This Standard Operating Procedures (SOP) document has been approved by the Head, Clinical Investigation Department (CID) at Naval Medical Center Portsmouth (NMCP) and endorsed by Research Subject Protection Division (RSPD) of CID at NMCP.

All human subjects research submitted for consideration by the NMCP Institutional Review Boards (IRBs) will be processed according to the policies and procedures detailed in this SOP.

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<td>Research Compliance Advisor</td>
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SCOPE AND PURPOSE

This Standard Operating Procedure (SOP) is a reference for IRB members and investigators. This SOP documents the policies and procedures for the Naval Medical Center-Portsmouth Institutional Review Board’s (IRB) review of human subjects research.

This SOP is written to comply with the applicable federal regulations including those promulgated by National Defense 32 CFR 219, U.S. Department of Health and Human Services (DHHS) 45 CFR 46, and the U.S. Food and Drug Administration (FDA) 21 CFR 50, 56, and 812.

The intent of the policy to review all human subject research is to foster high ethical standards in the conduct of research and to assure that uniform criteria are applied to protect the human subjects who take part in research.

INTRODUCTION

MISSION

The 1979 Belmont Report identifies three broad ethical principles under which human subjects research is conducted.

1. Respect for persons
2. Beneficence
3. Justice

The principle of “Respect for Persons” requires that each individual should be treated as autonomous, capable of making decisions about themselves and their personal goals. Potential research subjects should be given sufficient time and information upon which to base their decisions about participation.

The principle of “Beneficence” dictates that researchers should maximize the benefits of participating in research studies and minimize the possible risks.

The principle of “Justice” incorporates the question of who ought to receive the benefits of research and who ought to bear the burden of possible risks.

These three principles of the Belmont Report are implemented through the processes of informed consent, risk/benefit assessment, and fair subject selection and are the cornerstone of the IRB mission.

REGULATORY MANDATE FOR PROTECTING HUMAN SUBJECTS

THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (DHHS) REGULATIONS

The Department of Health and Human Services (DHHS) Regulations (45 CFR Part 46) presently include additional protections for pregnant women, human fetuses and neonates (Subpart B); prisoners (Subpart C); and children (Subpart D).
DHHS regulations at 45 CFR Part 46 Subpart A constitute the Federal Policy (Common Rule) for the protection of human subjects. This Common Rule applies to any human subject research supported by any of the seventeen Federal agencies, including DOD, which support human subject research.

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DEPARTMENT OF DEFENSE (DOD) REGULATIONS

Department of Defense (DOD) Regulations [32 CFR Part 219] are the same as that codified by DHHS as Subpart A of the DHHS regulations at 45 CFR Part 46, but does not include the additional DHHS Subparts. However, DOD and Navy policies, at DODI 3216.02 and SECNAV Instruction 3900.39D 6.a (6), respectively, require that research involving pregnant women, fetuses, neonates and children meet the additional protections of 45 CFR Part 46 Subparts B, C and D. The SECNAV Instruction 3900.39D also requires additional protections for mentally disabled individuals, economically or educationally disabled as well as other groups. (See also, Chapter 17 “Potentially Vulnerable Subject Groups”) The Surgeon General of the Navy through the Department of the Navy Human Research Protection Program (Code M00R) at the Bureau of Medicine and Surgery enforces DOD regulations for naval research activities.

DOD human subjects regulations apply to all human subjects research conducted by a DOD Component (i.e., intramural) and other research that is supported by a DOD Component (i.e., extramural) through a contract, grant, cooperative agreement or other arrangement (DODI 3216.02).
Note: Investigators receiving support from other Federal agencies, such as the National Institutes of Health (NIH), as well as other DOD components such as the Army and Air Force, must meet both those agencies’ and Navy requirements for the protection of human subjects.

**FOOD AND DRUG ADMINISTRATION (FDA) REGULATIONS**


In general, FDA human subjects regulations apply to clinical investigations and other research involving FDA-regulated products, including food and color additives, drugs, medical devices, biological products for human use, and electronic products, regardless of funding source.

Note: DODI 3216.02 deems the use of investigational new drugs, biological products or devices for purposes of Force Health Protection as non-research activities. Such activities are governed by DOD Directive 6200.2.

Prospective IRB review and approval are required for all clinical investigations and all other research involving FDA-regulated products for human research, even where an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) is not required.

**ASSURANCE OF COMPLIANCE**

As a matter of institutional policy, NMCP must meet the requirements of the DOD human subjects protection regulations for all research, without regard to funding source or other support. DOD requires that any Naval or Marine Corps activity conducting, supporting, or participating in a human research effort, regardless of sponsor or subject area, hold a current DOD Navy Assurance as granted by the Surgeon General of the Navy.

NMCP maintains DOD Navy Assurance N40003 for which the NMCP Commanding Officer serves as the Institutional Signatory Official. The NMCP IRB is the “IRB of record” for human subjects research conducted within Navy Medicine East.

**FEDERALWIDE ASSURANCE AND IRB REGISTRATION**

Because NMCP’s activities involve research supported by or in collaboration with other Federal agencies, NMCP must have an assurance accepted by those agencies. Accordingly, NMCP maintains a Federalwide Assurance of Protection for Human Subjects (FWA 00006001) approved by the DHHS Office for Human Research Protections (OHRP). The NMCP Commanding Officer is the Institutional authority for establishing and empowering the IRB and serves as the Institutional Human Subject Signatory Official (Institutional Official or IO) for the NMCP FWA.

It is also noted that NMCP IRBs must be registered with the Food and Drug Administration.
NMCP currently operates two Institutional Review Boards (IRB), under its FWA registered as IRB #1 - OHRP 00003882, and IRB #2 - OHRP 00003883.

DEFINITIONS

Research (as defined by DOD and FDA)

- “Research” as defined by 32 CFR 219 regulations is “a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge, or an equivalent definition”; and
- “Clinical investigation” means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(j) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

Human Subject (as defined by DOD and FDA)

- “Human subject” as defined by 32 CFR 219 regulations is “a living individual about whom a researcher conducting research obtains data through intervention or interaction with the individual, or identifiable private information, or an equivalent definition.”
- The FDA definition of “human subject” is an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient.
- The FDA definition includes an individual on whose specimen a device is used. For medical device studies involving in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.

Experimental Subject (as defined by DOD)

- An activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Examples of interventions or interactions include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject’s environment, the withholding of an intervention that would have been undertaken if not for the research purpose.

Private Information

- Federal regulations at 32 CFR 219.102(f) define private information as any information that an individual can reasonably expect will not be made public, and any information about behavior that an individual can reasonably expect will not be observed or recorded.

Identifiable

- Federal regulations at 32 CFR 219.102(f) define identifiable as the identity of the individual subject is or may readily be ascertained by the investigator or may be associated with the information.
Minimal Risk

- Federal regulations at 32 CFR 219.102(f) and 21 CFR 56.102(i) define minimal risk as the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Minimal Risk for Prisoners

- In the case of research involving prisoners, federal regulations at 45 CFR 46.303(d) define minimal risk as the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.
- Note: The involvement of prisoners of war, captured or detained persons as human subjects of research is prohibited by DODI 3216.02 and SECNAV instruction 3900.39d 6 a.(8).

Institutional Review Board (IRB)

- An IRB is an appropriately constituted group that has been formally designated to review and monitor research involving human subjects. In accordance with the DOD regulations, the Common rule, and FDA regulations, the IRB recommends protocol approval, requires modification to secure approval, or disapproves research. The IRB is also authorized to suspend or terminate research for continued non-compliance with the DOD regulations, the Common rule, FDA regulations, or its own findings or determinations.

Compliance Assist Visit

- A systematic independent review and evaluation (internal audit) of all study related activities and documents
- Not-for-Cause audit - randomly selected and scheduled by RCA with PI 15 days in advance allowing PI/research team to prepare; typically all studies will be reviewed within a 2 year time period
- Directed/For Cause audit – directed by CO, CID, IRB, RCA, or PI/AI based on reasonable cause issues, previous non-compliance, or safety issues; scheduled by RCA 5 days in advance

Informed Consent Process Observation

- The observation of the informed consent process conducted by the RCA at consent process observation visits. Consent process should include the required elements of consent referenced in the RSPD SOPs.

Consent Form Review

- The mandatory submission of signed subject consent forms, conducted concurrently with IRB Continuing Review. Signed consents are reviewed and audited to ensure regulatory compliance.
Preventative Action
- A process for detecting and preventing potential issues of noncompliance

Corrective Actions
- A process of addressing and resolving an existing non-compliance issue or violation

Source Document
- An original document or record from which to compile clinical data (such as an electronic medical record, clinical chart/note, lab/pathology report, or pharmacy dispensing record)

Regulatory Binder
- A binder provided by CID and highly recommended for all new research projects. Please contact the RCA to obtain a regulatory binder for your study documents. Binders will be reviewed for completeness at Compliance Assist Visits. No PHI will be stored in Regulatory Binders; subject signed consent forms, source documents, and data collection forms will be stored in a separate secure location; subject ID key must be stored separately and securely from consent forms

DETERMINATION THAT AN ACTIVITY IS RESEARCH

In determining if an activity is research the IRB will assess the following criteria:
- Is the activity a systematic investigation (including research development, testing and evaluation)?
- Is the activity designed to develop or contribute to generalizable knowledge?
- Does the activity involve human subjects?
  - Are data being obtained about one or more living individuals?
  - Are the data collected through an intervention (physical procedures by which data are gathered or manipulations of the subject or the subject’s environment that are performed for research purposes) or interaction (communication or interpersonal contact between investigator and subject) with the individual?
  - Is individually identifiable private information being obtained?
  - Does the data indicate that the identity of the subject is or may readily be ascertained by the investigator or associated with the information?
  - Does observation or recording take place, or is information collected which has been provided for specific purposes by an individual and which the individual can reasonably expect that it will not be made public (e.g., medical record being obtained)?

A decision tree used by the IRB in determining that an activity is research is located in Appendix A.

Activities generally not overseen by the IRB at the Command include:
- classroom research
- case reports (2 or less)
- surveillance activities
quality improvement or program evaluation projects unless they meet the definition of human subjects research

When the Command includes other activities outside the scope of activities covered by regulations or laws, the definition includes those activities (e.g., research on non-living individuals).

WHO IS ENGAGED IN RESEARCH

NMCP is considered engaged in research when, for the purposes of research project, its employees or agents obtain: (a) data about the subjects of the research through intervention or interaction with them; (b) identifiable private information about the subjects of the research; or (c) the informed consent of human subjects for the research.

Shared Responsibilities for Protecting Human Subjects

The ethical conduct of research is a responsibility shared by all involved in human research protection at NMCP. It requires cooperation, collaboration, and trust among NMCP administrators, investigators and their research staff, the subjects who enroll in research, and the IRB members and staff.

a. NMCP Institutional Responsibilities (32 CFR 219.103): As part of its commitment to responsible and ethical research efforts and in compliance with its written DOD Navy Assurance and Federalwide Assurance (FWA), NMCP has developed this Standard Operating Procedure for conducting human subject research, including how the IRB will review research, how investigators report unanticipated problems to the IRB and appropriate regulatory bodies, and other issues.

b. NMCP Commanding Officer Responsibilities: The NMCP Commanding Officer serves as the Institutional Signatory Official for NMCP’s FWA and DOD Navy Assurance. Under the terms of the DOD Navy Assurance, the Commanding Officer, NMCP is responsible for supervising and monitoring the conduct of human subject research conducted at NMCP, or by his/her employees or agents. Consequently, the NMCP Commanding Officer is responsible for ensuring the protection of human subjects as outlined in SECNAVINST 3900.39D, Section 8c.

This includes:

- Completing and documenting initial and continuing research ethics training and human subject protections training.
- Overseeing the development and implementation of NMCP policies governing the NMCP IRB, all NMCP human subject research and all NMCP investigators and research personnel.
- Maintaining open channels of communication among all parties involved in the NMCP human subject protection process.
- Ensuring that the NMCP IRB has sufficient meeting space and staff to support its substantial review and record keeping responsibilities.
- Overseeing the operation and administration of the NMCP IRB and determining that the IRB complies with all Federal, State, and local laws and regulations that govern research involving human subjects.
- Assuring that IRB members and investigators are appropriately knowledgeable to conduct research in accordance with ethical standards and all applicable regulations.
• Ensuring the independent review of research for scientific merit or scholarship prior to IRB review.
• Ensuring that DOD, DON, or other funds for research involving human subjects are not expended unless the requirements of the DOD Navy Assurance have been satisfied.
• Developing and implementing an educational plan for all persons involved in reviewing, approving, supporting, conducting, or managing research involving human subjects.
• Serving as the approval authority for human research protocols.
• Establishing and maintaining policies to ensure that the Commanding Officer, NMCP and IRB Chair are promptly notified regarding (i) any unanticipated problem involving risks to subjects or others; (ii) any serious or continuing non-compliance with IRB requirements by research investigators; or (iii) any for-cause suspension or termination of approval.
• Ensuring notification of Department of the Navy - Human Research Protection Program (DON HRPP), OHRP and FDA of such incidents in accordance with applicable Federal regulations. Such notice will be accomplished in coordination with the Head, RSPD and IRB Chair.
• Overseeing implementation of a research compliance monitoring process that provides monitoring reports, as appropriate, to the Institutional Signatory Official, IRB Chair and/or Vice Chair.
• For NMCP initiated research requiring an IND, serving as the IND holder and sponsor representative signing the FDA Form 1571.
• Negotiating appropriate written review agreements with participating institutions for collaborative research efforts.
• Forwarding the following to the Secretary of the Navy, via the chain of command for approval: (a) waivers of the requirement for informed consent under 10 USC 980; (b) exceptions from informed consent requirements for emergency research under 21 CFR 50.24 and in accordance with the requirements of 10 USC 980; and (c) requests for waiver of requirements of DON policy regarding human research protections.
• Forwarding to the Under Secretary of the Navy, via the chain of command, for approval: (a) research involving severe or unusual intrusions, either physical or psychological, on human subjects (e.g., consciousness-altering drugs, or mind controlling techniques); (b) research involving prisoners; (c) research with potentially or inherently controversial topics (such as those likely to attract significant media coverage or that might invite challenge by interest groups).

c. Directors’ and Department Heads’ Responsibilities: Directors and Department Heads are best positioned to oversee investigators under their supervision as well as determine whether resources such as space, personnel, etc., are appropriate to properly conduct the research. All submissions for IRB review must be routed through investigator’s chain of command.

d. Division Head, Office of Research Subjects Protection Division (RSPD) Responsibilities: The RSPD Head is delegated responsibility for managing the NMCP Human Research Protection Program, including the operations of the IRB. The RSPD Head:
• Ensures submission of properly executed institutional assurances in accordance with OHRP procedures and DOD regulations.
• Recommends appointment of IRB members to the Commanding Officer or delegated official.
• Develops and updates policies, procedures and forms related to the protection of human subjects.
• Communicates with other institutions to negotiate research review agreements.
• Develops, implements, and maintains compliance and training activities for the NMCP research program.
• Works closely with the IRB Chair, Vice Chair(s), members, staff and researchers to ensure compliance with laws and regulations to ensure the protection of human subjects in research.
• Serves as the primary resource concerning compliance issues.
• Coordinates communication with the Bureau of Medicine and Surgery (DON-HRPP) on human studies.
• Responds to DON HRPP’s requests or those of higher authority.
• Coordinates site visits as may occur by DOD, FDA, OHRP, or others.

e. RSPD Administrators and Staff Responsibilities. The RSPD administers, supports, guides and oversees the work of the NMCP IRBs to uphold ethical and regulatory standards and practices in human subject research at NMCP. RSPD staff report to the Division Head, RSPD for administrative matters.

f. Scientific Review Committee (SRC) Responsibilities. The SRC is NMCP’s panel charged with conducting a scientific review of all human subject research including research exempt from the human subject protection regulations conducted by NMCP and its investigators. The reviewers have the expertise to understand the background, aims, and methods of the research to determine if the research uses procedures consistent with sound research design and assess if the research design is sound enough to yield the expected knowledge. The SRC review differs from IRB review in that it involves assessing the research’s scientific quality and the investigator’s qualifications. All research protocols must receive scientific review before submission to the IRB. The SRC Editor will determine whether reliance on another institution’s scientific review is appropriate.

g. Institutional Review Board (IRB) Responsibilities. The NMCP IRB is formally designated to review and monitor research involving human subjects to protect the rights and welfare of the subjects. It also provides oversight and monitoring of such protections. In accordance with the Common Rule, DOD and FDA regulations, the IRB recommends approval, requires modification to secure approval, defers, tables, or disapproves research.

The NMCP IRB reviews all human subject research conducted (a) completely or partially at NMCP; (b) in approved off-site locations, facilities; and/or (c) by NMCP employees or agents while on official duty time, regardless of whether the research is funded or regulated by any government agency.
In limited circumstances (i.e., collaborative research ventures) and at the discretion of the Commanding Officer, NMCP may rely on the collaborative institution’s IRB in lieu of NMCP IRB review. (See also Chapter on collaborative research below) In such circumstances, NMCP retains responsibility for monitoring the conduct of research at NMCP facilities by its employees and agents.

The IRB must meet all of the reporting requirements as outlined in SECNAVINST 3900.39D paragraph 8e (6) which includes but is not limited to, reporting all suspensions or terminations of previously approved research protocols; the initiation of investigations of alleged non-compliance with human subject protections; unanticipated problems involving risks to subjects or others, or Serious Adverse Events (SAEs); all audits, investigations, or inspections of CID or the IRBs conducted by an outside entity (e.g., FDA or OHRP); or significant communication between the institutions conducting research and other federal departments and agencies regarding compliance and oversight.

h. Principal Investigators (PI) Responsibilities. As the individual responsible for the implementation of research, the PI bears direct responsibility for protecting every research subject. This responsibility starts with protocol design, which must minimize risks to subjects while maximizing research benefits and continues through the life of the project, including the informed consent process, regardless of which members of the research team actually obtain and document consent. Finally, the PI and all members of the research team must comply with the findings, determinations, and requirements of the IRB.

For DON supported intramural research, a PI must be a current federal employee (uniformed or civilian, staff, or trainee), covered under the Intergovernmental Personnel Act (IPA), or a consultant consistent with the requirements established by 5 USC 3109. Status as a contractor or federal retiree is not sufficient to qualify individuals as a PI for such research.

For DON supported extramural research, the PI must meet the criteria established by the institution that receives the award.

Principal Investigators:
- Review and follow the terms of NMCP’s FWA, DOD regulations and requirements for the protection of human research subjects, relevant DHHS and FDA regulations, and the Belmont Report.
- Ensure that the research complies with all applicable Federal, State, and Local regulatory requirements and with the determinations of the IRB.
- Obtain written determination of whether the proposed activity is research with human subjects or if it meets the definition of exemption according to 32 CFR 219.101.
- Ensure that all human subjects research conducted at NMCP and/or on official duty time, has received prospective review by the IRB and approval by the Commanding Officer.
- Responsible for assuring all key research personnel complete required training and are educated in all phases of the research, including recruitment of subjects, obtaining informed consent, providing necessary reports, and maintaining protocol hard source documents.
• Ensure that continuing IRB review and approval of the research are secured in a timely fashion.
• Ensure that no changes in approved research are initiated without prior review by the IRB and approval by the Commanding Officer, NMCP, except where necessary to eliminate apparent immediate hazards to subjects; and that no research is continued beyond the IRB-designated approval period.
• Ensure that all documents are signed by the Investigator and chain of command as appropriate.
• Obtain informed consent from research subjects or their legally authorized representatives and provide them with a signed and dated copy of the completed informed consent document prior to the start of the research, unless a waiver of the documentation is approved by the Commanding Officer, NMCP.
• Ensure that the IRB is notified in writing in a timely manner of (a) any injuries or unanticipated problems involving risks to subjects or others; (b) any serious adverse events experienced by subjects; (c) any adverse events reported to the study sponsor; (d) any serious or continuing non-compliance with applicable regulatory requirements or determinations of the IRB of which they become aware; and (e) protocol deviations of which the investigator becomes aware. The Principal Investigator is to follow the NMCP SOP for reporting unanticipated problems and adverse events.
• Maintain complete and accurate records regarding all communications with the IRB, the sponsor, and any Federal Agency, and make such records available to the NMCP Institutional Official and/or delegate immediately upon request.
• Make a final report to the NMCP IRB and to the sponsor after the completion or discontinuance of a research project, or of withdrawal of the exemption for a research project.
• Provide the IRB with copies of any reports or correspondence to or from any regulatory or compliance enforcement Federal agency, such as DON HRPP, OHRP, or FDA, that exercises oversight over the protection of human subjects in research in which they are involved.
• Complete and document initial and continuing research ethics and human subject protections training in accordance with NMCP and DON HRPP policy.
• Maintain hard source documents, including signed, dated laboratory and procedural reports. Such documents provide evidence that the PI has reviewed subject records applicable to the protocol, in an effort to ensure human subject protection and data integrity.

Without all required approvals for a research protocol involving research participants, the PI must not:
• enroll research participants in a study, acquire data, analyze data, or test specimens from research participants;
• present research information by publication, submission of publication, presentation at meetings, or other means;
• fund travel for conducting the research protocol or for activities directly related to the participation of research participants;
• fund any other activities for which approval of the research protocol for participation of research participants is required.
Preliminary activities normally required for the planning and implementation of a study, prior to active participation or enrollment of research participants in a specific protocol, are permissible. Please see *Activities Preparatory to Research* for more information.

If the PI deploys, an Amendment to name a replacement PI must be submitted before the deployment begins. The incoming PI may be someone who is already named as an AI on the study or may be someone new to the project. The existing PI may request to remain on the protocol as an AI. Upon their return from deployment, an Amendment may be submitted to return them to the role of PI.

If the PI leaves NMCP (through PCS, retirement *etc.*), the original research records must be retained at the facility. An Amendment to name a replacement PI must be submitted before the departure. The incoming PI may be someone who is already named as an AI on the study or may be someone new to the project. If a PCS investigator wishes to continue working on the study from their new location, the CO of the investigator’s new command must acknowledge this activity.

i. Associate Investigators (AI) Responsibilities. Associate Investigators are individuals who contribute to the creation and/or conduct of the study. The title of Associate Investigator applies to all members of the Research Team beyond the PI including, but not limited to, physicians, nurses, research coordinators (including those in clinical, regulatory, and/or administrative roles), and research assistants. An AI may be active duty, civilian or a contractor. Associate Investigators work under the supervision of the Principal Investigator and their responsibilities should be documented in a Delegation of Duties log. NMCP defines an AI as any individual contributing to the conduct of research or submitting study documentation to the IRB. This person must be a designated and approved member of the research team (*i.e.*, Associate Investigator). If an AI is a contractor, they must be cognizant of any limitations placed upon the kinds of work they can perform as well as restrictions as to which research projects they can participate in, as described in their Performance of Work Statement (which includes the Statement of Work). The PI, contractor, and Contracting Officer’s Representative (COR) should work together to facilitate research while adhering to contracting requirements. In the absence of the PI, an AI may sign protocol documents and submit reports although the PI must be copied on all email submissions to the IRB. Every member of the Research Team is responsible for protecting human subjects. As such, they have a strict obligation to comply with all IRB determinations and procedures; adhere rigorously to all protocol requirements; inform Investigators of all adverse reactions or unanticipated problems involving risks to subjects or others; oversee the adequacy of the informed consent process; and take whatever measures are necessary to protect the safety and welfare of subjects. AIs must complete CITI and Research Integrity training, as required by NMCP and DON HRPP, and submit a current CV.

Researchers at every level are responsible for notifying the IRB and Compliance Advisor promptly of any serious or continuing non-compliance with applicable regulatory requirements or determinations of the IRB of which they become aware, whether or not they
themselves are involved in the research. Researchers must also notify the IRB Chair, Vice Chair, RSPD Division Head, or Compliance Advisor directly of any compliance concerns.

**PHASES OF RESEARCH**

Research studies are generally divided into four phases:

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**PHASE I**

Phase I trials examine the first exposure of a drug in humans to establish safety and dosage ranges, as well as assess the potential toxicity of a new drug. Phase I trials generally involve a small group of healthy volunteers on an inpatient basis. This phase of research can last for several months to many years.

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**PHASE II**

Phase II clinical trials test the efficacy of drugs, continue to assess the safety of the treatments under study, and further assess dosing requirements. Subjects for Phase II research must have the condition for which the drugs or treatment is intended. For this reason, Phase II trials are more selective and stringent in determining who is selected to participate. Phase II clinical trials examine whether or not a subject’s medical condition improves, seeks to identify common side effects, learn if the dosage should be reduced or increased, and determine how the body responds to the varying drug dosages. Randomized groups of up to 300 subjects are typically used as volunteers in Phase II clinical trials, and these studies are typically double-blinded, where neither the researcher nor the subject knows which group is taking the drug and which group is receiving the placebo. Very few new drugs make it past Phase II research.

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**PHASE III**

Phase III clinical trials are used to definitively conclude the efficacy of a drug for a certain condition. Throughout the research, dosage levels are tested to determine which dose provides the most beneficial effects while offering the least negative side effects possible. This phase of clinical studies can also determine the effectiveness of the drug for different levels of the disease. Phase III clinical trials have the largest base of volunteers of all the phases, typically ranging from 300 to 3,000 participants who are afflicted with the targeted condition. Since Phase III research tests participants with similar demographic traits over the course of two to five years, this is the most time-consuming study in which to be involved. Although few drugs make it to the Phase III trial, nearly 80% of those drugs in Phase III provide enough data for a product to be submitted for approval by the Food and Drug Administration (FDA).

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**PHASE IV**

Phase IV clinical trials are conducted after the FDA approves the marketing of a drug by a pharmaceutical company. The purpose of Phase IV research is to examine the long-term effects of drugs over an extended time period for a larger group of people. Phase IV clinical studies are performed to continuously discover more information about these new drugs post marketing. Participants in Phase IV clinical trials are typically patients who receive the medication under the supervision of their physician, and data collection is commonly conducted in physicians’ offices, since this is where patients receive regular medical care. Phase IV clinical trials often capture information about the drug’s effect on certain types of people, such as pregnant women, or to test the drugs’ interaction with other medications patients are taking. Phase IV research can also be used to
find new markets for the drug for competitive analysis. Since Phase IV studies apply to a much larger group of people over a much longer period of time, the long-term effects and unique effects on different populations can be more accurately measured and detected.

GUIDELINES FOR REVIEW

REGULATORY CRITERIA FOR APPROVAL

In reviewing human subjects research proposals, the Board considers the following regulatory criteria:

1. Risks to participants are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose participants to risk.
2. Risks to participants are minimized whenever possible, by using procedures already being performed on the participants for diagnostic or treatment purposes.
3. Risks to participants are reasonable in relation to anticipated benefits, if any, to participants, and the importance of the knowledge that may be reasonably expected to result.
4. Selection of participants is equitable taking into account the purposes of the research, the setting in which the research will be conducted, the special problems of research involving vulnerable populations, the selection criteria and the recruitment procedures.
5. Informed consent will be sought from each prospective subject or the subject’s legally authorized representative, in accordance with, and to the extent required by 32 CFR 219/45 CFR 46.116/21 CFR 50.20.
6. Informed consent will be appropriately documented, in accordance with and to the extent required by 32 CFR 219/45 CFR 46.117/21 CFR 50.27.
7. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of participants.
8. When appropriate, there are adequate provisions to protect the privacy of participants and to maintain the confidentiality of data.
9. When some or all of the participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these participants.

The regulatory criteria for approval must be met for the research to be approved (with the exception of the last three when they are not applicable). This is required for initial, continuing and modification reviews, whether by convened IRB or by the expedited process.

Additionally, the Board pays particular attention to the ethical principles of Respect for Persons, Beneficence, and Justice by considering:

- The degree of risk to the subjects as represented by the categories of risk [minimal risk and greater than minimal risk].
- Whether the informed consent document contains all the elements of informed consent and if it accurately represents the procedures of the study.
- Whether the protocol could be considered coercive, particularly when the subject is extremely ill, or if a remuneration of any kind is offered for participation.
- Appropriate third party consent, when applicable.
• Assent of the child, or waiver of assent as appropriate.

INSTITUTIONAL STANDARDS FOR NMCP

The NMCP IRB functions under NAVMEDCENPTSVAS INSTRUCTION 6500.2G. The Navy Surgeon General, through the DON Human Research Protections Program (HRPP), is the primary authority for Navy medical research and embodies the requirements for the FDA and DHHS for conducting research on human subjects within NMCP. Per this instruction, all human subjects research conducted with NMCP oversight should meet the following standards.

1. The study must contribute to human benefit, and have reasonable prospects of yielding important results which are not known to be obtained by other methods or other means of study.
2. The number of subjects used will be kept to the minimum necessary to achieve the anticipated results.
3. The study will be conducted to avoid all unnecessary physical or mental discomfort, suffering, or injury.
4. No study will be initiated if there is any reason to believe that death or disabling injury is likely to occur as a result of participation.
5. The degree of risk to be taken shall never exceed that determined to be required by the urgency or importance of the objectives to which the study is related.
6. Preparations shall be made, and adequate facilities provided, to protect the human subject against all possibilities of injury, disability, or death.
7. Only persons possessing the requisite qualifications appropriate to the study shall conduct the study. These qualification may include, but are not limited to scientific, medical, physical, psychological, psychiatric, and others as are called for in the protocol. This determination will be made by the IRB based upon their considerations for subject protections and scientific merit.
8. The subject shall have no physical or mental conditions which will make participation more hazardous for him or her than it would be for a normal healthy person, unless such condition is a necessary prerequisite for the particular study involved.
9. The person conducting the study and each member of the investigative team shall be prepared to terminate the subject’s participation at any stage if they have reason to believe that continuation is likely to result in injury, disability, or death to the subject.
10. Research involving prisoners as subjects will include additional relevant protections found in Subpart C of the DHHS regulations (or equivalent protections as allowed by law) including, but not limited to: requiring Full Board review of the protocol and ensuring that the reviewing Board has at least one member who is qualified to represent prisoners.
11. Institutionalized mentally disabled persons will not be used.

CRITERIA FOR APPROVAL OF INVESTIGATORS

CID requires evidence from investigators to document their ability to conduct ethical research.

• Current curriculum vitae including college and post graduate degrees, dates obtained, military service, and local address. CVs must be updated every three years.
• Evidence of completion of ethics training for the protection of human subjects in research. Currently DON HRPP requires a program referred to as CITI training. This training must be repeated after three years.
CRITERIA FOR APPROVAL OF A RESEARCH MONITOR

A research monitor must be identified for all protocols reviewed as “greater than minimal” risk. Although not required, the services of a research monitor may also be used for “minimal” risk studies, at the discretion of the PI and the IRB. A research monitor should have expertise commensurate with the nature of risk(s) identified within the research protocol. The research monitor must be independent of the investigative team, although he/she may concurrently serve as the research monitor and an ombudsman or a member of the data safety monitoring board. More than one research monitor may be named to a study, particularly if different skills or experiences are necessary to adequately monitor the protocol.

The duties of a research monitor are tied to specific risks or concerns identified by the PI or Board about a particular project. The IRB must approve a written summary of the monitors’ duties, authorities, and responsibilities.

The research monitor may serve as a medical monitor, reviewing SAEs as they are discovered to determine if the events suggest a trend towards increased risk to subjects that would require additional safeguards, subject notifications, or an invoking of stopping rules.

The research monitor may perform oversight functions, such as observing subject recruitment, enrollment and consenting; oversight of study interventions and interactions between investigators and subjects; examining monitoring plans and reports; and review of data matching, data collection, and data analysis procedures.

To satisfy these two areas of responsibility, the research monitor may discuss the research protocol with the investigators, interview study subjects, and consult with others outside of the project about the research. In the event a problem is identified, they have authority to stop a research protocol in progress, remove individual subjects from a study, and take whatever steps are necessary to protect the safety and well-being of subjects until the IRB can assess the monitor’s report.

Research monitors are required to promptly report their medical monitoring and oversight monitoring observations and findings to the IRB or other designated official.

The CID requires evidence from research monitors to document their ability to conduct an ethical review of ongoing research.

- Current CV including college and post graduate degrees, dates obtained, military service, and local address. CVs must be updated every three years.
- The research monitor must possess the expertise necessary to successfully review SAEs and identify potential trends. Qualifications that demonstrate this expertise will vary depending on the type of research being conducted (biomedical, social/behavioral, etc.).
- Evidence of completion of ethics training for the protection of human subjects in research. Currently DON HRPP requires a course referred to as CITI training, which is good for 3 years, after which it must be repeated. When registering for this training the...
Research Monitor will identify his/her role in the research and will be directed to the correct training.

DON HRPP may waive the requirement to have a research monitor on a case-by-case basis when the inclusion of a research monitor is not necessary to provide additional protections for human subjects.

SUBJECT POPULATION

Each research proposal must clearly define the population to be studied so that appropriate ethical consideration may be taken. This includes identifying the proposed number of subjects to be enrolled to both experimental and control arms as well as the age range, reproductive capacity, and active duty status of subjects.

The IRB is charged with ensuring the appropriateness of the population of subjects to be used. Three specific populations are identified in the DHHS regulations as vulnerable and require additional regulatory review:

- Pregnant women, fetuses, and neonates, because of possible risks to the unborn or newborn child (45 CFR 46 Subpart B).
- Prisoners, because of their diminished autonomy and vulnerability to coercion (45 CFR 46 Subpart C).
- Children, including newborns, because of their vulnerability, diminished autonomy, and incomplete understanding (45 CFR 46 Subpart D).

Although these three populations are categorically defined as vulnerable, the Board also considers the need for appropriate similar safeguards for other vulnerable populations, such as research involving:

- human subjects and investigators in supervisor-subordinate relationships,
- human subjects with limited civil freedom (such as residents, clients, and persons subject to military discipline),
- human subjects with decisional or mental impairments,
- human subjects with a physical disability, or
- any other kind of human subjects in circumstances that may warrant provision of additional protections.

PREGNANT WOMEN, FETUSES OR NEONATES

When research involves pregnant women, fetuses, or neonates, the protocol must satisfy the criteria for approval of research in Subpart B of the DHHS regulations or equivalent protections as allowed by law.

- Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses.
- One of the following must be true:
  - 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
The risk to the fetus is not greater than minimal and the purpose of the research is the development of important generalizable knowledge which cannot be obtained by any other means.

- The DON HRPP 27 June 2012 training on *Modifications Required to Secure Approval and Subpart B Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research*, presented a textual change from “biomedical knowledge” to “generalizable knowledge” to DODI.3216.02. Part 7d. This modification permits approval of minimal risk research (with or without direct benefit) which produces knowledge that is not necessarily biomedical in nature, such as information obtained from the results of surveys and questionnaires. It also changed the existing instruction to state that Subpart B only applies to research involving “pregnant women as human subjects involved in research that is more than minimal risk and includes interventions or invasive procedures to the woman or the fetus”. Thus, the IRB is not required to consider *Subpart B Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research* during review of research approved under an exempt or expedited category.

- Any risk is the least possible for achieving the objectives of the research.
- For children who are pregnant, assent and permission are obtained in accordance with the regulations.
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy.
- Individuals engaged in the research have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.
- Individuals engaged in the research have no part in determining the viability of a neonate.

Criteria for approval of research involving neonates of uncertain viability:

- Where scientifically appropriate, preclinical and clinical studies have been conducted and provided data for assessing potential risks to neonates.
- Individuals engaged in the research have no part in determining the viability of a neonate.
- One of the following must be true:
  - The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective.
  
  or

  - The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there is no added risk to the neonate resulting from the research.

Criteria for approval of research involving nonviable neonates:
- Where scientifically appropriate, preclinical and clinical studies have been conducted and provided data for assessing potential risks to neonates.
- Individuals engaged in the research have no part in determining the viability of a neonate.
- Vital functions of the neonate are not artificially maintained.
- The research will not terminate the heartbeat or respiration of the neonate.
- There is no added risk to the neonate resulting from the research.
- The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means.

For studies involving pregnant women, fetuses, or neonates, the Board must determine if consent to participate must be obtained from the pregnant woman alone or from both the pregnant woman and the father/partner.

The consent of the pregnant woman alone is required if the research:
- Holds out the prospect of direct benefit to the pregnant woman.
- Holds out the prospect of direct benefit to both to the pregnant woman and the fetus.
- Holds out no prospect of benefit for the woman or the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important generalizable knowledge that cannot be obtained by any other means.

The consent of the pregnant woman and the father/partner is required if the research holds out the prospect of direct benefit solely to the fetus.

When the research involves neonates of uncertain viability, the consent of either parent or consent of either parent’s legally authorized representative is required if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity.

When the research involves non-viable neonates, the consent of both parents is required. Consent from one parent is permitted if the other parent is unable to consent because of unavailability, incompetence, or temporary incapacity. Consent by a legally authorized representative is not permitted.

In all consenting procedures for research involving pregnant women, fetuses or neonates, the father/partner’s consent need not be obtained if he is absent (as in cases of deployment or incarceration), incompetent, unknown, or the pregnancy resulted from rape or incest.

PRISONERS

When research involves prisoners, the protocol must satisfy the criteria for approval of research in Subpart C of the DHHS regulations or equivalent protections as allowed by law.

- The research represents one of the following categories:
  1. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects.
  2. Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects.
3. Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults).
   - For DHHS funded research, OHRP has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of its intent to approve such research.

4. Research on practices, both innovative and accepted that has the intent and reasonable probability of improving the health or well-being of the subject.
   - For DHHS funded research which requires the assignment of prisoners in a manner consistent with protocols reviewed by the IRBs to control groups which may not benefit from the research, the study may proceed only after OHRP has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of its intent to approve such research.

In addition to the four categories of permissible research identified in Subpart C, two additional categories are allowable:

5. Epidemiological research that meets the following criteria:
   - The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor associations for a disease.
   - The research presents no more than minimal risk.
   - The research presents no more than an inconvenience to the human subject.
   - Prisoners are not a particular focus of the research.

6. Research that would meet the criteria for approval under one of the Exempt categories can be conducted with a prisoner population, but must be reviewed by a convened IRB and meet the requirements of Subpart C and other applicable requirements.

- The following criteria also apply:
  - Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired.
  - The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers.
  - Procedures for the selection of participants within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners.
Unless the principal investigator provides justification in writing for following some other procedures, control participants are selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project.

Adequate assurance exist that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole. When there is a need for follow-up examination or care of participants after the end of their participation, adequate provisions are made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing participants of this fact. For prisoners, “minimal risk” means the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

For appropriate review and approval of a study involving prisoners, special requirements are placed upon the membership present at the IRB meeting:

- A majority of the IRB (exclusive of prisoner members) have no association with the prison involved, apart from their membership on the IRB.
- At least one IRB member is present at the meeting who is a prisoner or a prisoner representative with appropriate background and experience to serve in that capacity. The prisoner representative may be a prisoner, an employee of the prison, or an individual not affiliated with the prison. The prisoner representative must have knowledge of the culture(s) of the prisoners and knowledge of the prison operations.

Research intending to include prisoners as subjects cannot be reviewed by the IRB through an expedited review procedure.

