk" the investigator through the beginning of a research idea.

(b) Provide administrative, technical and policy guidance that may influence the investigator's proposal.

(c) Identify and resolve potential problems associated with the investigator's research including fiscal and legal implications.

(d) Assist the investigator with the actual proposal submission.

(e) Act as the advocate/liaison for the Institutional Review Board, Naval School of Health Sciences, and Food and Drug Administration (FDA) as appropriate.

(f) Track the investigators proposal through the review process and keep the investigator informed of its progress. Notify the investigator when their study is approved and when they may begin.

(g) Assist the investigator with ordering and obtaining supplies, equipment and other support for their study. Keep the investigator informed of their expenditures.

(h) Handle all requests for changes in the investigator’s proposal (i.e., consent form, investigator changes, increases in study duration, increases in subject enrollment, or minor revisions to the study itself. Inform the investigator of the approval of each revision so that the investigator may implement the change.

(i) Assist the investigator's research in preparing Annual Reports, FDA reports, or Completion/Termination Reports as needed.

(j) Endorse and submit the investigator’s requests for travel funds from the Naval School of Health Sciences to support presentation of the investigator’s research at conferences and meetings.

b. Who May Be A Principal Investigator (PI). The PI may be any federal employee (uniformed or civilian), covered under the Intergovernmental Personnel Act (IPA), or consultants consistent with the requirements established by 5 USC 3109. If the research involves patient care, the PI must be approved to provide patient care at the performing site. The PI is the individual who is primarily responsible for the documentation and conduct of a research project. If the PI is not billeted at NNMC, someone who is billeted at NNMC should be designated as the point of contact for the research project and be responsible for communicating with the PI for purposes of completing administrative requirements (e.g. continuing review, FDA reports, etc.) in a timely manner. Individuals must possess the required education, knowledge, skills, experience and expertise to serve in that position. The IRB ultimately has the responsibility to assess and verify the PI’s qualifications.

c. Principal Investigator (PI) Responsibilities. The Principal investigator is the individual who is primarily responsible for the actual execution of the clinical investigation. He/she is responsible for ensuring that all associate investigators are educated in all phases of research, including the recruitment of subjects, obtaining informed consent, providing necessary reports, and maintaining study documents.

Additional PI responsibilities:

(1) Must be familiar with all applicable regulations governing research and the NNMC Federal Wide Assurance (NNMC website)

(2) Comply with the Standards of Conduct (http://www.defenselink.mil/dodgc/defense_ethics/ethics_regulation/index.html).

(3) Complete the human subject education training (Contact the Clinical Investigation Department for the current websites), provide the education completion certificates to the Clinical Investigation Department. (The research project will not receive Commander, NNMC approval until the certificates are submitted)

(4) Insure that all procedures in approved protocols are performed and/or supervised by the listed investigator, technicians, residents, fellows or nurses.

(5) Will only enroll a subject into a study after the appropriate authority has approved the study and, when appropriate, the subject's primary care physician has granted approval for him/her to enter a study.

(6) Responsible for assuring that the prospective volunteer is not participating as a subject in other research that will significantly increase the research risks.

(7) Responsible for assuring the quality of each subject's consent is in accordance with current federal regulations.

(8) Appoint a medical monitor if the research project involves greater than minimal risk to the research subjects.

(9) Will not accept any outside personal remuneration for designing or conducting a study.

(10) Will obtain the proper NNMC or other appropriate clearance for all publication and abstracts.

(11) Must submit to the CID:

(a) Any source of outside funding by completing the Resource Requirements Form.

(b) An Annual Report delineating the study's progress and/or results during the previous fiscal year.

(c) A final report within 30 days following the successful completion or termination (abandonment) of a study.

(d) Reports of any adverse effects occurring in subjects during study participation.

(e) Reports of any significant new findings found during the course of the study that might affect the subject's willingness to continue their participation in the research project.

(12) Cooperate fully with the IRB during the continuing review audit, which is usually done prior to the anniversary month of the original IRB review and approval date.

(13) Maintain Privacy and Confidentiality of all records:

(14) Notify CID/IRB in writing if an investigator or other personnel have changed.

(15) Provide the CID/IRB with the appropriate information on the research protocol including initial information, notification of modifications, termination.

(16) Will maintain a study file that must be kept indefinitely following the completion or termination of the study. It is required that all research records (including a copy of the entire protocol, consent form, and amendments) be maintained in the offices of the investigator. These documents, the names and access information for all subjects, research data and the subject's research record (obtained through written consent) constitute the permanent record of research done on each subject. If the investigator leaves NNMC, the records must be turned in to CID, and the CID/IRB should be notified of the transfer prior to the investigator departure. The IRB, the CID, the BUMED, Office of Research Integrity & Ethics (ORIE), the FDA and/or other regulatory agencies responsible for the oversight of research may inspect this file at any time. Study files should be provided to CID upon the completion of the research.

d. CIP Calendar. Each fall the CID establishes the proposal review schedule for the year. (NNMC website). This schedule includes the submission deadline for new proposals and the IRB meeting dates.

This helps the investigator to plan their research proposal's timetable for submission.

e. Submission Procedure. Submit one (1) original and one (1) copy of the complete research proposal directly to the CID. Be sure that the proposal is complete, in the order of the checklist, all study pages are numbered, current version date is provided, and all signatures are obtained.

**2. Instructions and Guidelines for New Research Proposals.**

a. Section I – The Research Proposal. The investigators research proposal consists of two sections. Section I contains the research proposal itself while Section II contains the supporting documents. Each element of Sections I and II is explained in this guidebook. The forms to use when developing and submitting the proposal are included and follow the written explanation.

(1) Investigator checklist. This checklist is designed to assist you in assuring that all the elements of the Research Project and Bibliography are present, clear, and concise. Initial or list as not applicable (N/A) each item on this list based on the specific nature of the study. Both you and the CID staff will use this list to ensure your research proposal is complete before forwarding to the appropriate authority for review and approval.

(2) Proposal Cover Page. Fill in the blanks with the appropriate information and obtain the needed signatures.

(3) Table of Contents. Provide a table of contents that organizes your entire research proposal package, Section I and Section II. Use the checklist to assist you.

(4) Research Proposal Outline. A well-written research proposal should clearly answer these questions:

* What do you intend to do?
* Why is the work important to Navy Medicine?
* What has already been done?
* How are you going to do the work?

**Use the sample Research Proposal Outline provided.**

(a) Abstract. On a separate sheet of paper, provide a brief, one paragraph, and summation of the essential elements of the research proposal. Include the background for the study, the procedures to be used, and the end results expected to be achieved from the study.

(b) Specific Aims (Objectives). State concisely and realistically what the research is intended to accomplish or what hypothesis is to be tested. Be very clear so those individuals not in your specialty can follow how the background and significance lead logically to the questions being asked in the objectives.

(c) Background and Significance. Give a brief review of previously published work related to the proposed investigation. Discuss how the investigator's proposed project relates to the previous work done on this subject citing literature specific to the study. Cite supporting references.

(d) Preliminary Studies. As appropriate and applicable, summarize your accomplishments, and those of any associate investigators in this area of study to establish the investigators experience and competence to pursue the proposed project. Pertinent preliminary studies may be included, but appropriate publications and manuscripts should be included as an appendix. Include a list of supporting literature as indicated later in the proposal.

(e) Bibliography. References must be cited in context, reflect a thorough knowledge of current literature in the area of study, and use a standard format for citation. If a relevant bibliography is absent for the research topic, documentation of appropriate literature database searches should be provided.

(f) Experimental Design – Methods, Materials, and Statistical Design. It is the responsibility of the investigator to demonstrate adequate knowledge of the previously published related work and a CLEAR understanding of the work proposed in the study. This information should be easily understood WITHOUT ANY ADDITIONAL VERBAL EXPLANATION by the investigator. The proposal should stand by itself.

1. Discuss in detail the experimental design and the procedures to be used to accomplish the specific aims of the project. Include definition of subject material i.e., adolescent males, guinea pigs, etc.), type and number, experimental groups, treatment for each group, instrumentation, invasive/non-invasive methods, description of experimental controls and use of placebos. Explain the randomization procedures to be used and at what point randomization occurs. Keep in mind that homogeneity of the sample increases the validity of the data. Sample size should be small enough to permit completion of the project yet large enough to be able to detect differences. Justify sample size (e.g., power analysis). Where feasible and desirable, state the exact technique for assuring blinding of the subject and observer.

2. Describe any new methodology and its advantage over existing methodologies. Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims. Point out any procedures, situations or materials that may be hazardous to personnel and the precautions to be exercised (e.g., use of investigational agents, radioactive materials, or biohazardous substance).

3. State the rational for a human versus an animal model, if appropriate.

4. Specify statistical methodology (design and analysis). State the method used to analyze the data including the variables to be measured and how you plan to display the data in final form. Incorporate a strategy of data recorded, collections, and analysis including anticipated results and statistical confidence limits. Include how the data will be analyzed and interpreted (e.g., establish a database with collected information; statistical analyses to be applied to the collected data). If you require assistance with this please contact the CID office.

5. Provide an example of all data collection forms, tests, surveys, questionnaires, etc. Make sure there are no subject identifiers, code the forms, such as, subj. #1, #2, etc.

(g) Research Involving Human Subjects. Describe the characteristics of the subject populations such as their anticipated number, age, sex, ethnic background, and health status. Define study populations with criteria for inclusion and selection as well as exclusion of subjects. Set the inclusion and exclusion criteria in separate paragraphs for easy noting by reviewers. The selection of subjects should be equitable and free of coercion. The IRB will closely examine research involving vulnerable subject populations, such as military subjects, children, subjects with cognitive disorders, or economically or educationally disadvantaged subjects. The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design appropriate to the scientific objectives of the study. The research plan should describe the composition of the proposed study population in terms of sex/gender and racial/ethnic group, and provide a rationale for selection of such subjects. The investigator should indicate in their submission how they would avoid the appearance of coercion in the recruitment of subjects. Provide a detailed explanation of any extra precautions taken to safeguard the rights and welfare of subject populations. Specify how confidentiality, the subject’s care, and the corresponding data collected from them will be handled if subjects fail to respond to treatment, are terminated from the study or decide to withdraw from the study.

1. Identify what types of research material will be obtained from individually identifiable living human subjects in the form of specimens, records or data. Indicate whether the material or data will be obtained specifically for research purposes or whether existing specimens, records or data will be used. If existing specimens or data will be used provide the time frame, (i.e. July 1999 to Dec. 1999)

2. Explain how the subjects will be identified. Describe the consent procedures to be followed, including the circumstances under which consent will be sought, who will seek it, the information to be provided to prospective subjects and the methods documenting

consent. Clearly describe how initial contact is made and who will make it.

3. Describe any potential risk – physical, psychological, social or others and assess their likelihood and seriousness. Describe alternative treatments and procedures that might be advantageous to the subjects.

4. Describe the procedures for protecting against or minimizing any potential risks, including risks to confidentiality, and assess their likely effectiveness. Discuss the contingency plan for ensuring necessary medical or professional intervention if needed in the event of adverse effects to the subjects. Also, describe who will have access to the records and the provisions for monitoring the data collected to ensure the subjects' safety and confidentiality.

5. Use a master subject list to identify your subjects and assign each a study number. There should be only one master file kept by the principal investigator in a secure place separate from the data. All data collection forms and computerized databases with information should reflect only the subject's study number so that the data and the subject cannot be 'linked'. The master list should usually be destroyed at the conclusion of the study unless there is significant reason, (e.g., investigational drug use) to maintain it.