**WHEN A SUBJECT BECOMES A PRISONER**

The PI must promptly notify the IRB when a previously enrolled subject becomes a prisoner and the relevant research protocol was not reviewed by the IRB in accordance with Subpart C. If the intent is to allow continuing participation of the prisoner-subject, the notification should include submission of a protocol amendment to permit inclusion of the prisoner. Such an amendment is subject to review and approval by the IRB and DON HRPP.

Upon learning that a subject has become a prisoner, the IRB Chair will instruct the PI that all research interactions and interventions with the prisoner-subject (including the collection of PHI) must stop until the Board can review his request to modify the protocol to permit inclusion of this prisoner. If the PI asserts in writing that it is in the best interest of the prisoner-subject to continue participation on the study while a prisoner, the IRB Chair may allow the prisoner-subject to continue participation until the Board can consider the matter at a convened meeting.

At the convened meeting, the IRB will re-review the research protocol to ensure that the rights and well-being of the human subject, now a prisoner, are not in jeopardy. A prisoner representative (or an ad hoc reviewer who has the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative) must be present at the meeting for quorum to be reached. The research protocol cannot be reviewed using expedited procedures.
If the prisoner-subject can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner-subject’s confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human subjects from continuing as approved, the convened IRB may recommend approval of a change in the study to allow this prisoner-subject to continue to participate in the research. This approval is limited to the individual prisoner-subject and does not allow recruitment of prisoners as subjects. The research project does not have to meet one of the six allowable categories of research described above.

All decisions related to subjects who become prisoners must be reported to DON HRPP if the study is conducted by a DOD institution, or to OHRP if a collaborative non-DOD institution is the lead organization on the project.

TREATMENT OF DETAINEES

DOD Directive 2310.01E defines a “detainee” as:

Any person captured, detained, held, or otherwise under the control of DOD personnel (military, civilian, or contractor employee). It does not include persons being held primarily for law enforcement purposes, except where the United States is the occupying power.

Research involving a detainee is prohibited. The only exception to this prohibition is when an investigational new drug (IND) or investigational device (IDE) is offered to detainees, with the detainees’ informed consent, for the diagnosis or treatment of a medical condition when the same product would be offered to members of the U.S. Military Services in the same location for the same medical condition. This use must be consistent with established medical practice involving investigational drugs and devices.

CHILDREN

When research involves children, the protocol must satisfy the criteria for approval of research in Subpart D of the DHHS regulations or equivalent protections as allowed by law.

SERVICE MEMBERS AND THEIR STATUS AS ADULTS

All Active Duty Service members and all Reserve Component members in a federal duty status are considered adults for purposes of legal capacity to participate in human subjects research per DODI 3216.02 dated 20 October 2011. Participation of these individuals, therefore, is not subject to requirements of Subpart D. When service members are under 18 years of age (as may occur in the Marine Corps), students at the Academies, or trainees, the IRB will carefully consider the recruitment process and the necessity of such members to participate, but assignment of a pediatric risk rating for the research project in question is not required.

PEDIATRIC RISK RATING

A pediatric risk rating must be assigned to all research involving children.

OHRP regulatory citations:
- No greater than minimal risk to children is presented.
- Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.
- One parent may consent for participation of their child.

[45 CFR 46.405] - Greater than minimal risk, prospect of direct benefit
- Greater than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual participant, or by a monitoring procedure that is likely to contribute to the participant’s well-being.
- The risk is justified by the anticipated benefit to the participants.
- The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.
- Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.
- One parent may consent for participation of their child.

[45 CFR 46.406] - Greater than minimal risk, no prospect of direct benefit
- Greater than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual participant, or by a monitoring procedure which is not likely to contribute to the well-being of the participant.
- The risk represents a minor increase over minimal risk.
- The intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations.
- The intervention or procedure is likely to yield generalizable knowledge about the participants’ disorder or condition which is of vital importance for the understanding or amelioration of the participants’ disorder or condition.
- Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.
- Two parents must consent for participation of their child, unless one parent is unable to consent because of unavailability (as in cases of deployment or incarceration), incompetence, or temporary incapacity.

If the Board determines that a proposed study involving children meets the criteria for [45 CFR 46.406] - Greater than minimal and with no prospect for direct benefit, special consideration must be taken if wards of the state are to be enrolled; if the research is related to their status as wards; or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.
- The IRBs 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.
  - The advocate is 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
  - The advocate 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.
These risk assessments categories are pertinent in research with children conducted under the FDA as well.

**FDA regulatory citations**

[21 CFR 50.51] - Minimal risk
- Clinical investigations not involving greater than minimal risk.
- Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.
- One parent may consent for participation of their child.

[21 CFR 50.52] – Greater than minimal risk, but presenting the prospect of direct benefit
- Clinical investigations involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects.
- Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.
- One parent may consent for participation of their child.

[21 CFR 50.53] – Greater than minimal risk and presenting no prospect of direct benefit
- Clinical investigations involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subjects' disorder or condition.
- Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.
- Two parents must consent for participation of their child, unless one parent is unable to consent because of unavailability (as in cases of deployment or incarceration), incompetence, or temporary incapacity.

Additionally, a fourth category of pediatric research is permitted by the regulations, although rarely seen at NMCP.

[45 CFR 46.407] OHRP
- The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.
- The federal agency, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, determined either: [If not federally funded, the Command can substitute an equivalent mechanism.]
  - That the research falls into categories 1 through 3;
  - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children and the research will be conducted in accordance with sound ethical principles.

and
Clinical investigations not otherwise approvable that present an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

SUBJECTS WHO ARE DECISIONALLY IMPAIRED

Subjects who are decisionally impaired present a challenge for researchers. Examples of conditions that may cause decisional impairment include, but are not limited to, trauma, head injury (such as TBI), mental illness (such as dementia or depression), women in labor, or patients under anesthesia. Impairment may be temporary or permanent, and may move up and down the spectrum of impairment during the course of participation in a study. Investigators must carefully assess whether or not a subject is capable of making an informed decision about participation. In some situations, when it is known that impairment may occur at the outset of participation in research (as would be the case of a patient receiving anesthesia prior to surgery or a woman in labor), the investigators may want to approach these individuals about taking part in the study before they become impaired. For other patients, who are too impaired to consent for themselves, it may be possible to allow a Legally Authorized Representative (LAR) to consent for the patient’s enrollment. Per 32 CFR 219.102 (c), a legally authorized representative is “an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research”. When consent by a LAR is allowed by the IRB, every effort should be made to involve the patient in the decision as his condition permits. In such cases, the patient may be approached to provide assent to participation, or may be asked to consent to their continued participation if they regain the ability to do so. Please contact the IRB for guidance if a protocol is studying a population that holds the potential to be decisionally impaired.

MILITARY PERSONNEL AS SUBJECTS

As mentioned previously, the NMCP IRB considers the need for appropriate safeguards for other vulnerable populations beyond the three defined above. The very nature of research in a “chain-of-command” setting dictates that the Board identify potential challenges to the Belmont principle of “Respect for Persons” when reviewing research involving investigators and subjects in supervisor-subordinate relationships.

Superiors (e.g., military and civilian supervisors, unit officers, and noncommissioned officers) may not influence the decisions of their subordinates (e.g., junior enlisted personnel and equivalent civilians) regarding the choice to participate or not to participate as research subjects.

In an effort to protect the autonomy of subordinates, Superiors of Service members (e.g., unit officers, senior NCOs, and equivalent civilians) in the chain of command may not be present during recruitment sessions or during the consent process in which a member of a unit under their command is approached about participation in research. In situations where the superiors are also candidates for participation in the research, they will be approached separately from any of their subordinates.

This separation of supervisor from subordinate also pertains to the recruitment of DOD civilians as research subjects.
When the research activity has been determined to be greater than minimal risk and when recruitment occurs in a group setting, the IRB will appoint an ombudsman to monitor the recruitment process. The ombudsman will document that the voluntary nature of participation was clearly and adequately stressed and that the information provided about the research was clear, adequate, and accurate. The ombudsman may not have a role on the study team, but may be the Research Monitor. For a research activity that has been determined to be minimal risk and involves recruitment in a group setting, the IRB will determine if it is appropriate to appoint an ombudsman to monitor the recruitment process on a case by case basis. The decision to require an ombudsman will be based in part on the subject population, the consent process, and the recruitment strategy.

Regardless of risk level, review of a study that seeks to enroll DOD civilians in a group setting will include IRB discussion of whether or not it would be beneficial to appoint an ombudsman. Again, the study population, the consent process, and the recruitment strategy will be considered when making that decision.

If a protocol enrolls a population that may be vulnerable due to their subordinate relationship to the investigators, it is recommended that the PI identify this population using the “Other” choice in the IRB application forms.

EQUITABLE SUBJECT SELECTION

In making an assessment about whether selection of participants is equitable, the IRBs will take into account:

- The purposes of the research.
- The setting in which the research will be conducted.
- Whether prospective participants will be vulnerable to coercion or undue influence.
- The selection (inclusion/exclusion) criteria.
- Participant recruitment and enrollment procedures.
- The influence of payments to participants (if applicable)

If a protocol states that a specified sub-population is to be exclusively used (e.g., active duty only), a compelling reason must be given that justifies such a bias on the basis of scientific necessity or operational Navy need.

RISK/BENEFIT RATIO

The IRB requires that the risk/benefit ratio of a protocol be in equipoise and that safeguards be established by the investigator. The protocol must include a description of the anticipated risks, measures to minimize risks, and anticipated benefits to subjects.

Potential risks to subjects are a factor in determining the appropriate level of review required to approve a protocol. CID Research Subject Protections Division will work with the IRB Chair or Vice Chair to establish risk level. Most protocols found to be minimal risk will undergo exempt or expedited review by the IRB Chair or Vice Chair. Protocols found to be greater than minimal risk are presented to the full IRB who will review and make a formal risk determination.

MINIMAL RISK
Minimal risk means that the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. Certain risks inherent in life include the ordinary risks of public or private living; those risks associated with admission to a school or hospital; and the risks inherent in professional practice as long as these do not exceed the bounds of established and accepted procedures, including innovative practice applied in the interest of the individual patient, student, or client.

Minimal risk is not interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, research in a special population, such as emergency responders, pilots, divers, or soldiers in a combat zone, should not be deemed minimal risk because the study related activities appear negligible when compared against the inherent risks encountered in their work environment. Likewise, research conducted with a population having a medical condition that involves frequent medical tests or constant pain should not be identified as minimal risk because the study related risks pale in comparison to risks they encounter on a daily basis.

The fact that some types of research do not involve risks beyond those experienced in daily life situations does not mean that the investigator is any less responsible for his or her subjects.

**EXAMPLES OF MINIMAL RISK:**
1. Studies on the psychological and physiological effect of mild to moderate sleep loss.
2. Studies on movement and moderate exercise of asymptomatic adults where adverse effects are not anticipated.
3. Psychological studies of learning, conditioning, sensory perception, personality, judgment responses to speech, group situations, and childhood obesity.
4. Psychological studies where the subjects are not subjected to physiological or emotional stress.
5. Behavioral studies of development.
7. Clothing and textile studies under conditions of mild to moderate thermal stress.
8. Nutritional studies in which the subjects are not expected to ingest unusual diets which are deficient in essential nutrients.
9. Taste panel studies and taste tests involving common food ingredients or known, edible materials.

**GREATER THAN MINIMAL RISK**

Greater than minimal risk means anticipated risks in the proposed research exceed, either in probability or magnitude, those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. All research protocols that involve procedures that may induce potentially harmful, altered psychological or physical states or conditions, untried diagnostic and surgical procedures or devices; biopsy procedures; removal of organs or tissues for study, reference, transplantation, or banking; administration of drugs or radiation; use of indwelling catheters or indwelling electrodes; and procedures which require strenuous physical exertion fall into this category. In classifying research involving human subjects, the investigator and those who review the proposed use of subjects should follow logical principles and procedures to arrive at a well-reasoned decision.
EXAMPLES OF GREATER THAN MINIMAL RISK:

1. Psychological studies of hypnosis.
2. Adult exercise and fitness testing where the imposed workload substantially exceeds the customary physical activity of the individual.
3. Work studies where there is hard physical work and extremes of environmental temperature.
4. Physiological studies of sweating involving special nutrient regimens, dehydration, and work in thermally stressful surroundings.
5. Pharmacological studies of prescribed drugs.
6. Studies involving introduction of nasopharyngeal live viruses or the administration of vaccines and antibiotics.
7. Studies of the effects of prescribed tranquilizer drugs on driving skills.

If risks to subjects are great, the IRB may require the investigator to install additional protections:

1. More frequent data monitoring to assist with prompt detection of unanticipated harms and increased frequency or severity of expected harms.
2. Clear definition of stopping rules which will be invoked if potential harm to subjects outbalances possible benefit.

Benefits to participation cannot be guaranteed as research generally involves testing whether or not a treatment, procedure, or intervention will produce a benefit. Where randomization and/or use of a placebo are involved, the possibility of benefit may increase for one group of subjects while decreasing for another. The risk/benefit assessment must apply to all subjects participating in a study, thus, if one group may benefit while another will not, the study as a whole is said to present no benefit to subjects.

Research conducted with healthy volunteers, as in a Phase I trial, is usually identified as offering no benefit to participation.

Non-treatment studies must take care not to overstate potential benefits to participation, particularly where subjects may be severely ill or otherwise vulnerable to the therapeutic misconception that the primary purpose of the study is therapeutic rather than scientific.

PRIVACY AND CONFIDENTIALITY

The IRB is responsible for systematically evaluating proposed research for adequate provisions which protect the privacy interests of participants and to maintain the confidentiality of identifiable data.

PRIVACY

Privacy refers to a person’s desire to control the access of others to themselves.

In developing strategies for the protection of subjects’ privacy, consideration should be given to:

- The methods used to identify and contact potential participants.
- The settings in which an individual will be interacting with an investigator.
- The appropriateness of all personnel present for research activities.
- The methods used to obtain information about participants.
• The nature of the requested information.
• Information that is obtained about individuals other than the “target participants,” and whether such individuals meet the regulatory definition of “human participant” (e.g., a subject provides information about a family member for a survey).
• Privacy guidelines developed by relevant professional associations and scholarly disciplines (e.g., oral history, anthropology, psychology).
• How to access the minimum amount of information necessary to complete the study.

CONFIDENTIALITY

Confidentiality refers to the researcher’s agreement with the participant about how the participant’s identifiable private information will be handled, managed, and disseminated.

The research proposal should outline strategies to maintain confidentiality of identifiable data, including controls on storage, handling, and sharing of data.

• Methods to shield participants' identity and adequately protect participant privacy.
• Long-range plans for protecting the confidentiality of research data, including a schedule for destruction of identifiers associated with the data.
• Consent documents which clearly and adequately describe confidentiality risks to potential subjects.
• Consent documents which clearly define who will have access to the subject’s information and under what circumstances that data may be shared (i.e., government agencies, sponsors).

The IRB will ensure the use of appropriate methods for maintaining patient confidentiality, with due regard to the storage of identifiers and data, particularly when the information will be entered into an electronic data system.

• Data collection instruments and procedures should be carefully designed to limit the personal information to that which is absolutely essential to the activity.
• Data that include information which would reveal a subject’s identity should be stored in files accessible only to the principal investigator and his or her authorized research team members.
• As early as feasible, the data should be handled in coded form. Plans for the ultimate disposition of the data should be made, or if they are to be retained indefinitely, plans must be made for their continued security.
• The identity of subjects must not be released except with their expressed permission, unless required by law.
• Secondary analysis of stored data which involves identifiable subjects should specify if the new use is within the scope of the consent under which the data was originally collected; whether it is necessary and/or feasible to obtain consent for this new use, and how identifiers will be protected to maintain confidentiality beyond the original use of the data.
• The use of Social Security Number (SSN) shall be reduced or eliminated wherever possible.
• Use of the SSN includes the SSN in any form, including, but not limited to, truncated, masked, partially masked, encrypted, or disguised SSNs.
SSNs shall not be used in spreadsheets, hard copy lists (such as data collection tools and case report forms), electronic reports, or collected in surveys unless its inclusion meets one or more of the acceptable use criteria. The acceptable uses of the SSN are those that are provided for by law, require interoperability with organizations beyond the Department of Defense, or are required by operational necessities (see DODI 1000.30p).

SSNs may be used in approved forms and systems when they meet one or more of the acceptable use criteria as described in DODI 1000.30p.

CERTIFICATE OF CONFIDENTIALITY

Occasionally, research will involve the collection of highly sensitive information about individually identifiable subjects which the IRB determines requires special protections against the risks of investigative or judicial processes.

In such situations, the IRB may require that an investigator request a Certificate of Confidentiality (CoC) from the National Institutes of Health (NIH). The Certificate protects against the involuntary release of sensitive information about individual subjects for use in Federal, State, or local civil, criminal, administrative, legislative, or other legal proceedings.

The Certificate does not prohibit voluntary disclosure of information by an investigator, such as voluntary reporting to local authorities of child abuse or of a communicable disease. In addition, the Certificate does not protect against the release of information to DOD, DHHS or FDA for audit purposes. The conditions under which information may be released must be stated clearly and explicitly in the informed consent document.

It should be noted that NIH makes the final determination as to whether a Certificate will be granted for a particular research project. The NMCP IRB may require that an investigator request a Certificate from NIH, and may decide to disapprove research not granted a Certificate, but they cannot require an investigator to obtain a Certificate.

CONFIDENTIAL INFORMATION PROTECTION AND STATISTICAL EFFICIENCY ACT (CIPSEA)

DOD researchers may consider using the protections available under CIPSEA for particularly sensitive research activities when additional protections for confidentiality would improve participation and results.

A command may use the authority described in sections 501-513 of Public Law 107-347, Confidential Information Protection and Statistical Efficiency Act of 2002 (CIPSEA) to assure that data or information obtained under a pledge of confidentiality for exclusively statistical purposes will only be used for statistical purposes and will not be disclosed in identifiable form for any other purpose, except with the informed consent of the subject. This authority does not extend to research conducted by a contractor, grantee, or other non-federal collaborator. If a command or unit of the command has been designated as a statistical agency by the OMB, then they may identify agents (e.g., contractor, grantee, or other non-federal collaborator) who may assure that the use of data obtained under a pledge of confidentiality for exclusively statistical purposes will only be used for statistical purposes and will not be disclosed in identifiable form for any other purpose, except with...
the informed consent of the subject. Use of CIPSEA authority must be reported annually to Office of Management and Budget (OMB) by the Command.

For more specific information on invoking CIPSEA, contact CID for guidance.

SUBJECT COMPENSATION

DON regulations permit military personnel who are participating in research while on duty (i.e., not on leave and participating during their duty hours), to be compensated $50 for blood collection. The funds for subject compensation for blood draws may come directly from a federal or non-federal source. This compensation is an exception to section 5536 of title 5, US Code which prohibits federal personnel from being paid by any source other than their regular federal salaries while they are on duty. No other compensation is possible if subjects participate while they are on duty.

When the subjects of a study are civilian federal personnel, they may be compensated $50 for blood collection if the study is federally funded.

Military personnel who participate in research while they are off-duty are also eligible for compensation of $50 for blood collection. In addition, off-duty military personnel may be compensated for research participation other than blood draws in the same manner as human subjects who are not federal personnel. However, the funds for this compensation may not come directly from a federal source (funds from a federal contractor or other non-federal source are permissible). Civilian federal personnel are also eligible for compensation in this manner.

There are no restrictions relevant to the compensation of dependents as research subjects.

When payments are allowed, the IRBs will review payments to determine that:

- The amount of payment and the proposed method and timing of disbursement neither is coercive nor presents undue influence.
- Credit for payment accrues as the study progresses and not be contingent upon the participant completing the entire study.
- Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
- All information concerning payment, including the amount and schedule of payments, is set forth in the consent document.
- Payments in exchange for referrals of prospective participants (“finder’s fees” or “referral fees”) are unacceptable.
- Payments tied to the rate or timing of enrollment (“bonus payments”) are not permitted.

SUBJECT RECRUITMENT

The recruitment of subjects is considered the first step of the informed consent process. The feasibility of a recruitment plan and the tools to be used must be considered before initiation of a protocol and should be reassessed throughout the study. For this reason, the IRB must review the methods, materials, procedures, and tools used to recruit potential research subjects before they are implemented. Some of the more commonly used tools of recruitment include direct advertising (flyers, posters, press releases, brochures), media advertisements (newspaper, TV, radio, websites),
recruitment letters, review of medical charts and computerized databases, and presentations at community meeting places.

The IRB must review all plans for advertisement (including the actual posters, brochures, scripts for commercials, etc.) prior to their use. An advertisement/flier/broadcast can only be used exactly as it was written and for the specific purpose specified as reviewed by the IRB.

Note: In addition, investigators must obtain permission from the Director for Administration using the Request for Display form in order to have posters, table top displays, and/or pictures posted at NMCP.

The IRB will review all advertising to recruit subjects and will consider the following:

- The information contained in the advertisement.
- The mode of its communication.
- The final copy of printed advertisements.
- The final audio or video taped advertisements.

The IRB will not approve advertising that:

- States or implies a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.
- Includes exculpatory language.
- Emphasizes the payment or the amount to be paid, by such means as larger or bold type.
- Promises “free treatment” when the intent is only to say participants will not be charged for taking part in the investigation.

Advertisements are limited to the information prospective participants need to determine their eligibility and interest, such as:

- The name and address of the investigator or research facility.
- The purpose of the research or the condition under study.
- In summary form, the criteria that will be used to determine eligibility for the study.
- Brief list of benefits to participants, if any.
- The time or other commitment required of the participants.
- The location of the research and the person or office to contact for further information.

When allowing advertisements for FDA regulated research, the IRBs will review advertising to ensure that advertisements do not:

- Make claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling.
- Use terms, such as “new treatment,” “new medication,” or “new drug”, without explaining that the test article is investigational.
- Allow compensation for participation in a trial offered by a sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.
Any change to an approved advertisement or recruitment tool must be reviewed by the IRB and approved by the CO prior to being put into effect. If changes need to be made to an approved advertisement, the document must be sent to the IRB for review even if the change is minor (i.e., a contact number or name change). Seemingly minor changes can impact the entire message of an advertisement.

INTERNATIONAL RESEARCH

The mission of the Navy is often carried out in an international setting. Similarly, researchers at NMCP may have occasion to conduct research outside of the U.S.

When the IRB reviews research occurring in other countries the Board will:

- Ensure appropriate expertise and knowledge of the country(ies) either through IRB members or consultants.
  - Knowledge of local laws
  - Knowledge of cultural context
- Confirm the qualifications of the investigators and research staff for conducting research in the country(ies).
- Provide Initial review, Continuing review, Review of modifications, and conduct Post-approval monitoring.
- Handle complaints, non-compliance and unanticipated problems involving risk to participants or others.
- Ensure the consent document is appropriate, noting potential language issues.
- Coordinate and communicate with local IRBs when appropriate.

Additional safeguards for research conducted with international populations require that:

- The Command or investigator has permission to conduct research in that country by certification, or local ethics review.
- Research involving human subjects who are not U.S. citizens or DOD personnel, conducted outside the United States, and its territories and possessions, requires permission of the host country. The laws, customs, and practices of the host country and those required by this instruction will be followed. An ethics review by the host country, or local Navy IRB with host country representation, is required.
- The investigator follows all local laws, regulations, customs, and practices.
- Additional safeguards might not be applicable to social-behavioral research involving no more than minimal risk.

INFORMED CONSENT

The process of informed consent is one of the most important parts of planning a research study. It is important that human subjects exercise their right of free will in making the decision to participate. It is equally important that subjects be given correct information, comprehend what is being presented to them, and have time to make their own decision about participation. Although a signed consent form is a significant research document, it is the informed consent process represented by the signature that is central to the IRB mission.
The methods used to obtain consent may vary. They should be designed to fit the nature of the research, the frequency and magnitude of the risks involved, the research setting, the nature of the subjects who will participate, and the requirements of applicable policies, laws, and regulations.

An investigator shall seek such consent only under circumstances which provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate in the research, and which minimize the possibility of coercion or undue influence by the research staff.

“Enrollment” occurs when an informed, prospective subject undergoes the initial informed consent process and voluntarily agrees to participate in a research project. As such, at NMCP, a subject is defined as “enrolled” in research when the consent form is signed. When reporting subject enrollment numbers during the submission of Amendments or Continuing Review, Investigators are asked to distinguish between subjects who signed consent and subjects who meet all inclusion criteria, as some subjects who sign consent may be not progress to active participation due to screen failure.

**PROCEDURES FOR CONSENTING**

The investigator (PI, AI) will present the research project to the prospective subject. The explanation of the research project must include the purpose and nature of the study, the potential risks and benefits, an explanation of procedures and what is expected of the subject and for how long, and alternatives to the research. The explanation must also convey that refusal to participate in the study will not affect his/her medical care.

If the prospective subject is interested in participating in the study, the investigator will give the subject a copy of the Informed Consent Form (ICF), which must be in language understandable to them, and allow them adequate time to read it. The ICF must be a copy of the latest IRB reviewed and CO-approved version and must contain the CID stamp and be dated and initialed by CID staff.

When the prospective subject has finished reading the ICF, the investigator will return to discuss the research project and the document. The investigator will ask the prospective subject if they have any questions about the research project or the documents. The investigator will answer all of the subject’s questions.

Once all of the subject’s questions have been answered and the subject agrees to participate, the investigator will ask the subject to print their name and sign and date the ICF; a witness is not required. The investigator will make sure all items are signed and dated accurately and then print his or her name on the ICF, sign and date it in the presence of the subject. The investigator’s printed name must be legible. Each person signing the consent form must sign on the same date and in the presence of the other persons signing.

The PI or AI designated by the PI to perform consenting and named in the approved protocol, must conduct the person-to-person consenting procedure. It is not acceptable for a person not named in the protocol to perform the consenting process. It is not acceptable for the investigator to sign the consent form in the absence of the subject and/or on a different date than the subject.

If a mistake is made in signing, it should be corrected immediately by the person making the mistake. A single line should be drawn through the incorrect information and the corrected information written
next to the incorrect information. The person making the mistake should then initial and date the correction.

A copy of the ICF will be given to the subject or their representative. The original subject-signed ICF must be maintained by the investigator in a secure, private location. A copy of the subject-signed ICF is submitted to the CID Compliance Advisor at the time of the protocol’s next scheduled continuing review.

CID does not designate a particular location for the storage of subject consent forms, but leaves the identification of secure, private location to the discretion of the investigator.

Occasionally, a consent form revision will be under consideration by the IRB when a prospective subject is identified. In this situation, the PI may continue to use the existing approved, stamped consent form until the IRB has reviewed and the CO has approved the revised consent document, unless otherwise restricted by the IRB. The PI must display due diligence and be cognizant of the pending modifications impact when using a consent form which they know is under revision to enroll a subject. On the date the IRB recommends approval of the modified consent to the CO, the revised document becomes the current consent form and the prior version becomes outdated. This is true even if the newly revised consent has not yet been returned to the PI. The IRB will make a determination as to whether or not the PI may continue to use the previously approved ICF while the newly revised version is awaiting CO approval. This determination is made on a case by case basis and will take into consideration the study procedures and related risks, and it any substantive changes are present in the new version of the consent form.

It is possible that a protocol’s design will call for an alternative means of obtaining consent, such as an oral consent process for subject populations which are visually impaired or are illiterate, or consent in a group setting. Please contact the IRB for guidance in these situations as developing an alternative consent process requires special protections, such as use of a witness for oral consent or naming an Ombudsman for group consent scenarios.

**ELEMENTS OF CONSENT**

The NMCP sample consent template contains all of the following elements of informed consent:

1. A statement that the study involves research;
2. An explanation of the purpose of the research and the expected duration of the subject's participation;
3. A description of the procedures to be followed and identification of any procedures that are experimental;
4. A description of any foreseeable risks or discomforts to the subject, an estimate of their likelihood, and a description of what steps will be taken to prevent or minimize them;
5. A description of any benefits to the subject or to others that may reasonably be expected from the research. Monetary compensation is not a benefit. If compensation is to be provided to research subjects or healthy volunteers, the amount should be stated in the consent document;
6. A disclosure of any appropriate alternative procedures or courses of treatment that might be advantageous to the subject;
7. A statement describing to what extent records will be kept confidential, including a description of who may have access to research records;

8. For research involving more than minimal risk, an explanation and description of any compensation and any medical treatments that are available if research subjects are injured; where further information may be obtained, and whom to contact in the event of a research-related injury;

9. An explanation of whom to contact for answers to pertinent questions about the research and the research subject's rights; and

10. A statement that participation is voluntary and that refusal to participate or discontinuing participation at any time will involve no penalty or loss of benefits to which the subject is otherwise entitled.

When appropriate, one or more of the following elements of information should also be included in the consent form:

- If the subject is or may become pregnant, a statement that the particular treatment or procedure may involve risks, which are currently unforeseeable, to the subject or to the embryo or fetus;
- A description of circumstances in which the subject's participation may be terminated by the investigator without the subject's consent;
- Any costs to the subject that may result from participation in the research;
- What will happen if the subject decides to withdraw from the research and how withdrawal will be handled;
- A statement that the Principal Investigator will notify subjects of any significant new findings developed during the course of the study that may affect them and influence their willingness to continue participation;
- The approximate number of subjects involved in the study;
- The amount of remuneration/compensation, if any, that will be provided to subjects.
- When appropriate, a statement concerning an investigator’s potential financial or other conflict of interest in the conduct of the study.
- If the study involves the use of an FDA regulated product (such as an IND, IDE or HDE) a statement that subjects can access study information at [http://www.ClinicalTrials.gov](http://www.ClinicalTrials.gov).

The IRB will determine that in seeking consent, the regulatory criteria for the consent process have been met and the required disclosures will be provided to each participant or a legally authorized representative in accordance with the regulations.

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**WAIVER OF DOCUMENTATION OF CONSENT OR WAIVER OF INFORMED CONSENT**

A Waiver of Documentation of Informed Consent or Waiver of Informed Consent may be appropriate for some research.

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**WAIVER OF DOCUMENTATION CONSENT**

Waiver of Documentation of Consent is a means by which the IRB can release investigators from the requirement to obtain a signed consent form for some or all subjects. Examples of studies for which a Waiver of Documentation of Consent may be appropriate include research in which unintended disclosure of participation or data may cause harm to subjects (including psychological pain and embarrassment, loss of social standing, economic injury, loss of employment, potential for legal
action, loss of insurability, etc.) or studies that involve questionnaires or surveys in which completion of the instrument implies consent.

The IRB may waive documentation of consent if it finds:

- That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
- That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

Even if a waiver of documentation of consent has been granted, a consent process must still be in place. The consent process must include all the required elements and should generally take the form of an information sheet or verbal script, which must be submitted to the IRB in support of the Waiver request.

**WAIVER OR ALTERATION OF CONSENT**

Waiver or Alteration of Consent is a means by which the IRB can release the investigator from the requirement that informed consent be obtained from subjects prior to their participation in research. Examples of studies for which a Waiver of Consent may be appropriate include, but are not limited to, retrospective chart reviews or prospective research involving deception.

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

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

An IRB shall require documentation of informed consent except as follows: The IRB 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.

If the research subjects meet the DOD definition of “experimental subjects,” then a Waiver of consent may only be granted by the Assistant Secretary of Defense for Research and Engineering ASD(R&E) if all the following conditions are met:

1. The research is necessary to advance the development of a medical product for the Military Services.
2. The research may directly benefit the individual experimental subject.
3. The research is conducted in compliance with all other applicable laws and regulations.
Waiver of Consent is not permitted for research involving FDA-regulated devices, drugs or biologics.

CONSENTING IN RESEARCH INVOLVING PREGNANT WOMEN/FETUSES/NEONATES

Consent requirements for research involving pregnant women are dependent upon the distribution of risks and benefits between the pregnant woman and her fetus.

Consent from the **mother alone** is required when the research holds:

- the prospect of direct benefit to the pregnant woman, or
- 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 but 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.

Consent from the **mother and the father/partner** is required when the research holds out the prospect of direct benefit solely to the fetus.

**Consent Decision Chart for Pregnant Women and Fetuses**

<table>
<thead>
<tr>
<th>Risk is minimal</th>
<th>Direct benefit to mother only</th>
<th>Direct benefit to mother and fetus</th>
<th>Direct benefit to fetus only</th>
<th>No direct benefit or societal benefits only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother's consent</td>
<td>Mother's consent</td>
<td>Mother and father's consent*</td>
<td>Mother's consent</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk is greater than minimal</th>
<th>Direct benefit to mother only</th>
<th>Direct benefit to mother and fetus</th>
<th>Direct benefit to fetus only</th>
<th>No direct benefit or societal benefits only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother's consent</td>
<td>Mother's consent</td>
<td>Mother and father's consent*</td>
<td>NOT APPROVABLE BY LOCAL IRB</td>
<td></td>
</tr>
</tbody>
</table>

* In all consenting procedures for research involving pregnant women/fetuses, the father/partner’s consent need not be obtained if he is absent (as in cases of deployment or incarceration), incompetent, unknown or the pregnancy resulted from rape/incest.

CONSENTING IN RESEARCH INVOLVING PRISONERS

Consent procedures for research involving prisoners are challenged by the limited privacy and inherently coercive living arrangements of potential subjects.

The appropriateness of prisoner research as well as the planned procedure for obtaining informed consent from prisoners is established by the IRB during the initial and continuing approval process. In support of the regulatory requirements, investigators must ensure that:

- Consent information is presented to the prisoners in a language that is understandable to them, and
- Each prisoner is informed in advance that participation in the research will have no effect on his or her eligibility for parole.

CONSENTING IN RESEARCH INVOLVING CHILDREN

PARENTAL PERMISSION FOR MINORS

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RSPD SOP
For children less than 18 years of age, parental or guardian consent is required for their participation in research. Consent documents should be addressed to the parent and refer to “your child” throughout.

State law concerning emancipation may impact how consent and assent are approached. For example, in the State of Virginia, a pregnant minor may give consent for her newborn to participate in research, but may not consent for her own participation – consent of her parent(s) and assent of the pregnant minor would be required.

Commands under Navy Medicine East must be aware of their obligations to local state law.

**WAIVER OF PARENTAL PERMISSION**

If a research protocol is designed for a subject population for which parental or guardian permission is not a reasonable requirement to protect the child subjects, the IRB may waive consent provided that an appropriate mechanism for protecting the children who will participate is substituted for parental permission.

For a waiver to be granted, four criteria must be satisfied.

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

A waiver of parental permission is not permitted for research involving FDA-regulated devices, drugs or biologics.

**ASSENT OF THE CHILD**

Participation of children in research requires not only parental permission but also the assent of the child. A child’s failure to object to participation should not be construed as assent. Although there is no fixed age at which assent should be sought, investigators should obtain assent from children considered able to provide it. Ideally, assent should be attempted for children ages 8 through 17, depending on the subject’s level of maturity and capacity for judgment. It is assumed that children ages 0 through 7 are not capable of giving assent. The IRB and investigators should use best judgment on a case-by-case basis as to the ability of a child to assent. The assent form must contain a brief lay language description of the study (what the child is being asked to do as a participant and what risks or benefits they may incur), and a clear explanation of how they may withdraw from the study if they choose to do so. Every attempt should be made to discuss issues related to both physical risks and harms (a needlestick may be frightening and painful) as well as psychological risks and harms (questionnaire responses about drinking or sexual behavior that will be shared with a parent may result in embarrassment or punishment).

Investigators should be mindful that long-term studies may require a plan for obtaining consent from subjects who enrolled as minors and reached the age of maturity during their participation.

**WAIVER OF ASSENT OF THE CHILD**
The investigator may waive the assent of the child if he/she determines the child does not have the capacity to give assent due to the level of maturity or psychological state of the child. The reasoning behind the decision to waive assent should be documented during the consent process. If the study is to be conducted over many years, the investigator should consider if the child will gain a level of maturity during their participation which will permit assent at some time in the future.

**OVERVIEW OF ASSENT OF THE CHILD**

The physician and parents/guardians may override a child’s decision not to participate, if it is determined to be in the best interest of the child to do so, as may be the case in research involving life-threatening diseases. In such pediatric studies, the Board determines whether the override of non-assent may be appropriate. Children who are not cognitively impaired and who are fourteen years of age or older are presumed by the IRB to be capable of making their own decision regarding participation in a research study. In most cases, the decision of children ages 14 years or older should not be overridden.

**HIPAA PROTECTIONS**

HIPAA is the Health Insurance Portability and Accountability Act of 1996, a federal law that protects personal medical information and recognizes the rights to relevant information of caregivers and others directly involved in providing or paying for care.

The three main components of HIPAA are:

- Uniform standards for electronic transactions;
- Security for information transmitted;
- Privacy rights of individuals

Two goals of HIPAA are to:

- Create uniform, comparable national data on utilization, payments, epidemiological patterns, and clinical practices;
- Enable patients to control uses and disclosures of their private health information (PHI).

The IRB plays a role in the protection of privacy of research subjects. The Privacy Rule portion of HIPAA requires that patients/research subjects give authorization for the use of their private health information. The intended use of the PHI, with whom it will be shared, how it will be protected, and its disposition at the end of the study must be stated in the protocol. The authorization for the use of PHI is contained in the Privacy Act Statement in the template Informed Consent Form.

There are situations where PHI may be used without authorization from the individual. This may occur when:

- Documentation is obtained by the IRB for a Waiver of Authorization of the Use of PHI;
- Representation is made by the researcher that the PHI use or disclosure is “preparatory to research;” or
- PHI being sought is on decedents.

**WAIVER OF AUTHORIZATION FOR THE USE OF PHI**

The IRB may approve a Waiver of HIPAA authorization if it can be established that:
a. The use or disclosure of the PHI involves no more than minimal risk to the privacy of individuals based on, at least, the presence of the following elements:

1. An adequate plan to protect health information identifiers from improper use and disclosure.
2. An adequate plan to destroy identifiers at the earliest opportunity consistent with conduct of the research (absent a health or research justification for retaining them or a legal requirement to do so).
3. Adequate written assurances that the PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

b. The research could not practicably be conducted without the waiver or alteration.

c. The research could not practicably be conducted without access to and use of the PHI.

**PREPARATORY TO RESEARCH**

The Privacy Rule (Section 164.512) applies to the use of protected health information (PHI) in those activities preparatory to research that are necessary to prepare a research protocol for a grant application, for IRB review, or for similar purposes preparatory to research.

Activities preparatory to research may include:

- The development of research questions and hypotheses;
- The determination of study feasibility (in terms of the available number and eligibility of potential study participants); and
- The development of eligibility (inclusion and exclusion) criteria.

The Privacy Rule allows NMCP to use or disclose to an investigator PHI preparatory to research without authorization by the subject (patient). However, NMCP must have documentation from the investigator, either in writing or orally, that:

- The use or disclosure of the PHI is solely to prepare a research protocol or for similar purposes preparatory to research,
- The researcher will not remove any PHI from NMCP, and
- PHI for which access is sought is necessary for research purposes.