6. Discuss why the risks to the subjects are reasonable in relation to the anticipated benefits to the subjects and in relation to the importance of the knowledge that may be reasonably expected to result.

7. If a subject is a beneficiary and not active duty they may receive payment for their participation in the research. An active duty member may receive up to $50.00 per blood draw only for a total amount of $250.00.

8 For research involving military personnel, unit officers and noncommissioned officers (NCOs) shall not influence the decisions of their subordinates to participate or not to participate as research subjects. Unit officers and senior NCOs in the chain of command shall not be present as the time of research subject solicitation and consent during any research recruitment sessions in which members of units under their command are afforded the opportunity to participate as research subjects. When applicable, officers and NCOs so excluded shall be afforded the opportunity to participate as research subjects in a separate recruitment session. During recruitment briefings to a unit where a percentage of the unit is being recruited to participate as a group, an ombudsman not connected in any way with the proposed research or the unit shall be present to monitor that the voluntary nature of individuals participants is adequately stressed and that the information provided about the research is adequate and accurate.

(h) Medical Monitor: Medical monitors shall be an approved health care provider. IRBs will ensure that the role(s) of the monitor during subject selection, enrollment, participation, and/or follow-up have been specified in writing.

The Medical Monitor:

a. Is to be assigned to studies involving greater than minimal risk.

b. Must be credentialed and privileged at the National Naval Medical Center or satellite and have a projected rotation date of more than one year after assignment as a Medical Monitor.

c. Shall be independent of the investigative team and shall not be from the same primary department that is conducting the research.

d. Shall possess sufficient educational and professional experience to serve as the subject/patient advocate. Shall not be from the same primary department conducting the research.

e. Will ensure that the enrollment of subjects is in compliance with the protocol's inclusion and exclusion criteria. The medical monitor may be assigned to assess one or more of the following phases of a research project: subject recruitment, subject enrollment, data collection, of data storage and analysis.

f. Shall provide a Letter of Intent stating they are willing to assume the responsibility of the medical monitor.

g. Shall provide a current curriculum vita.

h. Review all adverse events and principal investigator's recommendations (e.g. no change in the consent form) prior to submission to NNMC's IRB.

i. Review amendments and comment on whether the amendment increases the risk level to subjects and/or increases the risk/benefit ratio.

j. At the discretion of the IRB, the medical monitor may be assigned to discuss research progress with the principal investigator, interview subjects, consult on individual cases, or evaluate adverse event reports.

k. Shall promptly report discrepancies or problems to the IRB.

l. Shall have the authority to stop a research study in progress, remove individual subjects from a study, and take whatever steps are necessary to protect the safety and well being of research subjects until the IRB can assess the medical monitor's report.

m. The designed medical monitor will ensure that the replacement medical monitor will be briefed regarding pertinent situations in the study to date. Formal transfer of responsibilities will be acknowledged in the form of a signed memorandum that will be filed in the research protocol.

Provide a letter of intent from the medical monitor and a Curriculum Vita for the appointed individual when submitting your research proposal, if greater than minimal risk.

(i) Investigational Agents. The requirement for an Investigational New Drug (IND) for any drug, including those which are

FDA approved but might be used in a research project for a non-FDA approved indication, route, dosage, etc. is determined jointly by 21 CFR, and the risks to the subject. If the investigator plans to use any drugs in this manner, contact CID so that they may assist this process. Investigational agents (drugs, devices and/or biologics) to be used in the study must be adequately justified, stating why present methods are inadequate. For each drug attach a copy of the Investigational Drug Clinical Information Brochure, and for devices include a copy of the manufacturer's information booklet. Identify the source, sponsor and method for obtaining the agents (e.g., the involvement of the local pharmacist in the project). The CID will provide the appropriate pre-typed Food and Drug Administration (FDA) Forms 1571 and/or 1572.

Investigational devices are regulated under separate Investigation Device Exemption (IDE) guidelines. Please contact the CID staff to discuss the requirements and procedures. There is a separate procedure for the use of investigational drugs or devices in an Emergency One-Time Use or in the Treatment Use situation. Contact the CID for more specific information and guidance. The CID will forward the proposal to the Food and Drug Administration after the Institutional Review Board's review and approval has been received.

1. FDA Form 1571, Investigational New Drug Application (IND). If the National Naval Medical Center, Bethesda, Maryland wishes to sponsor an investigation agent, biologic product or device not yet approved by the FDA, and not sponsored by another organization for clinical testing, a FDA Form 1571 must by completed. The Commander, NNMC, must sign the original FDA Form 1571. (CID will complete.)

2. FDA Form 1572, Statement of Investigator. A Phase I, II, or III trial is an initial investigational trial conducted on a limited number of patients for treatment or prevention of a specific disease to determine safety and efficacy of the treatment. To ensure that each investigator is qualified for the study and the facilities are adequate, the sponsor must obtain a FDA Form 1572 from the Principal Investigator (also listing associate investigators), which is then submitted with other material to the FDA as a part of the total information for which the sponsor is accountable.

(j) Research In Retrovirology. All clinical research involving studies with subjects identified as positive HIV-1, HIV-2, or HTLV-1 will be forwarded by the CID staff to the BUMED HIV Program Division (BUMED – 37) for screening prior to IRB review. Describe in detail the regimen of therapeutic agents to be used and how data will be collected in natural history studies. Outline in detail the parameters to be evaluated, time sequence of proposed clinical trials, long-term follow-up cases and storage of the data.

(k) Research Involving Animals. CID will accept the Animal Use Justification Form from other institutions with the following information being provided:

1. Justification for the choice of the species, selected for the experimental design for the research project.

2. Identify the species, strains, ages, sex, rate of use and total number of animals to be used, and the source of the animals.

3. Identify the veterinary personnel participation in the study to care for the animals involved in the research project.

4. Describe the procedures to avoid unnecessary discomfort, pain or injury to the animals, such as surgical anesthesia, post-trauma analgesia, tranquilizing drugs, and comfortable restraining measures.