The data collected may not subsequently be used for research, but may only be used to determine if there are adequate data and subjects to conduct research. If adequate data are found, a research protocol must then be submitted to the IRB for review and approved by the CO. The data originally collected during preparation may not be used in the research, but once the protocol has been approved, the database or medical records may be revisited and data re-collected for use in research. This research protocol may include a request for a waiver of authorization for use of PHI. Alternatively, once approved, the investigator may contact potential subjects to obtain their authorization to use their PHI.

Prior to conducting a data search preparatory to research, an investigator must complete an *Activities Preparatory to Research* form and submit to the Head, RSPD by email. This notification does not require a research protocol or require scientific review. The Head, RSPD will reply to the investigator notifying them that they may or may not proceed with the data query.
RESEARCH ON DECEDENTS

The Privacy Rule allows NMCP to use or disclose to an investigator PHI of decedents without authorization from their next of kin or personal representative, a Waiver of Authorization for the Use of PHI, or a data use agreement. However, NMCP must have documentation from the researcher, either in writing or orally, that the:

- PHI is being sought solely for research on the decedents;
- PHI being sought is necessary for research; and
- Documentation of the death of decedents is provided (if requested).

Prior to conducting or collecting decedent PHI, an investigator must notify the Head, RSPD by email. Research on decedents does not require IRB review.

MINIMUM PHI NECESSARY

Researchers must not only be specific about the information that they will use or disclose, but must also limit their use or disclosure of PHI to the minimum necessary. Under the Privacy Rule, viewing or using a patient's entire record for research purposes is not permitted, unless a specific justification has been made to and approved by the IRB that all PHI contained in the record is necessary.

USE OR DISCLOSURE OF DE-IDENTIFIED INFORMATION

PHI may be used if it is stripped of the identifiers currently defined by the Privacy Rule. Once the identifiers have been removed, it is no longer considered PHI and is referred to as “de-identified” or a “Limited Data Set”.

PHI identifiers include all of the following:

1. Names
2. All geographical subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code, if according to the current publicly available data from the Bureau of the Census:
   a. The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and
   b. The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.
4. Phone numbers
5. Fax numbers
6. Electronic mail addresses
7. Social Security numbers
8. Medical record numbers
9. Health plan beneficiary numbers
10. Account numbers
11. Certificate/license numbers
12. Vehicle identifiers and serial numbers, including license plate numbers
13. Device identifiers and serial numbers
14. Web Universal Resource Locators (URLs)
15. Internet Protocol (IP) address numbers
16. Biometric identifiers, including finger and voice prints
17. Full face photographic images and any comparable images
18. Any other unique identifying number, characteristic, or code (note this does not mean the unique code assigned by the investigator to code the data)

PHI may also be used or disclosed if a knowledgeable statistician determines that the risk of identifying an individual subject from the information is “very small” and documents the methods and results used to come to that conclusion.

Psychotherapy notes (used only by a psychotherapist) are held to a higher standard of protection because they are not part of the medical record and were never intended to be shared with anyone else.

Investigators, as part of the Covered Entity NMCP, may use or disclose health information that is de-identified without restriction under HIPAA rules. The research, though, is still subject to IRB rules. Investigators seeking to use this health information must demonstrate that the information has been de-identified using either statistical verification of de-identification or by removing certain pieces of information from each record as specified in the Privacy Rule.

TRANSPORATION OF PII AND PHI

Each NMCP member (whether military, civilian, contractor, or volunteer) is responsible for protecting the personally identifiable information (PII) and protected health information (PHI) of all Department of Defense (DoD) beneficiaries and complying with federal laws such as the Privacy Act of 1974 and the HIPAA Privacy and Security Rules, implemented within the Military Health System (MHS) by appurtenant DoD Regulations including: DoD 5400.11-R, “Department of Defense Privacy Program,” DoD 6025.18-R, “DoD Health Information Privacy Regulation,” DoD 8580.02-R, “DoD Health Information Security Regulation,” and DoD Memorandum, “Encryption of Sensitive Unclassified Data at Rest on Mobile Computing Devises and Removable Storage Media”, July 3, 2007. To comply with these laws and regulations, NMCP members should apply administrative, technical and physical safeguards to ensure the confidentiality, integrity and availability of PII and PHI.

For further information regarding breach response procedures, contact the NMCP HIPAA office at 757-953-6812 (HIPAA Privacy) or 757-953-0094 (HIPAA Security).

HIPAA PROTECTIONS FOR CID ADMINISTRATIVE STAFF

1. CID staff will protect PII & PHI of patients, fellow staff members, research subject records, and committee members including, but not limited to the IRB, IACUC, and Scientific Review Committee.
2. Staff will not discuss PII & PHI unless there is a need to know.
3. Computer screens will be minimized if user is not at the screen.
4. Computers will be logged off when not in use and CAC removed
5. Paper shredders and recycling bins are located in the secure reception area for PII & PHI. Call Recycling when 2/3 full at 953-5625.
6. Social Security numbers will be blacked out on all documents that are to be faxed or mailed.

7. Faxing should be used for non-routine or urgent information. The preferred way to send confidential information is by mail. Command HIPAA FAX cover sheets should be used.

8. When mailing or guard mailing information it should be double sealed. Address both envelopes with the destination and recipient. Mark mail with “Sensitive material for recipient’s eyes only.”

9. Protect all PII & PHI with cover sheets. Information should not be left out for others to see.

10. Emails that contain PII shall be encrypted and digitally signed. Messages shall include the terms “FOUO, Privacy sensitive.”

11. Emails that contain PII shall contain a privacy act disclaimer.

12. Staff are responsible for birth month training on privacy topics at MHS learn.

13. The NMCP HIPAA Officer shall address all privacy issues, 953-6812.

14. The NMCP HIPAA Security Officer shall address security issues, 953-0094

INVESTIGATOR CONFLICT OF INTEREST

It is the responsibility of the Principal Investigator to notify the CID when a potential for Conflict of Interest (COI) exists, whether significant financial interests (entitlements to payments in connection with the research not directly related to the reasonable costs of the research) or otherwise. It is the responsibility of the IRB to ensure that any potential COI does not pose a possible risk to subjects or potential subjects involved in the study. The IRB’s concern about an investigator’s possible COI is in the impact on human subjects’ protection, specifically clinical decision-making by the investigator, the integrity of the consent process, and the integrity of the research (and thus its merit and the merit of putting subjects at risk).

In evaluating whether a researcher has a COI, the following items may be considered:

1. Is the researcher or any family member (spouse, child, domestic partner) the inventor of any item (drug, device, program, method, etc.) being evaluated in this research project?

2. Does the researcher or any family member (spouse, child, domestic partner):
   - Have any financial interest in or relationship with the sponsor of this research project?
   - Have any financial relationship with the manufacturer of the item (drug, device, program, method, etc.) being evaluated in this research project?
   - Have any other financial interest or relationship with a competitor of the sponsor of this research project that might be affected by this research project?
   - Have any other financial interest or relationship that might be affected by this research project?
   - Have any non-monetary incentives or interests that may affect or be affected by the conduct of this research project and that may affect the protection of the human subjects involved in this research project?

3. Does the arrangement with the sponsor include financial bonus payments related to speed of enrollment or any milestones?
4. Will a company in which the researcher has an interest receive materials from this research project?

5. Does the researcher plan to pay referring physicians or other persons a “finder’s fee” or present them with “gift-in-kind”?

Researchers must disclose whether they, family members, or any other person responsible for the design, conduct or reporting of the research have a conflict of interest.

When a member of the research team is identified as having a conflict of interest, the PI must submit a brief description of each conflicted person’s role on the study. This information will be evaluated by the CID and/or the IRB as to whether or not their conflict has the potential to influence the collection, analysis, or interpretation of data or impacts subject recruitment.

Strategies for the management of an actual or potential conflict of interest may include one or more of the following:

- Include a statement in the beginning of the Consent Form explaining the investigator’s relationship and interests with the sponsor.
- Monitoring of research by independent reviewers;
- Modification of the research plan;
- Disqualification of an investigator or investigators from participation in some or all portions of the research project;
- Disapproval of the study.

Where cases of conflict exist, the IRB has the final authority regarding evaluation, including any management plan, in determining whether the research can be approved and has the final authority to make a recommendation to the Commanding Officer.

IMPACT OF LOCAL STATE LAW

The NMCP IRB serves as the IRB of record for Navy Medicine East. As such, the research reviewed and approved by the IRB takes place in several states other than Virginia. For many of the states in question, there is no mention medical research within their state law. For states that do cover the conduct medical research within their Code however, an assessment of the impact of state law upon federal law must be considered on a case by case basis. Contact CID for guidance.

For research conducted in Virginia, the sections of the Code of Virginia 32.1-162.16-20 regarding human research do not apply to NMCP as NMCP is required to follow federal regulations 32 CFR 219, DODI 3216.02 and SECNAVINST 3900.39D.

PROCESS OF INITIAL PROTOCOL REVIEW

Forms and applications related to initial review of human subjects research and subsequent post-approval actions for the research are available on the NMCP SharePoint page or by request from the IRB Administrators.

AUTHORITY TO APPROVE

All protocols submitted in accordance with NAVMEDCENTPTSVAINST 6500.2G, and SECNAVINST 3900.39D are reviewed by the IRB to determine if they meet the criteria for full,
exempt or expedited review. Full Board protocols will be reviewed at a convened meeting of the IRB. Exempt and Expedited protocols will be reviewed by the IRB Chair (or Vice-Chair). If the Chair concurs with the determination that the proposal is considered Exempt or Expedited, he/she will review and, when satisfied that the criteria for approval have been met, will recommend the protocol for approval by the CO. If the CO approves, the investigator will be notified by CID to begin research. No research may begin and no data may be collected prior to CO approval. Data collected prior to IRB review and CO approval may not be used for research or publication. Investigators are advised not to collect data under process improvement criteria with the intention of later turning this into useable research data. There is no regulation that permits retroactive IRB review and CO approval.

**AUTHORITY TO DISAPPROVE**

The IRB Chair may not disapprove exempt or expedited research. Only the Full Board may disapprove research. However, the IRB Chair and IRB Administrators may advise the investigator that disapproval is likely and how to modify the protocol to obtain a recommendation to the CO for approval. Once the Chair has recommended approval to the CO, the Commanding Officer, NMCP, may approve or disapprove the research. But the Commanding Officer, NMCP, may not approve research that has been disapproved by the IRB and that has not been recommended to the Commanding Officer.

**BASIC SCIENCE**

Per NAVMEDCENPTSVAINST 6500.9A, basic science research, not involving living human beings (e.g., cadaver studies, materials testing, cell culture, histology) are classified as non-human research and do not require IRB review. Basic science research protocols do not involve living animal subjects and are not subject to IACUC review. Examples of basic science research include, but are not limited to, human cadaver research where no personal identifiers are collected or reported, animal tissue research in which no animal has been purposely killed in order to obtain the tissue, or cell culture research.

Basic science protocols must have scientific merit but will not undergo a separate scientific review, with the exception of cadaveric research.

Research on human cadavers will be sent for separate scientific review, in compliance with Navy regulations (SECNAVINST 3900.39D). Individual body parts are not considered cadavers. All cadaver research must comply with applicable state laws regulating organ donation for science or research. If the research involves direct connections, coded connections, or other links of private identifiable information between deceased and living individuals, then the protocol must be submitted to the IRB.

CID performs the review and approval of these protocols. Basic science research must be approved by the Commanding Officer before initiation and requires annual review.

Submission of a CV and Research Integrity training are required for investigators but human research ethics training, such as CITI, is not required.

**AUTHORITY TO APPROVE BASIC SCIENCE**
Basic science research is not subject to IRB or IACUC review or approval. Basic science research will be approved by Head, CID and forwarded to the Commanding Officer for final approval. Basic science projects will be reviewed annually by CID for tracking purposes, and require Amendments for protocol or personnel modifications, and submission of a Final Report to close the project at the conclusion of the research. Investigators will be notified when annual continuing reviews are due.

**ANIMAL RESEARCH**

Non-human animal research is not subject to IRB review or approval. Research with animal subjects comes under the purview of the Institutional Animal Care and Use Committee (IACUC), housed within CID. Please see the IACUC requirements for protocols using animals.

**NOT HUMAN SUBJECTS RESEARCH DETERMINATION**

**PROJECTS THAT DO NOT CONSTITUTE RESEARCH**

The Institutional Review Board (IRB) is responsible for protecting the rights and welfare of human subjects in research. As a result, the first question a researcher should consider with respect to IRB review requirements is whether the project fits the definition of research. For assistance, please see the Research Determination Decision Tree in the Appendices.

DHHS regulations define research as “systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge”.

While some activities are typically outside the realm of research (e.g., operational activities such as defined practice activities in public health and medicine, or internal management activities such as quality improvement, quality assessment and program evaluation), some of these activities may constitute research in circumstances where there is a clear intent to contribute to generalizable knowledge. Often, determining whether a project constitutes research under federal and institutional regulations can be a complex process that involves assessing the project intent, design, and dissemination of results.

**Research** intends to develop or contribute to generalizable knowledge (e.g., testing hypotheses). Investigators are motivated to conduct research because of individual professional goals and requirements (e.g., seeking promotion; obtaining grants). Research projects are designed to develop or contribute to generalizable knowledge and may involve randomization of individuals to different treatments, regimens, or processes. Intent to publish or present is generally presumed at the outset of a project as a part of professional expectations or obligations. Dissemination of the study results usually occurs in research/scientific publications or another research/scientific forum. The results are expected to develop or contribute to generalizable knowledge by filling a gap in scientific knowledge or supporting, refining, or refuting results from other research studies.

**Quality Assurance or Quality Improvement (QA/QI)** intends to assess or improve an internal practice or process within a particular institution or ensure it conforms with expected norms. Individuals are motivated to undertake the project regardless of whether or not they may benefit professionally from conducting the project. It is not designed to develop or contribute to generalizable knowledge, and generally does not involve randomization to different practices or processes. The findings of the study are expected to directly affect institutional practice and identify corrective action(s) needed. Intent to publish or present is generally not presumed at the outset of the project. Dissemination of information
often does not occur beyond the institution evaluated, but may occur in quality improvement publications. When published or presented to a wider audience, the intent is to suggest potentially effective models, strategies, assessment tools or provide benchmarks or base rates rather than to develop or contribute to generalizable knowledge.

Program Evaluation (PE) intends to improve a specific program. Individuals are often motivated to conduct the project only because it has been mandated by a funding source or as part of an operational assessment. The project is not designed to develop or contribute to generalizable knowledge and does not involve randomization of individuals, although it may involve the comparison of variations in programs. The findings of the evaluation are expected to directly affect the conduct of the program and identify improvements. Intent to publish or present is generally presumed at the outset of the project. Dissemination of information back to the program stakeholders and participants is expected. When published or presented to a wider audience, the intent is to suggest potentially effective models, strategies, assessment tools or provide benchmarks or base rates rather than to develop or contribute to generalizable knowledge.

If there are no plans to generalize a QA/QI or PE project and the sole intent is to evaluate or improve a process or function within a program or institution, IRB review is most likely not required. However, even if the PI believes that a project does not constitute research, the IRB must determine that the project does not fall under their oversight. This determination will be made by the IRB Chair, Vice-Chair, or designee and communicated in writing to the PI.

RESEARCH NOT INVOLVING HUMAN SUBJECTS

DHHS regulations define human subject as “a living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual, or identifiable private information”.

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

Projects involving only coded private information or human biological specimens may not constitute research involving human subjects.

Information is considered to be **coded** if:

- Identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private
information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code);

and

- A key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Research involving only coded private information or specimens does not involve human subjects if the following conditions are both met:

1. The private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals

and

2. The investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
   - The key to decipher the code is destroyed before the research begins;
   - The investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased;
   - There are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
   - There are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

Depending on the study design, it may be appropriate to engage an Honest Broker to maintain the key. An Honest Broker is a neutral intermediary who collects and collates pertinent information regarding the data source, replaces identifiers with a code, and releases only coded information to the researcher. An Honest Broker may not be affiliated with the project, but may, for example, be a member of the medical records office who performs the query and provides a de-identified data set to the investigator.

Projects involving coded private information or human biological specimens may be determined to not be research involving human subjects, and therefore, not subject to IRB review. This determination will be made by the IRB Chair, Vice-Chair, or designee and the determination will communicated in writing to the PI.

The FDA has separate definitions for what constitutes research. If the project includes use of a drug, device or biologic, it may be subject to FDA regulations and require IRB review even if it would not appear to meet the criteria for human subjects research under the DHHS regulations.

Per DODI 3216.02, the following activities are NOT research involving human subjects:
   - Activities carried out solely for purposes of diagnosis, treatment, or prevention of injury and disease in Service members and other mission essential personnel under
force health protection programs of the Department of Defense, including health
surveillance pursuant to section 1074f of Reference (g) and the use of medical
products consistent with DoD Instruction 6200.02 (Reference (x))*.

- Authorized health and medical activities as part of the reasonable practice of medicine
  or other health professions undertaken for the sole purpose of patient treatment.
- Activities performed for the sole purpose of medical quality assurance consistent with
  section 1102 of Reference (g) and DoDI 6025.13 (Reference (y)).
- Activities performed solely for an OT&E project where the activities and project meet
  the definition of OT&E as defined in section 139(a)(2)(A) of Reference (g).
- Activities performed solely for assessing compliance of individuals and organizations
  with requirements applicable to military, civilian, or contractor personnel or to
  organizational units, including such activities as occupational drug testing,
  occupational health and safety reviews, network monitoring, and monitoring for
  compliance with requirements for protection of classified information.
- Activities, including program evaluation, customer satisfaction surveys, user surveys,
  outcome reviews, and other methods, designed solely to assess the performance of
  DoD programs where the results of the evaluation are only for the use of Government
  officials responsible for the operation or oversight of the program being evaluated and
  are not intended for generalized use beyond such program.
- Survey, interview, or surveillance activities and related analyses performed solely for
  authorized foreign intelligence collection purposes, as authorized by DoDI 5240.01
  (Reference (z)).

* Reference (g): Sections 139(a)(2)(A), 980, 1074f, and 1102 of title 10, United States Code
  o Reference (x): DoD Instruction 6200.02, “Application of FDA Rules to Department of
    Defense Force Health Protection Program,” 27 Feb 08Reference (y):
  o DoD Instruction 6025.13, “Medical Quality Assurance (MQA) and Clinical Quality
    Management in the Military Health System (MHS),” 17 Feb 11Reference (z):
  o DoD Directive 5240.01, “DoD Intelligence Activities,” 27 Aug 07

CASE REPORTS OF UP TO TWO PATIENTS

Case reports of one or two patients do not fit the DOD definition of research, are not considered
research, and do not require IRB review or approval. One or two patients are not sufficient numbers
for minimal systematic evaluation nor for statistical analysis. Informed consent is not required by IRB
regulations for case reports of one or two patients. However, case report journals often require
informed consent from patients in order to publish. A patient informed consent form for this purpose
(different from a research subject consent form) can be found on the CID SharePoint page.

CASE REPORTS OF THREE OR MORE PATIENTS

Case reports involving a retrospective review of three or more patients with similar symptoms
planned for a single publication are considered research and must be approved by the IRB process.
This is because three cases begin to meet the Navy definition of research – a “systematic investigation
designed to develop or contribute to generalized knowledge.” Considerations of risk and informed
consent apply.

SPONSORED PROTOCOL REQUIREMENTS
Sponsored protocols (e.g., NCI) are required to include local context considerations along with submission of the approved sponsored protocol documents. The local context considerations are identified and reported to the IRB by the NMCP Principal Investigators via annual and study-specific Worksheets. Local context considerations for the NMCP include, but are not limited to, state and local laws, conflict of interest policies, boilerplate language for inclusion in the consent document, and any other institutional requirements. Additional local context considerations include, but are not limited to, resources available to support research, extent of existing research responsibilities, informed consent process information, including descriptions of vulnerable populations eligible for enrollment and safeguards used to protect those populations. Privacy and confidentiality protections, in addition to any unique study-specific considerations, are also reviewed by the IRB as part of local context.

Sponsored protocols are exempt from completing the literature review section at the time of continuing review.

Investigators will have the responsibility to report to the NMCP IRB any potential unanticipated problems or serious or continuing noncompliance.

Investigators will have the responsibility to notify CID at least 30 days in advance of an external audit and must submit external audits/monitoring reports to CID within 10 days after receipt.

**COMMAND APPROVAL OF EXTRAMURAL RESEARCH**

Some research that occurs at NMCP is conducted under the purview of an extramural IRB. An IRB agreement (i.e., IAIR or IIA) must in place before NMCP can be an approved site for extramural research protocols. Extramural research of this nature is subject to the requirement for CO approval for all initial and post-approval actions described in SECNAVINST 3900.39D. Investigators must complete the CID form for Command Approval of Review Conducted by the Extramural IRB and submit documentation of the reviewing IRB’s approval of the action, approval of as NMCP as a research site, and approval of local items (such as consent forms or recruitment materials to be used at NMCP, as well as approval of NMCP investigators). The Command Approval of Review Conducted by the Extramural IRB form can be found on the CID SharePoint page or by email request to the Head, RSPD. Upon receipt, the Head, RSPD will package the action for presentation to the CO. When CO signature is obtained, the Head, RSPD will communicate the approval to the Investigator via email.

If the local NMCP site or local protocol documentation is part of an external audit, investigators will have the responsibility to notify CID at least 30 days in advance of a protocol audit and must submit a copy of the external audit/monitoring reports to CID within 10 days after receipt.

**PROCESS FOR REVIEW OF HUMAN SUBJECTS RESEARCH**

Please see the flow chart describing the process for the initial review of human subjects research in Appendix C.

**SCIENTIFIC REVIEW**

Prior to IRB review, each protocol will undergo scientific review by persons at NMCP who possess demonstrated experience in medicine and research. Scientific review is conducted separately from IRB review to allow the IRB to focus on human subject protections issues rather than on study design and
scientific validity. CITI training or the equivalent will be required of scientific reviewers and must be renewed every three years.

If a protocol is eligible for exempt or expedited review, it will be distributed electronically to subject matter experts per the Scientific Review Committee Electronic (SRCE) process. If a protocol will be reviewed by the Full Board, it will be distributed to the Scientific Review Committee (SRC) for consideration. If the level of review required for a protocol changes during the IRB process (for example, expedited review becomes Full Board review) the Scientific Editor, Scientific Review Committee Chair, or IRB Chair/Vice Chair may, at their discretion, either accept the existing scientific review determination or require that the protocol receive an additional scientific review along the alternate review path.

COMPOSITION OF THE SCIENTIFIC REVIEW COMMITTEE (SRC)

The SRC will be composed of at least five members, including senior scientists from NMCP and the CID staff biostatistician. Members will be selected who are experts qualified by knowledge, experience, and training to review human subjects research protocols for scientific merit, study design, feasibility, and methodology. The minimum membership consists of the SRC Chair, two clinicians qualified by training and experience to participate in the scientific review process and a biostatistician. The membership will reflect a balance of scientific and clinical expertise. Quorum for a committee meeting is three voting members, but a larger, broader committee may be required to review complex protocols and to share the burden of primary review.

NMCP Department Heads will be asked to nominate qualified individuals to serve as voting committee members on the SRC. If selected, it is the responsibility of the Department Chair to ensure that their personnel actively and effectively participate in the SRC process. Department Chairs are encouraged to make effective service a performance review criteria. It is important that professional staff regard this as an honor to be nominated and as a performance requirement to serve.

The SRC will utilize additional Subject Matter Experts (SMEs) who will participate as needed for the review of complex, specialized research projects. These individuals can be internal or external. There is no restriction on their employment status. They will not be voting members. The SRC Chair will coordinate with CID when SMEs are needed to review a research project.

The CID Head will designate an SRC Administrator who will be the administrative contact for the SRC process.

SCIENTIFIC REVIEW COMMITTEE PROCEDURES

SCIENTIFIC REVIEW - EXEMPT AND EXPEDITED REVIEW PROCESS

Exempt and expedited protocols will be reviewed by the Scientific Review Committee Electronic process. The SRCE will be composed of persons from NME and surrounding academic communities who possess demonstrated experience in medicine and research. CITI training or the equivalent will be requested of scientific reviewers. SRCE members will be contacted by email by the Scientific Review Committee Editor and will provide reviews electronically. Reviewers will receive the research plan, data collection sheets, and reviewer checklist (Appendix E).
Two to three reviews will be sought: two from within the applicant's department or specialty and one from outside their department. All reviews need to be rated as “acceptable” to be forwarded to the IRB.

Reviewers will be contacted and are expected to complete reviews within one week. If a review is not returned within that time period, a subsequent reviewer will be found to conduct the review.

Based upon the scientific reviews the SRC Editor will decide if the protocol can go forward to the IRB or should be returned to the PI for revision.

If the protocol is returned for revision, the investigator will be asked to highlight the protocol revisions in yellow and to respond to each of the reviewer’s comments by describing the action taken or the basis for not taking a recommended action. The SRC Editor will judge if investigator’s response satisfies the scientific reviewer’s questions. If it does, then that scientific review is deemed “acceptable”. If it does not, then the Editor may return the protocol to the Investigator for additional information or forward back to the Scientific Reviewer for additional comment.

When the scientific review is complete, the SRC Administrator will share copies of the anonymous Scientific Reviewer checklists with the PI. These checklists, as well as any reviewers’ comments, investigator’s itemized reply, and revised materials will be included for IRB consideration.

A flow chart of scientific review for SRCE is located in Appendix D.

SCIENTIFIC REVIEW - FULL BOARD REVIEW PROCESS

The committee will meet up to once per month or as needed, to be determined by the SRC Chair and Editor.

The submission pathway is primarily an administrative issue. Proposals are submitted through CID as defined below.

The CID office will forward the proposal package to the SRC Administrator and the Editor if it is deemed in need of SRC review and if the package is sufficiently complete. A package is considered sufficiently complete if it includes the completed research plan, a sponsor’s protocol and/or Investigator’s Brochure (when appropriate), the, all data collection forms, and any external reviews.

- Review by the SRC may be waived if the proposal has received an external scientific review. The decision to waive will be made by the SRC Editor.
- Packages will be distributed to the SRC and assigned to Members for review in consultation with the Chair. The Scientific Reviewer Form will be provided to the SRC reviewers to facilitate their evaluation of the project.

The Chair will manage the style of the scientific review. The committee meetings are conducted live and the investigator or his/her designated representative who is knowledgeable about the protocol may attend in person or by telephone.

The SRC may convene by electronic means, but in only rare instances should scientific review be conducted without direct, live communication. An example might be multi center trials where written
documentation of prior scientific review is not available. In this case the protocol is distributed and following review, approved electronically.

Two primary reviewers will be assigned to each protocol. The Scientific Reviewer Forms will be used and will become part of the protocol record. The SRC will decide which revisions are required and which are simply recommended.

A third review of each protocol will be provided by the Biostatistician.

The SRC Administrator will draft minutes of the SRC meeting, summarizing the protocol review. The minutes should state whether the proposal is approved, approved with revisions, requires resubmission after modifications, or is disapproved. The basis for these judgments will be clearly outlined for the investigator. Vague guidance, such as “background section is incomplete”, and requirements for non-substantive changes will be avoided.

- Modifications will be classified as required or recommended. The SRC Administrator incorporates comments from the entire SRC into the required/suggested changes, maintaining anonymity of each reviewer, although an SRC reviewer may contact the principal investigator directly for information if they wish. Typographical and grammatical errors are generally listed separately from scientific revisions. Required modifications must be addressed by the Investigator, although sometimes the response may be a thorough explanation of why the modification is not in the best interests of the research.
- Human subjects protection issues are not the purpose of scientific review. However, experienced reviewers may point out issues that are likely to be of concern to the IRB for the investigator to consider.

Investigators must include comments in a cover letter or email addressing their response to requested or recommended modifications. It is particularly important that the PI justify their decision to decline making a change.

The SRC will decide whether the requested revisions must return to the convened committee, may be reviewed outside of the full committee by the primary reviewers, or may be accepted by the SRC Chair or the SRC Editor. Review of the revisions must ensure that the modifications completely and effectively address the concerns raised at the initial review. Any additional changes should be reviewed for scientific integrity. Either the primary reviewers, the Chair, or the Editor may direct revisions back to the convened SRC at their discretion.

The SRC Administrator will provide the IRB Administrator with the revised protocol and scientific review materials.

**SCIENTIFIC REVIEW OF AMENDMENTS**

1. The CID staff, in consultation the IRB Chair/Vice Chair and the SRC Chair will evaluate protocol amendments to determine if they substantively impact the science of a protocol. If so, the amendment may be reviewed for scientific validity.
2. The SRC Chair will assess the amendment and determine if it should be evaluated by full or expedited SRC review. The SRC Administrator will manage the amendment through the SRC
review process as for a new protocol and will forward approved amendments to the IRB Administrator.

IRB REVIEW

Each submitted protocol will undergo administrative and human subjects’ protection review by the IRB Administrator. When complete, the protocol will go to the IRB.

To ensure an effective review by the IRB, a full description of the planned research (i.e., a research plan or protocol) must be submitted with the Initial Review Application. The research plan/protocol provides the reader with background information of the problem under study, including the study rationale, a detailed plan for conducting the research involving human research participants, a discussion of the potential importance of the research, and a bibliography for the background section and research plan.

When the investigator is conducting sponsored multi-center research (such as through COG, NRG, or a pharmaceutical sponsor), both the full sponsored protocol and a Local Context for Sponsored Research (LCSP) form must be submitted. The LCSP documents ways in which local conduct of the research differs from that described in the sponsored protocol (if at all), and describes how the project will be undertaken at NMCP, including recruitment, consenting, adverse event reporting, and significance to Navy medicine. The bibliography within the sponsored protocol satisfies the requirement for a background section literature search.

For initial review of research by a convened IRB, application materials include:

- The IRB Application,
- The full protocol/research plan and/or a LCSP containing the relevant information to determine whether the proposed research fulfills the regulatory criteria for approval, including any protocol modifications previously approved by the IRB,
- Request for Waiver of Authorization for the Use of PHI (if applicable)
- Proposed consent document(s) or request for Waiver of Consent,
- Recruitment materials (flyers, announcements, text of recruitment emails),
- CV and documentation of CITI and Research Integrity training for PI and Associate Investigators, and
- Supplemental materials, such as an agreement (CRADA, MOU, etc.), Investigator Brochure, drug package inserts, data collection tools (case report forms, data spreadsheets, questionnaires, subject diaries, etc.) subject ID key, and letters of support.

Please note that the following items are not required, but are considered best practice:

- A visual representation of the timing for recruitment and screening procedures which lead to the consent process be included in the research plan (as a diagram, flow chart, or table),
- A proposed Delegation of Duties Log explaining the role for each member of the Research Team. The PI should, for example, identify some AIs as able to perform consent, but assign different responsibilities, be they clinical, regulatory, or administrative, to others. Awareness of the duties each member of the Research Team will perform allows the IRB to adequately assess the qualifications of Research Team
members and provides insight into the logistical details of how the protocol will be undertaken.

One to two designated reviewers are assigned, each receiving all the materials submitted in support of the application and a reviewer checklist which becomes part of the record. IRB members not assigned as designated reviewers also receive the application supporting materials.

Designated reviewers are assigned by the IRB Administrator who identifies the member as having the appropriate scientific expertise to conduct an in-depth review of the protocol. If the research involves participants likely to be vulnerable to coercion or undue influence, the IRB Administrator ensures that at least one IRB member knowledgeable about or experienced in working with such participants is present at the meeting. Should this personnel requirement not be satisfied, the protocol is tabled to a later agenda.

**SPECIAL AREAS OF CONSIDERATION DURING INITIAL REVIEW**

The Belmont Report’s principle of Respect for Persons, incorporates at least two ethical convictions. First, individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The concept of autonomy can be broken down into mental capacity, or the ability to understand and process information, and voluntariness, or freedom from the control or influence of others. Therefore, subjects have full autonomy when they have the capacity to understand and process information, and the freedom to volunteer for research without coercion or undue influence from others. When a subject has limitations on either capacity or voluntariness, then the subject is vulnerable. Examples of subjects with a lack of capacity are children and individuals with progressive dementia that is not reversible. Examples of subjects with a potential lack of voluntariness are subjects in emergency situations, subjects in hierarchical social structures, subjects who are economically or educationally disadvantaged, subjects who are marginalized in society, or subjects with fatal or incurable diseases.

During Initial Review, the Board takes special care in consideration of vulnerable populations to be enrolled in research at NMCP. In the IRB Application and Research Plan, investigators are required to identify if their population is *categorically vulnerable* (such as newborns, minors, pregnant women/fetuses, and decisionally impaired persons) or if they are *potentially vulnerable* due to the hierarchical structure of the Navy (such as military [active duty], civilian [dependents, retirees] or both.

Review of the documents to be used for recruitment and the consent process are also scrutinized to be sure they are accessible to the population to be enrolled and are free from coercive elements. The Board considers if the consent/assent process, as described in the submission materials, is satisfactory for women and their partner or the father of their unborn child, in the case of research involving pregnant women or fetuses; minors and their parents or guardians, in the case of research involving children; and adults of diminished capacity and their caregivers, in the case of research involving decisionally impaired persons. Copies of the checklists for vulnerable populations used by the Board to review protocols are located in Appendix H.
For more information on the ethical conduct of research in vulnerable populations, please see the Office for Human Research Protections (OHRP) website at www.hhs.gov/ohrp or the Collaborative Institutional Training Initiative (CITI) website at www.citiprogram.org.

COMMUNICATION WITH THE INVESTIGATOR

After a meeting, the IRB Administrator communicates the substance of the Board’s review to the investigator via email.

- The decision to recommend CO approval, disapprove or require modifications to secure a recommendation for approval.
- A detailed summary of any modifications or clarifications required by the IRB as a condition for the IRB to recommend approval.
- If an IRB decides to disapprove a research activity, a statement of the reasons for its decision and giving the investigator an opportunity to respond in person or in writing.
- If changes are requested, the investigator is told if the modifications may be returned to the Chair for review or if the changes must be presented back to the Full Board. The dates for upcoming meeting agendas are provided to the investigator to help facilitate timely resubmission.
- A response to the IRB’s request for changes is expected within six months of investigator receipt. If the IRB Administrator does not receive the investigator response or see evidence of any progress towards resolution of the changes, the protocol will be presented to the Head, CID for Administrative Withdrawal.

When both IRB recommendation for approval and completion of an associated agreement, such as a CRADA or MOU, etc. (if any) are documented, the study is forwarded to the CO.

- The IRB Administrator will notify the investigator via email that their materials have been sent to the CO for approval. Investigators are reminded that they may not initiate research until command approval has been granted.
- Investigators are instructed that they may begin their research once command approval has been received in CID. In this communication, the IRB Administrator provides the investigator with a formal letter of approval and announces that the study may be initiated upon receipt of the email.

Throughout the life of a study, IRB Administrators will contact investigators via email to notify them of both expedited and Full Board actions related to their protocol.

Such communications include, but are not limited to:

- notice of upcoming continuing review
- notice of requirements for securing a recommendation for approval of continuation as dictated by expedited reviewer or by the full committee
- notice of continuation approval
- notice of requirements for securing a recommendation for approval of an amendment as dictated by expedited reviewer or by the full committee
- notice of amendment approval
- notice of requirements for securing acceptance of serious adverse event reports as dictated by expedited reviewer or by the full committee
• notice of acceptance of serious adverse event reports
• notice of requirements for securing acceptance of an acknowledge receipt only report as dictated by expedited reviewer or by the full committee
• notice of acceptance of an acknowledge receipt only report
• notice of the need for updated CITI training for investigators on study (as appropriate)
• notice of requirements for securing a recommendation for approval of a final report as dictated by expedited reviewer or by the full committee
• notice of final report approval

The IRB Administrator also distributes expedited and Full Board approved study materials to the PI and an additional research team member, if applicable, such as a Research or Regulatory Coordinator.

PROCEDURES/REQUIREMENTS FOR EXEMPT AND EXPEDITED REVIEW

EXEMPT

In research protocols where human subjects incur minimal risk and no informed consent is required, such studies may be considered “exempt” based upon 32 CFR 219.101 (b).

Examples of this type of research include retrospective chart reviews, use of removed tissue or fluids, or non-invasive diagnostic procedures, so long as no patient identifiers are included in the data collected and no temporary or permanent list of subjects is compiled.

Investigators may view identifiers while reviewing data (often approved with a Waiver of Authorization for the Use of PHI), but may not record identifiers.

| Category | Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular or special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods. |
| Category 2 | Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) the information is recorded in such a manner that the subjects can be identified, directly or through identifiers; and (ii) disclosure of the subject's responses places them at risk of civil or criminal liability or is damaging to their financial standing, employability, or reputation. |

Please note that Exempt Category 2 is not approvable in pediatric populations.

| Category 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 2 of this section if: (i) the human subjects are elected or appointed officials or candidates for public office; or (ii) Federal statute(s) require(s) without exception that confidentiality of the personally identifiable information be maintained throughout the research and thereafter. |

| Category 4 | Research involving the collection or study of existing data, documents, records, |
pathological specimens, if these sources are publicly available or if the information is recorded so that subjects cannot be identified, directly or through identifiers.

Please note that Exempt Category 4 involves research on existing data only.
* “Existing data” is defined by the regulations as data that exists before the study is proposed to an institutional official or to an IRB. NMCP defines this date as the date of initial submission.
* Documentation of existing data to be collected should be identified in the protocol as “data collected for this study is limited to data, documents, records, or pathological specimens, [in existence prior to DATE] OR [existing between DATE and DATE].

| Category 5 | Research and demonstration projects which are conducted by or subject to the approval of Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:  
(i) Public benefit or service programs;  
(ii) procedures for obtaining benefits or services under those programs;  
(iii) possible changes in or alternatives to those programs or procedures; or  
(iv) possible changes in methods or levels of payment for benefits or services under those programs. |
|---|---|
| Category 6 | Taste and food quality evaluation and consumer acceptance studies,  
(i) if wholesome foods without additives are consumed; or  
(ii) if a food is consumed that contains a food ingredient at or below the level and for use found to be safe, by the FDA or approved Environmental Protection Agency or the Food Safety and Inspection Service of the Department of Agriculture. |

To request an exempt initial review, the investigator must submit an Exempt Human Research Application Form, complete with Research Plan, CV, CItI, and Research Integrity training documentation for the PI and Associate Investigators, and supplemental documents such as a request for Waiver of Authorization for the Use of PHI, data collection tools, subject questionnaires, or letters of support.

If a request for changes is made by the IRB at any time during the review process, the response is expected within six months of investigator receipt. If the IRB Administrator does not receive the investigator response or see evidence of any progress towards resolution of the changes, the protocol will be presented to the Head, CID for Administrative Withdrawal.

Reviewers make use of a checklist to assist with the determination that a protocol meets the 32 CFR 219.111 criteria for approval, and that the research is approvable under one or more exempt categories. Reviewers also receive checklists associated with the regulatory criteria for approving research in vulnerable populations (pregnant women/fetuses, prisoners, and children) as appropriate.

**EXPEDITED**

Research that involves only minimal risk to human subjects and is listed in one or more categories by the OHRP may be considered for expedited review. Expedited research must include informed consent unless a waiver is requested and approved by the IRB.