5. Describe the euthanasia method to be used and reason for its selection.

6. Provide the Animal Use Committee review and approval letter from the other institution.

(l) References. List references as required reviewing the background information and to support and justify your proposal. The references should be cited within the body of the text and listed in a bibliography at the end. There is NO SPECIFIC FORMAT required for listing references.

(5) Categories Of Research That May Be Reviewed through an Expedited Review Procedure[1]

If you think your proposal meets the criteria for expedited or exempted review, please review the following criteria and notify the CID office when submitting your proposal.

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 subject 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

[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. 110.

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) and 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[2], 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 unsimulated 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 that routine proghylactic 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 non-invasive 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

[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).

generally eligible for expedited review, including studies of cleared medical devices for new indication.)
Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input or 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) eletrocardiography, electroencephalography, 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 material (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 had determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

(6) Exempted Protocols-This determination must be made by the Chairperson of the IRB

Certain categories of research proposals involving human subjects may be **exempt** from the regular review procedures. These research proposals will also receive the expedited review procedure at NNMC. (§46.101b of 45 CFR Part 46).

1. Research that is conducted or supported 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 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.

2b. 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 categories 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 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 reasonable 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. Note: A HIPAA waiver may be required, contact the Clinical Investigation Department for assistance.

Certain surveys require coordination and review by the Deputy Chief of Naval Operations (Manpower, Personnel and Training (OP-01). Refer to OPNAVINST 5300.8A. This review can be accomplished concurrently with the research process.

The procedures for **expedited** review shall not apply to protocols submitted within the following categories:

1. Projects using subjects, which necessitate the use of third party consent.
2. Projects requiring Secretary of the Navy or BUMED approval.
3. Projects involving severe and unusual intrusion, either physical or psychological on the person of the human subject.
4. Projects involving potential political or public embarrassment to the Department of the Navy.
5. All classified projects.
6. Projects requiring funding in the amount of $5000.00 and over from CID.

(7) Resources and Funding. Chief, BUMED approves the funding to support the Navy research offices at the local Navy teaching hospitals following review of annual budget requests from the comptroller of each Navy teaching hospital. The Navy CIP is funded from Health Care Operations money (e.g., O&M, N funds). Once funds are allocated to the hospital, it is the responsibility of the CO and Comptroller to support the clinical investigation research program. The Head, CID, determines the amount of funding actually awarded to each research study. There are other sources of non-Navy support for research such as:

(a) Grants. A grant is an award of funds, services, or tangible or intangible property from a non-profit organization in support of the CID that is pursuant to a written agreement.

1. Grant applications for non-federal research funds (e.g., corporate entities organized for profit, such as pharmaceutical companies) cannot generally be accepted for product evaluation, and extra care must be used to avoid any appearance of conflict of interest.

2. Grant applications for federal and non-federal (non-profit organizations) research funds must be endorsed by the local Commanding Officer.

3. The grantor must be notified in writing that the grant will be made to the government on behalf of the treatment facility, and is not for personal use of an individual. The original grant application, together with the completed protocol formats requested by CID, would be reviewed by the local Staff Judge Advocate and Comptroller, and forwarded with the local CO's endorsement to the granting agency.

(b) Gifts. A gift is any donation of funds, services or tangible or intangible property from a non-DoD, profit or non-profit organization, for which there is no compensation or promise of compensation on behalf of the donor.

1. Navy Medical Department personnel will **not** initiate requests for gifts.

2. Gifts received in support of the CIP must be approved by the chain of Command.

3. Investigational agents (e.g., drugs, devices or biologics) may be accepted by the Commander for research projects, when the agent is not available for sale, has no market value, and is in direct support of an approved research project.

(c) Henry M. Jackson Foundation for the Advancement of Military Medicine (HMJFAMM). The Jackson Foundation is a non-profit scientific and educational organization specifically authorized by Congress, which can provide a mechanism to apply for and receive extramural grants in support of clinical research projects. Usually these grants are for multi-year studies, from for-profit companies and would be administered and managed by the Foundation and not by the comptroller of the teaching hospital. In effect, all civilian personnel matters, travel requirements and procurement procedures for equipment and supplies would be done by the Foundation.

1. Eligibility for the Foundation services requires either a Uniformed Services University of the Health Sciences (USUHS) adjunct academic appointment or a Foundation Guest Scientist Appointment which confers on active duty health care professionals the equivalent status of an Assistant Professor or above at the University. A Guest Scientist may be a staff member of a teaching hospital who is at least one year out of a residency program and possesses the academic background and capabilities to be considered qualified for a faculty position at the University, and is credentialed in a treatment facility.

2. Investigational agents receive special attention by the Foundation, who in turn establishes special agreements between the CO of the teaching hospital, the principal investigator, the Foundation and the for-profit company. A similar understanding is established with the grant donor concerning a non-restrictive publication policy. Courtesy copies are provided to the company 30-60 days prior to publication for review and not for clearance approval.

3. The protocol review for grants via the Foundation includes the following:

| **ADJUNCT FACULTY MEMBER** | **GUEST SCIENTIST** |
|---|---|
| (1) CO, Teaching Hospital | (1) CO, Teaching Hospital |
| (2) CO, NSHS | (2) CO, NSHS |
| (3) USUHS Department Chairman | (3) USUHS-Research Administration & HMJFAMM |
| (4) USUHS-Research Administration & HMJAMM | (4) University Extramural Protocol Review Committee |
| (5) USUHS-Assurance Review | (5) USUHS-Assurance Review |
| (6) Funding Agency | (6) Funding Agency |

A MOU has been established between BUMED and HMJFAMM to coordinate efforts in utilizing services available from the Foundation.

(d) Work For Private Parties. For information concerning policies, responsibilities, charges and fees consult with the CID staff. Carefully consider all options before negotiating with a commercial company (i.e., drug company, for supplies or financial support. The company might ask for access and/or ownership of the consistent with DOD or DON policies. Consider using CID funds for the drug and placebo.