Examples of expedited research include acquisition of tissue or body fluids, non-invasive, and minimal risk diagnostic procedures. Retrospective and prospective chart reviews may be conducted on data not originally collected for research purposes.
<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Category 1</strong></td>
<td>Clinical studies of drugs and medical devices only when condition (a) or (b) is met.</td>
</tr>
<tr>
<td>a.</td>
<td>Research on drugs for which an investigational new drug application (21CFR 312) is not required.</td>
</tr>
<tr>
<td>b.</td>
<td>Research on medical devices for which</td>
</tr>
<tr>
<td>(i)</td>
<td>an investigational device exemption application (21CFR 812) is not required; or</td>
</tr>
<tr>
<td>(ii)</td>
<td>the medical device is being used in accordance with its cleared/approved labeling.</td>
</tr>
<tr>
<td><strong>Category 2</strong></td>
<td>Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:</td>
</tr>
<tr>
<td>a.</td>
<td>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</td>
</tr>
<tr>
<td>b.</td>
<td>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.</td>
</tr>
<tr>
<td><strong>Category 3</strong></td>
<td>Prospective collection of biological specimens for research purposes by noninvasive means.</td>
</tr>
<tr>
<td>Examples:</td>
<td></td>
</tr>
<tr>
<td>(a)</td>
<td>hair and nail clippings in nondisfiguring manner;</td>
</tr>
<tr>
<td>(b)</td>
<td>deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;</td>
</tr>
<tr>
<td>(c)</td>
<td>permanent teeth if routine patient care indicates a need for extraction;</td>
</tr>
<tr>
<td>(d)</td>
<td>excreta and external secretions (including sweat);</td>
</tr>
<tr>
<td>(e)</td>
<td>uncanulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying dilute citric solution to the tongue;</td>
</tr>
<tr>
<td>(f)</td>
<td>placenta removed at delivery;</td>
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<tr>
<td>(g)</td>
<td>amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;</td>
</tr>
<tr>
<td>(h)</td>
<td>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;</td>
</tr>
<tr>
<td>(i)</td>
<td>mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;</td>
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<tr>
<td>(j)</td>
<td>sputum collected after saline mist nebulization.</td>
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<tr>
<td><strong>Category 4</strong></td>
<td>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.)</td>
</tr>
<tr>
<td>Examples:</td>
<td></td>
</tr>
<tr>
<td>(a)</td>
<td>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</td>
</tr>
<tr>
<td>Category 5</td>
<td>Research involving materials (data, documents, records, or specimens) that have previously been collected* for any purpose, provided the materials were not collected for the currently proposed research.**</td>
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* Please note that Expedited Category 5 includes materials “that have previously been collected”.

  ✓ Data “that has been collected” is defined as “existing data”, which is defined by the regulations as data that exists before the study is proposed to an institutional official or to an IRB. NMCP defines this date as the date of initial submission.

  ✓ Documentation of existing data to be collected should be identified in the protocol as “data collected for this study is limited to data, documents, records, or pathological specimens, [in existence prior to DATE] OR [existing between DATE and DATE].

** DoDI 3216.02, dated 08 Nov 11, alters the 45 CFR 46 language for Expedited Category 5 from “materials that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis)” to “materials that have previously been collected for any purpose, provided the materials were not collected for the currently proposed research.”

Per DON HRPP guidance 11 Mar 15, the DoDI 3216.02 does not limit or expand Expedited Category 5 as listed in the Federal Register (60364-60367 of 09 Nov 98). Projects using prospective data can continue to be reviewed and approved under Expedited Category 5, as long as this category continues to be appropriate for the study.

<table>
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<tr>
<th>Category 6</th>
<th>Collection of data from voice, video, digital, or image recordings made for research purposes.</th>
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</table>

| Category 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. |

To request an expedited initial review, the investigator must submit an Expedited Human Research Application Form, complete with Research Plan, consent document(s) or request for Waiver of Consent, CV, CITI, and Research Integrity training documentation for the PI and Associate Investigators, and supplemental documents such as requests for Waiver of Authorization for the Use of PHI, a data collection tool, subject questionnaire, or letter of support.
If a request for changes is made by the IRB at any time during the review process, the response is expected within six months of investigator receipt. If the IRB Administrator does not receive the investigator response or see evidence of any progress towards resolution of the changes, the protocol will be presented to the Head, CID for Administrative Withdrawal.

Reviewers make use of a checklist to assist with the determination that a protocol meets the 32 CFR 219.111 criteria for approval and that the research is approvable under one or more expedited categories. Reviewers also receive checklists associated with the regulatory criteria for approving research in vulnerable populations (pregnant women/fetuses, prisoners, and children) as appropriate.

CHART OR RECORDS REVIEW RESEARCH

Chart or records review research is a protocol design frequently undertaken at NMCP. It is generally eligible for review and approval under Exempt Category 4 or Expedited Category 5.

<table>
<thead>
<tr>
<th>Exempt Category 4</th>
<th>Research involving the collection or study of existing data, documents, records, pathological specimens, if these sources are publicly available or if the information is recorded so that subjects cannot be identified, directly or through identifiers.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expedited Category 5</td>
<td>Research involving materials (data, documents, records, or specimens) that have previously been collected for any purpose, provided the materials were not collected for the currently proposed research.</td>
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</table>

An application tailored to chart review or records review protocols is available on the CID SharePoint page. Specific information relevant to the selection, collection, manipulation, and storage of records data research is requested.

APPROVALS

Once all requirements have been satisfied, the IRB Administrator presents the study to the IRB Chair for signature. If the project has an agreement associated with it (such as CRADA, MOU, etc.), the IRB Administrator must receive evidence that the agreement process is complete before the study may be forwarded to the Commanding Officer with a recommendation for approval. No research may begin until this final approval is given.

The Commanding Officer may overrule a recommended approval by the Board, if in his/her judgment s/he regards such research as inappropriate for conduct within NMCP. However, neither the Commanding Officer, DON HRPP, nor any other higher echelon of command, may overrule an IRB’s recommendation for disapproval, nor may a higher echelon of command remove any of the safeguards put in place by the IRB.

CO signed documents are returned to the IRB Administrator for final packaging prior to submission to DON HRPP by RSPD. The IRB Administrator then distributes approved study materials to the PI and an additional research team member, if applicable, such as a Research or Regulatory Coordinator.

If the study is being conducted at an extramural command (such as NHCL, NHJX, or NHPC), the RSPD will provide the IRB reviewed materials for electronic presentation to the extramural command CO for approval. Upon receipt, signed documents will be returned to the RSPD for final packaging prior to
submission to DON HRPP. The IRB Administrator then distributes approved study materials to the PI and an additional research team member, if applicable, such as a Research or Regulatory Coordinator.

The expiration date of a protocol is calculated as a maximum of 364 days from the date of IRB review and recommended approval.

For studies requiring Full Board review, the expiration date is calculated as follows.
- If approval is recommended as submitted, the expiration date is calculated from the date of the meeting at which the Board voted to recommend approval.
- If changes are required to secure a recommendation for approval and the investigator’s response may receive expedited review by the IRB Chair or Vice-Chair, then the expiration date is calculated from the date of the Chair’s signature on the application form.
- If changes are required to secure a recommendation for approval and the investigator’s response requires Full Board review, then the expiration date is calculated from the date of the meeting at which the changes are reviewed.

For studies qualifying for Exempt or Expedited review, the expiration date is calculated from the date of the Chair or Vice Chair recommendation for approval, which is documented by their signature on the application form.

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<thead>
<tr>
<th>Timing of Recommendation for Approval</th>
<th>Expiration Date Calculated from</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Full Board protocol recommended as submitted</td>
<td>Date of meeting</td>
</tr>
<tr>
<td>New Full Board protocol recommended pending changes which may receive expedited review by the Chair</td>
<td>Date of Chair signature on application</td>
</tr>
</tbody>
</table>
| New Full Board protocol recommended pending changes which require consideration by the convened Board  
  • Revisions recommended as submitted  
  • Revisions recommended pending changes which may receive expedited review by the Chair | Date of meeting when changes are reviewed  
  Date of Chair signature on application |
| New Exempt/Expedited protocol recommendation | Date of Chair signature on application |

Study records include the date of the convened meeting (if applicable), date of Chair recommendation for approval, and date of CO approval to document the movement of the protocol approval process up the chain of command.

At the time of initial approval of a research project, the IRB specifies the duration of the approval period and the interval after which continuing review must occur (e.g., 4 months, 6 months, or 1 year) in order for the research to continue. In addition to specifying a time interval, the IRB may also specify a subject enrollment number as a threshold for determining when continuing review should occur. For example, at the time of initial review and approval of a high-risk clinical trial, the IRB might require that continuing review occur either in 6 months or after 5 subjects have enrolled, whichever occurs first. Duration of approval may be shortened from 364 days at the discretion of the IRB, but may not be lengthened beyond 364 days. Protocols fall out of compliance the day following their expiration date.
ACTIVITIES PERMITTED IN AN APPROVED ACTIVE STUDY

An active research project is one that has current CO approval. The following activities are permitted.

- **Preliminary activities:**
  - advertisement
  - recording of identifiable private information for research purposes

- **Interaction or intervention with research participants or potential research participants:**
  - recruitment
  - enrollment
  - protocol-directed intervention or interaction
  - notification of subjects concerning their randomization status or study results
  - participant follow-up

- **Use of identifiable private information (PHI or PII) for research purposes:**
  - data analysis involving medical records or research data containing PHI or PII
  - data transmission of PHI or PII
  - data transmission of de-identified data
  - preparation of a study publication
  - internal or external audit
  - Post Approval Monitoring (PAM) conducted by the Research Compliance Advisor who is a staff member of CID

PROCESS FOR REVIEW OF POST-APPROVAL ACTIONS

Please see the flow chart describing the process for the review of post-approval actions in Appendix G.

ACTIONS TO BE REVIEWED BY THE IRB FOLLOWING INITIAL APPROVAL

CONTINUING REVIEW

A periodic report (continuing review) is required of all active protocols. Reviews of ongoing research studies will be conducted at annual intervals or at intervals determined by the IRB at the time of approval of the protocol.

The IRB determines the frequency of continuing review for each research project necessary to ensure the continued protection of the rights and welfare of research subjects. More frequent review (i.e., more frequently than once per year) may be appropriate, for example, when the risks to subjects warrants more frequent reassessment. When deciding on an appropriate interval for continuing review, the IRB examines:

- The nature of any risks posed by the research project;
- The degree of uncertainty regarding the risks involved;
- The vulnerability of the subject population;
- The experience of the investigators in conducting research;
- The IRB’s previous experience with the investigators (e.g., compliance history, previous problems with the investigator obtaining informed consent, or prior complaints from subjects about the investigator);
- The projected rate of enrollment; and
• Whether the research project involves novel interventions.

Duration of approval may be shortened from 364 days at the discretion of the IRB, but may not be lengthened beyond 364 days.

To perform a thorough continuing review, the IRB considers:
• Whether the approved protocol (including amended versions) is being followed.
• Whether any unapproved modifications have been implemented.
• Whether all additions or deletions of investigators have been reported and approved.
• If investigational agents are used, whether the investigators filed FDA-1572.
• Whether any adverse or unexpected reactions occurred.
• Whether the approved consent document is being used.
• Whether the appropriate procedures for obtaining informed consent are being used.
• Whether copies of the signed informed consent document are being filed appropriately.
• Whether there is expected direct benefit to the subjects enrolled in this project.
• Whether the benefits of the study continue to outweigh the risks.
• Whether all safeguards that were initially implemented by the IRB are still adequate and in place.
• Any significant new findings that have arisen from the review process and that may be related to participants’ willingness to continue participation are provided to participants.
• If subject or record accrual is proceeding as expected. This is assessed by examining whether or not there have been unanticipated challenges to enrollment or if a large number of subjects are being withdrawn or lost to follow-up.

The IRB may determine that a project needs verification from sources other than the investigators (e.g., compliance assist visit) that no material changes have occurred since previous IRB review. The requirement for an independent study audit may be driven by:
• random selection of protocols;
• complex studies involving unusual levels or types of risk to subjects;
• projects conducted by investigators who previously have failed to comply with the regulatory requirements or procedures established by the IRB; and
• studies where concern about possible material changes occurring without IRB review have been raised based upon information provided in the continuing review report or from other sources.

EVALUATION OF CONTINUING REVIEW

The IRB determines if a continuing review submission requires full (convened) board or expedited review.

Full (convened) board studies
Continuing reviews of studies that were originally approved by the full (convened) board may be scheduled for Full Board review if:
• the project continues to pose greater than minimal risks to subjects
• subjects were active during the period of review, or
- the study has an IND or IDE number associated with it.

Exempt and Expedited studies
Continuing reviews of studies that were originally approved under an exempt or expedited category may receive expedited review if the risks to subjects remain minimal. The IRB must determine that the protocol:
- Continues to be approvable under an exempt or expedited category of research.
- Continues to meets the 32 CFR 219.111 regulatory criteria for approval

Reviewers may not disapprove continuation of a study, but should present their review to the Full Board for determination.

A study originally approved by the full (convened) board may qualify for expedited review under Expedited Category 8 or 9.

<table>
<thead>
<tr>
<th>Category 8</th>
<th>Continuing review of research previously approved by the IRB at a convened meeting as follows:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a. Where</td>
</tr>
<tr>
<td></td>
<td>(i) the research is permanently closed to the enrollment of new subjects;</td>
</tr>
<tr>
<td></td>
<td>(ii) all subjects have completed all research-related interventions; and</td>
</tr>
<tr>
<td></td>
<td>(iii) the research remains active only for long-term follow-up of subjects; OR</td>
</tr>
<tr>
<td></td>
<td>Where no subjects have been enrolled and no additional risks have been identified; OR</td>
</tr>
<tr>
<td></td>
<td>where the remaining research activities are limited to data analysis.</td>
</tr>
</tbody>
</table>

Under expedited review Category 8a “long-term follow-up” includes research interactions that involve minimal risk to subjects (such as quality of life surveys) and the collection of follow-up data from procedures or interventions that would have been performed as part of routine clinical practice to monitor a subject for disease progression or recurrence.

With respect to Category 8b, “no subjects have been enrolled” is interpreted to mean that no subjects have ever been enrolled at NMCP.

Under expedited review Category 8c, the IRB may conduct expedited continuing review when the only remaining research activity is the analysis of data.

<table>
<thead>
<tr>
<th>Category 9</th>
<th>Continuing review of research previously approved by the IRB at a convened meeting that meets the following conditions:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. The research is not conducted under an investigational new drug application (IND) or an investigational device exemption (IDE);</td>
</tr>
<tr>
<td></td>
<td>2. Expedited review categories (2) through (8) do not apply to the research;</td>
</tr>
<tr>
<td></td>
<td>3. The IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk to the subjects; and</td>
</tr>
<tr>
<td></td>
<td>4. No additional risks of the research have been identified</td>
</tr>
</tbody>
</table>

Expedited Category 9 allows the Board to perform expedited continuing review on minimal risk studies that required Full Board approval because they did not qualify for approval under expedited categories
1-7. An approval process can occur in this manner when a study procedure is ineligible for expedited approval (for example inclusion of x-ray, which are prohibited in Category 4, or blood draws that are of a volume or frequency higher than that permitted in Category 2). Category 9 may be used only if the research continues to involve minimal risk and there have been no additional risks identified since the initial review.

Regardless of the level of review required for continuation, reviewers make use of a checklist to assist with the determination that the study continues to meets the 32 CFR 219.111 criteria for approval. Reviewers also receive checklists associated with the regulatory criteria for approving research in vulnerable populations (pregnant women/fetuses, prisoners, and children) as appropriate. Both expedited and Full Board reviews make use of a single primary reviewer.

To request continuation, an investigator should submit a Continuing Review report and literature search, consent form(s) for continuing enrollment (if applicable) and supplemental documents, such as study progress reports, data collection tools, and questionnaires. Investigator initiated Full Board protocols require inclusion of a literature search for articles published since the most recent IRB review. The PI is expected to review the results of the search, identify relevant articles, and briefly comment upon how the new literature impacts the project. When the investigator is conducting sponsored multi-center research (such as through COG, NRG, or a pharmaceutical sponsor) which requires Full Board review, inclusion of sponsor materials such as a progress report or annual report satisfies the requirement for a literature search. Requests for continuation of an Exempt or Expedited protocol contain essentially the same materials as those sent to the Full Board, with the exception that a new literature search is not required. Copies of signed consent forms from subjects enrolled during the reporting period (if applicable) are submitted to the Research Compliance Advisor for review.

When preparing a study that involves collaboration for either expedited or Full Board continuing review, the IRB Administrator will seek evidence that agreements are in good standing. This information is important, as the Board may not feel that it is appropriate to approve continuation of a protocol or approve consent forms or recruitment materials if investigators are unable to conduct the study because an agreement is not in place. Every effort should be made to present information about the status of an agreement with the materials for review. If an agreement is not in good standing, the IRB may choose to approve Full Board continuing reviews pending documentation that an agreement is complete, or approve expedited continuing reviews but delay reporting of the action to the CO until the agreement is in place.

For continuing reviews requiring presentation to the Full Board, the expiration date is calculated from the date of the meeting. This is true even if the IRB establishes changes required to secure a recommendation for approval to continue which can be accepted by the Chair or Vice Chair through subsequent expedited review. For continuing reviews conducted by expedited review, the expiration date is calculated from the date the Chair or Vice Chair signs the continuing review report.

Per SECNAVINST 3900.39D a request for study continuation is recommended to the Commanding Officer by the IRB, but is not final until approval is obtained from the Commanding Officer. This approval is documented when the minutes in which the action is reported are signed by the CO. When a study moves past the current expiration date, all protocol activity must stop and may not resume until the CO-signed minutes are returned to CID. At that time, the IRB Administrator finalizes the continuing
review event package and distributes approved study materials to the PI and an additional research team member, if applicable, such as a Research or Regulatory Coordinator, noting that protocol activities may resume.

Consent forms approved for continued use at the time of continuing review are re-versioned to reflect the new date of IRB review (in the document footer) and new study expiration date (within the approval stamp). See Appendix F for sample approval stamps.

When a consent form is updated to a new version in conjunction with a continuing review, the new consent form becomes the current version upon signature by the IRB. Due to the requirement for CO approval of all actions prior to implementation, this sometimes results in a situation where investigators find themselves unable to access the current consent version during the period of time between IRB review and CO approval. In an attempt to minimize this delay, the NMCP IRB may permit the investigator to continue using the previously approved consent version to enroll subjects while the revised consent form associated with the continuing review awaits approval by the CO. The IRB Chair/Vice Chair or designated reviewer makes this determination at the time of review. If he/she chooses to disallow use of the previous consent, justification for this decision must be provided. Communication of the Board’s decision to permit use of a previous consent version is communicated to the investigator.

There are consequences if an investigator fails to submit a continuing review before study expiration. Although CID will provide reminders of upcoming continuing review at one hundred twenty, ninety, sixty, and thirty days prior to expiration, the responsibility of submission remains with the investigator. If Continuing Review does not take place before the expiration date of previous approval, the study will fall out of compliance. Submission of a report does not constitute a continuing review. There must be adequate time for the IRB to receive, review, and approve the report before the expiration date of the study. If the request for continuation is received prior to expiration but insufficient time is available to perform the IRB review, then the study will enter an unapproved status.

During the period of unapproved status, all interventions and interactions with current participants must stop and no recruitment activities, including enrollment, may be performed. Data collection, sharing and analysis are defined as research-related activities and are also subject to this stoppage. One exception is if the IRB finds an over-riding safety concern or ethical issue such that stopping the treatment or intervention poses a threat to the life or welfare of a subject.

If the request for continuation is not received prior to expiration, the protocol will fall out of compliance. As with studies in unapproved status, all interventions and interactions with current and potential participants must stop and no data analysis may be performed. The exception for continuing treatment or intervention to mitigate a threat to the life or welfare of a subject also applies.

Upon study expiration, the IRB Administrator will take steps to present the study to the convened IRB for Administrative Termination for Non-Compliance. Investigators are encouraged to submit Final Report materials prior to the convened meeting to avoid Administrative Termination. An investigator is welcome to submit an administratively terminated protocol back to the IRB as a new application. This should be done with the appropriate new protocol application (Exempt, Expedited or Full Board),
updated materials (literature search, instruments, data collection tools, recruitment materials, consent
forms, etc.), a description of the data the PI wishes to include from the administratively terminated study
(if any), a justification for why the IRB should permit access to these data for this new project, and a
description of any additional data that will be collected.

Access to subject records, signed consent forms, to PHI, or PII is permitted for the purpose of
completing an application to reinstate the study or final report but is not allowed for further extraction
of data. Data analysis of de-identified data is permitted for use in preparing an application for
reinstatement of the protocol, a final report, or preliminary manuscript. Publication approval will not
be given if a protocol is expired. The protocol must be officially closed and in good standing before
CID will recommend publication approval. In order to use data already collected, an expired study
must be reinstated by the IRB through approval of a new application, or by submission and approval
of a Final Report with a request for completion.

A PI may not submit a new study for consideration by the IRB while other protocols under his/her
supervision are in non-compliance.

CID is required to report evidence of continuing non-compliance to DON HRPP. The threshold for
identification of an investigator exhibiting continuing non-compliance is three occasions where he/she
does not submit a continuing review on time, or fails to submit a continuing review at all.

AMENDMENTS

A request for modification of study materials must be approved by the IRB before the change may be
implemented. Whether the changes are substantive enough to require review by the Full Board is
initially assessed by CID, but ultimately left to the discretion of the IRB Chair or Vice Chair.

In general, Full Board review will be required if any of the following changes are requested:
- Increase drug dosage or device maximum setting higher than that already approved by
  the IRB.
- Addition of a procedure (that does not qualify for expedited review) to those
  procedures already approved by the IRB.
- Increase the risk portion of the risk-benefit relationship beyond that already approved
  by the IRB.
- Increase of compensation or services provided to subjects to the degree that the Board
  must consider if the increase is coercive.
- Alteration of subject population to the degree that the IRB must consider if the change
  is equitable regarding subject selection.
- Change in the safeguards established for vulnerable populations to the degree that the
  Board must consider if the rights and welfare of subjects are adequately protected.
- Addition or subtraction of a study arm which involves the potential for increased risk
  to subjects, or requires the subject to receive new information.
- Significant alteration of study design.
- Change in PI and/or Research Monitor

If an investigator is submitting an Amendment that involves changes to a sponsored protocol, all
materials (both originating from the sponsor and from the site) must be submitted promptly to the
IRB for review. Local approval of the Amendment must be completed within a 90-day window from the date of the sponsor's release of documents.

Substantive amendments to approved research may undergo scientific review prior to presentation to the IRB if deemed appropriate (see SCIENTIFIC REVIEW OF AMENDMENTS).

If the modifications to be made are minor, the Amendment may be approved through expedited review.

Minor changes include, but are not limited to:

- The addition of an “expeditable” procedure [as described in the expedited review categories presented above].
- Deletion of a procedure which results in a reduction of risk, and does not alter the scientific objectives or validity of the protocol.
- Administrative changes.
- A reasonable increase in the number of subjects who are permitted to enroll in the study.
- Change to Associate Investigator.
- Addition of an advertisement or other subject materials if they are not coercive.
- Change in Enrollment Status (close or re-open enrollment) if the change did not result from a safety issue.

In addition, the IRB Administrators approve administrative personnel changes such as the addition or removal of an Associate Investigator, as long as no other modifications which would require consideration by the IRB Chair/Vice Chair/ or designated reviewer, are included in the Amendment request. If additional non-local personnel are added to a study through an amendment, an appropriate collaborative agreement (CRADA or MOU) must be in place or obtained prior to approval.

Regardless of the level of review required for approval of an Amendment, reviewers make use of a checklist to assist with the determination that the study continues to meets the 32 CFR 219.111 criteria for approval. Reviewers also receive checklists associated with the regulatory criteria for approving research in vulnerable populations (pregnant women/fetuses and children) as appropriate. Both expedited and Full Board review processes make use of a single primary reviewer.

To request an Amendment, an investigator should submit an Amendment form and documents with highlighting to indicate revisions. Highlighted documents may include such items as protocols, consent form(s), investigator brochures, questionnaires, or advertising. If a change in study personnel is requested, the Amendment (personnel) Supplemental form must be submitted, documenting the incoming research team member’s Human Use Assurance and Conflict of Interest statement. Current CV and documentation of CITI training for incoming personnel must be included. Materials required for expeditable amendments are the same as those required for Full Board amendments.

As with continuing reviews, when a protocol amendment has been submitted for review, the IRB Administrator will seek evidence that agreements are in good standing for collaborative protocols. If an agreement is not in good standing, the IRB may, at their discretion, approve Full Board
amendments pending documentation that an agreement is complete, or delay review of expedited amendments until agreements are in place.

Modifications requested by Amendment must receive final approval from the Commanding Officer after IRB review. This approval is documented when the minutes in which the action is reported are signed by the CO. Study changes may not be implemented until the CO-signed minutes are returned to CID. At that time, the IRB Administrator finalizes the Amendment package and distributes approved study materials to the PI and an additional point of contact (i.e., approved research team member), noting that the modifications may take effect. Investigators must be mindful of this requirement for CO approval when developing a timeline for submission of their Amendment to the IRB.

In rare situations, changes in approved research are initiated without prior IRB review to eliminate apparent immediate hazards to subjects or others. Should this occur, the investigator must report the change to the IRB within one business day. This notice must include information concerning how the investigator intends to notify active subjects to the change. If the emergent change involves the premature completion of a study, the investigator must supply justification for the early termination and a plan for notifying active subjects. Upon receipt, the IRB Chair reviews the modifications to determine whether each change was consistent with ensuring the participants’ continued welfare.

Consent forms which are modified within the scope of an amendment are re-versioned to reflect the new date of IRB review (in the document footer). The study expiration date (within the approval stamp) remains unchanged.

When a consent form is updated to a new version in conjunction with an amendment, the new consent form becomes the current version upon signature by the IRB. Due to the requirement for CO approval of all actions prior to implementation, this sometimes results in a situation where investigators find themselves unable to access the current consent version during the period of time between IRB review and CO approval. In an attempt to minimize this delay, the NMCP IRB may permit the investigator to continue using the previously approved consent version to enroll subjects while the revised consent form associated with the amendment awaits approval by the CO. The IRB Chair/Vice Chair or designated reviewer makes this determination at the time of review, and must justify why it is inappropriate to continue using the previous document, as would be the case, for example, if a new risk has been introduced, or if new information is presented which may impact the subject’s decision to continue participating in the study. Communication of the Board’s decision to permit use of a previous consent version is communicated to the investigator.

ADVERSE EVENTS

The term adverse event is defined as any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal finding in a physical exam or laboratory report), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research.

At NMCP events are categorized as Adverse Events (AEs) or Serious Adverse Events (SAEs), depending on three criteria: Seriousness, expectedness, and relatedness to the research. An SAE must include all three criteria. Events which do not meet all three criteria are identified as AEs.
SAEs and AEs each have different reporting requirements. When an investigator has doubts whether all three criteria are met they should contact CID.

THREE CRITERIA REQUIRED FOR AN SAE

- An event that is serious, e.g., when the patient outcome is:
  - Death
  - Life-threatening
  - Hospitalization (initial or prolonged)
  - Disability or Permanent Damage
  - Congenital Anomaly/Birth Defect
- An event is defined as unexpected when it was not foreseen or expected at the time of the occurrence, or is occurring at a rate that is higher than that expected.
- An event is defined as related when it is likely to have resulted from the conduct of the research. This relationship may expand beyond study procedures, drug, or device.

SAEs are not limited to physical harms. They may include psychological, societal, and financial harms as well, such as psychological pain and embarrassment, loss of social standing, economic injury, loss of employment, potential for legal action, or loss of insurability, etc.

REPORTING REQUIREMENTS AND PROCEDURES FOR LOCAL SAEs

If an investigator believes a local adverse event is an SAE, the investigator must contact CID within one business day of discovery. CID will inform the IRB Chair, or the Vice Chair in the absence of the Chair, via email and phone call. The emails will “carbon copy” the Director of Professional Education (DPE) to allow for situational awareness of the SAE. RSPD will report the event to the Commanding Officer as soon as possible after determining the event is an SAE. CID will notify DON HRPP that an SAE is under investigation and follow up by email. The Local Serious Adverse Event Form and supporting documentation must be submitted to CID within five business days and will be forwarded to the IRB for review at the next available meeting.

If the local event does not meet all three criteria for an SAE, it will be classified as an AE and will be reported to the IRB at next continuing review. At the discretion of the Chair, an AE may be brought to the Full Board at the next available meeting.

Head RSPD will facilitate these communications and will keep DPE and DON HRPP informed.

In its review of an SAE report, the Board must discuss the report, establish if it qualifies as an SAE, and determine if the event suggests an increase in risk to subjects that would require additional safeguards, subject notifications, or protocol suspension. The Board may require the investigator to notify active or completed subjects and offer guidance for continuing medical oversight as appropriate.

Local SAEs that occur in protocols which involve an IND must be reported to FDA by the sponsor of the IND. The investigator is responsible for notifying the sponsor about the event as per sponsor guidelines.
A sponsor of a research protocol may have different criteria than NMCP for defining and reporting an SAE. Reporting an event as an SAE to a sponsor does not mean that event will also meet NMCP criteria.

**REPORTING REQUIREMENTS FOR NON-LOCAL SAES**

Non-local SAEs and safety reports are reviewed by the Full Board as they are reported by the sponsor to determine if any changes are required to the protocol assigned risk level, or review cycle. The Board also decides if subjects should be notified of any new information that may impact their decision to continue participation in the study.

Reportable events include:

- Non-local SAEs and safety reports involving risks to participants or others.
- Unanticipated problems – problems that were not foreseen or expected at the time of the occurrence, or that are occurring at a rate that is higher than expected.
- Changes the protocol made without prior IRB review to eliminate an apparent immediate hazard to a research participant.
- Information from the sponsor that indicates a change to the risks or potential benefits of the research.
- Sponsor imposed suspension for risk related issues.
- An interim analysis or safety monitoring report indicating that the frequency or magnitude of harms or benefits may be different from those initially presented to the IRB.
- Protocol violations (meaning an accidental or unintentional change to the IRB reviewed protocol) that harm participants or that may increase the risk of harm.
- A publication about another study indicating that the frequency or magnitude of harms or benefits may be different from those initially presented to the IRB.
- Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.

**REPORTING REQUIREMENTS FOR LOCAL ADVERSE EVENTS**

Local Adverse Events (that clearly do not meet all three criteria for an SAE) do not have to be reported immediately to CID but should be submitted in summary form to the IRB at time of continuing review. AEs may also be reported to the IRB more frequently if required to do so by a study sponsor.

Investigators may contact CID at any time regarding the criteria for adverse events and reporting requirements, without triggering the need for a formal, immediate report.

**EXTRAMURAL COMMANDS AND REPORTABLE EVENTS**

The term “Local” will also be used to apply AEs and SAEs at extramural commands for which the NMCP IRB conducts reviews. Reporting requirements described above will apply except that reports will be made to the Commanding Officer of the extramural command rather than the Commanding Officer, NMCP. For example, extramural commands should still report local SAEs to CID within one business day. CID will contact the IRB Chair. The investigator will determine if an SAE has occurred, and, if so, CID will notify the Commanding Officer of the extramural command and DON HRPP. AEs will be reported at time of continuing review.
UNANTICIPATED PROBLEMS

Unanticipated problems (UPs) describe an array of events that may occur during the conduct of a study. They may be broadly characterized as protocol deviations, protocol violations, or serious unanticipated problems, in order of increasing severity.

PROTOCOL DEVIATION

A protocol deviation is any change, divergence, or departure from the study design or procedures of a research protocol and that has not been approved by the IRB. A protocol deviation may originate from the investigators or the subjects. The following examples of protocol deviations may be elevated to protocol violations depending on the impact upon subjects and the magnitude of the event.

Examples of protocol deviations:

- Subject study visit out of window.
- Inappropriate documentation of informed consent, including:
  - Signed and dated consent form missing from study file.
  - Signed and dated consent form is missing pages.
  - Subject signature or investigator signature is absent
  - Someone other than the subject dated the consent form
  - Copy of consent document was not given to the person signing the form
  - Use of invalid consent form, (i.e., consent form without IRB stamp, or outdated/expired consent form)
- Failure to follow the approved study procedure that does not affect subject safety or data integrity, and may include:
  - Study procedure conducted out of sequence
  - Omitting an approved portion of the protocol
  - Failure to perform a required lab test
  - Subject was asked to repeat a procedure because the specimen/sample/data was lost or damaged
  - Study visit conducted outside of required timeframe
  - Subject failed to return study medication
  - Inclusion of more subjects’ records than the number approved by the IRB.
  - Inclusion of subjects’ records outside of the data window approved by the IRB for a retrospective records review protocol.

REPORTING REQUIREMENTS FOR PROTOCOL DEVIATIONS

Events identified as protocol deviations may be submitted upon discovery, at the discretion of the PI, using the Protocol Deviation/Violation Reporting form. If a PI elects NOT to report an event upon discovery, then it must be it must be reported and summarized at the time of continuing review using Appendix B within the Continuing Review Report. Protocol Deviations identified during the course of a Compliance Assist Visit should be submitted upon discovery.

Protocol deviations will be reviewed by the IRB Chair to determine if any changes are required to the protocol, assigned risk level, or review cycle, or if subjects should be notified of any new information that may impact the their decision to continue participation in the study. The Chair may refer protocol deviations to the Full Board or may report them as expedited actions at the next IRB meeting.
PROTOCOL VIOLATIONS

A protocol violation is a deviation from the approved protocol that may affect the subject's rights, safety, or well-being and/or the completeness, accuracy and reliability of the study data.

Please note that events which are unexpected, related to the protocol, and place the subject or others at risk of harm may be categorized as UPIRTSOs and have escalated reporting requirements. Please contact CID for guidance.

Examples of protocol violations:
- Wrong medication given to subject
- Drug/study medication dispensing or dosing error
- Enrollment of a subject not meeting all inclusion/exclusion criteria
- Study procedures initiated before informed consent was obtained
- Enrollment of subjects after approval of a study has expired
- Enrolling more subjects than the number approved for participation in a prospective intervention study.
- Implementation of unapproved recruitment procedures or materials
- Performing study procedures which have not been approved
- Failure to report serious adverse events to the IRB and/or sponsor
- Failure to follow data/safety monitoring plan
- Loss or theft of data or breach of data security

REPORTING REQUIREMENTS FOR PROTOCOL VIOLATIONS

CID must be notified of a protocol violation by telephone or email within five business days of discovery. Relevant documents and materials must be submitted to the IRB within five business days of notification to CID using the Protocol Deviation/Violation Reporting form.

Protocol violations will be reviewed by the IRB Chair to determine if any changes are required to the protocol, assigned risk level, or review cycle, or if subjects should be notified of any new information that may impact the their decision to continue participation in the study. The Chair may refer protocol violations to the Full Board or may report them as expedited actions at the next IRB meeting.

SERIOUS UNANTICIPATED PROBLEMS (UPIRTSO)

Federal and DOD regulations [32 CFR 219.103(b)(5) and 21CFR56.108(b)(1); DODINST 3216.02] require the IRB to ensure that investigators promptly report “any unanticipated problems involving risk to subjects or others” (UPIRTSO). A UPIRTSO is a serious unanticipated problem and is defined by meeting all three of the following criteria:

1. It is unexpected (in terms of nature, severity, or frequency) given the procedures described in the research protocol documents (e.g., the approved research protocol and informed consent document) and the characteristics of the human subject population being studied.
2. It is related or possibly related to participation in the research (in this Instruction, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research).

3. The problem may place the subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized, even if no harm has actually occurred.

UPIRTSOS may include any of the above protocol deviations or violations if the three criteria are also met.

If an investigator believes a local unanticipated problem is an UPIRTSO the investigator must contact CID within one business day of discovery. CID will inform, via email and phone call, the IRB Chair, or the Vice Chair in the absence of the Chair. The emails will “carbon copy” the Director of Professional Education (DPE) to allow for situational awareness of the UPIRTSO. The IRB Chair will discuss the event with the PI and consult with others if necessary to determine if it is in fact an UPIRTSO. If the IRB Chair and the PI agree the event was a UPIRTSO, the IRB Chair will report the event to the Commanding Officer as soon as possible and not later one business day after learning of the event. CID will notify DON HRPP that an UPIRTSO is under investigation and follow up by email. The Local Serious Unanticipated Problem Form and supporting documentation must be submitted to CID within five business days of the PI and IRB Chair’s decision and will be forwarded to the IRB for review at the next available meeting.

In case the IRB Chair and the PI disagree, the Chair has the authority to make the final decision on classification of the unanticipated problem.

If the event does not meet all three criteria for an UPIRTSO, it will be classified as an unanticipated problem and will be reported to the IRB at next continuing review. At the discretion of the Chair, the unanticipated problem may be brought to the Full Board at the next available meeting.

Head RSPD will facilitate these communications and will keep DPE and DON HRPP informed.

In its review of an UPIRTSO, the Board must discuss the report, establish if it qualifies as an UPIRTSO, and determine if the problems suggest an increase in risk to subjects that would require additional safeguards, subject notifications, or protocol suspension. The Board may require the investigator to notify active or completed subjects and offer guidance for continuing medical oversight as appropriate.

REPORTING REQUIREMENTS FOR LOCAL UNANTICIPATED PROBLEMS

Local unanticipated problems that clearly do not meet all three criteria for an UPIRTSO do not have to be reported immediately to CID but should be submitted in summary form to the IRB at time of continuing review. Unanticipated problems may also be reported to the IRB more frequently if required to do so by a study sponsor.

Investigators may contact CID at any time regarding the criteria for adverse events and reporting requirements, without triggering the need for a formal, immediate report.

EXTRAMURAL COMMANDS, UNANTICIPATED PROBLEMS AND UPIRTSOS.
The term “Local” will also be used to apply unanticipated problems and UPIRTSOs at extramural commands for which the NMCP IRB conducts reviews. Reporting requirements described above will apply except that reports will be made to the Commanding Officer of the extramural command rather than the Commanding Officer, NMCP. For example, UPIRTSOs should be reported to CID within one business day. CID will contact the IRB Chair. The Chair and investigator will determine if an UPIRTSO has occurred, and, if so, the Commanding Officer of the extramural command and DON HRPP will be notified. Unanticipated problems will be reported at time of continuing review.

**FINAL REPORTS**

Final reports must be submitted to the IRB to properly end the research project. A final report may be submitted to request either **Completion** or **Closure without Completion**. Final reports of protocols initially reviewed by the Full Board, which do not qualify for expedited continuing review, will be presented to the Board for consideration at a convened meeting. Final reports for protocols reviewed through the exempt or expedited process, and those Full Board studies which qualify for expedited continuing review under Category 8 or 9, are presented to the Chair for expedited review.

**REQUEST FOR COMPLETION**

An investigator may request completion of their study if all study procedures have concluded. For this to be appropriate, subjects’ active participation and follow up must have ended and no further contact with subjects may occur. There may be no further access to subject records, consent forms, coded lists that can be used to identify subjects, or to data containing PHI or PII. All data collection from medical records or hospital databases must be complete, and no actions may be outstanding in the IRB (such as amendments or adverse events). The investigator may continue to access the collected data for data analysis and manuscript creation, but may not re-enter medical records or hospital databases for purposes of additional data collection. Submission of signed consent forms to the Compliance Advisor is required at time of study closure. Following approval of the Final Report by the IRB and the CO, the investigator is no longer obligated to report to the IRB and the project is not considered to be an active research protocol. The Navy remains the owner of the data and data sharing agreements, such as CRADAs, may still apply. Manuscripts must receive publication approval from the Command Publication Officer at NMCP. Investigators changing to another command should follow that command’s publication requirements. Authorship is at the discretion of the investigators. To request completion, the investigator should submit a Final Report, indicating the intent to complete, and any manuscripts, presentations, abstracts, or summary of findings which have been developed.

**REQUEST FOR CLOSURE-WITHOUT COMPLETION**

An investigator may request closure without completion of their study if the protocol needs to be abandoned for reasons such as lack of progress; lack of enrollment; failure to meet power for statistical analysis, lack of personnel to conduct the study (due to PCS for example) or discovery in the literature that a similar study has been completed elsewhere and continuation would produce no additional, useful results. There may be no further contact with subjects or access to subject records, consent forms, coded lists that can be used to identify subjects, or to data containing PHI or PII. Data collected under a protocol that is closed without completion may not be published and the assigned IRB number may not be used on an application requesting publication approval. Data analysis of de-identified data is permitted for use in preparing a new protocol only. The protocol plan may be shared for the purpose of preparing a new protocol. All study materials, including those contained within a regulatory binder, collected data, and signed consent forms, must be sent to the Compliance Advisor.
in CID and may not be retained by the PI and/or his/her department. CID prefers that these documents be sent to the Compliance Advisor as a PDF, either emailed or saved to a shared drive. An attestation that all original documents have been destroyed must accompany the PDF. Upon receipt, the Compliance Advisor will forward the items for archiving.

To request closure without completion, the investigator should submit a Final Report, indicating the intent to close. The report should include the number of subjects/records enrolled and a summary of the activity that occurred during the final reporting period. The IRB may require the investigator to notify active or completed subjects of the early closure and provide information on the cause of the closure or offer guidance for continuing medical oversight as appropriate.

### TERMINATION OR ADMINISTRATIVE TERMINATION FOR NON-COMPLIANCE

Termination is the closure of a protocol that is generally done by the IRB for cause and must be reported to DON HRPP (SECNAVINST 3900.39D). Studies which expire without submission of a continuing review or a final report are presented to the IRB for administrative termination for non-compliance. The PI and Department Head will receive notice of the IRB’s decision to administratively terminate a protocol for non-compliance via email.

Data collected under a protocol that is terminated or administratively terminated for non-compliance may not be published and all identifiable data and links to subjects must be destroyed. All study materials, including those contained within a regulatory binder, collected data, and signed consent forms, must be sent to the Compliance Advisor in CID and may not be retained by the PI and/or his/her department. CID prefers that these documents be sent to the Compliance Advisor as a PDF, either emailed or saved to a shared drive. An attestation that all original documents have been destroyed must accompany the PDF. Upon receipt, the Compliance Advisor will forward the items for archiving.

A PI may not submit a new study for consideration by the IRB while other protocols under his/her supervision are in non-compliance.

### SUSPENSION AND TERMINATION BY EXTERNAL BODIES

If a protocol is suspended, terminated, or closed to enrollment for cause by a sponsor or lead institution in a multicenter trial, then the investigator must contact CID immediately and plan to submit a report to be presented to the IRB at the next available meeting. CID will contact the IRB Chair to determine if additional actions should be taken. The investigator provides the IRB with an explanation of the action, report on the ongoing treatment of subjects (on or off study), plans for notifying subjects, arrangements for medical care, transferring care, and withdrawal of subjects, if necessary.

Suspension refers to halting research for immediate protection of subjects who may be at risk resulting from, for example, serious adverse events, protocol violations, or scientific misconduct and Termination refers to closing a research project for the same purposes.

Although the terms “suspension” and “termination” both refer to serious actions, they may be used differently by sponsors and the IRB. The IRB will evaluate the use of these terms in correspondence.
from sponsors or lead institutions in a multicenter trial and make their decisions and report accordingly.

CID will notify the Commanding Officer and DON HRPP of suspensions for cause by an external body within five (5) days of receiving notice from the investigator.

**NON-COMPLIANCE AND SCIENTIFIC MISCONDUCT**

Non-compliance is failure to follow the regulations or the requirements and determinations of the IRBs. Serious non-compliance is intentional or unintentional violation of the protocol increasing subject risk. This includes violations to the requirements of and determinations of the IRB. Continuing non-compliance is repetition of same or similar behavior following advice from the IRB, CID, or others involved in the research.

If an investigator does not abide by the federal regulations (such as failure to complete continuing reviews, protocol deviations, and improper consenting) the IRB may be called upon to suspend or terminate approval of the research not being conducted in accordance with the IRB’s requirements or that had been associated with unexpected serious harm to participants. Continuing non-compliance by investigators requires escalating notification of next in chain of command, *e.g.*, Department Heads, Directors. All suspensions are reported to the Director of Professional Education, Executive Officer, and Commanding Officer.

Deviation from approved protocol procedures is considered non-compliance. Intentional and unintentional deviations are reported by the principal investigator to the Head, CID. Head, CID contacts the IRB Chair (or Vice Chair) and may ask for a temporary suspension while the situation is evaluated and until all parties can be contacted. The Chair may order a complete or partial suspension of activities, keeping risk to subjects foremost.

Improper consenting procedures are non-compliance and may call for a suspension by the Head, CID or the IRB Chair or Vice Chair. Such a suspension will halt all further consenting of new subjects and may also postpone other research activities until the issue can be resolved.

Subject complaints about research which go unreported are defined as non-compliance and may call for a suspension by the Head, CID or the IRB Chair or Vice Chair.

Results of both internal and external audits must be submitted to the IRB. Failure to submit the results of an audit is considered non-compliance and may call for a suspension by the Head, CID or the IRB Chair or Vice Chair.

CID is responsible for reporting IRB actions to the appropriate institutional officials and to DON HRPP any serious or continuing non-compliance by investigators with the requirements and the determinations of the Board.

Resolution of non-compliance by the IRB may depend upon many factors. The IRB may require re-education of all investigators, re-evaluation of the protocol and/or submission of an amendment to modify procedures that may no longer be practical, re-consent of all active subjects, observation of the consent process and the conduct of the research by the Board or by a third party, or permanent
discontinuation of the research. These examples are not intended to be exhaustive and the Board must be flexible in determining the best corrective action plan for each non-compliance event.

In the event that there is reasonable suspicion that a researcher is engaged in unethical or improper behavior, the following actions may be taken that may eventually lead to charges of scientific misconduct:

- All protocols conducted by the researcher should be immediately suspended and study records from affected protocols impounded.
- The Head, CID will investigate scientific misconduct according to NAVMEDPTSVAINST 6500.10.

**PUBLICATION APPROVAL**

Investigators are encouraged to publish or present “authored works” from studies which are successfully completed, but publication approval must be obtained prior to distribution. Per NAVMEDCENPTSVAINST. 5720.46A, an authored work is defined as any written document or oral presentation prepared in the author’s professional capacity and intended to be published to the general public. An authored work also includes any written document or oral presentation prepared in the author’s personal capacity that contains information that may adversely affect national security, threaten the safety or privacy of US Government personnel or their families, violate the privacy of citizens of the US, or be contrary to law. This includes any authored work that is to be transmitted via internet (blog, podcast, twitter, etc.), mass broadcast, and mass email are subject to publication approval.

An investigator may prepare an authored work before or after closing the associated study with the IRB, but may not re-enter medical records or hospital databases for purposes of additional data collection after protocol closure.

From time to time, an investigator leaves NMCP for another command during the course of their research. When this occurs and the project is ongoing, a new NMCP PI should be named and the study transitioned to the new leadership before the location change occurs. If the study has been closed, then the departing PI may take copies of the de-identified data with them to their new location, but PHI and PII may not leave the originating command. Publication approval for authored works will be granted by the command where the investigator is located at the time of publication. An investigator who separates from the Navy may also take copies of de-identified data with them for future publication under the same restrictions. Similarly, if a researcher arrives at NMCP with de-identified data from a research project completed elsewhere, publication approval will be granted by NMCP pending verification of previous IRB review. In both situations, the required manuscript text (usually in the methods section) and ethics oversight statement will indicate where the research was conducted.

To request publication approval, a Request for Publication Approval (RPPA) form must be submitted to CID a minimum of two weeks before the journal or conference deadline. Approval must be obtained prior to publication, presentation, or commitment to a conference.

**DISPOSITION OF STUDY MATERIALS/DATA RETENTION**
The DHHS protection of human subjects regulations require institutions to retain records of IRB activities and certain other records frequently held by investigators for at least three years after completion of the research (45 CFR 46.115(b)). IRB related materials should be disposed of per Navy instruction at the conclusion of the three years.

All identifiable data including data collection tools, case report forms, source documents, signed consent forms must remain at the initial study site. Regulatory documents and/or regulatory binder should remain at initial study site.

All study materials and documentation must remain at the initial study site in a secure, locked location 3 years following the closure of the study according to research regulations; 6 years for HIPAA; and for any additional period of time as required by a study sponsor or department record retention policy.

Primary data analysis should occur while the study is open and under IRB oversight. De-identified, aggregate form data ONLY may be re-analyzed after study closure. Once a study is closed, investigators may not go back to the identifiable data unless they request and are approved to re-open the study through the IRB.

**PROTOCOLS REQUIRING OVERSIGHT BY THE FDA**

**USE OF INVESTIGATIONAL TEST ARTICLES**

An Investigational New Drug Application (IND) is a request for authorization from the FDA to administer an investigational drug or biological product to humans. Together, the investigator and the IRB will determine if the proposed protocol requires an IND.

**DETERMINING IF AN IND IS NEEDED**

To determine if an IND is needed for a given protocol, an investigator should consider if human subjects will receive an unapproved drug or if human subjects will receive an approved drug for an unapproved use.

The FDA has set specific requirements for making an IND application. Forms required for application include:

- Form FDA 1571: The Investigational New Drug Application Form
- Form FDA 3674: Certification of Compliance
- Form FDA 1572: Statement of Investigator Form
- Cover Letter
- Study Protocol describing the methodology to be used and an analysis of the protocol demonstrating its scientific soundness.
- Monitoring Plan which will verify that:
  - The rights and well-being of human subjects are protected.
  - The reported trial data are accurate, complete, and verifiable from source documents.
  - The conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s).
• Case Report forms used to collect data for your research

When submitting an application, the Commanding Officer of NMCP is identified as the sponsor of that IND, unless there is an existing IND held by another sponsor. The Head, CID will manage the IND and make the 1571 submission on behalf of the Commanding Officer.

CID will provide guidance to investigators when submitting an IND application to FDA.

Alternatively, if another entity (such as a drug company) already holds an IND for the drug or device which is consistent with the proposed research, the investigator may approach the company about conducting the protocol under their IND. Documentation of a valid IND/IDE number should be provided to the IRB with the protocol submission. When participating in industry sponsored IND/IDE research, the sponsor should supply the investigator with the Investigational Drug Clinical Information Brochure (IDCI) for IND studies or the manufacturer’s brochure for IDE studies. All significant side effects described in the brochure must be represented within the protocol and consent documents submitted for IRB review.

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### IND APPLICATION APPROVAL PROCESS

In general, the FDA will respond within 30 days of submission with an acknowledgement letter and an IND number.

This means that the IND has been successfully filed, however, the clinical investigation cannot start until 30 days after the IND has been received by the FDA, unless earlier notification by FDA is received, stating, that the studies may begin.

After sending this acknowledgment of receipt, the FDA may respond in one of two ways.

- The FDA may request additional information and may place clinical holds on the study or research. The study cannot begin until all concerns raised by the FDA have been responded to satisfaction.
- The FDA may conclude that the project is exempt. An exemption means that the study or research may be conducted without filing an IND application.

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### IND POST APPROVAL

After approval of an IND, the Sponsor and Investigator are still subject to conditions set forth by the FDA.

The FDA has set responsibilities for the sponsor/investigator of clinical trials:

- Conduct the study according to the most current approved protocol.
- Clinical monitoring must be conducted by a qualified individual and monitoring must be documented.
- Obtain informed consent
- The study protocol must be followed and if a change is made in the protocol, a protocol amendment must be sent to and approved by the FDA.
- Adverse events must be reported to the FDA.
- Annual progress reports must be sent to the FDA.
- Maintain adequate record keeping of drug disposition.
• Maintain adequate data collection forms/case report forms
• Maintain adequate safety reports.
• Label all drug products with an investigational drug label.

If NMCP is the sponsor of an IND, annual reports will be prepared and submitted to the FDA by CID. CID will request summary information for this report from the investigator.

OFF LABEL USE

Good medical practice and the best interests of patients require that physicians use legally available drugs, biologics and devices according to their best knowledge and judgment. If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the product's use and effects. Use of a marketed product in this manner when the intent is the "practice of medicine" does not require the submission of an Investigational IND, IDE or review by an IRB. Physicians who are considering employing this process are encouraged to contact CID to ensure that their plans are consistent with this guidance as there may be other factors that would call for a different procedure. Note that off label use is similar to compassionate use, described below, except that off label use involves a marketed drug or device, while compassionate use procedures are for unapproved drugs and devices. Compassionate use requires IRB review.

INVESTIGATIONAL USE OF APPROVED MARKETED PRODUCTS

The investigational use of approved, marketed products differs from the situation described above. "Investigational use" suggests the use of an approved product in the context of a clinical study protocol. When the principal intent of the investigational use of a test article is to develop information about the product's safety or efficacy, submission of an IND or IDE may be required.

However, the clinical investigation of a marketed drug or biologic does not require submission of an IND if all six of the following conditions are met:

• it is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the drug;
• it is not intended to support a significant change in the advertising for the product;
• it does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
• it is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively];
• it is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7]; and
• it does not intend to invoke 21 CFR 50.24.

To conduct a clinical investigation of a marketed drug or biologic without submission of an IND, the PI must provide justification of these six criteria to the IRB, who will determine the appropriateness of the request.

ABBREVIATED INVESTIGATIONAL DEVICE EXEMPTION (IDE)
When research is conducted to determine the safety or effectiveness of a device, the investigator and study protocol should document that:

- The device has an IDE issued by the FDA;
- The device fulfills the requirements for an abbreviated IDE.
  - The device is not a banned device.
  - The sponsor labels the device in accordance with 21 CFR §812.5.
  - The sponsor obtains approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval.
  - The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator’s care, consent under 21 CFR §50 and documents it, unless documentation is waived.
  - The sponsor complies with the requirements of 21 CFR §812.46 with respect to monitoring investigations;
  - The sponsor maintains the records required under 21 CFR §812.140(b) (4) and (5) and makes the reports required under 21 CFR §812.150(b) (1) through (3) and (5) through (10);
  - The sponsor ensures that participating investigators maintain the records required by 21 CFR §812.140(a)(3)(i) and make the reports required under §812.150(a) (1), (2), (5), and (7); and
  - The sponsor complies with the prohibitions in 21 CFR §812.7 against promotion and other practices.
- The device fulfills one of the IDE exemption categories:
  - A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.
  - A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.
  - A diagnostic device, if the sponsor complies with applicable requirements in 21 CFR §809.10(c) and if the testing:
    - Is noninvasive.
    - Does not require an invasive sampling procedure that presents significant risk.
    - Does not by design or intention introduce energy into a participant.
    - Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
  - A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put participants at risk.
A custom device as defined in 21 CFR §812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

The investigator should include documentation of the sponsor’s assigned risk determination (significant risk or non-significant risk). The IRB will concur with the risk determination or request review by the FDA if they disagree with the sponsor’s assessment.

CID will monitor command responsibilities regarding local sponsorship of an investigational drug/device to include liability. The possibility of the transfer of the investigator must be addressed with due regard to the responsibility for subject follow-up and record-keeping requirements. It is important to identify where subject records are maintained and who will be named PI to continue the study after the departure of the established PI.

PLANNED RESEARCH IN EMERGENCY SETTINGS

Planned research in emergency settings is a planned protocol conducted in life-threatening, emergent situations where the requirement to obtain prospective informed consent has been waived by the IRB. The investigational plan for Emergency Research must be approved in advance by the FDA and the IRB and publicly disclosed to the community in which the research study will be conducted.

The IRB with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation finds and documents each of the following:

- The research activity is subject to regulations codified by the Food and Drug Administration (FDA) at Title 21 CFR part 50 and will be carried out under an FDA investigational new drug application (IND) or an FDA investigational device exemption (IDE).
- The application clearly identifies the protocols that will include participants who are unable to consent.
- The research participants are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which might include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
- Obtaining consent is not feasible because:
  - The participants will not be able to give their consent as a result of their medical condition.
  - The intervention under investigation must be administered before consent from the participants’ legally authorized representatives is feasible.
  - There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
- Participation in the research holds out the prospect of direct benefit to the participants because:
  - Participants are facing a life-threatening situation that necessitates intervention.
  - Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence supported the
potential for the intervention to provide a direct benefit to the individual participants.

- Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of participants, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

- The clinical investigation could not practicably be carried out without the waiver.

- The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each participant within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent.

- The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

- The IRB has reviewed and approved consent procedures and a consent document consistent with §50.25. These procedures and the consent document are to be used with participants or their legally authorized representatives in situations where use of such procedures and documented is feasible.

- The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a participant’s participation in the clinical investigation consistent with the paragraph below.

- Additional protections of the rights and welfare of the participants will be provided, including, at least:
  - Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the participants will be drawn.
  - Public disclosure to the communities in which the clinical investigation will be conducted and from which the participants will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits.
  - Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and investigators of the study, including the demographic characteristics of the research population, and its results.
  - Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation.
  - If obtaining consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the participant’s family member who is not a legally authorized representative, and asking whether he or she objects to the participant’s participation in the clinical investigation.
    - The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
- Procedures are in place to inform, at the earliest feasible opportunity, each participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, of the participant’s inclusion in the clinical investigation, the details of the investigation and other information contained in the consent document.

- There is a procedure to inform the participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, that he or she might discontinue the participant’s participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.

- If a legally authorized representative or family member is told about the clinical investigation and the participant’s condition improves, the participant is also to be informed as soon as feasible.

- If a participant is entered into a clinical investigation with waived consent and the participant dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the participant’s legally authorized representative or family member, if feasible.

- The protocol is performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identified such protocols as protocols that may include participants who are unable to consent.

- The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists.

- If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation.

At NMCP, investigators must incorporate consent by subjects or their legally authorized representative into their study protocol. Although the regulatory criteria for planned emergency research allows for waiver of consent, DOD does not permit exception from consent in planned emergency research unless a waiver is obtained from the Secretary of Defense. Thus, for planned emergency research to be conducted at NMCP, the Secretary of Defense must be included in the development of the protocol from the very beginning. Please contact CID for guidance in developing a protocol for planned emergency research.

**REQUIREMENTS FOR REVIEW OF SINGLE-PATIENT COMPASSIONATE USE**

Occasionally, a physician may want to request a Single Patient IND for Compassionate Use as a means of providing an unapproved drug or other product for the care of a single patient who has failed standard therapy. This request should be made for use of an unapproved drug for continuing treatment – not in a life threatening situation. Upon receiving permission from the manufacturer, the investigator must submit to the IRB. A request for Compassionate Use is placed on an agenda for review in the same manner as a Full Board initial review. Treatment of the patient may not begin until final approval of the Compassionate Use request has been granted by the IRB and Commanding Officer.
Materials to be included in a Request for Compassionate Use are:

- Letter requesting a single patient IND for Compassionate Use. Correspondence must include contact information for the requesting physician (phone, pager, fax, and email).
- Brief Clinical History of the patient including the diagnosis, the disease status, prior therapy, response to prior therapy and the rationale for requesting the proposed treatment.
- Proposed Treatment Plan including the dose, route, planned duration, monitoring procedures and modifications (e.g., dose reduction or treatment delay) for toxicity. Reference a published protocol or journal article if appropriate.
- Investigator Brochure (if available)
- Informed Consent specific to the patient to be treated. Since the Compassionate Use is not research, words such as “research” or “study” should be avoided in this consent form. Terms such as “compassionate use”, “compassionate use access clinical trial”, or “compassionate use access of [product]” are preferred.
- Investigator CV and CITI training certificates are not required, but Research Integrity training is required.
- Letter of support from an un-involved physician. The letter should state that the physician has reviewed the patient record and concurs with the decision to treat with a single patient IND for Compassionate Use.
- Drug Supply Reference Statement which would name the supplier or manufacturer and a statement that a Letter of Authorization to cross reference an appropriate IND of the supplier or Drug Master File (DMF) of the manufacturer is included. The treating physician must contact the supplier or manufacturer for such a statement.
- FDA Form 1571, which will be completed by CID on behalf of the Commanding Officer.
- FDA Form 1572, identifying the treating physician as the investigator. Form 1572 and other forms can be downloaded from the Internet.

For more information, please see the FDA website.

**REQUIREMENTS FOR REVIEW OF EMERGENCY USE**

From time to time, a patient is confronted by a disease or condition that is life threatening or severely debilitating. If this patient has failed standard therapy or no standard acceptable treatment is available, the treating physician may wish to request Emergency Use of an investigational drug or other product for which the FDA has issued an IND or IDE. In such a situation, there is not sufficient time to obtain IRB review and CO approval through the normal process. Upon receiving permission to use the test article from the manufacturer, the investigator must submit a request for Emergency Use to the IRB.

Materials to be included in a Request for Emergency Use are:

- Letter requesting Emergency Use of a test article. Correspondence must include contact information for the requesting physician (phone, pager, fax, and email).
- Brief Clinical History of the patient including diagnosis, disease status, prior therapy, response to prior therapy, and rationale for requesting the proposed treatment.
• Proposed Treatment Plan including the dose, route, planned duration, monitoring procedures and modifications (e.g., dose reduction or treatment delay) for toxicity. Reference a published protocol or journal article if appropriate.
• Investigator Brochure (if available)
• Discussion of the informed consent process. Consent must be sought from the patient or, if unable to consent for themselves, from the patient’s legally authorized representative. The consent process must include all appropriate elements of consent (purpose, procedures that are experimental, foreseeable risks and how they will be minimized, possible benefits, treatment alternatives, confidentiality, options if the patient is injured, investigator contact information, and voluntariness). The informed consent must be documented in writing.
• Investigator CV and CITI training certificate.
• Letter of support from an un-involved physician. The letter should state that the physician has reviewed the patient record and concurs with the decision to treat with a single patient IND for Emergency Use.
• Drug Supply Reference Statement which would name the supplier or manufacturer and a statement that a Letter of Authorization to cross reference an appropriate IND of the supplier or Drug Master File (DMF) of the manufacturer is included. The treating physician must contact the supplier or manufacturer for such a statement.
• FDA Form 1571, which will be completed by CID on behalf of the Commanding Officer.
• FDA Form 1572, identifying the treating physician as the investigator. Form 1572 and other forms can be downloaded from the Internet.

Requests for Emergency Use may be reviewed by the IRB Chair through expedited review. The investigator must report the Use to the IRB within five (5) business days. The notice should include a description of the apparent success or failure of the test article as well as a summary of the patient’s current condition. Follow-up reports are reviewed by the Board associated with the Chair who reviewed the Use. Any subsequent use of the test article for this indication must have IRB review and CO approval before initiating treatment.

For more information, please see the FDA website.

**HUMANITARIAN USE DEVICE EXEMPTION (HDE)**

A Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year. The Humanitarian Device Exemption (HDE) regulations permit use of such devices in patients. Although treatment under an HDE is not defined as research, the IRB is charged with oversight for these activities. A request for HDE use must receive IRB review and CO approval before the device is administered.

Requests for HDE use are presented to the Full Board for review. Continuing review may be performed through expedited review procedures unless the IRB determines that Full Board review should be performed. The Board’s decision whether to permit expedited continuing review must be documented at the time of initial review.
To submit a request for HDE use, the investigator should prepare materials similar to those that accompany a new Full Board protocol application (see the IRB Review section), but because this activity is not research, the documents will differ slightly.

Materials to be included in a Request for HDE Use are:

- NMCP IRB Full Board Application
- Investigator CV and CITI training certificates are not required.
- The device manufacturer’s product labeling, clinical brochure, and/or other pertinent manufacturer informational materials (such as a patient information booklet, etc.).
- The FDA HDE approval letter (typically obtained from the manufacturer).
- Treatment plan or device use protocol
- Informed consent (see the Elements of Consent section)
  - Because the device is approved for clinical use by the FDA, words such as “research” or “study” should be avoided in this consent form. Terms such as “device use” or “HDE activity” are preferred.
  - The consent should educate the patient about HDEs. Suggested language is: “Your medical care will involve the use of (specify device), which has been approved by the U.S. Food and Drug Administration (FDA) under an HDE. An HDE permits access to a device that is used to diagnose or treat a disease or condition that affects fewer than 4000 individuals in the US per year and for which no comparable device is available. The FDA approves a device under an HDE based primarily on evidence that it does not pose a significant risk of injury to the patient and that the potential benefit of the device to the health of the patient outweighs the risks of its use. The FDA approval is based on limited data documenting its effectiveness in humans. Its use does not involve research.”

A Request for HDE use receives the same oversight as a research protocol, including required annual continuing review and the submission of Amendments, SAEs, and a Final Report.

For more information, please see the FDA website.

RESEARCH COMPLIANCE PROGRAM OVERVIEW

MISSION

The mission of the Research Compliance Program at Naval Medical Center Portsmouth, Clinical Investigation Department (NMCP CID), is to provide guidance and oversight to Principal Investigators and research staff throughout Navy Medicine East (NME) to ensure regulatory compliance across all aspects of clinical research. This is achieved through an internal audit and evaluation process as well as continuing education.

INTRODUCTION

The following Standard Operating Procedures (SOPs) describe the policies and procedures established by the Research Compliance Program at NMCP CID. The goal of the program is to support the clinical research efforts and ethical standards of conduct of NME research by providing periodic regulatory oversight, including compliance assist visits and consent form review, as well
as continuing education and training in regard to the regulatory standards of clinical research conduct.

As required by Department of the Navy Human Research Protection Program (DON HRPP), all DON research is subject to ongoing evaluation to ensure ethical standards in clinical research practice including regulatory compliance and proper informed consent processes. At the direction of DON HRPP BUMED, NMCP CID implemented the Research Compliance Program to include post approval monitoring and internal auditing of all studies including Human Subjects Research. Compliance Assist Visits, much like internal audits, include the review and evaluation of study protocols, research plans, consent forms, data collection, source documentation, subject eligibility, and recruitment methods. Evaluation of the consent process occurs through observation of the investigator-subject consenting process. Subject signed consents are also reviewed concurrently with IRB Continuing Review submissions to ensure the current approved consent documents are being utilized and completed with accuracy. Investigators are held accountable when research is not compliant with regulatory standards and offered guidance in order to achieve compliance.

As the Research Compliance Program (RCP) falls under the NMCP Research Subjects Protections Division at CID, the following RCP policies draw from the regulatory standards referenced in Research Subjects Protection Division (RSPD) SOPs and comply with Federal Regulations including those promulgated by the DOD, DON HRPP, the Department of Health and Human Services (DHHS), and the Food and Drug Administration (FDA). Ethical standards in clinical research involving Human Subjects were established historically and draw from the guiding principles referenced in the Nuremberg Code, Belmont Report, and Declaration of Helsinki.

GOALS

Research Compliance Program Goals

- Confirm NME research is compliant with DON HRPP and NMCP IRB regulatory standards and policies through an internal audit process that includes the evaluation of the research methods and confirms regulatory compliance
- Provide continuing education for existing research activities and training for new Principal Investigators (PIs) and research team members
- Observe and evaluate investigator-subject consent processes
- Ensure investigator accountability for research activities and reporting

RESEARCH COMPLIANCE ADVISOR (RCA) ROLE

Regulatory

Evaluate research to ensure regulatory compliance

- Conduct compliance assist visits to review and evaluate documentation and research procedures following Command approval
- Audit research protocol files held by CID including archived IRB study documents
- Perform directed/for cause audits of research activities as directed by the IRB/CID/CO
• Observe consent process and documentation to ensure compliance with DON HRPP standards
• Review/audit/archive consent documentation submitted by NME sites at time of IRB Continuing Review
• Provide guidance to investigators and research staffs regarding corrective and/or preventative action plans
• Ensure investigator/research staff training is compliant with NMCP IRB and DON HRPP standards
• Manage database of compliance related activities including compliance assist visits, consent form review, and consent process observations
• Oversight of CITI and Research Integrity Training

Training

Provide ongoing education for Principal and Associate Investigators
• Schedule and facilitate specific training based on recognized deficiencies as well as current areas of interest
• Provide guidance to investigators regarding regulatory standards and IRB compliance
• Meet with new investigators to review regulatory documentation standards and IRB policies
• Conduct individual meetings and regulatory follow up as needed
• Provide written guidance and communication as appropriate
• Visit other NME sites to perform compliance assist visits and training
• Update and maintain Research Compliance Program SOPs as needed

COMPLIANCE AND EVALUATION

The Research Compliance Program includes post approval review and evaluation (internal auditing) of all studies involving Human Subjects Research at NME. All study related materials are subject to review and evaluation including research plans, consent documentation, collected data, and source documents. The program is implemented by the Research Compliance Advisor who performs periodic regulatory oversight of NME research protocols on a rotating and for cause basis. The three standard post approval monitoring methods include:
• Compliance Assist Visits
• Consent Process Observation
• Signed Consent Form Review

The RCA will meet with investigators during visits to evaluate research activities and provide guidance to researchers. Any findings from Compliance Assist Visits and Consent Process Observations will be reviewed with the PI and research team at the time of the visit and also be reported to the IRB. Based on findings, the PI and research team will be given 10 business days to take corrective action and submit appropriate documentation to the IRB including necessary Amendments, Protocol Deviations/Violations, and/or Corrective Action and Preventative Action Plans. Failure to do so may result in study suspension or termination as determined by the IRB.
The authority to require corrective action of an investigator resides with CID, the IRB, and Commanding Officer (CO).

Issues of non-compliance may also be reported by the PI or research team members to the RCA or CID in order to document regulatory issues and/or internally resolve issues of non-compliance at any time (see Non-Compliance Reporting).

NOTE: Studies undergoing external monitoring or sponsor audits are required to notify the Head, Research Subjects Protection Division at least one week in advance of the audit. Additionally, monitoring reports and/or audit results are to be submitted to the Head, RSPD within 10 business days of receipt of the final report.

**COMPLIANCE ASSIST VISIT**

Compliance assist visits are systematic independent reviews and evaluations of all study related activities and documents. All NME research studies are subject to review and compliance oversight as required by the DON. Studies are selected at random (not for cause audit) and will typically be evaluated at least once within the life of the protocol. However CID and/or the NMCP IRB may review any research study at any time as deemed necessary or for cause (directed audit).

(See Appendix I.1 to reference expectations of a Compliance Visit.)

**PROCEDURES**

**Scheduling**

- The RCA will contact the Principal Investigator to schedule a Compliance Assist Visit at least 10 business days in advance. Visits may take anywhere from 1-3 days based on the volume of data, source documentation, consent forms, and the degree of site preparation prior for the visit
- If the PI/AI does not reply to the RCA within 5 business days with availability for the visit, then the RCA will follow-up with another e-mail prior to contacting the COC.
- The RCA will then email confirmation of the agreed upon date and time of visit. This will also include the RCA’s request for a designated area and computer as well as a research team member available during the review. At this time, the RCA will send a Compliance Assist Visit checklist to the research team to use as a guide to prepare for the visit

**Visit**

- At the site visit, the RCA will first meet with the PI/AI to discuss expectations of the visit and respond to questions and concerns regarding the study
- The RCA will then review study documentation according but not limited to the Compliance Assist Visit checklist
- A Consent Process Observation will also be scheduled (if applicable)
- At the completion of the site visit, the RCA will meet with the PI and AI(s) to debrief the visit and discuss findings as well as any required corrective actions
The final report will be presented to the IRB and then archived with study materials at CID. The IRB will make any final determination based on the reported findings.

**Follow Up**
- If required, the site will submit requested corrective documents to the IRB and/or develop a Corrective and Preventative Action Plan (CAPA); all corrective actions plans along with required IRB documents (i.e., amendments, deviations, etc.) will be emailed to the RCA for review within 10 business days of the visit and prior to IRB submission.

**Reporting**
- Compliance Assist Visit findings and corrective actions will be reviewed with the IRB Chair and/or Board who may require sanctions or actions resulting from the findings.
- The RCA will inform the PI of the Chair and/or Board’s final determinations.
- The RCA final report including original Compliance Assist Visit checklist and any corrective actions will be archived as part of the protocol file.

**DOCUMENTATION FOR REVIEW**

All study related documentation is subject to review during a Compliance Assist Visit. A computer and research team member must be available to assist with review of all documentation. The following documentation should be prepared for the RCA prior to the visit as applicable:
- Initial Approval packages to include: letters of approval with Head, CID signature, Scientific Review, IRB recommendation and CO approvals, AI signatures on Human Use Assurance and Conflict of Interest Statement, Support statement with signature, Research Plan stamped with version and date of IRB recommended approval, Informed Consent stamped with version and date of IRB recommended approval, if applicable, Waiver of Consent and/or Waiver of Authorization for the Use of PHI, if applicable), and data collection tools
- Continuing Review Approvals
- Amendment Approvals
- Current Research Plan
- Associated CRADA/DSA/MOU/EPA
- Research charts/subject binders (source documents, data collection forms, eligibility/screening logs)
- Subject recruitment and accrual (subject log)
- Associated certificates if applicable (lab, radiology)
- Delegation of Duty Log
- Monitoring Log
- CITI training, Research Integrity training, and CVs
- Prior audit files
- Signed consent forms
- Database for retrospective studies
• Safety Reporting/Protocol Deviations/Protocol Violations

In addition
• A Regulatory Binder is highly recommended to organize all regulatory documentation including approval documentation, research plans/consent documents, and training certificates/CVs; file hard copies of all regulatory documents in binders with tabs (CVs and training certificates may be stored electronically if a memo in the binder references the location of the documents)
• All signed Consent Forms will be reviewed for completeness including all signatures and dates, correct consent form version and current IRB stamp, and verified against subject eligibility documentation
• Subject Eligibility will be verified against inclusion/exclusion criteria; subject screening logs including screen fails will be reviewed as well as subject ID key
• Data Collection review will be conducted to evaluate data integrity and PI accountability. Case Report Forms and other data collection forms will be reviewed against source documents. This review will ensure that all data being transcribed into data collection forms are accurate, consistent, complete, and in accordance with the study protocol
• The PI/AI should prepare source documentation (electronic or hard copy) prior to RCA visit to minimize disruption to the site during the Compliance Assist Visit and expedite the review process

CONSENT PROCESS OBSERVATION

Observation of the informed consent process will be conducted by RCA at scheduled Consent Process Observation visits and/or in conjunction with Compliance Assist Visits. The goal of these observations is to ensure the consent process is conducted in compliance with IRB and DON HRPP requirements and that required signatures are obtained in the required timeframe. (See Appendix I.2 to reference expectations of a Consent Process Observation.)

PROCEDURES
• The RCA will contact the PI/AI by email to establish a date to observe a consenting procedure; the RCA may also request a Consent Process Observation at the time of a Compliance Assist Visit
• The research team will reply by email within 5 business days to confirm date of consent process observation
• The RCA will communicate with the PI/AI by email confirming the date of consent observation and goals of the review. The RCA will provide the Consent Process Observation checklist for the PI/AI to review prior to the date of observation
• The RCA will meet with the consenting investigator at the agreed time prior to Consent Process Observation. The RCA will review the process and ask the investigator if s/he has concerns prior to proceeding. The consenting investigator will introduce the RCA to his/her potential subject prior to starting the observation process noting that the observation is an evaluation of the investigator
• Following the consent process, the RCA will review the checklist and discuss findings.
• If required, the site will submit necessary corrective documents to the IRB (such as Protocol Deviation) and/or develop a Corrective and Preventative Action Plan (CAPA); submission of any corrective actions will be emailed to the RCA within 10 business days of visit prior to being forwarded to the IRB.
• The RCA will report to the IRB the results and/or findings and corrective actions in regard to the Consent Process Observation. The IRB will determine if further action is required and the RCA will inform the PI if the IRB has subsequent final determinations.
• The RCA final report, including Consent Observation checklist and corrective actions will archived as part of the protocol.

**CONSENT FORM REVIEW**

A mandatory review of signed consent forms is conducted by the RCA at the time of Continuing Review and at study closure. Signed consent forms for the respective Continuing Review period (roughly one year) or period between last Continuing Review and closure are submitted directly to the RCA. (See Appendix I.3 for Consent Form Review checklist and Appendix I.4 for Consent Submission Process.)

Signed consents will be reviewed and audited to ensure regulatory compliance with the following requirements:

- Consent forms reflect current stamped IRB version
- All pages of consent form are present
- Subject/PI/AI signatures present
- Consenting investigator is an approved member of the research team
- All signatures reflect subject enrollment date
- Screen failed consent forms are included with submission
- Assent/Waiver of Assent signature(s) present if applicable

**Procedure for Submission**

- All signed subject consent forms (from the respective Continuing Review period or period of time between the last Continuing Review and study closure) will be submitted to the RCA via encrypted email or AMRDEC Safe (see Appendix I.4 for Consent Submission Process) concurrently with Continuing Review submission.
- Up to 10 consent documents may be scanned into one PDF and sent via encrypted email or if number of consent documents exceeds 10, use the AMRDEC Safe system to transfer documents scanning up to 10 consents in one PDF.
- Notify the RCA via email regarding your submission and include the IRB # and study title, PI, and number of total subjects enrolled (and screen failed) during the CR reporting period (approximately one year).
- Include the subject identifier log in your submission (appendix A of the Continuing Review form).
• Consent review findings will be communicated via email to the PI and presented to the IRB
• If required, the PI will submit necessary corrective actions (such as protocol deviation/note to file) and/or develop a Corrective and Preventative Action Plan (CAPA); submission of the corrective actions will be emailed to the RCA within 10 business days of the report and then submitted to the IRB
• Continuing Review approval (and new stamped consent forms) or study closure will not be released by the IRB until issues of non-compliance have been resolved
• Subject signed informed consent documents will be electronically archived by CID however the PI is accountable for maintaining all original consent documents for the duration of the study, per HIPAA and DON data retention guidelines, and in accordance with study sponsor or department requirements.