1. “Private Parties” is a term that collectively covers many categories of individuals, corporations or companies, and certain state and local municipality entities, which receive, work, services, and materials from Department of the Navy activities. A general feature of Department of the Navy transactions with private parties is that the recipient must provide funds in advance of the services or materials to be received. Additionally, private parties are assessed full costs for all services provided to them.

2. A condition precedent to providing services or materials to private parties is that the Department of the Navy will not be placed in the position of providing competition with commercial organizations in the private economy if these are available to provide

the services or materials requested. Clinical investigation conducted in cooperation with a for-profit institution must be based on established user charges for fair market value.

(e) Memorandum of Understanding (MOU)/Cooperative Research and Development Agreement (CRADA). A MOU/CRDA is required if collaborative efforts involve the transfer of funds and/or services between other teaching hospitals and:

- Foreign authorities or institutions.
- U.S. state/local authorities or civilian institutions.
- Other Navy or Marine Corps activities, excluding agreements within BUMED commands.

The local JAGC and comptroller must review and approve the MOU and CRADA for those protocols over which the Commander possesses approval authority.

(f) Interservice Support Agreement (ISA). The basic objective of the ISA is to allow transfer of materials and services between and within government agencies to achieve greater CIP support (e.g., a CIP between two DOD agencies, or a DOD agency and a non-DOD federal agency).

(g) If you are collaborating with a Principal Investigator from another institution, you must submit documentation of the proposals IRB review and approval (scientific, human use and/or funding) from the collaborating institution, and a Letter of Intent from outside sources who have indicated a willingness to support the research efforts. This letter should outline exactly what they will be providing to the research.

**Instruction and Guidelines for New Research Proposals**

b. Section II – Supporting Documentation. The page numbers on the Table of Contents for each form correspond to the paragraph numbers listed below.

(1) Verification Worksheet. Complete only questions 1 through 5. You and your Service Line Leader/Department Head sign in the spaces provided. The CID will complete question #6 and obtain the other necessary information and signatures.

(2) Resource Requirements. Aside from the research proposal itself, this information is critical to document the support you require to conduct your research. Determine all the various types of support, monetary and non-monetary, you will need. All the resources you need should be consolidated on this form.
Answer questions 1-8 as directed below:

Questions 1-4 are self-explanatory.

Question 5. Budget for your study using the following guidelines:

List only the total cost for each expense element/category and for which year of the study the funding is needed. List detailed cost on a separate sheet by expense element.

Mark any critical items needed at the onset of the study with an asterisk (*).

All equipment supporting research is centrally owned and managed by the CID. Although the equipment may be used in another Department's spaces, it must be returned to the CID upon completion of the research project.

EXPENSE ELEMENTS

Q5a. U = Personnel. List all personnel uniquely involved in this study, including their present position, and proposed hours/week. Include the annual salary. Calculate salary and benefits applicable ONLY to those civilian personnel UNIQUE to the study.

Q5b. M = Rentals and Utilities. List the rented or leased item (s), the cost/year, what is covered in the rental, does rental include maintenance? If not, is it needed?

Q5c. P = Preventive Maintenance of Equipment. List each piece of equipment including name, model and year of purchase, and the maintenance cost/year. List what specifically is needed in the maintenance contract.

Q5d. Q = Purchased Services Contracts. This includes fees for services performed for your research such as:

1) Lab tests or other diagnostic tests sent to a reference lab. This is the most frequently used type of purchased services for a clinical study.

2) Consultants' fees – Give the name and institutional affiliation for any consultants who have agreed to serve in this capacity. Include consulting physicians in connection with patient care. Briefly describe the number of days of consultation; the expected rates of compensation or other costs.

3) Housing and care for animals.

Letters of Intent. If you plan to use a purchased service contact, you must provide a "service and price quote" from the company. It should indicate what service will be done at what cost (i.e., Reference Lab x will provide lab assay "z" at $7.50/assay".

Q5e. T = Supplies. Using an attached sheet, provide a detailed list of all consumable supplies (i.e., including item name, ordering number, quantity required, cost per item and total cost needed. Indicate whether supplies are needed "up front" by marking with (*). If supplies are needed for on going years, spread the divide cost over the years taking into consideration subject enrollment rate, or usage rate, or shelf life of the item. Provide the company name and address from which supplies will be purchased.

Q5f. W = Non-Investment Equipment. Non-investment equipment is a non-expendable item with a per unit acquisition cost of less than $14,999.00. List name of equipment and cost. Submitting the appropriate paperwork for your equipment now will allow the CID to expeditiously order your items when your study is approved. This will decrease the time delays between the ordering and receipt of equipment necessary to complete your study.

Q5g. W = Investment Equipment. This type of equipment has an acquisition cost greater than $15,000 per unit. Does equipment have a Navy stock number or being purchased from an outside source? All equipment justifications must be submitted in accordance with Naval regulations and accompany this submission.

Q5h. Y = Printing and Reproduction. Include purchasing or printing of forms needed to conduct your project. Include costs of publication and reprints after study completion.

Q5i. Other Expenses. Include any other expenses necessary to conduct your study, (i.e., TAD to collect data at another facility. Be sure to include a justification).

Travel. Office of Research Integrity & Ethics disburses travel funds in support of Clinical Investigation Program studies, which are either active or completed. Estimate the approximate amount

needed (include registration fees, travel and per diem) under the appropriate year. Contact to the CID to obtain the proper forms to request Clinical Investigation travel funds.

Question 6. Sources of Support. List the total amount of funds provided or if other institutions/agencies are providing support (i.e., personnel and/or supplies for this study).

Question 7. Nongovernment Support Statement. Answer question7a through 7e as completely as possible.

You must be specific and clear in delineating "who" is providing "what" so that the CID can easily draft the agreement or contract. It is a good idea to get an "informal" letter of intent from the collaboration agency delineating what exactly they will be providing to the research.

Question 8. Personnel Support: Fill in the information requested. The CID will calculate the total man-years of support.

(3) Departmental Impact Statement. When a research project utilizes NNMC resources, (e.g. laboratory, radiology, pharmacy, patients records, clinic or ward patients) an impact statement from the utilized resource may be required to ensure availability of the resource for research purposes. Fill in the proposal title and your name. If you do not require any support from other service lines, write in "Not applicable". Obtain your Service Line Leader's/Department Head signature.

(4) Investigator List and Standards of Conduct. Fill out completely for each investigator. If an investigator has privileges at NNMC along with his/her primary duty at another duty station, list "NNMC Privileges" after the primary duty station name.

(5) Curriculum Vitae. Provide a current curriculum vita for each investigator on your study. Be sure the current version date is in the upper right hand corner.

(6) Consent Form. Use the standard consent form format as this contains the minimum requirements for informed consent under HHS and FDA regulations. The Privacy Act statement is also required. Address the item in each paragraph clearly and concisely.

Third Party or Minor Consent. Modify the text of the consent form to indicate "my child", "my ward", etc. when third party or minor consent is anticipated. Use the modified signature block for the consent form as shown in the example. The Privacy Act Statement remains the same.

If a third party permission is given by the parent of a minor or a legal guardian, next-of-kin, or other legally authorized third party representative of any individual, the following conditions must be met:

a. The prospective participant in the research must be legally incapable of giving informed consent.

b. The measures used in the research must be intended to be beneficial to the participant.

c. Investigators must demonstrate that the individual providing permission is legally authorized to do so.

d. The permission is legally effective in the locale(s) where it is obtained and the research exposure of the participant takes place.

Assent. In designing procedures for seeking a child's assent to participate in research, investigators should aim to create assent processes that consider and respect the child and the family as a unit as well as individually. The process for requesting assent should

a. be developmentally appropriate given the ages and other characteristics of the children to be approached;

b. provide opportunities for children to express and discuss their willingness or unwillingness to participate;

c. clarify for parents and children (as appropriate) the degree of control that each will have over the participation decision; and

d. when appropriate, describe to children and parents the kinds of information about the child that will or will not be shared with the parents.

(7) Drug Literature. Include any information you may have on the manufacturing, indications, dose, side effects etc. for the drugs you will be using in your research. A package insert or the information from a current PDR is acceptable. This information is critical especially when using FDA approved drugs in a Non-FDA approved manner.

(8) Device Literature. Same as above.

(9) FDA Form 1571 Investigational New Drug Application (IND). If the National Naval Medical Center, Bethesda wishes to sponsor an investigational agent or biologic product not yet approved by the FDA, and not sponsored by another organization for clinical testing, a FDA Form 1571 must be completed. The original FDA Form 1571 must be signed by the Commander, NNMC. Upon review and approval of the proposal, CID will forward the FDA Form 1571 and a copy of the proposal to the FDA for their review, approval and assignment of an investigational new drug (IND) number. The CID will complete the required FDA 1571.

(10) FDA Form 1572 Statement of Investigator. A Phase I, II, or III trial is an initial investigational trial conducted on a

limited number of patients for treatment or prevention of a specific disease to determine safety and efficacy of the treatment. To ensure that each investigator is qualified to perform the study and the facilities are adequate, the sponsor must obtain a FDA Form 1572 from the principal investigator and submit it with other material to the FDA as a part of the total information for which the sponsor is accountable. The CID will provide this pre-typed form for your signature.

(11) Animal Use. Provide the outside institution's animal use form, the institution's review and approval letter along with Section II of the CID guideline forms. Be sure to use the guidelines attached to this form.

# Informed Consent Requirements

The purpose of this section is to assist the investigator by providing guidance on how to obtain valid informed consent from potential volunteer research subjects. The informed consent process is fundamental to ensuring the continuous and adequate disclosure of information and research related risks and benefits.

## THE PROCESS OF INFORMED CONSENT

Research subjects are rarely aware of research activities prior to an initial presentation by the principal investigator or a member of the principal investigator's study team. The initial phase of consent requesting participation in a research activity commonly begins with the first contact between the subject and the investigator. Many subjects make their decision regarding whether to participate in research during the initial contact. As a result, the greatest potential for misunderstanding exists in the initial consent process. Researchers are encouraged to provide sufficient time for a potential subject to reflect on the nature of participation during the important initial presentation of a research activity. When subjects are presented with numerous research and clinical options, the consent process should include a clear description of the possible ramifications resulting from each option presented. The presentation should not include specific "leading" information about whether to participate in any particular project.

By providing a potential subject with understandable information in an initial session regarding complex research issues, potential subjects will have an improved comprehension of the elements within the consent form and provide a more informed consent for participation in the research.

The second step in the consent process is the presentation of the consent form to subjects. The investigator should separate the research consent form from other clinical information or hospital admission forms. Subjects should not be asked to sign hospital consent documents for clinically indicated procedures at the same time as the presentation of the research consent form.

A member of the study team should ensure that the subject reads the consent form. After the subject reads the consent form, the member of the study team should ask the subject if he/she understands the information contained in the form. In situations where the ability of the subject to understand the form is in question, for example, the form includes complex scientific information or the subject is possibly educationally or mentally challenged, the member of the study team may wish to ask questions of the subject to ensure an understanding of the basic elements of the consent form.

All efforts should be made to offer potential subjects sufficient time to consider the information contained in the consent form. The subject should have time to decide if they are willing to participate in the research. The subject should be given an opportunity to take the consent form home and sign the form on a return visit or the subject may be left alone to consult enrollment with family or friends. If the individual decides to participate, he/she would sign the consent form, the principal investigator would co-sign the form, and a witness would sign the document. The subject would receive a copy of the document; a copy would go in the subjects' inpatient and/or outpatient medical file. The principal investigator would keep the original. The witness may not be part of the research project.