COMMONLY RECOGNIZED COMPLIANCE ISSUES WITH INFORMED CONSENT DOCUMENTATION

• Signature date inconsistent with study enrollment date; signature date occurs AFTER study related procedures
• Consenting investigator not approved on study
• Partial or incomplete documentation/consent document
• Incorrect consent version (no current IRB stamp)
• Enrollment/consent occurs during period new consent form is pending CO approval and the previous version was not approved for use
• Draft used (prior to approval)
• Pages are missing from the document submission
• Investigator dated the consent form for the subject
• Dates differ between investigator and subject
• Telephone consent conducted without prior approval
• Screen fail consent forms not submitted or accounted for on Continuing Review form

STUDY INITIATION VISIT

Principal Investigators who have not conducted research at NMCP or have not previously served in a Principal Investigator capacity at NMCP are required to meet with the RCA prior to the initiation of research. Once the study has received recommended approval by the IRB, contact the RCA to schedule a Study Initiation Visit. This visit will include a review of research practices, implementation of Regulatory Binder, proper data security methods, and consenting guidance if applicable. Associate investigators/ coordinators are highly encouraged to attend as well. Regulatory binders will be issued at these visits.

NON-COMPLIANCE REPORTING

Non-compliance is the failure to follow federal, state, or local regulations or policies governing human subjects research. This includes institutional policies related to human subjects research and determinations of the IRB. Issues of non-compliance may violate or challenge the ethical standards of research referenced in, but not limited to, the NMCP RSPD policies, SECNAV Instruction, DON HRPP regulations, and Federal Regulations including the Common Rule and FDA Standards.
compliance may result in the suspension or termination of research studies as determined by CID, the IRB, or the CO; the authority to require corrective action of a Principal Investigator resides with CID, the IRB, and the CO.

The RCA will report issues of non-compliance to CID and the IRB Chair and/or Board promptly in order to protect the integrity of NMCP research and the protection of human research subjects.

DEFINITIONS

- Allegations of non-compliance are unproven assertions or reports of non-compliance
- Non-compliance is the failure to follow federal, state, or local regulations or policies governing human subject research, institutional policies related to human subject research, or determinations of the IRB. This may pertain to the principal investigator, associate investigator, or any member of the research team

Serious/Continuing Non-Compliance

Serious non-compliance constitutes issues that increase the risk to study subjects. These issues may adversely affects the rights, welfare, and safety of the research subjects or adversely affect the scientific integrity of the study. Willful violation of policies and/or federal regulations may also constitute serious non-compliance. Continuing non-compliance is a pattern of non-compliance and may also constitute serious non-compliance.

REPORTING ALLEGATIONS OF NON-COMPLIANCE

Investigators and research team members are encouraged to report any potential, suspected, observed, or apparent non-compliance to the RCA, Head, CID/ RSPD or CO, immediately via email, telephone, or office visit. Reports may be anonymous and personnel reporting non-compliance issues or welfare concerns will be protected under the “Whistleblower Protection Act.” Reporting mechanisms are as follows:

- phone call to Head, CID or RSPD at 757-953-5939 or RCA at 757-953-5473
- submit an anonymous email via link on the CID SharePoint or Internet page
- schedule a meeting with or email the Institutional Official (CO)

Reports of non-compliance may also be the result of internal or external audits, based on IRB review, or from discussion with IRB Chairs, supervisors, or colleagues. Regardless of how issues arise, all allegations of non-compliance must be referred to the RCA and/or IRB and will be investigated and communicated to the PI.

HANDLING ALLEGATIONS OF NON-COMPLIANCE

All allegations of non-compliance will be reviewed by the Head CID. Allegations may be referred to the IRB or CO for evaluation as applicable and stipulated in the RSPD SOPs. Within one week of receiving a report of potential non-compliance, the RCA will conduct an investigation (Directed/For Cause audit) and will determine whether the allegation has a basis in fact. If circumstances warrant a longer period, the respective Chair and/or Board may approve an extension.
and the reason for the extension will be documented. If the allegations have a basis in fact, the process will be reported to the IRB Board for deliberation during an IRB meeting.

HANDLING (PROVEN) NON-COMPLIANCE

All proven non-compliance issues will be reviewed by the IRB Chair and referred to the Full Board for deliberation. The Board will evaluate and determine whether the non-compliance potentially represents serious and/or continuing non-compliance. If circumstances warrant, the Board may require the PI and/or research staff present the intended corrective and preventative actions at the Board meeting. To ensure subject protection and data safety, the RCA will closely monitor the study for compliance oversight in the future and conduct follow up audit activities.

Research non-compliance may also include failure to submit documentation to the IRB within the required time frame. Instances of non-compliance may include:

- Failure to follow approved study protocol and research methods
- Failure to properly consent subjects
- Failure to protect subject confidentiality and maintain appropriate data security methods
- PI leaves command without transferring study to new PI
- Personnel conducting research are not approved research team members
- Enrollment of more subjects than approved
- Failure to submit Continuing Review documentation annually
- Failure to submit signed Consent Forms annually
- Failure to submit timely documentation requesting Closure
- Failure to submit other IRB required documents (*i.e.*, SAEs, Protocol Violations, or Amendments)
- Failure of PI to ensure research team training is up to date

Issues of non-compliance will be reviewed by CID and/or the IRB and necessary actions including study termination may result. When a study is administratively terminated by the IRB, chain of command is notified. Reports of non-compliance are also reported to BUMED as required. In addition, no study data may be used for publication and study materials and data must be turned over to CID immediately following protocol termination.

INVESTIGATOR REQUIRED TRAINING AND EDUCATION

As required by DON HRPP, all personnel conducting research at NMCP must be appropriately qualified as determined by education, training, and licensure referenced in the RSPD SOPs. All PIs and AIs are also required to complete on-line training in proper research conduct and the protection of human subjects including DON specific CITI Training and Research Integrity training.

**Training requirements**

- CITI Training Modules – Investigators and Key Research Personnel – Biomedical for Human Subjects (three year expiration)
- Research Integrity Training (one time training through CID Sharepoint)
- CV (three year expiration from date of submission)
Procedures

- Any new study submission to the IRB should include all investigator (PI and AI) CITI Training certificates and CVs
- Continuing Reviews should include any renewed CITI Training or CVs for investigators with expired documents
- Amendments should include CITI Training and CVs for new research team members only
- The IRB Administrators and/or RCA will review the submissions and will accept or deny the submission
- The PI/AI should file all CITI Training and CVs in the Regulatory Binder (a memo in binder referencing location of electronic files for these documents is acceptable)
- Current training is required for all PIs/AIs on all active studies. Protocols undergoing IRB Continuing Review or Amendment will be reviewed for current training however the PI is accountable that all research staff training remain current as long as study is active

Training documentation will be reviewed at Compliance Assist Visits; any expired or lapsed training will be considered a finding.

IRB ADMINISTRATION

The Institutional Review Boards (IRBs) are hospital-recognized committees that are charged with assuring the scientific merit of protocols and the protection of the human subjects.

The NMCP IRBs serve as the IRB of record for Navy Medicine East. CID coordinates research within this geographic area of responsibility to provide effective and necessary IRB review to supported commands.

MEMBERSHIP

The IRB shall be composed of no fewer than five (5) members. The IRB shall be sufficiently qualified through the maturity, experience, and expertise of its membership, to ensure respect for its advice and counsel both for its determination of the scientific merit of a protocol, and for safeguarding the rights and welfare of human subjects. No Board shall consist entirely of members of a single profession or entirely of members, officers, employees, agents of, or persons who are otherwise associated with the in-house activity or contractor facility concerned. Members of the Board must be government employees, including the non-affiliated community representative. A fiscal representative may be appointed as a non-voting member in order to have access to approved protocol budgets.

To ensure expertise in review of protocols in the type of research to be conducted and the subject population, the IRBs first rely upon the diversity of personnel available to serve as members. Especially in the medical community, most IRB members have served at different MTFs inside and outside CONUS and with different branches of the military. In this way they have experience with
different populations of subjects and their dependents. For protocols that are outside the expertise of members, ad hoc reviewers or consultants will be invited to review, to offer opinions and to participate in meetings. These members are not appointed to the Board and do not vote. Head, RSPD will consult with the IRB Chairs and Vice-Chairs to determine if this external expertise is needed. (see further description below under Ad Hoc Reviewers.)

Based on unforeseen Navy commitments including deployment for war and natural disasters, alternate members shall be appointed to ensure the availability of the Board to convene scheduled meetings. As there are two IRBs, each member of one Board shall serve as an alternate on the other Board. Alternates will be designated based upon their similar expertise and may serve as alternates for more than one member and in more than one discipline, although they may only represent one member at a single meeting. If both the regular and alternate members are present, only one may vote. During deployment, IRB members may retain their appointment but will not be counted toward the quorum until they return and are ready to resume committee membership activities.

CHAIR

Membership will include a non-voting Chair who is an Officer (0-4 or above) or civilian federal employee. The Chair may be, for example a Medical Officer; Medical Service Officer, Nurse Officer, Judge Advocate, Hospital Corps or Enlisted, Chaplain Officer, staff, resident, and an affiliated or non-affiliated member.

The Chair’s responsibilities include calling the meeting to order, leading the Board’s progress through the agenda, calling for a vote, and calling for adjournment of the meeting. The Chair signs recommended approvals resulting from the actions at the meeting and approves meeting minutes prior to presentation to the CO. The Chair shares responsibility for reviewing and recommending approval of exempt and expedited actions with the Vice Chair.

VICE CHAIR

One or more Vice Chairs may be appointed to the IRB. The Vice Chair may be selected from the same rank and Corps criteria as the Chair. The Vice-Chair is a voting member who steps into the role of non-voting Acting Chair should the Chair be absent from the meeting. The Vice Chair shares responsibility for reviewing and recommending approval of exempt and expedited actions with the Chair.

ACTING CHAIR

When the IRB Chair is not present for a convened meeting, the Vice Chair shall act as Chair. When neither the Chair nor Vice Chair are in attendance, an Acting Chair will be selected by consensus of the members present. The Acting Chair will sign the documents, including the minutes, for the meeting they are called upon to lead, attesting the actions of the IRB. However, the Acting Chair will not sign recommended approval of expedited and exempt protocols unless designated by the Commanding Officer, NMCP.

IRB MEMBER TRAINING

All IRB members will take the CITI Department of the Navy “IRB Chairs, Vice Chairs, and Members” as described in the DON HRPP Education Policy after initial their appointment to the IRB.
This training must be repeated every three years as directed by DON HRPP. CID will maintain IRB member certificates and CVs. In addition all members will complete the research integrity training.

Information concerning “hot topics” are presented at each convened IRB meeting and made available to investigators or other interested parties upon request.

REPORTING IRB MEMBERSHIP TO DON HRPP

CID will keep a membership roster for each IRB which identifies the scientific/non-scientific and affiliated status for member. The roster is checked monthly for accuracy. The roster includes those members and alternate members who are currently appointed to the Board. Members who are deployed or unavoidably assigned TAD will not be included in the membership roster that month and will not be counted toward the quorum. The membership roster also identifies alternate members and the primary members or class of primary members for whom each alternate member could substitute.

Information maintained on each IRB member includes:

- Name
- Rank
- Earned degree(s)
- Indication of expertise such as board certification, licenses, etc., sufficient to describe each member’s chief anticipated contribution to deliberations.
- Any employment or other relationship between each member and the institution; for example, full-time employee, part-time employee, a member of governing panel board, paid or unpaid consultant.
- Areas of expertise for which they may act as alternate members.

DESCRIPTION OF ALL COMPONENTS

Components of Naval Medical Center Portsmouth include:

- Yorktown Branch Health Clinic
- Naval Shipyard Norfolk Branch Health Clinic
- Sewells Point Branch Health Clinic
- Tricare Prime Clinic Chesapeake
- Tricare Prime Clinic Virginia Beach
- Sewells Point Dental Clinic
- USNS COMFORT (T-AH 20)
- NSA Northwest Branch Health Clinic
- NAVSTA Norfolk Branch Health Clinic
- Boone Branch Health Clinic
- Branch Health Clinic Dam Neck Annex
- Branch Health Clinic Naval Air Station Oceana

TRAINING FOR MEMBERS OF THE RESEARCH TEAM

All researchers at NMCP are required to document human subjects’ protection training prior to initiating research. Initial and continuing training requirements are satisfied by completion of CITI training modules established by DON HRPP.
Currently DON HRPP requires an initial course referred to as CITI Department of the Navy “Investigators and Key Research Personnel-Biomedical” for investigators. Completion of the course satisfies the training requirement for three years, after which the training must be repeated to gain another three years. Other courses available through CITI, such as the “Good Clinical Practice (GCP)”, “Responsible Conduct of Research (RCR)”, and “IRB Reference Resource” are great opportunities for further learning, but are optional only and do not satisfy the training requirements established by DON HRPP. Alternate CITI training modules may be used to document ethics training on a case by case basis.

As training requirements are changed by DON HRPP policy, this SOP will defer to those changes as training certificates expire and for investigators taking the training for the first time.

All researchers at NMCP are also required to document research integrity training in accordance with BUMEDINST 6500.3 and NAVMEDCENPTSVAINST 6500.6C. The content of research integrity training is established by the Research Integrity Leader and supported by the Head, CID.

To successfully complete research integrity training a researcher must:
- View the “Introduction to Research Ethics” video;
- Read “On Being A Scientist”
- Read BUMEDINST 6500.3
- Read BUMEDINST 3910.2

The training may be accessed on the NMCP SharePoint site via Training and Education.

Compliance Advisor under the guidance of Head CID is responsible for maintaining personnel records for all completed research integrity training. The Head, CID with full support of Research Integrity Leader will maintain records of all personnel training and subsequent education as part of the compliance program oversight.

RESEARCH FUNDING

Investigators are encouraged to seek funding for their research projects. Funds may be acquired from Federal sources, such as the National Institutes of Health (NIH) and the National Science Foundation (NSF); private granting agencies, such as the Bill Gates Foundation; academia, such as the University of Virginia; Army Research, Development, Test and Evaluation (RDT&E) program “P6” monies, and from BUMED, such as the Wounded, Ill, and Injured (WII) program. CID offers support services for researchers, including identification of funding opportunities, and assistance with the crafting and submission of competitive grant applications. Please contact CID at for more information.

RESEARCH COLLABORATION AGREEMENTS

It is in the best interest of the hospital, and is required by regulations, to pursue necessary collaboration agreements with outside agencies in the pursuit of research. It is important for the individual researcher to appropriately pursue such Interagency Support Agreements (ISSA), Memoranda of Understanding (MOU), Cooperative Research and Development Agreements (CRADA), or Educational Partnership Agreements (EPA). CID will review each protocol for evidence that there will be outside agencies, governmental or otherwise, involved in the research, and then assure that in such a situation an appropriate agreement exists in the proper format. Each
agreement must be reviewed by the Fiscal and Legal Departments. Such approval is necessary before ultimate protocol approval can be gained from the Commanding Officer, NMCP.

CID will assist in the preparation and approval process and ensure that all collaborative research requiring an agreement has agreements in place prior to final approval of the research by the Commanding Officer. IRB Administrators must have documentation from the CRADA Officer or their designee, that an agreement has been finalized before a study can be forwarded to the Commanding Officer for approval. The agreements process takes considerable time and may be routed at the same time a research protocol is being reviewed by the IRB. Investigators are encouraged to contact CID early in the research submission process for assistance.

Investigators conducting collaborative research should be aware that their project must be approved by all required organizations before human subjects are recruited or any other research activities with human subjects begin. The IRB may recommend approval of a research protocol contingent upon its approval by other organizations (e.g., required reviews can be conducted in parallel).

CID monitors the performance of each CRADA at least annually, in conjunction with the IRB Continuing Review process for the associated protocol.

For more information about the CRADA process, please see NAVMEDCENPTSVAINST 6500.8A.

**HRPO REVIEW OF CONTRACTOR COMPLIANCE IN SUPPORT OF DOD-CONDUCTED (INTRAMURAL) HUMAN SUBJECTS RESEARCH**

Research of this nature requires Human Research Protection Official (HRPO) approval for all new protocols and post-approval actions for contractor supported intramural DoD research involving human subjects. These protocol activities are individually reviewed by the HRPO prior to approval by the NMCP Commanding Officer. The activities are then compiled into monthly reports which are reviewed by the local program officer at NMCP. The HRPO reports are delineated by contract number and are submitted monthly to the Contracting Officer at Naval Medical Logistics Command (NAVMEDLOGCOMM) and the Department of Navy Human Research Protections Program (DON HRPP).

For more information about HRPO requirements, please see DFARS Clause 252.235-7004 entitled “Protection of Human Subjects”, SECNAVINST 3900.39D and DoDI 3216.02.

**CONDUCT OF BUSINESS**

There are two IRBs at the Naval Medical Center Portsmouth, IRB-1 and IRB-2. Both are provided administrative support by the Research Subjects Protection Division (RSPD) and Clinical Investigation Department (CID), but are otherwise independent Boards with direct authority from the Commanding Officer.

- IRB-1 meets the second Wednesday of each month IRB-2 meets the fourth Wednesday of each month. Meetings are held in an appropriate conference room. Protocols are assigned for review on the next available meeting agenda.
Exceptions to scheduling new protocols for review are made on a case-by-case basis at the discretion of the Head of RSPD in order to accommodate emergency applications and other unusual situations that may arise.

AGENDA

An agenda for each meeting is prepared by the IRB Administrator. The agendas present the Board with items for action (such as continuing reviews, new protocols, amendments, serious adverse events and final reports) as well as items for which action has been taken by the Chair or Vice Chair which require notification of the Board (such as events recommended for approval through exempt or expedited review). The agenda also serves as a vehicle for announcements and continuing education of members. The Administrators distribute the meeting agenda to the IRB approximately one week prior to the meeting to allow Board members sufficient time to complete their review of the protocols or events to be discussed.

CONTINUING EDUCATION

Ongoing continuing education of human subjects research ethics and IRB concerns will be provided at monthly meetings by the IRB Chair with the assistance of the IRB Administrator. Continuing education will be recorded in the minutes of each meeting.

ATTENDANCE REQUIREMENTS

A convened (full) board meeting requires:

- Attendance of a majority of IRB members
- Attendance of at least one member whose primary concerns are in non-scientific areas.
- Attendance of at least one member who represents the general perspective of participants.
- Attendance of a prisoner representative if the IRB reviews research involving prisoners.

The presence of a non-affiliated member is not a quorum requirement, [DoDI 3216.3.b 08 Nov 11] but the IRB encourages the non-affiliated member to attend each meeting.

QUORUM

A quorum shall consist of a majority of voting members on the IRB (with the exception of deployed members) and must include at least one physician and one non-scientist. If a member leaves the room for any reason, (for example, a conflict of interest) the number or category counted toward a quorum shall likewise be reduced. If the quorum is lost the IRB cannot vote or take any official action until a quorum is restored. Members may participate by teleconference if they have all the meeting materials available to them. There is no written proxy voting. Members in attendance will sign a roster for each meeting and will be identified by name in the minutes if, and when, they leave the meeting after call to order. The Chair shall determine the presence of a quorum with the assistance of the IRB Administrator.

A majority of votes cast must be obtained in order for a motion to be approved. A majority means more than half. Abstentions do not count in tallying the vote negatively or positively. Abstentions are a refusal to vote and when members abstain, they are in effect only contributing to a quorum. The names of members, their vote or abstention, or the reason for their vote are not recorded.
AD HOC REVIEWERS

The IRBs may, at their discretion, invite individuals/consultants with competence in special areas to assist in the review of complex issues which require expertise in addition to that available to the IRB. If it is determined that outside expertise is required for review, CID will approach potential consultants for service to the Board. These individuals will be identified as ad hoc reviewers at the beginning of the meeting. They perform review and participate in discussion but do not vote. The consultant’s expertise in the particular area of discussion will be documented by CID and noted in the minutes. Ad hoc reviewers should not have a conflict of interest with the protocol to be reviewed.

The IRB Chair/Vice Chair and CID will evaluate each protocol to determine whether a consultant is needed. An IRB Member may also request a consultant if they feel unable to provide an adequate review.

The IRB Chair/Vice Chair will defer the study to another meeting or IRB, or obtain consultation if there is not appropriate scientific/scholarly or representational expertise on the committee.

IRB MEMBERS WITH CONFLICT OF INTEREST

No IRB may have a member participate in the review of any project in which the member has a conflicting interest except as a source of information.

IRB members with a conflicting interest:
- Will be excluded from discussion except to provide information requested by the IRB.
- Will be excluded from voting.
- Will be not counted towards quorum when absent from the meeting.
- IRB members with a conflict will be documented in the minutes as being absent with an indication that a conflict of interest was the reason for the absence.

Voting members in the same department as a PI or AI may remain in the room for discussion and voting as long as they do not have a conflict of interest with the protocol being reviewed.

Voting members in the same department as PI or AI may be critical reviewers.

If the IRB Chair is a PI or AI on the study he/she must not preside over the discussion or voting of that protocol and should leave the room during those phases.

If the IRB Chair is a member of the same Department as the PI or AI, a determination will be made in conjunction with the Head, RSPD as to whether the Chair should preside over the discussion and voting.

If the Chair or Vice-Chair has a conflict of interest, they will not be permitted to perform expedited or exempt actions for that protocol.

VOTING

During a vote, the Chair calls for each member to indicate their choice of for, against, or abstention. Members may indicate their vote verbally (as with Aye or Nay) or visually (with a raised hand). The
IRB Administrator records the vote upon each action for inclusion in the meeting minutes. Should a motion fail, the Administrator alerts the Board that the motion did not pass. The Board may resume discussion, make another motion, or table the action for re-review at a later time.

Common actions that the IRB may take during the review of protocols include recommending approval, tabling, disapproval, and acceptance.

These actions stem from the authority to conduct human research at a Navy MTF. The authority to conduct research belongs to the Surgeon General (SG). The SG may delegate this authority to Commanders, Commanding Officers, and Officers in Charge of a Command. This authority may not be further sub-delegated.

At NMCP only the Commanding Officer has the authority to approve research and research-related documents including, but not limited to, research protocols, IRB minutes, CRADAs, MOUs, and Institutional Agreements for IRB Review (IAIR). In the absence of the Commanding Officer and when assuming the legal role as “Commanding Officer, Acting”, the Executive Officer may sign these same documents.

During a meeting, any member may make a motion for action to be taken by the IRB at the committee level. Following this action, the IRB will make a recommendation to the Commanding Officer. Generally an assigned reviewer will make a motion for the agenda item being discussed, but this is not a requirement.

The IRB may review revised consent forms with an Amendment or at the time of Continuing Review. When the Board recommends approval for the revised consent, the Board will need to determine if the Investigator may/may not continue to use the previously approved version of the consent form to enroll subjects while the revised consent form associated with the continuing review or the amendment awaits approval by the CO. The IRB should consider all aspects of the proposed consent changes, to ensure no harm may come to subjects from use of the prior consent version. The IRB will include this determination in their motion for deliberation and vote.

The preferred language for actions is as follows:

\textbf{Recommend approval}  
- The preferred language for the motion by the IRB is:
  - “I move to recommend approval of (protocol number), [if applicable - involving a vulnerable population of (children, pregnant women/fetuses, prisoners, \textit{etc.})] with (minimal or greater than minimal) risk [and for pediatric research - the prospect of direct benefit or no prospect of direct benefit] and (annual or semi-annual) review.”
  - If the consent is revised: “The PI may continue to use the prior version of the consent while awaiting CO approval” or “The PI may not use any version of consent until the new version of the consent is approved by the CO.”
  - Approval will be recommended to the Commanding Officer.
Recommend approval pending requirements (return to Full Board or review by the Chair)

- The preferred language for the motion by the IRB if the requirements may be reviewed by the Chair is:
  - “I move to recommend approval of (protocol number), [if applicable - involving a vulnerable population of (children, pregnant women/fetuses, prisoners, etc.)] with (minimal or greater than minimal) risk [and for pediatric research - the prospect of direct benefit or no prospect of direct benefit] and (annual or semi-annual) review, ‘pending completion of requirements, giving the Chair authority to review.’ or ‘pending completion of requirements to be returned to the Full Board.’”
  - If the consent is revised: “The PI may continue to use the prior version of the consent while awaiting CO approval” or “The PI may not use any version of consent until the new version of the consent is approved by the CO.”
  - Changes that may be returned to the Chair for final IRB review are those that have been clearly defined by the IRB, and which, if made as instructed, would be recommended for approval by the Full Board. Examples may include, but are not limited to:
    - Confirmation of specific assumptions or understandings on the part of the IRB regarding how the research will be conducted.
    - Submission of additional documentation (such as CITI training)
    - Precise language changes to protocol or informed consent documents.
    - Precise changes to protocol or informed consent documents along with clearly stated parameters that the changes must satisfy.
  - Changes that should be returned to the convened Board are those for which the Board has not provided specific language. Changes of clarity are needed where it is uncertain how the investigators will respond. Changes are requested that the IRB members specifically wish to see as a group:
    - Clarifications requested for stopping criteria.
    - Questions about the statistical methodology.
    - Questions about how referrals will be obtained.
    - Questions about how privacy will be maintained.
    - Questions about the qualifications of the Research Monitor.
    - Concerns about the plan for research related injuries.
    - Questions about military enrollment.
    - Lack of all recruitment materials.
    - Lack of all study related materials.
    - Questions about how participants will be identified.
    - Questions about measures to ensure subject privacy.

Table

- The IRB has the authority to table a protocol. The Board may choose to table a protocol if the materials presented for review do not provide enough information, or sufficient clarity of information, for the members to make a decision to approve or disapprove.
• The preferred language for the motion by the IRB is:
  o “I move to table (protocol number) [cite reason].”
• This action is reported in the minutes.
• The investigator will get a full, detailed report of weaknesses and suggestions for improvement as it is expected that a revision will be submitted.

**Disapprove**
• The IRB has the authority to disapprove a protocol. The Board should indicate if the protocol has merit and approval may be possible with revision, or if the scientific or ethical basis of the research is so weak that a recommendation for approval will not be possible.
• The language for the motion by the IRB is:
  o “I move to disapprove (protocol number) [cite reason].”
• The Commanding Officer may not approve a protocol unless it is recommended for approval by the IRB.
• The Commanding Officer may disapprove a protocol that has been recommended for approval by the IRB. The Commanding Officer may disapprove a protocol for any reason for example, if he/she finds that the goals of the research do not meet the mission of the command, even if the IRB found the study ethically and scientifically sound.

**Accept**
• The IRB may accept items presented for review. Such items are not recommended to the CO, but the Board accepts them as a means of acknowledging receipt. For example, the IRB may accept a list of adverse events that occurred at another command, or the Board may accept actions completed under expedited or exempt review by the Chair and/or Vice Chair. Upon acceptance, no further action by the full committee is required. The Board may take further action on an accepted item if they determine that the information presented impacts the risk/benefit ratio or if the new information should be presented to local subjects. In these cases, a separate action by the Board would be initiated.
• Example motion language is provided to IRB members.

**IRB MINUTES**

Following each meeting of the IRB, minutes will be prepared by the IRB Administrator and reviewed by the IRB Chair, RSPD Head and Head, CID. Creation of the minutes should be completed within one week. The draft of the minutes is electronically distributed to the Board for review, revision, and acceptance. Members who fail to respond to the electronic distribution are considered not to have cast a vote. IRB recommended approval of the minutes is reflected by a simple majority vote of the quorum. Documentation of the Board’s vote is reported at the next convened meeting. Upon receiving recommended approval by the IRB, the IRB Administrator attaches an Executive Summary, and presents the minutes to the IRB Chair for signature. The minutes are then forwarded to the Commanding Officer. In the absence of the Commanding Officer, the Executive Officer (acting Commanding Officer) will sign the minutes. When returned to CID, the official copy of the minutes is scanned and sent to DON HRPP.
IRBs minutes will document:

- Attendance in support of quorum, expertise, and diversity, documented by dated signature.
- Attendance of staff, and guests.
- Continuing Education presented to members.
- Distinct discussion for each action, to include
  - A written summary of the discussion.
  - The basis for requiring changes or disapproving research.
  - The vote, documenting voting members for, against, and abstaining.
  - When an alternate member replaces a primary member.
  - The names of IRB members who leave the meeting because of a conflict of interest along with the fact that a conflict of interest is the reason for the absence.
  - The approval period for initial and continuing review.
  - When a study involves a waiver of consent or waiver of documentation of consent.
  - Vulnerable populations to be enrolled in the study:
    - Research involving pregnant women, fetuses, and neonates.
    - Research involving prisoners.
    - Research involving children.
    - Research involving decisionally impaired individuals.
  - Risk assessment including appropriate OHRP or FDA citations for children.
  - The rationale for significant risk/non-significant risk FDA device determinations (if applicable).
  - Deletion or substantive modification of information concerning risks or alternative procedures contained in a DHHS-approved sample consent document. (if applicable).

Minutes also provide a reporting mechanism by which the Board is notified of expedited and exempt actions which have been completed by the Chair and Vice Chair, as well personnel changes completed by the IRB administrators. This includes initial approval of protocols, continuing reviews, amendments, final reports, and acknowledge-receipt-only items.

**MAINTENANCE OF RECORDS**

CID is accountable for the proper maintenance and availability of approved protocols. Complete and accurate study records are essential.

A complete IRB file includes documents associated with the entire life cycle of a protocol, from initial review to final report.

Materials maintained in the study file include:

- Applications
- Protocols and/or Research Plans
- Documentation of Scientific Review
- Evidence of scientific review if performed by an external body
- Approved consent documents
- DHHS-approved sample consent document(s) and protocol(s), if applicable
- Records of continuing review activities
- Records of modifications
- Reports of injuries to participants
- Statements of significant new findings provided to participants
- Reports of study completion or termination
- Significant correspondence between the IRB and investigators
- Reviewer checklists which identify the exempt or expedited category under which the protocol received initial and/or continuing approval.
- Justification for granting Waiver of Consent or Waiver of Documentation of Consent
- Justification for granting Waiver of Authorization for the Use of PHI
- Reviewer checklists which demonstrate that requirements for the inclusion of vulnerable populations have been met
  o Research involving pregnant women/fetuses/neonates
  o Research involving prisoners
  o Research involving children
- Records needed to document determinations required by laws, regulations, codes, and guidance
- Documentation of Emergency Use

IRB records relating to research that qualify as permanent records will be maintained at CID electronically. Hard copy records are retained for a period of time and then sent to permanent storage per SECNAVINST 5210.8D, the most current guidance from DON. Draft and duplicate copies may be retained as needed but should be destroyed as soon as practical.

CID permits inspection and copying of IRB records by authorized representatives of federal agencies or departments at reasonable times and in a reasonable manner.

**SELF ASSESSMENT**

CID monitors all aspects of the research submission, approval, and reporting process and tracks these data in a comprehensive Excel spreadsheet. Data reports are made to the command monthly and include all active protocols from time of submission to the Commanding Officer’s final approval and beyond. These metrics provide performance measures of investigators, scientific reviewers, CID staff, and IRBs in the time taken at each stage of the process. These data allow assessment of trouble areas that can then be targeted for improvement.

IRB Chairs and members are provided with evaluation forms for self-assessment and for assessment by CID. These evaluation forms are be distributed and collected annually. Feedback will be provided individually to those needing assistance.

CID conducts re-review of new protocols reviewed by the IRB for the effective use of the reviewer checklists that include regulations and criteria for approval. Effective and consistent use of the checklists will be a topic of education if warranted.

Adequacy of scientific reviews is evaluated by reports from IRB members assigned to review protocols. Members can report directly to the Chair and CID and will also report this in their review
checklist. A question regarding the adequacy of the scientific review is included added to the Full Board and Expedited checklists. Scientific reviewers that consistently get poor ratings may be counseled to provide more in-depth review or may be dropped from the roster.

RESEARCH QUESTIONS

Information about various aspects of research may be found on the CID SharePoint page on the NMCP intranet and the CID web page on the NMCP website on the internet. Research related documents are also available by request from the IRB Administrators.

For more information, please call CID at 757-953-5939.

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APPENDIX A – RESEARCH DECISION TREE

Chart 1: Is an Activity Research Involving Human Subjects Covered by 45 CFR part 46?

Start here.

Is the activity a systematic investigation designed to develop or contribute to generalizable knowledge? [45 CFR 46.102(d)]

YES → Activity is research. Does the research involve obtaining information about living individuals? [45 CFR 46.102(f)]

NO → Activity is not research, so 45 CFR part 46 does not apply.

YES → Does the research involve intervention or interaction with the individuals? [45 CFR 46.102(f)(1), (2)]

NO → The research is not research involving human subjects, and 45 CFR part 46 does not apply.

YES → Is the information individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information)? [45 CFR 46.102(f)(2)]

NO → NO

YES → Activity is research involving human subjects. Is it conducted or supported by HHS? [45 CFR 46.101(a)(1)]

NO → NO

YES → Is the research covered by an applicable OHRP approved assurance created under 45 CFR 46.103?

NO → Is the research exempt under 45 CFR 46.101(b), 45 CFR part 46, subpart A requirements apply to the research. As appropriate, subpart B, C, and D requirements also apply.

YES → Unless exempt under 45 CFR 46.101(b), 45 CFR part 46, subpart A requirements apply to the research. As appropriate, subpart B, C, and D requirements also apply.

NO → Go to Chart 2

AND

Other Federal, State and local laws and/or regulations may apply to the activity. [45 CFR 46.101(f)]
Chart 2: Is the Research Involving Human Subjects Eligible for Exemption Under 45 CFR 46.101(b)?

- Has HHS prohibited exemption of the human subjects research? (All research involving prisoners, some research involving children.) [Footnote 1 to 45 CFR 46.101(i), 45 CFR 46.401(b)]
  - NO
    - Will the only** involvement of human subjects be in one or more of the following categories?
      - Research conducted in established or commonly accepted educational settings, involving normal education practices?
        - YES -> Exemption 45 CFR 46.101(b)(1) may apply. Go to Chart 3
        - AND/OR
          - Research involving the use of educational tests, survey procedures, interview procedures, or observation of public behavior?
            - YES -> Exemption 45 CFR 46.101(b)(2) or (b)(3) may apply. Go to Chart 4
            - AND/OR
              - Research involving collection or study of existing data, documents, records, or pathological or diagnostic specimens?
                - YES -> Exemption 45 CFR 46.101(b)(4) may apply. Go to Chart 5
                - AND/OR
                  - Research studying, evaluating, or examining public benefit or service programs?
                    - YES -> Exemption 45 CFR 46.101(b)(5) may apply. Go to Chart 6
                    - AND/OR
                      - Research involving taste and food quality evaluation or consumer acceptance studies?
                        - YES -> Exemption 45 CFR 46.101(b)(6) may apply. Go to Chart 7
                        - NO

  - YES
    - No exemptions to 45 CFR part 46 apply. Provisions of 45 CFR subpart A apply, and subparts B, C and D also apply if subjects are from covered vulnerable populations. Go to Chart 8

** "Only" means that no non-exempt activities are involved. Research that includes exempt and non-exempt activities is not exempt.
Chart 3: Does Exemption 45 CFR 46.101(b)(1) (for Educational Settings) Apply?

From Chart 2

Is the research only conducted in established or commonly accepted educational settings? (Including but not limited to schools and colleges. May include other sites where educational activities regularly occur.)

NO

Research is not exempt under 45 CFR 46.101(b)(1).

Go to Chart 8

YES

Does the research study involve only normal education practices? (Such as research on regular and special education instructional strategies, or research on effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.)

NO

YES

Research is exempt under 45 CFR 46.101(b)(1) from all 45 CFR part 46 requirements.
Chart 4: Does Exemption 45 CFR 46.101(b)(2) or (b)(3) (for Tests, Surveys, Interviews, Public Behavior Observation) Apply?

From Chart 2

Does the research involve only the use of educational tests, survey procedures, interview procedures, or observation of public behavior?

YES

Does the research involve children to whom 45 CFR part 46, subpart D applies?

YES

Is the information obtained recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and could any disclosure of the human subjects' responses outside the research reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation?

NO

NO

Research is not exempt under 45 CFR 46.101(b)(2).

However, the 45 CFR 46.101(b)(3) exemption might apply.

Are the human subjects elected or appointed public officials or candidates for public office? (Applies to senior officials, such as mayor or school superintendent, rather than a police officer or teacher.)

NO

NO

Research is not exempt under 45 CFR 46.101(b)(2) or (b)(3).

Go to Chart 8

YES

Does any Federal statute require without exception that the confidentiality of personally identifiable information will be maintained throughout the research and thereafter?

NO

YES

Research is exempt under 45 CFR 46.101(b)(3) from all 45 CFR part 46 requirements.

Research is exempt under 45 CFR 46.101(b)(2) without exception from 45 CFR part 46 requirements.
**Chart 5: Does Exemption 45 CFR 46.101(b)(4) (for Existing Data Documents and Specimens) Apply?**

From Chart 2

Does the research involve only the collection or study of *existing* data, documents, records, pathological specimens, or diagnostic specimens? *

(“Existing” means existing before the research is proposed to an institutional official or the IRB to determine whether the research is exempt.)

---

**YES**

Are these sources *publicly available*?

---

**YES**

Research is exempt under 45 CFR 46.101(b)(4) from all 45 CFR part 46 requirements.

**NO**

Will information be *recorded by the investigator* in such a manner that the subjects *cannot be identified*, directly or through identifiers linked to the subjects?

---

**YES**

Go to Chart 8

**NO**

Research is not exempt under 45 CFR 46.101(b)(4) from 45 CFR part 46 requirements.

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* Note: See OHRP guidance on research use of stored data or tissues and on stem cells at http://www.hhs.gov/ohrp/policy/index.html#tissues and #stem, and on coded data or specimens at #coded for further information on those topics.
Chart 6: Does Exemption 45 CFR 46.101(b)(5) (for Public Benefit or Service Programs) Apply?

From Chart 2

Is the research or demonstration project conducted or approved by the Department or Agency Head?

YES

Does the research or demonstration project involve only the study, evaluation, or examination of:

Public benefit or service programs;

YES

NO

Procedures for obtaining benefits or services under public benefit or service programs;

YES

NO

Possible changes in or alternatives to public benefit or service programs or to procedures for obtaining benefits or services under public benefit or service programs;

YES

NO

Possible changes in methods or levels of payment for benefits or services under those public benefit or service programs?

YES

NO

Research is not exempt under 45 CFR 46.101(b)(5).

Go to Chart 8

Research is exempt under 45 CFR 46.101(b)(5) from all 45 CFR part 46 requirements.*

* Note: See OHRP guidance on exemptions at http://www.hhs.gov/ohrp/policyindex.html#exempt for further description of requirements for this exemption.
Chart 7: Does Exemption 45 CFR 46.101(b)(6) (for Food Taste and Acceptance Studies) Apply?

From Chart 2

Does the research involve only a taste and food quality evaluation or a food consumer acceptance study?

YES

Are wholesome foods without additives consumed?

YES

Research is exempt under 45 CFR 46.101(b)(6) from all 45 CFR part 46 requirements.

NO

Is food consumed that contains a food ingredient, agricultural chemical, or environmental contaminant at or below the level found to be safe by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture?

YES

NO

Research is not exempt under 45 CFR 46.101(b)(6).

Go to Chart 8
Chart 8: May the IRB Review Be Done by Expedited Procedures Under 45 CFR 46.110?*

From Chart 2, 3, 4, 5, 6, or 7

Has the research been previously reviewed and approved by the IRB?

YES → Is the review a continuing review? [45 CFR 46.109(d)]

NO → Does the research present no more than minimal risk to human subjects and does the research involve only procedures included in categories 1 through 7 on the list of categories of research that may be reviewed through an expedited review procedure? [45 CFR 46.110(b)(1)]

YES → Review by convened IRB is required.