**The consent process does not end with the signing of a consent form.** Research is an on-going process, which involves the constant re-evaluation of current information and procedures. Therefore, investigators are ethically obligated to keep subjects apprised of all issues related to their participation in the study. For example, a sponsor may, during the course of a study, decide to supply a drug free-of-charge to subjects following their participation in the research. The new information should be presented to research subjects in a written form and the subjects should be asked to sign a copy of the form or to sign a revised consent form. Likewise, adverse events may occur during a research activity that would directly affect whether a prospective or enrolled subjects would wish to continue in a particular research activity. Subjects must also receive the new information as a part of the consent process. Information also may arise regarding the study, which should be shared with previously enrolled subjects after their completion of the study, or a specific treatment or procedure.
**Investigators should note that the IRB requires review and approval prior to an investigator providing subjects with new research information.**

## WRITING THE CONSENT FORM

The consent form is intended to serve as only one aspect of an on-going dialogue between the investigator and the subject. Subjects are autonomous and should voluntarily give their consent to participate in research. As a result of their voluntary participation, subjects reserve the right to withdraw their participation from the research without prejudice. Therefore, the consent form should serve as just one element in an equal exchange of information between the investigator and the subject and not a binding contract between two parties.

The design of the consent form should carefully reflect the process of informed consent, i.e., introduce the investigator to the subject; indicate why the subject has been asked to participate in the study; articulate the purpose of the study; clearly separate the research procedures from any standard treatment; inform the subject's of the risks and benefits of participation and ultimately document the subject's willingness to participate in the project. The consent form

must also contain the alternative procedures or courses of treatment that may be available. Oftentimes the consent form is too technical and includes scientific jargon that can render alternatives to participate incomprehensible and ultimately intimidating to a subject. Studies have found that most subjects read at a sixth grade level or lower. Therefore, consent forms should avoid or define technical jargon or terminology, adjust for educational background and age, and provide translations for subjects who are not facile in English.

Consent forms that contain medical language, social science terminology, and metric equivalents for quantities are routinely returned to investigators for modification. If the subject cannot understand the consent form they cannot give informed consent for their participation in the research. The IRB suggests that investigators have a colleague or staff person, not familiar with the field of research, review the consent form for content and readability prior to submitting the form for Committee review.

A typical problem for research requesting blood draws or biopsies is the use of metric measurements in the consent form. Most subjects do not understand metric measurements, i.e., how much blood in 10 cc; therefore, the Committee commonly requests the translation of metric measurements into teaspoons, tablespoons, etc. In a similar spirit, biopsies should be described or equated with a commonly recognized amount.

The CID can provide a glossary of medical terms to assist with the writing of the consent form, NNMC website.

HIPAA

The Privacy Rule introduces new standards for protecting the privacy of individuals' identifiable health information held by a covered entity or its business associates. For covered entities, the Privacy Rule sets minimum standards for how PHI may be used and disclosed and how individuals can have control of their health information, including for research purposes. For independent researchers who are not subject to the Privacy Rule, the Rule may affect access to such information.

The Privacy Rule was not intended to impede research. Rather, it provides ways to assess vital information needed for research in a manner that protects the privacy of the research subject. The Privacy Rule describes methods to de-identify health information such that it is no longer PHI or governed by the Rule. If de-identified the research in an Authorization document describing the research uses and disclosures of PHI and the rights of the research subject. When obtaining the Authorization form is not practicable, an IRB or Privacy Board could waive or alter the Authorization requirement. The Privacy Rule also provides alternatives to obtaining an Authorization or a waiver or an alteration of this requirement, such as limited data sets or with representations provided for certain research activities. The Privacy Rule also contains a provision that "grandfathers" research that is going before the compliance date to facilitate compliance with the Rule.

Many researchers are accustomed to complying with Federal and State regulations that protect participants from research risks: some of these regulations even require, as applicable, a researcher to describe privacy and confidentiality protections in an informed consent. While the Privacy Rule may add to these privacy protections, researchers are aware of the importance of protecting research subjects from foreseeable research risks, including risks to privacy. Understanding how and why the Privacy Rule protects the privacy of identifiable health information is an important step in understanding how covered entities implement the Rule's standards.

Because the Privacy Rule is new and introduces new standards for how PHI is handled by covered entities, researchers and their institutions may have questions about the Rule. Researchers are encouraged to contact the Clinical Investigation Department at 301-295-2275, or the Privacy Officer at 301-295-0991 for guidance.

**HIPAA Research Road map***

| | | |
|---|---|---|
| Are you intending to collect data on any of the 18 personal health identifiers?<br>1. Names<br>2. Street address, city, county, 5-digit zip code<br>3. Months and dates (years are OK) and ages >89 (unless all persons over 89 years are aggregated into a single category)<br>4. Telephone numbers<br>5. Fax numbers<br>6. E-mail addresses<br>7. Social security number<br>8. Medical record number<br>9. Health plan beneficiary number<br>10. Account number<br>11. Certificate/license number<br>12. Vehicle identification number (VIN) and/or license plate number<br>13. Device identifiers and serial numbers<br>14. URLs (Uniform Resource Locators)<br>15. Internet protocol address number<br>16. Biometric identifiers, such as finger and voice prints<br>17. Full face photographic images or any comparable images<br>18. Any other unique identifying number, characteristic, or code such as patient initials | No → | HIPAA does not apply. |
| Yes | | |
| Will the Protected Health Information (PHI) be completely de-identified, based on one of these criteria?<br>a. The data collection forms and database will be stripped of all 18 identifiers, and the Master Link irrevocably destroyed shortly after subject enrollment.<br>b. A statistician can verify that there is less than a "very small" risk that an individual's identity can be detected. | Yes → | No Authorization or Waiver is necessary. |
| No | | |
| Can you limit your collection of personal health identifiers to just dates, city/state/zip, and/or "other unique identifier" (#18 above)? (defined as a "limited data set" in HIPAA-speak) | Yes → | Provide a Data Use Agreement. No Authorization or Waiver is necessary. |
| No | | |
| Is obtaining patient Authorization "impracticable," as determine by the IRB? (protocol may qualify as "HIPAA minimum risk" – see DoD regulation 6025.LL-R, C7.9.2). | Yes → | Request Waiver in protocol, but disclosure must be tracked. |
| No | | |
| Is data collection "preparatory to research" in order to determine how many potential research subjects meet study recruitment criteria? | Yes → | No Authorization necessary. |
| No | | |
| Research subject will need to sign Authorization – the Authorization should be separate from the informed consent form. | | |