NO → Does the review involve a minor change in approved research during the (one year or less) period of approval? [45 CFR 46.110(b)(2)]

YES → Go to Chart 9

NO → Is the research classified? [Paragraph (D) of Categories of Research That May Be Reviewed By an IRB through an Expedited Review Procedure.]

YES → Are measures in place to make risks no more than minimal?

NO → Go to Chart 10

YES → Research is eligible for IRB review through expedited procedures. Agency head may restrict, suspend, terminate or choose not to authorize an institution’s or IRB’s use of the expedited review procedure. [45 CFR 46.110(d)]

NO → Could identification of subjects put them at risk of criminal or civil liability, or be socially or economically damaging? [Paragraph (C) of Categories.]

YES → Research is eligible for IRB review through expedited procedures. Agency head may restrict, suspend, terminate or choose not to authorize an institution’s or IRB’s use of the expedited review procedure. [45 CFR 46.110(d)]

NO → Go to Chart 9

* Note: See expedited review categories and OHRP guidance on the use of expedited review procedures at http://www.hhs.gov/ohrp/policy/index.html#expedited for further information on expedited review.
**Chart 9: Can Continuing Review be Done by Expedited Procedures Under 45 CFR 46.110?**

1. **From Chart 8**
   - Has the research been *previously reviewed* and approved by the IRB using *expedited* procedures? **YES**
   - NO

2. **Has conditions changed** to make the research *eligible* for expedited review under the *applicability criteria and categories 1 through 7* on the list of categories that may be reviewed by expedited procedures (e.g., research is within those categories and experience confirms research to be of greater than minimal risk)? **[45 CFR 46.110(a)]**
   - YES
   - NO

3. **Category 8**
   - (a) For this site:
     - Is the research permanently closed to enrollment of new subjects? **and**
     - Have all subjects completed all research-related interventions? **and**
     - Does the research at this site remain active only for long-term follow-up of subjects? **YES**
   - NO

4. **(b) Have no subjects been enrolled at this site?** **and**
   - Have no additional risks been identified anywhere? **NO**

5. **Research is eligible for IRB review through expedited procedures.**

6. **Have conditions changed such that the research is no longer eligible for expedited review (e.g., protocol change, or experience shows research to be of greater than minimal risk)?** **YES**

7. **Review by convened IRB is required.**

8. **NO**

9. **Go to Chart 10**

10. **Has the IRB determined and documented at a convened meeting that the research involves no greater than minimal risk?** **YES**

11. **NO**

12. **Is the research conducted under an IND or IDE?** **YES**

13. **NO**

**Note:** See expedited review categories, OHRP guidance on the use of expedited review procedures and on continuing review at [http://www.hhs.gov/ohrp/policy/index.html#expe and continuing for further information on expedited review.**
Chart 10: Can Informed Consent Be Waived or Consent Elements Be Altered Under 45 CFR 46.116(c) or (d)?

**(Note: If subjects include children to whom 45 CFR part 46, subpart D applies, an alternative provision for waiver of parental permission might apply. [See 45 CFR 46.408(c)])

From Chart 8 or 9

Will the research or demonstration project be conducted by or subject to the approval of state or local government officials? [45 CFR 46.116(c)(1)]

NO

Will the research involve greater than minimal risk, as defined in Section 46.102(i)? [45 CFR 46.116(c)(1)]

NO

Is it practicable to conduct the research without the waiver or alteration? [45 CFR 46.116(d)(3)]

NO

Will waiving or altering the informed consent adversely affect the subjects' rights and welfare? [45 CFR 46.116(d)(2)]

NO

Will pertinent information be provided to subjects later, if appropriate? [45 CFR 46.116(d)(4)]

YES

NO

Waiver of informed consent or alteration of consent elements is allowed if IRB documents these findings and approves waiver or alteration.

YES

Is the project designed to study, evaluate, or otherwise examine: (i) Public benefit of service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs? [45 CFR 46.116(c)(1)]

NO

YES

Is it practicable to conduct the research without the waiver or alteration? [45 CFR 46.116(c)(2)]

NO

Go to Chart 11

The project is not practicable to conduct the research without the waiver or alteration.

* Note: See OHRP guidance on informed consent requirements in emergency research at http://www.hhs.gov/ohrp/policy/index.html#emergency for further information on emergency research informed consent waiver.
Chart 11: Can Documentation of Informed Consent Be Waived Under 45 CFR 46.117(c)?

From Chart 10

Would the consent document be the only record linking the subject and the research and would the principal risk be potential harm resulting from a breach of confidentiality? [45 CFR 46.117(c)(1)]

NO

Does the research present no more than minimal risk and involve no procedures for which written consent is normally required outside the research context? [45 CFR 46.117(c)(2)]

YES

IRB may waive the requirement for a signed consent form for some or all subjects.

AND

IRB may require investigator to provide subjects with a written statement regarding the research. [45 CFR 46.117(c)]

If IRB Allows Waiver of Documentation Under 45 CFR 46.117(c)(1)

Investigator will ask each subject if he or she wants documentation linking the subject with the research. [45 CFR 46.117(c)(1)]

Subject’s wishes will govern whether informed consent is documented. [45 CFR 46.117(c)(1)]

NO
APPENDIX B – INITIAL REVIEW OF HUMAN SUBJECTS RESEARCH FLOWCHART

Key:  EM - Exempt Protocol  
EP - Expedited Protocol  
FB - Full Board Protocol
APPENDIX C-SCIENTIFIC REVIEW COMMITTEE (SRC) ELECTRONIC FLOWCHART

**Protocol Received**
- IRB Administrator receives protocol electronically

**Protocol Preparation**
- SRC Administrator forwards protocol to SRC Editor
  - Editor strips away all but research protocol

**External Review**
- SRC Editor forwards protocol to 3 external reviewers
- Each reviewer is given 1 week to return evaluation form with feedback

**IRB/IACUC Review**
- Reviewer recommends approval “as is”
- SRC Editor forwards protocol to the SRC Administrator for assignment to the IRB / IACUC

**Protocol Returned to PI**
- Reviewer recommends Changes
- SRC Editor returns protocol to PI with recommendations for changes

**Protocol Resubmission**
- PI makes appropriate changes to protocol and resubmits it to SRC Editor for review
- SRC Editor forwards to SRC Administrator for IRB/IACUC review
APPENDIX D – SCIENTIFIC REVIEWER FORM

NMCP Scientific Reviewer #

Title:  
Principal Investigator:  
Date Review completed:  

Thank you for taking your time to complete the scientific review of this protocol. Please use the form below to evaluate the protocol. There are two parts to this evaluation form. The first includes the table below which provides a general evaluation and overview. The second part requires a written response to questions 1 – 14.

The applications are to be considered confidential. If you cannot review an application, contact the Scientific Review Editor who can obtain an appropriate outside opinion. Respect for the privacy of the investigators’ ideas is also important. Misappropriation of intellectual property, including the unauthorized use of ideas or unique methods obtained from a privileged communication is considered plagiarism and falls under the definition of scientific misconduct. Your review will be returned to the principle investigator and forwarded with the protocol to the IRB in confidence. Neither the PI nor the IRB will know who performed the scientific review.

Part 1: Criteria for Evaluating Scientific Merit

<table>
<thead>
<tr>
<th>Objective/Condition</th>
<th>Acceptable</th>
<th>Not Acceptable</th>
<th>Absent</th>
<th>Not Applicable</th>
<th>Comments Attached</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objectives: Clearly stated purpose of study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Background and Rationale: Justification for conducting the study, results of similar or pilot data, current literature cited</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothesis: Hypothesis is testable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Design: Adequate to determine stated objectives</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Data Collection: Measures adequate to test hypothesis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eligibility Criteria: Specific inclusion/exclusion requirements</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precautions to Minimize Procedural Risks</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Outcome Characteristics and Endpoint Definitions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statistical Analysis and Sample Size: reviewed by a qualified statistician</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completeness of IRB proposal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall Assessment</td>
<td>Forward to IRB</td>
<td></td>
<td>Return to PI for changes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RSPD SOP Page 135
Part 2: Written Criteria and Feedback:

Consider all aspects of the research protocol. Do not describe the investigator's plans; rather make evaluative statements about the strengths and weaknesses based on criteria described below. A strong application will contain good ideas, address important issues, and generate confidence that the investigator(s) will make a significant impact. Do not insist on a hypothesis-driven approach if the research is sound and will move the field forward. Be concise; longer reviews are not necessarily better. Sample critiques are less than 2 pages long. Where possible, try to put the strengths and weaknesses in perspective by indicating their relative magnitude. Do not consider issues outside of scientific merit in your critique such as current or past funding levels or personal situations of the investigator.

1. Are the proposed methods suited to the stated objective?

2. Is the project likely to produce any new or useful information?

3. Do the investigators clearly outline the significance of the results that might be obtained?

4. Is the description of the approach clear enough to permit adequate evaluation?

5. Do the investigators appear to be familiar with recent pertinent literature?

6. Has the overall design of the study been carefully thought out?

7. Are the stated objectives realistic?

8. Do the hypotheses rest on sufficient evidence, are they clearly stated, and are they testable?

9. Have the statistical aspects of the approach been given sufficient consideration?
10. What is the strength of the Proposal?

11. What is the weakness of the Proposal?

12. Other Comments:

13. Overall Evaluation:


15. Additional Comments:
APPENDIX E – DOCUMENT APPROVAL STAMPS

RESEARCH PLAN:

The Research Plan stamp is populated as shown below:

<table>
<thead>
<tr>
<th>Version:</th>
<th>Version Identifier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date:</td>
<td>IRB Signature Date</td>
</tr>
<tr>
<td>CID:</td>
<td>IRB Administrator Initials</td>
</tr>
</tbody>
</table>

Research Plans are re-stamped when modifications occur, resulting in a new version identifier and IRB review date.

CONSENT FORM:

The Consent Form stamp and document footer are populated as shown below:

<table>
<thead>
<tr>
<th>Study Expiration Date</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>CID Version</td>
<td>Identifier</td>
</tr>
<tr>
<td>Protocol Version</td>
<td>Identifier</td>
</tr>
<tr>
<td>Protocol Date</td>
<td>Date</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Identifier</th>
<th>IRB Signature Date</th>
<th>IRB Administrator Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td>CID Version</td>
<td>ICF Date</td>
<td>IRB Administrator</td>
</tr>
</tbody>
</table>

Consent forms are re-stamped when modifications occur, resulting in a new CID version identifier and potentially a new protocol version identifier and protocol date. Consent forms are also re-stamped at the time of continuing review, resulting in a new study expiration date and new CID version identifier.

Information in the document footer is updated in conjunction with stamping, to reflect the new CID version, consent date, and initials of the IRB Administrator.
**2. IS THIS PROJECT RESEARCH?**

If yes to any of the following, the project is research and may require oversight by the IRB:

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the activity an investigation?</td>
<td></td>
</tr>
<tr>
<td>Is the investigation systematic?</td>
<td></td>
</tr>
<tr>
<td>Is the systematic investigation designed to develop or contribute to knowledge?</td>
<td></td>
</tr>
<tr>
<td>Is the knowledge the systematic investigation is designed to develop or contribute generalizable?</td>
<td></td>
</tr>
</tbody>
</table>

**COMMENTS:**

**3. DOES THIS PROJECT INVOLVE HUMAN SUBJECTS?**

If yes to any of the following, the project is human subjects research and requires oversight by the IRB:

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the investigator conducting the research gathering data about living individuals?</td>
<td></td>
</tr>
<tr>
<td>Will the investigator gather that data through either of the following mechanisms?</td>
<td></td>
</tr>
</tbody>
</table>

**COMMENTS:**

**4. DOES THIS PROJECT INVOLVE PRIVATE OR IDENTIFIABLE INFORMATION?**

If yes to any of the following, the project is human subjects research and requires oversight by the IRB:

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Will the investigator gather data about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place? (Private Information)</td>
<td></td>
</tr>
<tr>
<td>Will the investigator examine data provided by individuals for specific purposes in which the individuals can reasonably expect that it will NOT be made public, such as a medical record? (Private Information)</td>
<td></td>
</tr>
<tr>
<td>Can the individuals' identities be readily ascertained or associated with the information by the investigator? (Identifiable Information)</td>
<td></td>
</tr>
</tbody>
</table>

**COMMENTS:**

**5. DOES THE PROJECT INVOLVE HUMAN SUBJECTS UNDER FDA REGULATIONS?**

If yes to any of the following, the project is human subjects research and requires oversight by the IRB:

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>An individual will be the recipient of any test article (drug, device, biologic) or as a control</td>
<td></td>
</tr>
<tr>
<td>An individual on whose specimen a medical device will be tested</td>
<td></td>
</tr>
<tr>
<td>Will data generated from this project be used to support an application to the FDA?</td>
<td></td>
</tr>
</tbody>
</table>

**COMMENTS:**
6. DOES THIS PROJECT INVOLVE CODED DATA OR SPECIMENS?
If no to any of the following, the project is human subjects research and requires oversight by the IRB.

<table>
<thead>
<tr>
<th>Code</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code), and</td>
</tr>
<tr>
<td>2</td>
<td>A key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.</td>
</tr>
</tbody>
</table>

- **YES**  
  The holder of the key (serving as an Honest Broker) and the investigator have entered into an agreement prohibiting the release of the key to the investigator under any circumstances, until the individuals are deceased.
  - **Honest Broker**: A neutral intermediary who collects and collates pertinent information regarding the data source, replaces identifiers with a code, and releases only coded information to the researcher.

- **YES**  
  The investigator has documentation of written policies and operating procedures from a repository or data management center that prohibits the release of the key to the investigators under any circumstances, until the individuals are deceased.

- **YES**  
  There are other legal requirements prohibiting the release of the key to the investigator, until the individuals are deceased.

**COMMENTS:**

7. IS THE PROJECT QUALITY ASSURANCE OR QUALITY IMPROVEMENT (QA/QI)?
If no, the project is human subjects research and requires oversight by the IRB.

- **YES**  
  The purpose of the project is to assess or improve an internal practice or process within a particular institution or a facility that conforms with expected norms. The findings of the study are expected to directly affect institutional practice and identify corrective action(s) needed. Dissemination of information often does not occur beyond the institution evaluated, but may occur in quality improvement publications.
  - When published or presented to a wider audience, the intent is to suggest potentially effective models, strategies, assessment tools or provide benchmarks or base rates rather than to develop or contribute to generalizable knowledge.

**COMMENTS:**

8. IS THE PROJECT PROGRAM EVALUATION (PE)?
If no, the project is human subjects research and requires oversight by the IRB.

- **YES**  
  The purpose of the project is to improve a specific program. The findings of the evaluation are expected to directly affect the conduct of the program and identify improvements. Dissemination of information back to the program stakeholders and participants is expected.
  - When published or presented to a wider audience, the intent is to suggest potentially effective models, strategies, assessment tools or provide benchmarks or base rates rather than to develop or contribute to generalizable knowledge.

**COMMENTS:**
9. Per DODI 3216.02, the following activities are NOT research involving human subjects:

- **YES** ☐ **NO** ☑ Activities carried out solely for purposes of diagnosis, treatment, or prevention of injury and disease in Service members and other mission essential personnel under force health protection programs of the Department of Defense, including health surveillance pursuant to section 1074 of Reference (g) and the use of medical products consistent with DoD Instruction 6200.02 (Reference (w)).

- **YES** ☐ **NO** ☑ Authorized health and medical activities as part of the reasonable practice of medicine or other health professions undertaken for the sole purpose of patient treatment.

- **YES** ☐ **NO** ☑ Activities performed for the sole purpose of medical quality assurance consistent with section 1102 of Reference (g) and DoD 6025.13 (Reference (y)).

- **YES** ☐ **NO** ☑ Activities performed solely for an OT&E project where the activities and the project meet the definition of OT&E as defined in section 139(a)(2)(A) of Reference (g).

- **YES** ☐ **NO** ☑ Activities performed solely for assessing compliance of individuals and organizations with requirements applicable to military, civilian, or contractor personnel or to organizational units, including such activities as occupational drug testing, occupational health and safety reviews, network monitoring, and monitoring for compliance with requirements for protection of classified information.

- **YES** ☐ **NO** ☑ Activities, including program evaluation, customer satisfaction surveys, user surveys, outcome reviews, and other methods, designed solely to assess the performance of DoD programs where the results of the evaluation are only for the use of Government officials responsible for the operation or oversight of the program being evaluated and are not intended for generalized use beyond such program.

- **YES** ☐ **NO** ☑ Survey, interview, or surveillance activities and related analyses performed solely for authorized spy, foreign intelligence collection purposes, as authorized by DoD 5240.01 (Reference (z)).

**COMMENTS:**

Reference (g): Sections 139(a)(2)(A), 380, 1074, and 1102 of title 42, United States Code.
Reference (y): DOD Instruction 6025.13, "Medical Quality Assurance (MQA) and Clinical Quality Management in the Military Health System (MHS)," 17 Feb 11.

**IRB Determination:**

- ☐ Not Human Subjects Research: No IRB Oversight Required
- ☐ Human Subjects Research: IRB Review and Approval Required
- ☐ I do not have any conflicts of interest regarding this project

**Printed Name of IRB Reviewer/Chair/Vice Chair:**

**Signature:**

**Date:**
1. BASIC STUDY INFORMATION

<table>
<thead>
<tr>
<th>Protocol Title:</th>
<th>Reviewer:</th>
</tr>
</thead>
</table>

2. SUBJECT INFORMATION

Does this research involve human subjects?

- [ ] YES
- [ ] NO

- [ ] Children: Age range of participants:
- [ ] Pregnant Women/Infants
- [ ] Prisoners
- [ ] Active Duty Military
- [ ] Mentally Disabled Persons
- [ ] Economically Disadvantaged Persons
- [ ] Educationally Disadvantaged Persons
- [ ] Other: __________________________

3. RESEARCH INFORMATION

Please indicate which exemption category applies to this protocol. For the category marked, include a brief description in the section below, describing how the category applies to the research study.

Note: All of the activities described in the protocol must fit into a category below for the protocol to be Exempt. More than one category may be selected.

- [ ] Category 1 – 32 CFR §219.101 (b)(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.

  Briefly describe how this category applies to the research: __________________________________________

- [ ] Category 2 – 32 CFR §219.101 (b)(2) (Does not apply to children)
  Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
  i. information obtained as recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
  ii. any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

  Briefly describe how this category applies to the research: __________________________________________

- [ ] Category 3 – 32 CFR §219.101 (b)(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.

  Briefly describe how this category applies to the research: __________________________________________

- [ ] Category 4 – 32 CFR §219.101 (b)(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.

  Briefly describe how this category applies to the research: __________________________________________
<table>
<thead>
<tr>
<th>Category 5 - 32 CFR §219.101(b)(5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research and demonstration projects which are conducted by or subject to the approval of department or agency heads and which are designed to study, evaluate, or otherwise examine:</td>
</tr>
<tr>
<td>i. Public benefit or service programs;</td>
</tr>
<tr>
<td>ii. Procedures for obtaining benefits or services under those programs;</td>
</tr>
<tr>
<td>iii. Possible changes in or alternatives to those programs or procedures; or</td>
</tr>
<tr>
<td>iv. Possible changes in methods or levels of payment for benefits or services under those programs.</td>
</tr>
<tr>
<td>Briefly describe how this category applies to the research:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category 6 - 32 CFR §219.101(b)(1) or 21 CFR §56.100(d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taste and food quality evaluation and consumer acceptance studies:</td>
</tr>
<tr>
<td>i. If wholesome foods without additives are consumed or</td>
</tr>
<tr>
<td>ii. If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.</td>
</tr>
<tr>
<td>Briefly describe how this category applies to the research:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Were the 32 CFR 219.111 criteria for approval met?</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
</tr>
<tr>
<td>1. Risks to subjects are minimized:</td>
</tr>
<tr>
<td>i. By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk; and</td>
</tr>
<tr>
<td>ii. Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.</td>
</tr>
<tr>
<td>2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects and the importance of the knowledge that may reasonably be expected to result;</td>
</tr>
<tr>
<td>3. Selection of subjects is equitable</td>
</tr>
<tr>
<td>4. Informed consent will be sought from each prospective subject or the subject’s legally authorized representative, in accordance with, and to the extent required by 32 CFR 219.116?</td>
</tr>
<tr>
<td>i. If no, has a Waiver of Informed Consent approved by the IRB?</td>
</tr>
<tr>
<td>5. Informed consent will be appropriately documented, in accordance with, and to the extent required by 32 CFR 219.117?</td>
</tr>
<tr>
<td>i. If no, has a Waiver of Documentation of Informed Consent approved by the IRB?</td>
</tr>
<tr>
<td>6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects</td>
</tr>
<tr>
<td>7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data</td>
</tr>
<tr>
<td>8. Are there adequate protections for the confidentiality of data?</td>
</tr>
<tr>
<td>9. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IRB Action:</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Full Board Review</td>
</tr>
<tr>
<td>Date Reviewed</td>
</tr>
<tr>
<td>Recommendation to IRB:</td>
</tr>
<tr>
<td>☐ Approve as submitted</td>
</tr>
<tr>
<td>I do not have any conflict of interest regarding this study</td>
</tr>
</tbody>
</table>

Printed Name of IRB Chair/Vice Chair | Signature | Date |
1. BASIC STUDY INFORMATION

<table>
<thead>
<tr>
<th>Protocol Title:</th>
<th>Reviewer:</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI:</td>
<td></td>
</tr>
</tbody>
</table>

2. SUBJECT INFORMATION

<table>
<thead>
<tr>
<th>Does this research involve human subjects?</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ YES</td>
</tr>
<tr>
<td>☐ Children: Age range of participants:</td>
</tr>
<tr>
<td>☐ Pregnant Women/Fetuses</td>
</tr>
<tr>
<td>☐ Prisoners</td>
</tr>
<tr>
<td>☐ Active Duty Military</td>
</tr>
</tbody>
</table>

3. RESEARCH INFORMATION

Expeditied research presents no more than “minimal risk” to the participant. “Minimal risk” means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

The IRB expeditied review process is not used when identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability, or be damaging to the subject’s financial standing, employability, insurability. IRB Reviewers are asked to consider these risks and indicate on the checklist concerns about these issues. Full committee review is required to allow for thoughtful consideration and debate about whether information collected about the participant would place him/her at risk of criminal or civil liability, or be damaging to the subject’s financial standing, employability, insurability.

Please indicate which expedited category applies to this protocol. For the category marked, include a brief description in the section below, describing how the category applies to the research study.

Note: All of the activities described in the protocol must fit into a category below for the protocol to be Expedited. More than one category may be selected.

☐ Category 1 – Clinical Drug Studies and Medical Devices
Clinical Drug Study; Research on drugs for which an investigational new drug (IND) application is not required.

Medical Devices: Research on medical devices for which:
(a) an Investigational Device Exemption (IDE) application is not required;
(b) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

Briefly describe how this category applies to the research: ________________________________

☐ Category 2 – Collection of blood samples by finger stick, heel stick, ear stick or venipuncture, as follows:

From healthy, non-pregnant adults who weigh at least 110 pounds, the amounts drawn may not exceed a total of 550 mL during an 8 week period and collection may not occur more frequently than 2 times per week.

From other adults and from children, consideration must be given to the age, weight and health of the subjects, the collection procedure, the total amount of blood to be collected and the frequency with which it will be collected: the amounts drawn may not exceed the lesser of 50 mL or 3 mL per kg during an 8 week period and collection may not occur more frequently than 2 times per week.

Briefly describe how this category applies to the research: ________________________________
CIP#  
IRB  
Naval Medical Center Portsmouth Institutional Review Board  
Expedited Review of New Research – IRB Reviewer Form

☐ Category 3 – Prospective collection of biological specimens for research purposes by noninvasive means.

Examples:
(a) hair and nail clippings in a non-disturbing manner;
(b) deciduous teeth at time of exfoliation as 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) unaccomplished saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or salt 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) supragingival 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, toenails or mouth washings;
(j) sputum collected after saline nebulization

Briefly describe how this category applies to the research.

☐ Category 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; this includes studies of cleared medical devices for new indications.)

Examples:
(a) physical sensors that are applied 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, electroneuromyography, 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.

Briefly describe how this category applies to the research.

Note 1: Research that requires any invasive procedures (with the exception of those listed in Category 4 above) is considered as involving greater than minimal risk and is not appropriate for Expedited Review.

☐ Category 5 – Research involving materials (data, documents, records, or specimens) that have previously been collected for any purpose, provided the materials were not collected for the currently proposed research.∗

∗ DoDI 3216.02, dated 08 Nov 11, alters the 45 CFR 46 language for Expedited Category 5 from materials that have been collected or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis) to materials that have previously been collected for any purpose, provided the materials were not collected for the currently proposed research.

Per DoD HRPP guidance 19 Mar 15, the DoDI 3216.02 does not limit or expand Expedited Category 5 as listed in the Federal Register (80/364–80/387 of 08 Nov 98). Projects using prospective data can continue to be reviewed and approved under Expedited Category 5, as long as this category continues to be appropriate for the study.

Note: Data that have been collected* are defined as “existing data,” which are defined by the regulations as data that exists before the study is proposed to an institutional official or to an IRB.

For retrospective records review studies, existing data to be collected should be identified in the protocol as “data, documents, records, or pathological specimens existing prior to [DATE] or between [DATE and DATE].

Briefly describe how this category applies to the research.
CIP#  
IRB  
Naval Medical Center Portsmouth Institutional Review Board  
Expedited Review of New Research – IRB Reviewer Form

☐ Category 6 – Collection of data from voice, video, digital or image recordings made for research purposes  
Briefly describe how this category applies to the research:  

☐ Category 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.  
Briefly describe how this category applies to the research:  

<table>
<thead>
<tr>
<th>Were the 32 CFR 219.111 criteria for approval met?</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Risks to subjects are minimized:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and</td>
<td></td>
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<tr>
<td>• Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Risks to subjects are reasonable in relation to anticipated benefits. If any, to subjects, and the importance of the knowledge that may reasonably be expected to result.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Selection of subjects is equitable.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Informed consent will be sought from each prospective subject or the subject’s legally authorized representative, in accordance with, and to the extent required by 32 CFR 219.116?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• If no, has a Waiver of Informed Consent approved by the IRB?</td>
<td></td>
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<tr>
<td>5. Informed consent will be appropriately documented, in accordance with, and to the extent required by 32 CFR 219.117?</td>
<td></td>
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<tr>
<td>• If no, has a Waiver of Documentation of Informed Consent approved by the IRB?</td>
<td></td>
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<tr>
<td>6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.</td>
<td></td>
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<tr>
<td>7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.</td>
<td></td>
<td></td>
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<tr>
<td>8. Are there adequate protections for the confidentiality of data?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects: (pregnant women/citizens, children, prisoners, mentally disabled, economically/educationally disadvantaged, deployed active duty)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IRB Action:  
☐ Full Board Review  ☐ Expedited Review

Date Reviewed:  
Review Cycle:  
Risk Level: ☐ Minimal Risk  ☐ N/A Greater than Minimal Risk

Recommendation to IRB:  ☐ Approve as submitted:  ☐ Approve pending requirements  ☐ Forward to Full Board

☐ I do not have any conflict of interest regarding this study

Printed Name of IRB Chair/Vice Chair  Signature  Date:  

Page 3 of 3  Version 15 February 2016
1. BASIC STUDY INFORMATION

Protocol Title: 
PI: 
Reviewer: 

2. SUBJECT INFORMATION

Does this research involve human subjects?

- [ ] YES
- [ ] NO

- [ ] Children: Age range of participants __________
- [ ] Mentally Disabled Persons
- [ ] Pregnant Women/Fetuses
- [ ] Economically Disadvantaged Persons
- [ ] Prisoners
- [ ] Educationally Disadvantaged Persons
- [ ] Other: __________
- [ ] Active Duty Military

3. RESEARCH INFORMATION

Exempt and Expedited research present no more than "minimal risk" to the participant. "Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

The IRB exempt/expedited review process is not used when identification of the subjects would reasonably place them at risk of criminal or civil liability; or be damaging to the subject's financial standing, employability, insurability.

IRB Reviewers are asked to consider these risks and indicate on the checklist concerns about these issues.

Please indicate which exempt or expedited category applies to this protocol. For the category marked, include a brief description in the section below, describing how the category applies to the research study.

Research in which the investigator receives and examines a de-identified data set may be eligible for Exempt approval.

Research in which the investigator receives or examines subject identifiers may be eligible for Expedited approval.

- [ ] EXEMPT Category 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.

Briefly describe how this category applies to the research: ____________________________

- [ ] EXPEDITED Category 5 – Research involving materials (data, documents, records, or specimens) that have previously been collected for any purpose, provided the materials were not collected for the currently proposed research.

* DoD 3216.02, dated 06 Nov 11, alters the 45 CFR 46 language for Expedited Category 5 from materials that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis) to materials that have previously been collected for any purpose, provided the materials were not collected for the currently proposed research.

Per DoD 3216.02 guidance 11 Mar 15, the DoD 3216.02 does not limit or expand Expedited Category 5 as listed in the Federal Register (80344-60367 of 19 Nov 98). Projects using prospective data can continue to be reviewed and approved under Expedited Category 5, as long as this category continues to be appropriate for the study.

Note: Data "that have been collected" are defined as "existing data", which are defined by the regulations as data that exists before the study is proposed to an institutional official or to an IRB.

For retrospective records review studies, existing data to be collected should be identified in the protocol as "data, documents, records, or pathological specimens existing prior to [DATE] or between [DATE and DATE]."

Briefly describe how this category applies to the research: ____________________________
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<tr>
<td>9</td>
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</tbody>
</table>

**IRB Action:**

- [ ] Full Board Review
- [ ] Expedited Review

**Date Reviewed:**

**Review Cycle:**

**Risk Level**

- [ ] Minimal Risk
- [ ] Greater than Minimal Risk

**Recommendation to IRB**

- [ ] Approve as submitted
- [ ] Approve pending requirements
- [ ] Forward to Full Board

- [ ] I do not have any conflict of interest regarding this study.

**Printed Name of IRB Chair/Vice Chair**

**Signature**

**Date**
# Naval Medical Center Portsmouth Institutional Review Board
## Full Board Review of New Research – IRB Reviewer Form

## 1. BASIC STUDY INFORMATION

<table>
<thead>
<tr>
<th>Protocol Title:</th>
<th>Reviewers:</th>
</tr>
</thead>
</table>

## 2. SUBJECT INFORMATION

**Does this research involve human subjects?**
- [ ] YES
- [ ] NO

- [ ] Children: Age range of participants
- [ ] Mentally Disabled Persons
- [ ] Pregnant Women/Fetuses
- [ ] Educationally Disadvantaged Persons
- [ ] Prisoners
- [ ] Other:

## 3. RESEARCH INFORMATION

### GENERAL

- Does the study involve a systematic investigation?
- Is the primary goal to develop or contribute to generalizable knowledge?
- Does the use of human subjects have research relevance?
- Are there ethical problems regarding the study's design and conduct?
- Do any apparent immediate risks exist?
- Does the study meet the definition for "minimal risk" (i.e., the risks of harm anticipated in the proposed research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests)?

### IRB PROTOCOL SIGNIFICANCE

- Is this Social Behavioral Research?
- Is this Biomedical Research?
- Is the research anonymous?
- Does the research design carry enough likelihood of yielding data sufficient to warrant risks to subjects?
- Is the design adequate to answer questions?
- Are the aims/objectives likely to be achievable within a given time period?
- Is the design described and adequately justified?

### RESEARCH DESIGN AND METHODS

- Are the study procedures and study visits clearly outlined and described?
- Are all procedures described clearly defined as either research related or completed as part of the subject's clinical care (regardless of study participation)?
- Are subjects being evaluated at intervals that are sufficiently frequent so as to identify and prevent untreated problems?
- If not already listed, does this study require an IND or IDE?
- Where appropriate, have alternative procedures that might be advantageous to the potential research subjects been described?

### DATA COLLECTION AND STATISTICAL CONSIDERATIONS

- Is the study population appropriate for the goals of the study? (consider both the nature and size of the sample)
- Is there a statistical justification for the sample size?
- Is the proposed statistical treatment of the data appropriate for the design of the study?
<table>
<thead>
<tr>
<th><strong>HUMAN SUBJECTS</strong></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the criteria for inclusion of subjects appropriate?</td>
<td></td>
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<tr>
<td>Are the criteria for exclusion of subjects appropriate?</td>
<td></td>
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<tr>
<td>If children are being enrolled into the study, did the investigator include the appropriate justification for inclusion of children? Refer to “children” checklist.</td>
<td></td>
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<tr>
<td>If prisoners are being enrolled into the study, did the investigator include the appropriate information for inclusion of prisoners? Refer to “prisoner” checklist.</td>
<td></td>
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<tr>
<td>If the study involves the recruitment and/or study of decisionally impaired subjects, has the investigator included all elements required? Refer to “decisionally impaired” checklist.</td>
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<tr>
<td>If the study involves the recruitment and/or study of pregnant women has the investigator provided appropriate justification? Refer to “pregnant women/fetuses” checklist.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>RECRUITMENT PROCEDURES</strong></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is recruitment strategy adequate?</td>
<td></td>
<td></td>
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<tr>
<td>Are recruitment materials included &amp; appropriate (ads, phone screen script, emails)</td>
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<tr>
<td>Is there a vulnerable population involved in this study? Identify population</td>
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<tr>
<td>Is justification for vulnerable population adequate?</td>
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<tr>
<td>Are methods of subject recruitment legal, ethical and free from coercion or undue influence?</td>
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</table>

<table>
<thead>
<tr>
<th><strong>RISKS/BENEFIT RATIO</strong></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are risks and benefits in the protocol consistent with risks/benefits in the consent?</td>
<td></td>
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<tr>
<td>Are all the risks (including known incidence) clearly described?</td>
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<tr>
<td>Have adequate safeguards been adopted to reduce risk exposure as much as possible?</td>
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<tr>
<td>Is there description of study design safeguards such that if the research protocol needs to be modified, or changes in the risk level occur, they will be appropriately and timely brought to the attention of the IRB for review and approval?</td>
<td></td>
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</tr>
<tr>
<td>Does the protocol outline specific steps that will be taken (i.e. during study participation, after study participation, and with the publication of study results) to ensure that the subject’s participation in the research study and respective data will be confidential?</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th><strong>BENEFITS</strong></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
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</thead>
<tbody>
<tr>
<td>Are the potential benefits to the subject (if any) clearly described?</td>
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<tr>
<td>Do the potential benefits to the subject and/or society outweigh the risks being incurred?</td>
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</table>

<table>
<thead>
<tr>
<th><strong>COSTS AND PAYMENTS</strong></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the financial obligations of the subject, the sponsor and the institution clearly described?</td>
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<tr>
<td>Do any payments seem sufficient yet not large enough to be coercive?</td>
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<tr>
<td>Does the compensation meet the DoD requirements?</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>QUALIFICATIONS OF INVESTIGATORS</strong></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do the principal investigator and co-investigators have the appropriate academic and clinical credentials and experience for this study?</td>
<td></td>
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<tr>
<td>If the principal investigator is a staff member, graduate student or trainee of the Institution, have appropriate faculty support and supervision been guaranteed?</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>BIBLIOGRAPHY/REFERENCES</strong></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Were appropriate references cited in the research protocol to support the research design and risks and benefits of the study?</td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>CONSENT – GENERAL CONSIDERATIONS</strong></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is clear, concise, non-technical language used throughout?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>CONSENT – BASIC ELEMENTS</td>
<td>YES</td>
<td>NO</td>
<td>NA</td>
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<td>--------------------------</td>
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<tr>
<td>A statement that the study involves research</td>
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<tr>
<td>A clear statement of the purpose of the study</td>
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<tr>
<td>A statement of the expected duration of the subject’s participation</td>
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<tr>
<td>A complete description of the procedures to be followed</td>
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<tr>
<td>Identification of any procedures which are experimental</td>
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<tr>
<td>A description of any reasonable foreseeable risks or discomforts, including invasion of privacy</td>
<td></td>
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<tr>
<td>A description of any benefit resulting from the research, either to the subjects or to others</td>
<td></td>
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<tr>
<td>A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant</td>
<td></td>
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<tr>
<td>A statement informing subject extent of confidentiality of records</td>
<td></td>
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<tr>
<td>An explanation of whom to contact for answers to pertinent questions about the research or about problems or concerns</td>
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</tr>
<tr>
<td>An explanation of whom to contact for answers to pertinent questions about the research participant’s rights, information or input</td>
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<tr>
<td>A statement that this is voluntary</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>A statement that the subject is free to withdraw from the study at any time without penalty or loss of benefits that the subject is otherwise entitled to</td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CONSENT – FOR RESEARCH INVOLVING MORE THAN MINIMAL RISK</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>An explanation as to whether any compensation is available if injury occurs</td>
<td></td>
<td></td>
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<tr>
<td>If compensation is available, what it consists of, or where further information may be obtained</td>
<td></td>
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</tr>
<tr>
<td>An explanation as to whether any medical treatments are available if injury occurs</td>
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<table>
<thead>
<tr>
<th>CONSENT – ADDITIONAL ELEMENTS</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
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</thead>
<tbody>
<tr>
<td>A description of the possible risks to the subjects which are currently unforeseeable</td>
<td></td>
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<tr>
<td>A description of the circumstances under which the subject’s participation may be terminated</td>
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<tr>
<td>A description of any financial costs to the subject that may result from participation in the research or withdrawal from the research</td>
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<tr>
<td>A description of the consequences of a subject’s decision to withdraw from the research and procedures for orderly termination</td>
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<tr>
<td>A description stating that subjects will be informed of significant new findings that may relate to their willingness to continue participating</td>
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<thead>
<tr>
<th>CONSENT – STUDY DESCRIPTION</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
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<tbody>
<tr>
<td>Is there a clear explanation of the reason particular subjects are invited to participate?</td>
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<tr>
<td>Is it clearly stated that the subject is participating in a research study?</td>
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<tr>
<td>Is the approximate number of subjects to be studied noted (including gender and age range)?</td>
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<tr>
<td>Are all procedures accurately described as either research related or completed as part of the subject’s clinical care (regardless of study participation)?</td>
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<tr>
<td>If the study involves the use of questionnaires, is there a description of the general content and time required to complete them?</td>
<td></td>
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<tr>
<td>Is the total volume of blood to be drawn (if any) described in tablespoons or teaspoons or ounces?</td>
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<tr>
<td>Are samples being collected and stored? If so, is it specified where the samples are stored, how they are identified, how long they will be stored, and who will have access to the samples?</td>
<td></td>
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</table>
### CONSENT – ALTERNATIVE TREATMENTS

- If applicable, have all alternative treatments been satisfactorily described?
- Is the language included in this section the same as that included in the protocol?

### CONSENT – CONFIDENTIALITY

- Have adequate measures been taken to protect subjects from breaches of confidentiality and/or invasion of privacy?
- Did the investigator use a statement describing the extent to which confidentiality of records identifying the subject will be maintained?
- Does the section sufficiently state who will have access to subject records (e.g., the FDA, study sponsor, Compliance and Risk Management)?
- If the use and disclosure of medical record information or other PHI are used as part of the research study have HIPAA regulations been addressed?