* Note: HIPAA is a complex law, and its research application is still subject to interpretation. This Roadmap is subject to revision as the interpretation of the law evolves. For more information, see DoD regulation 6025.LL-R March 10, 2003

## The Clinical Investigation Department Website

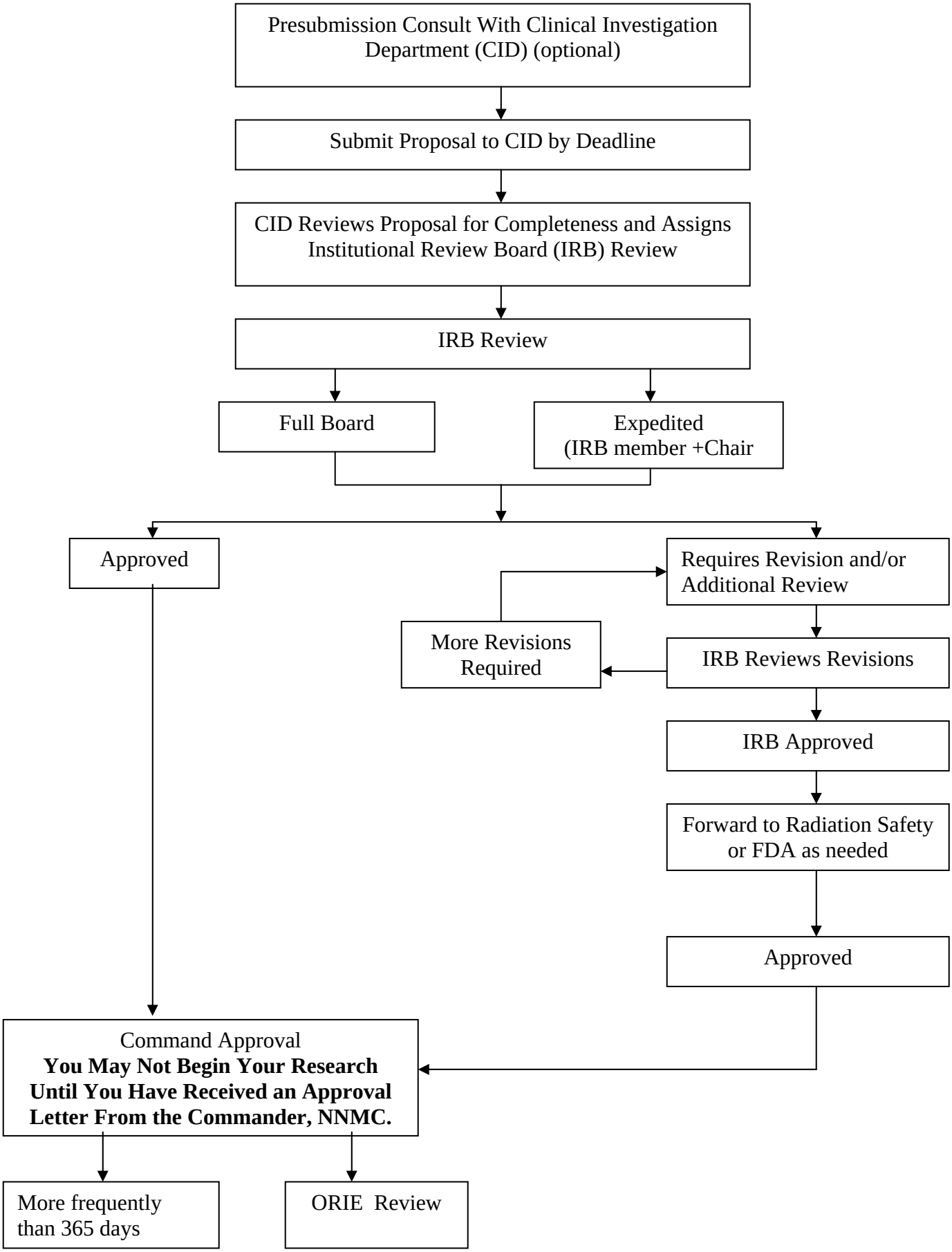
NNMC website:

To find the Clinical Investigation Department Web page you have to be able to access the secure NNMC Site. We are listed under the link websites.

The website contains

- Point of contact information
- Federal Rules and Regulations for research
- Information on Protection of Human Subjects Training
- The Research proposal submission forms
- The IRB meeting Calendar
- Other useful links.
- Glossary

www.stanford.edu
www.med.umich.edu
www.windor.igs.net
www.som.tulane.edu


Presubmission Consult With Clinical Investigation Department (CID) (optional)
Submit Proposal to CID by Deadline
CID Reviews Proposal for Completeness and Assigns Institutional Review Board (IRB) Review
IRB Review
Full Board
Expedited (IRB member +Chair
Approved
Requires Revision and/or Additional Review
More Revisions Required
IRB Reviews Revisions
IRB Approved
Forward to Radiation Safety or FDA as needed
Approved
Command Approval
You May Not Begin Your Research Until You Have Received an Approval Letter From the Commander, NNMC.
More frequently than 365 days
ORIE Review