### CONSENT – RIGHT TO WITHDRAW

- Is this section clearly worded and non-coercive?
- Are the risks of subject withdrawal stated (if applicable)?
- Are reasons why a subject might be withdrawn from the study by investigators clearly defined?

### CONSENT – COMPENSATION FOR INJURY

- Is the standard statement or other satisfactory wording included?

### CONSENT – VOLUNTARINESS?

- Is there an appropriate line for the date and signature of the subject?
- Is there a parental permission section included if children are included in the study?
- Are there appropriate signature spaces for the child to sign assent?
- If the protocol provides a justification for the use of proxy consent, are there appropriate signature spaces included?

### CONSENT – HIPAA AUTHORIZATION

- If the use and disclosure of medical record information is completed as part of the research study have HIPAA regulations been addressed?

### CONSENT – MULTICENTER STUDIES

- If the study involves international sites, has the investigator included all applicable information (e.g., FWAs for federally funded studies, local IRB approval, translated consent forms as well as a back-translation)?
- If the study involves non-local sites (i.e. outside of the institution) has local IRB approval been obtained?

### ACCOMPANYING CHECKLISTS

- Research Involving Pregnant Women/Fetuses
- Research Involving Children
- Research Involving Prisoners
- Research Involving Decisionally Impaired Adults
CIP# Naval Medical Center Portsmouth Institutional Review Board Full Board Review of New Research – IRB Reviewer Form

<table>
<thead>
<tr>
<th>Were the 32 CFR 219.111 criteria for approval met?</th>
<th>YES</th>
<th>NO</th>
</tr>
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<tbody>
<tr>
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IRB Action:
- [ ] Full Board Review
- [ ] Expected Review

Date Reviewed: Review Cycle: Risk Level: [ ] Minimal Risk [ ] Greater than Minimal Risk

Recommendation to IRB:
- [ ] Approve as submitted
- [ ] Approve pending requirements
- [ ] Table
- [ ] Disapprove
- [ ] I do not have any conflict of interest regarding this study

Printed Name of IRB Reviewer/Chair/Vice Chair: Signature: Date:
## BASIC USE INFORMATION

<table>
<thead>
<tr>
<th>CU Title</th>
<th>Reviewers</th>
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<tr>
<td>PI:</td>
<td></td>
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## COMPASSIONATE USE INFORMATION

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<tr>
<th>Question</th>
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<tr>
<td>FDA Single Patient Compassionate Use?</td>
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<tr>
<td>FDA Intermediate-size Patient Population Compassionate Use?</td>
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<tr>
<td>FDA Treatment Protocol Compassionate Use (designed for use in larger patient populations)</td>
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<table>
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<th>Drug</th>
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<tr>
<th>Device</th>
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<tbody>
<tr>
<td></td>
<td>Market Approved</td>
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## ITEMS TO CONSIDER

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<tr>
<th>Question</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has a brief clinical history of the patient including diagnosis, disease status, prior therapy, response to prior therapy, and rationale for requesting the proposed treatment been provided?</td>
<td></td>
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<tr>
<td>Has a proposed CU treatment plan been provided?</td>
<td></td>
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<tr>
<td>Has use of the CU drug/device been justified?</td>
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<tr>
<td>Are the risks of treatment with the CU drug/device acceptable?</td>
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<tr>
<td>Has a letter of support from an un-involved physician, concurring with the decision to treat with the CU drug/device been provided?</td>
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<tr>
<td>Have supporting documents from the sponsor/manufacturer been provided?</td>
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<tr>
<td>Are consent/assent materials acceptable?</td>
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Were the 32 CFR 219.111 criteria for approval met?

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<thead>
<tr>
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| 1. Risks to subjects are minimized:  
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| 2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. |     |     |
| 3. Selection of subjects is equitable |     |     |
| 4. Informed consent will be sought from each prospective subject or the subjects legally authorized representative, in accordance with, and to the extent required by 32 CFR 219.117:  
   - If no, has a Waiver of informed Consent approved by the IRB? |     |     |
| 5. Informed consent will be appropriately documented, in accordance with, and to the extent required by 32 CFR 219.117:  
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| 6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. |     |     |
| 7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. |     |     |
| 8. Are there adequate protections for the confidentiality of data? |     |     |
| 9. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects.  
   (Applicable if study involves pregnant women/mothers, children, prisoners, mentally disabled persons, economically/educationally disadvantaged persons, deployed active duty personnel) |     |     |

IRB Action:

- Full Board Review

Date Reviewed:  
Review Cycle:

Recommendation to IRB:

- Approve as submitted  
- Approve pending requirements  
- Table  
- Disapprove

☐ I do not have any conflict of interest regarding this CU request.

Printed Name of IRB Reviewer/Chair/Vice Chair:  
Signature:  
Date:
1. BASIC STUDY INFORMATION

<table>
<thead>
<tr>
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<tbody>
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<td></td>
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</table>

2. SUBJECT INFORMATION

Does this research involve human subjects?

- [ ] YES
- [x] NO

- [ ] Children: Age range of participants
- [ ] Pregnant Women/Fetuses
- [ ] Prisoners
- [ ] Active Duty Military
- [ ] Mentally Disabled Persons
- [ ] Economically Disadvantaged Persons
- [ ] Educationally Disadvantaged Persons
- [ ] Other: __________

3. RESEARCH INFORMATION

This study was approved under Exempt Category:

- [ ] Category 1 [Educational practices-instructional techniques and curricula]
- [ ] Category 2 [Educational tests, surveys, interviews, and public behavior]
- [ ] Category 3 [Educational tests, surveys, interviews, and public behavior-public officials]
- [ ] Category 4 [De-identified existing data, records or specimens]
- [ ] Category 5 [Public benefit and service programs]
- [ ] Category 6 [Taste and food quality]

Below, please indicate concurrence that continuation under this category is still appropriate.

- [ ] Category 1 – 32 CFR §219.101 (b)(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.

  Continuation under this category is still appropriate? __________

- [ ] Category 2 – 32 CFR §219.101 (b)(2) (Does not apply to children)
  
  Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless
  
  i. information obtained as recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects, and
  
  ii. any disclosure of the human subjects’ responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, or reputation.

  Continuation under this category is still appropriate? __________
<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Continuation under this category is still appropriate?</th>
</tr>
</thead>
</table>
| 3 | **Category 3 – 32 CFR §219.101 (b)(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 | **Category 4 – 32 CFR §219.101 (b)(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. |
| 6 | **Category 6 - 32 CFR §219.101 (b)(5)** | Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:  
  i. Public benefit or service programs  
  ii. Procedures for obtaining benefits or services under those programs;  
  iii. Possible changes in or alternatives to those programs or procedures; or  
  iv. Possible changes in methods or levels of payment for benefits or services under those programs. |
| 6 | **Category 6 – 32 CFR §219.101(b)(1) or 21 CFR §56.106(d)** | Taste and food quality evaluation and consumer acceptance studies:  
  i. if wholesome foods without additives are consumed or  
  ii. if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe; or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. |

Continuation under this category is still appropriate? ____________________________
<table>
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<tr>
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**IRB Action**

- [ ] Full Board Review
- [ ] Expedited Review

**Date Reviewed:**

**Review Cycle:**

**Risk Level:**

- [ ] Minimal Risk
- [ ] Greater than Minimal Risk

**Recommendation to IRB:**

- [ ] Approve as submitted
- [ ] Approve pending requirements

- [ ] I do not have any conflict of interest regarding this study

**Printed Name of IRB Chair/Vice Chair:**

**Signature:**

**Date:**

---

*Page 3 of 3  Version 15 February 2016*
1. BASIC STUDY INFORMATION

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2. SUBJECT INFORMATION

Does this research involve human subjects?
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- [ ] NO

- [ ] Children: Age range of participants
- [ ] Mentally Disabled Persons
- [ ] Pregnant Women/Fetuses
- [ ] Economically Disadvantaged Persons
- [ ] Prisoners
- [ ] Educationally Disadvantaged Persons
- [ ] Active Duty Military
- [ ] Other:

3. RESEARCH INFORMATION

This study was approved under Expedited Category:
- [ ] Category 1 (Clinical studies of drugs or medical devices with no IND/IDE)
- [ ] Category 2 (Collection of blood sample)
- [ ] Category 3 (Prospective non-invasive collection of biological specimens for research purposes)
- [ ] Category 4 (Collection of data though non-invasive routine clinical practices)
- [ ] Category 5 (Data, records, or specimens that have previously been collected for any purpose, provided the materials were not collected for the currently proposed research)
- [ ] Category 6 (Data from voice, video, digital, or image recordings made for research purposes)
- [ ] Category 7 (Individual / group characteristics or behavior, research using survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance)

This study was approved under Full Board review, and is eligible for review under Category:
- [ ] Category 8 (Permanently closed to enrollment, subjects completed, study open only for long-term follow up of subjects, no subjects enrolled and no additional risks identified, only data analysis remains)
- [ ] Category 9 (Categories two through 8 do not apply, but convened IRB has determined that the research involves no greater than minimal risk and no additional risks have been identified)

Below, please indicate concurrence that continuation under this category is still appropriate.

- [ ] Category 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.
  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 being used in accordance with its cleared/approved labeling.

- [ ] Category 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;
  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.

Continuation under this category is still appropriate?
Category 3 - Prospective collection of biological specimens for research purposes by noninvasive means.

Examples:
(a) Raw and hair clippings in noninvasive manner;
(b) Caudal teeth at time of extraction 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) Uncultured saliva collected either in a stimulated fashion or simulated by chewing gumbase or wax or by applying dilute nitric 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) Muscular and skin cells collected by buccal swabbing or eavestskin swab; or mouth washings;
(j) Sputum collected after saline mist inhalation.

Continuation under this category is still appropriate?

Category 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 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, electromyography, 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.

Continuation under this category is still appropriate?

Category 5

Research involving materials (data, documents, records, or specimens) that have previously been collected for any purpose, provided the materials were not collected for the currently proposed research.

* DoD 3216.02, dated 06 Nov 11, alters the 45 CFR 46 language for Expedited Category 5 from materials that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis) to materials that have been previously collected for any purpose, provided the materials were not collected for the currently proposed research.

Per DoD HRPP guidance 11 Mar 15, the DoD 3216.02 does not limit or expand Expedited Category 5 as listed in the Federal Register (80FR 62667 of 09 Nov 98). Projects using prospective data can continue to be reviewed and approved under Expedited Category 5, as long as the category continues to be appropriate for the study.

Note: Data "that have been collected" are defined as "existing data," which are defined by the regulations as data that exists before the study is proposed to an institutional office or to an IRB.
For retrospective records review studies, existing data to be collected should be identified in the protocol as "data, documents, records, or pathological specimens existing prior to [DATE] or between [DATE and DATE].

Continuation under this category is still appropriate?

Category 6

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

Continuation under this category is still appropriate?
### Category 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.

Continuation under this category is still appropriate?

### Category 8
Continuing review of research previously approved by the convened IRB as follows:
- 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
- Where no subjects have been enrolled and no additional risks have been identified; or
- Where the remaining research activities are limited to data analysis.

Continuation under this category is still appropriate?

### Category 9
Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through (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.

Continuation under this category is still appropriate?

---

### Study Status:

<table>
<thead>
<tr>
<th>Choose one</th>
<th>or</th>
<th>Choose One</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolment not yet begun</td>
<td></td>
<td>Subject / Records Activity Ongoing</td>
</tr>
<tr>
<td>(Study approved but has not initiated)</td>
<td></td>
<td>(Interaction / Intervention / Collection ongoing)</td>
</tr>
<tr>
<td>Enrolment Open</td>
<td></td>
<td>Subject / Records Activity Complete</td>
</tr>
<tr>
<td>(Subjects / records accrual ongoing)</td>
<td></td>
<td>(Only long term follow-up of subjects remains)</td>
</tr>
<tr>
<td>Enrolment Closed</td>
<td></td>
<td>Data Analysis Only</td>
</tr>
<tr>
<td>(Subjects / records accrual no longer occurring)</td>
<td></td>
<td>(Remaining research activities limited to data analysis)</td>
</tr>
</tbody>
</table>

### Continuing Review form has documented:

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. The number of subjects / records enrolled.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Number of male and female subjects.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. The ethnicity of subjects.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. The number of subjects withdrawn and/or lost to follow-up and an explanation for why this occurred.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Comments:**

### Since the last IRB review were there:

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Adverse events, untoward events, or outcomes experienced by participants.</td>
<td></td>
</tr>
<tr>
<td>b. Unanticipated problems and/or unanticipated problems involving risks to participants or others.</td>
<td></td>
</tr>
<tr>
<td>c. Complaints about the research.</td>
<td></td>
</tr>
<tr>
<td>d. Amendments or modifications.</td>
<td></td>
</tr>
<tr>
<td>e. Internal or external audits</td>
<td></td>
</tr>
</tbody>
</table>

**Comments:**

### New factors affecting study assessment have been included:

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Interim findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. DSM5 reports or other relevant multi-center trial reports</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Other relevant information (particularly changes to the risk/benefit ratio identified during the review period)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Comments:**
**Additional considerations for continuing review:**

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>Does the protocol need verification from sources other than the investigator that no material changes have occurred since the last review?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b.</td>
<td>Are there significant new findings concerning this research that might affect the willingness of participants to continue to take part in the research? If there are significant new findings, state how they will be provided to participants, or if not provided, explain rationale.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c.</td>
<td>Are consent form(s) incorrect or incomplete? Consent forms are re-visited to reflect the IRB approval signature or each subsequent continuing review. The Investigator MAY continue to use the previously approved version of the consent form for enrolled subjects while the revised consent form associated with this Amendment awaits approval by the CO. If NO, explain why.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Comments:**

---

**Were the 32 CFR 219.11f criteria for approval met?**

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Risks to subjects are minimized: By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or therapeutic purposes.</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Selection of subjects is equitable.</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 32 CFR 219.11f? If no, has a Waiver of Informed Consent approved by the IRB?</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Informed consent will be appropriately documented, in accordance with, and to the extent required by 32 CFR 219.11f? If no, has a Waiver of Documentation of Informed Consent approved by the IRB?</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects?</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Are there adequate protections for the confidentiality of data?</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects. (Applicable if study involves pregnant women/infants, children, prisoners, mentally disabled persons, economically/educationally disadvantaged persons, deployed active duty personnel.)</td>
<td></td>
</tr>
</tbody>
</table>

---

**IRB Action**

- [ ] Full Board Review
- [ ] Expedited Review

**Date Reviewed:**

**Review Cycle:**

**Risk Level:**

- [ ] Minimal Risk
- [ ] Greater than Minimal Risk

---

**Recommendation to IRB**

- [ ] Approve as submitted
- [ ] Approve pending requirements

[ ] I do not have any conflict of interest regarding this study

**Printed Name of IRB Chair/Vice Chair**

**Signature**

**Date**
# Naval Medical Center Portsmouth Institutional Review Board
## Full Board Continuing Review – IRB Reviewer Form

### 1. Basic Study Information

<table>
<thead>
<tr>
<th>Protocol Title:</th>
<th>Expiration Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI:</td>
<td>Reviewer:</td>
</tr>
<tr>
<td>BUMED code:</td>
<td></td>
</tr>
</tbody>
</table>

### 2. Subject Information

**Does this research involve human subjects?**

- [ ] Yes
- [ ] No

- [ ] Children
- [ ] Age range of participants: ________
- [ ] Pregnant Women/Fetuses
- [ ] Prisoners
- [ ] Active Duty Military
- [ ] Mentally Disabled Persons
- [ ] Economically Disadvantaged Persons
- [ ] Educationally Disadvantaged Persons
- [ ] Other: ________

**This study was approved under Full Board review**

### 3. Research Information

**Study Status:**

- [ ] Choose one:
  - Enrolment not yet begun  
    (Study approved but has not initiated)
  - Enrolment Open  
    (Subject/records accrual ongoing)
  - Enrolment Closed  
    (Subject/records accrual no longer occurring)

- [ ] Choose one:
  - Subject/Records Activity Ongoing  
    (Interaction/Intervention/Collection ongoing)
  - Subject/Records Activity Complete  
    (Only long-term follow-up of subjects remains)
  - Data Analysis Only  
    (Remaining research activities limited to data analysis)

**Continuing Review form documented:**

- a. The number of subjects/records enrolled: 
- b. Number of male and female subjects: 
- c. The ethnicity of subjects: 
- d. The number of subjects withdrawn and/or lost to follow-up and an explanation for why this occurred: 

**Comments:**

**Since the last IRB review were there:**

- a. Adverse events, untoward events, or outcomes experienced by participants: 
- b. Unanticipated problems and/or unanticipated problems involving risks to participants or others: 
- c. Complaints about the research: 
- d. Amendments or modifications: 
- e. Internal or external audits: 

**Comments:**

**New factors affecting study assessment have been included:**

- a. Literature search and assessment of how new publications impact the research project: 
- b. Interim findings: 
- c. DSM5 reports or other relevant multi-center trial reports: 
- d. Other relevant information (particularly changes to the risk/benefit ratio identified during the review period): 

**Comments:**

*Page 1 of 2  Version 15 February 2016*
**Additional considerations for continuing review:**

<table>
<thead>
<tr>
<th>a. Does the protocol need verification from sources other than the investigators that no material changes have occurred since the last review?</th>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>b. Are there significant new findings concerning this research that might affect the willingness of participants to continue to take part in the research? If there are significant new findings, state how they will be provided to participants, or if not provided, explain rationale.</td>
<td>YES</td>
<td>NO</td>
<td>N/A</td>
</tr>
<tr>
<td>c. Are consent form(s) incorrect or incomplete?</td>
<td>YES</td>
<td>NO</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*Consent form(s) are re-versioned to reflect the IRB approval signature on each subsequent continuing review.*
- The Investigator MAY continue to use the previously approved version of the consent form to enroll subjects while the revised consent form associated with this Amendment awaits approval by the CD.
- If NO, explain why.

**Comments:**

**Were the 32 CFR 219.111 criteria for approval met?**

<table>
<thead>
<tr>
<th>1. Risks to subjects are minimized:</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>- By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and.</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>- Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>3. Selection of subjects is equitable.</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 32CFR219.116?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>- If no, has a Waiver of Informed Consent approved by the IRB?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>5. Informed consent will be appropriately documented, in accordance with, and to the extent required by 32 CFR 219.117?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>- If no, has a Waiver of Documentation of Informed Consent approved by the IRB?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.</td>
<td>YES</td>
<td>NO</td>
</tr>
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<td>7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.</td>
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<td>NO</td>
</tr>
<tr>
<td>8. Are there adequate protections for the confidentiality of data?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>9. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects. (Applicable if study involves pregnant women/adolescents, children, prisoners, mentally disabled persons, economically/educationally disadvantaged persons, deployed active duty personnel.)</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

**IRB Action:**
- [ ] Full Board Review  [ ] Expedited Review

**Date Reviewed**

**Review Cycle:**

**Risk Level:**
- [ ] Minimal Risk
- [ ] Greater than Minimal Risk

**Recommendation to IRB:**
- [ ] Approve as submitted
- [ ] Approve pending requirements
- [ ] Table
- [ ] Disapprove

[ ] I do not have any conflict of interest regarding this study.

**Printed Name of IRB reviewer/Chair/Vice Chair**

**Signature**

**Date**

---

Page 2 of 2  Version 15 February 2016
BASIC STUDY INFORMATION

Protocol Title:  
PI:  
Reviewer:  
BUMED code:  
Reviewed:  

1. What is the current level of risk for the protocol:
   - [ ] Minimal Risk
   - [ ] Greater than Minimal Risk
   - [ ] EM_____
   - [ ] EP_____
   - [ ] FB_____

2. Will the changes requested in this Amendment impact the risk assessment?
   - [ ] No, Risk level stays the same
   - [ ] Yes, Risk level increases
   - [ ] Yes, Risk level decreases

3. Is the change a minor amendment that meets either/both of the following criteria:
   - [ ] Minor changes to currently approved research.
   - [ ] All of the proposed changes are found by the reviewer to involve no more than minimal risk and are approvable under an Exempt or Expedited Category.
     If yes, Expedited review is appropriate. If not, Full Board review is required.

<table>
<thead>
<tr>
<th>Are there consent form changes associated with this Amendment?</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The Investigator may continue to use the previously approved version of the consent form to enroll subjects while the revised consent form associated with this Amendment awaits approval by the CO.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>If NO, explain why:</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Is documentation from other reviews required? (such as scientific, radiation safety, pharmacy, laser safety, occupational safety, etc.)</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Are any endorsements required? (e.g. from Command relying on other IRB)</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Was the Amendment reviewed and approved before implementation of the changes?</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>• If no, was the change implemented to eliminate an immediate apparent hazard?</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Does the amendment represent new information that needs to be provided to past, present, and/or future subjects?</th>
<th>YES</th>
<th>NO</th>
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<tbody>
<tr>
<td>• Has a plan to notify completed and/or active subjects been included?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were the 32 CFR 219.111 criteria for approval met?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>-------------------------------------------------</td>
<td>-----</td>
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<tr>
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<td></td>
</tr>
</tbody>
</table>

IRB Action:
- Full Board Review  
- Expedited Review

Date Reviewed: [ ]  
Review Cycle: [ ]  
Risk Level: [ ] Minimal Risk  
[ ] Greater than Minimal Risk

Recommendation to IRB: [ ] Approve as submitted  
[ ] Approve pending requirements  
[ ] Table  
[ ] Disapprove

☐ I do not have any conflict of interest regarding this study.

Printed Name of IRB Reviewer/Chair/Vice Chair: [ ]  
Signature: [ ]  
Date: [ ]
## BASIC STUDY INFORMATION

**Protocol Title:**

**PI:**

**Reviewer:**

**B/L/MED code:**

**Reviewed:**

<table>
<thead>
<tr>
<th>Changes made</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Change of PI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Addition/Removal of Associate Investigators</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Change of Research Monitor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**What is the current level of risk for the protocol:**

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Minimal Risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ Greater than Minimal Risk</td>
<td></td>
<td></td>
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</tbody>
</table>

**Review level:**

<table>
<thead>
<tr>
<th>Review Level</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ EM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>□ EP</td>
<td></td>
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</tr>
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<td>□ FB</td>
<td></td>
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</table>

**Are there consent form changes associated with this Amendment?**

- The Investigator may continue to use the previously approved version of the consent form to enroll subjects while the revised consent form associated with this Amendment awaits approval by the CO.

**If NO, explain why:**

**Is documentation from other reviews required?**

(such as scientific, radiation safety, pharmacy, laser safety, occupational safety, etc.)

**Are any endorsements required? (e.g. from Command relying on other IRB)**

**Was the Amendment reviewed and approved before implementation of the changes?**

- If no, was the change implemented to eliminate an immediate apparent hazard?

**Does the amendment represent new information that needs to be provided to past, present, and/or future subjects?**

- Has a plan to notify completed and/or active subjects been included?

## IRB Action:

- [ ] Full Board Review
- [ ] Expedited Review
- [ ] Administrative Review

**Date Reviewed:**

**Review Cycle:**

**Risk Level**

- [ ] Minimal Risk
- [ ] Greater than Minimal Risk

**Recommendation to IRB**

- [ ] Approve as submitted
- [ ] Approve pending requirements
- [ ] Table
- [ ] Disapprove

- [ ] I do not have any conflict of interest regarding this study

**Printed Name of IRB Reviewer**

**Chair/Vice Chair or Designee**

**Signature**

**Date**
BASIC STUDY INFORMATION

Protocol Title: ________________________________
PI: ________________________________ Reviewer: ________________________________
BUMED code: ________________________________ Reviewed: ________________________________

Project Status

<table>
<thead>
<tr>
<th>Total Subjects IRB Approved</th>
<th>Total Subjects Enrolled</th>
<th>Total Subjects Currently Active</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Enrollment:  
- Open
- Closed

Risk Rating:  
- Minimal
- Greater than Minimal

Level:  
- EM
- EP
- FB

Brief Description of Item to be Acknowledged:

In your opinion, are any follow-up actions required in response to this item?
- YES
- NO

In your opinion, are changes to the protocol or informed consent warranted as a result of this item?
- YES
- NO

In your opinion, do subjects need to be notified of information contained in this item?
- YES
- NO

IRB Action:
- Full Board Review
- Expedited Review

Date Reviewed: ________________________________
Review Cycle: ________________________________
Risk Level:  
- Minimal Risk
- Greater than Minimal Risk

Recommendation to IRB:  
- Approve as submitted
- Approve; pending requirements
- Table
- Disapprove
- I do not have any conflict of interest regarding this study

Printed Name of IRB Reviewer/Chair/Vice Chair: ________________________________
Signature: ________________________________
Date: ________________________________

1. BASIC STUDY INFORMATION

Protocol Title: 
PI: 
URNED code: FR
Expiration Date: 
Reviewer: 

2. SUBJECT INFORMATION

Vulnerable populations participating in this study:
- N/A
- Children: age range of participants
- Pregnant Woman
- Prisoners
- Active Duty Military
- Mentally Disabled Persons
- Economically Disadvantaged Persons
- Educationally Disadvantaged Persons
- Other:

3. RESEARCH INFORMATION

This study was approved under:
- Full Board review
- Greater than minimal Risk
- Minimal Risk
- Expedited review
  - Category 1 [Clinical studies of drugs or medical devices with no NOIDE]
  - Category 2 [Collection of blood sample]
  - Category 3 [Prospective non-invasive collection of biological specimens for research purposes]
  - Category 4 [Collection of data through non-invasive routine clinical practices]
  - Category 5 [Data, records, or specimens that have been previously collected for any purpose, provided the materials were not collected for the currently proposed research]
  - Category 6 [Data from voice, video, digital, or image recordings made for research purposes]
  - Category 7 [Individual/group characteristics or behavior; research using survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance]
- Exempt review
  - Category 1 [Educational practitioner-instructional techniques and curricula]
  - Category 2 [Educational tests, surveys, interviews, and public behavior]
  - Category 3 [Educational tests, surveys, interviews, and public behavior; public officials]
  - Category 4 [De-identified existing data, records or specimens]
  - Category 5 [Public benefit and service programs]
  - Category 6 [Taste and food quality]

4. THE INVESTIGATOR REQUESTS

- Completion: Has a data summary been submitted? 
  - YES
  - NO
- Closure not completed: Has a justification for closure been provided? 
  - YES
  - NO

5. WILL COMPLETION/CLOSURE OF THIS STUDY RESULT IN THE POTENTIAL FOR RISKS OR HARM TO SUBJECTS?

- YES
- NO

If yes, describe the risks or harm.

6. DO SUBJECTS NEED TO BE NOTIFIED OF THIS COMPLETION/CLOSURE?

- YES
- NO

If yes, state what information needs to be communicated.

7. DO YOU AGREE THAT COMPLETION/CLOSURE-WITHOUT COMPLETION IS APPROPRIATE?

- YES
- NO

NOTE: No subjects may be active and no actions may be pending completion for closure to be appropriate.

IRB Action:
- Full Board Review
- Expedited Review

Date Reviewed: 
Review Cycle: 
Risk Level: Minimal Risk
Greater than Minimal Risk

Recommendation to IRB:
- Approve as submitted
- Approve pending requirements
- Table
- Disapprove

I do not have any conflict of interest regarding this study.
### Basic Study Information

<table>
<thead>
<tr>
<th>Protocol Title:</th>
<th>Expiration Date:</th>
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<tbody>
<tr>
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</table>

<table>
<thead>
<tr>
<th>Reviewer:</th>
<th>Meeting Date:</th>
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<tbody>
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</tbody>
</table>

### Subject Information

- **Vulnerable populations participating in this study:**
  - [ ] N/A
  - Children: age range of participants: ______
  - Pregnant Women
  - Prisoners
  - Active Duty Military
  - Mentally Disabled Persons
  - Economically Disadvantaged Persons
  - Educationally Disadvantaged Persons
  - Other: ______

### Research Information

- **This study was approved under:**
  - [ ] Full Board review
  - Minimal Risk
  - Greater than Minimal Risk
  - Greater than Minimal Risk [now eligible for review under EP8]

- [ ] Expedited review
  - Category 1: Clinical studies of drugs or medical devices with no IND/IDE
  - Category 2: Collection of blood sample
  - Category 3: Prospective non-invasive collection of biological specimens for research purposes
  - Category 4: Collection of data through non-invasive routine clinical practices
  - Category 5: Data, records, or specimens that have previously been collected for any purpose, provided the materials were not collected for the currently proposed research.
  - Category 6: Data from voice, video, digital, or image recordings made for research purposes
  - Category 7: Individual/group characteristics or behavior, research using survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance

- [ ] Exempt review
  - Category 1: Educational practices-instructional techniques and curricula
  - Category 2: Educational tests, surveys, interviews, and public behavior
  - Category 3: Educational tests, surveys, interviews, and public behavior-public officials
  - Category 4: De-identified existing data, records, or specimens
  - Category 5: Public benefit and service programs
  - Category 6: Taste and food quality

### Subject Status

<table>
<thead>
<tr>
<th>Total Subjects IRB Approved:</th>
<th>Total Records IRB Approved:</th>
</tr>
</thead>
<tbody>
<tr>
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</table>

<table>
<thead>
<tr>
<th>Total Subjects Enrolled:</th>
<th>Total Records Collected:</th>
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<tbody>
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</table>

<table>
<thead>
<tr>
<th>Total Subjects Currently Active:</th>
<th>Record collection:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ongoing</td>
</tr>
</tbody>
</table>

[ ] Enrollment Open  [ ] Enrollment Closed
- If an investigator does not abide by the federal regulations (such as failure to complete continuing reviews, protocol deviations, and improper consent) the IRB may be called upon to suspend or terminate approval of the research not being conducted in accordance with the IRB's requirements or that had been associated with unexpected serious harm to participants.

- Continuing non-compliance is repetition of same or similar behavior following advice from the IRB, CID, or others involved in the research.

- Continuing non-compliance by investigators requires escalating notification of next in chain of command, e.g., Department Heads, Directors. All suspensions are reported to the Director of Professional Education, Deputy Commander, and Commander.

**Justification for Request for Administrative Termination:**

In your opinion, are any follow-up actions required in response to this item?
- [ ] YES: ________________________________
- [ ] NO

In your opinion, do subjects need to be notified of this administrative termination?
- [ ] YES: ________________________________
- [ ] NO

In your opinion, does this item represent continuing non-compliance by the PI, Research Staff, or Department?
- [ ] YES: ________________________________
- [ ] NO

**IRB Action:**

- [ ] Full Board Review

**Date Reviewed:** ____________

**Review Cycle:** ____________

**Risk Level**
- [ ] Minimal Risk
- [ ] Greater than Minimal Risk

**Recommendation to IRB:**
- [ ] Approve as submitted
- [ ] Approve pending requirements
- [ ] Table
- [ ] Disapprove

- [ ] I do not have any conflict of interest regarding this study.

Printed Name of IRB Reviewer/Chair/Vice Chair: ____________________________

Signature: ____________________________

Date: ____________________________
**BASIC STUDY INFORMATION**

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<tr>
<th>Protocol Title:</th>
<th>Reviewer:</th>
<th>BUMED code:</th>
</tr>
</thead>
</table>

Per DoD 3216.02, the applicability of Subpart B is limited to research involving pregnant women as human subjects involved in research that is more than minimal risk and includes interventions or invasive procedures to the woman or the fetus.

- This checklist is not required if a protocol is [select one]
  - Approved under Exempt or Expedited categories
  - Full Board research assessed as minimal risk
  - Full Board research assessed as greater than minimal risk which does not include interventions or invasive procedures

<table>
<thead>
<tr>
<th>Research Involving Pregnant Women Criteria</th>
<th>Y</th>
<th>N</th>
<th>N/A</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, has been conducted and provide data for assessing potential risks to pregnant women and fetuses.</td>
<td></td>
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<tr>
<td>One of the following is true:</td>
<td></td>
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</tr>
<tr>
<td>- 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.</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>- The risk to the fetus is not greater than minimal and the purpose of the research is the development of important generalizable knowledge which cannot be obtained by any other means.</td>
<td></td>
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<tr>
<td>Any risk is the least possible for achieving the objectives of the research.</td>
<td></td>
<td></td>
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<tr>
<td>For children who are pregnant, assent and permission are obtained in accordance with the regulations.</td>
<td></td>
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<tr>
<td>No inducements, monetary or otherwise, will be offered to terminate a pregnancy.</td>
<td></td>
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</tr>
<tr>
<td>Individuals engaged in the research have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Individuals engaged in the research have no part in determining the viability of a neonate.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Consent/ Permission Criteria</th>
<th>Y</th>
<th>N</th>
<th>N/A</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>The consent of the mother is obtained in accordance with consent regulations 32 CFR 219.116 &amp; 117.</td>
<td></td>
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</tr>
<tr>
<td>If the research holds out the prospect of direct benefit solely to the fetus, then the consent of the father is also obtained in accordance with the regulations, except that the father's consent does not need to be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.</td>
<td></td>
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<tr>
<td>Individuals providing consent are fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Were the 32 CFR 219.11 criteria for approval met?</td>
<td>YES</td>
<td>NO</td>
<td></td>
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<tr>
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<td>-----------------------------------------------</td>
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<tr>
<td>1</td>
<td>Risks to subjects are minimized:</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and</td>
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<tr>
<td></td>
<td>• Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.</td>
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<tr>
<td>2</td>
<td>Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result</td>
<td></td>
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<tr>
<td>3</td>
<td>Selection of subjects is equitable.</td>
<td></td>
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<tr>
<td>4</td>
<td>Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 32CFR219.116?</td>
<td></td>
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<tr>
<td></td>
<td>• If no, has a Waiver of Informed Consent approved by the IRB?</td>
<td></td>
<td></td>
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<tr>
<td>5</td>
<td>Informed consent will be appropriately documented, in accordance with, and to the extent required by 32 CFR 219.117?</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• If no, has a Waiver of Documentation of Informed Consent approved by the IRB?</td>
<td></td>
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<tr>
<td>6</td>
<td>When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.</td>
<td></td>
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<tr>
<td>7</td>
<td>When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.</td>
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<tr>
<td>8</td>
<td>Are there adequate protections for the confidentiality of data?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>9</td>
<td>When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects. (Applicable if study involves pregnant women/fetuses, children, prisoners, mentally disabled persons, economically/educationally disadvantaged persons, deployed active duty personnel.)</td>
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</table>

**IRB Action:**

- [ ] Full Board Review
- [ ] Expedited Review

**Date Reviewed:**

**Review Cycle:**

**Risk Level:**

- [ ] Minimal Risk
- [ ] Greater than Minimal Risk

**Recommendation to IRB:**

- [ ] Approve as submitted
- [ ] Approve pending requirements

- [ ] I do not have any conflict of interest regarding this study.

**Printed Name of IRB Reviewer/Chair/Vice Chair**

**Signature**

**Date**
DOD Directive 2310.01E defines a "detainee" as: Any person captured, detained, held, or otherwise under the control of DOD personnel (military, civilian, or contractor employee). It does not include persons being held primarily for law enforcement purposes, except where the United States is the occupying power.

Research involving a detainee is prohibited. The only exception to this prohibition is when an investigational new drug (IND) or investigational device (IDE) is offered to detainees, with the detainees' informed consent, for the diagnosis or treatment of a medical condition when the same product would be offered to members of the U.S. Military Services in the same location for the same medical condition. This use must be consistent with established medical practice involving investigational drugs and devices.

An Amendment must be submitted when a previously enrolled subject becomes a prisoner and the relevant research protocol was not reviewed and approved by the IRB in accordance with Subpart C, and the intent is to allow continuing participation of the prisoner-subject.

<table>
<thead>
<tr>
<th>Research Involving Prisoners Criteria</th>
<th>Y</th>
<th>N</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;</td>
<td></td>
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<tr>
<td>(ii) Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;</td>
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<tr>
<td>(iii) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of his intent to approve such research;</td>
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<tr>
<td>(iv) Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which these studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of the intent to approve such research.</td>
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</table>
The Board shall review and approved research only if it finds that:

<table>
<thead>
<tr>
<th></th>
<th>Y</th>
<th>N</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>The research under review represents one of the categories of research permissible under 546.306(a)(2); <strong>AND</strong></td>
<td></td>
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<tr>
<td>(2)</td>
<td>Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired; <strong>AND</strong></td>
<td></td>
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<tr>
<td>(3)</td>
<td>The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers; <strong>AND</strong></td>
<td></td>
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<tr>
<td>(4)</td>
<td>Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project; <strong>AND</strong></td>
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<tr>
<td>(5)</td>
<td>The information is presented in language which is understandable to the subject population; <strong>AND</strong></td>
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<tr>
<td>(6)</td>
<td>Adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; <strong>AND</strong></td>
<td></td>
<td></td>
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<tr>
<td>(7)</td>
<td>Where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners’ sentences, and for informing participants of this fact.</td>
<td></td>
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<tr>
<td>Were the 32 CFR 219.111 criteria for approval met?</td>
<td>YES</td>
<td>NO</td>
<td></td>
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<tr>
<td>-------------------------------------------------</td>
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<td></td>
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**IRB Action:**
- [ ] Full Board Review
- [ ] Expedited Review

**Date Reviewed:**

**Review Cycle:**

**Risk Level:**
- [ ] Minimal Risk
- [ ] Greater than Minimal Risk

**Recommendation to IRB:**
- [ ] Approve as submitted
- [ ] Approve pending requirements

- [ ] I do not have any conflict of interest regarding this study.

**Printed Name of IRB Reviewer/Chair/Vice Chair:**

**Signature:**

**Date:**

**Page 3 of 3 Version 15 February 2016**
# Basic Study Information

<table>
<thead>
<tr>
<th>Protocol Title:</th>
<th>Reviewer:</th>
<th>BUMED Code:</th>
</tr>
</thead>
</table>

### Identification of Population

<table>
<thead>
<tr>
<th>Are children aged 0-17 to be enrolled in this study?</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are subjects wards of state or any other agency?</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

If yes,
- The IRB requires 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.
- The advocate is 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.
- The advocate 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.

### Criteria to include children in research: CHOOSE ONE

#### Minimal Risk

<table>
<thead>
<tr>
<th>Category 1: [45 CFR 46.404 or 21 CFR 50.51]</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>
- No greater than minimal risk to children is presented

**OR**

#### Greater than Minimal Risk

<table>
<thead>
<tr>
<th>Category 2: [45 CFR 46.405 or 21 CFR 50.52]</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>
- Greater than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual participant, or by a monitoring procedure that is likely to contribute to the participant's well-being.
- The risk is justified by the anticipated benefit to the participant.
- The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.

<table>
<thead>
<tr>
<th>Category 3: <strong>[45 CFR 46.406 or 21 CFR 50.53]</strong></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>
- Greater than minimal risk to children is presented by an intervention or procedure that does NOT hold out the prospect of direct benefit for the individual participant, or by a monitoring procedure which is not likely to contribute to the well-being of the participant.
- The risk represents a minor increase over minimal risk.
- The intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations.
- The intervention or procedure is likely to yield generalizable knowledge about the participants' disorder or condition which is of vital importance for the understanding or amelioration of the participants' disorder or condition.

**Wards of the state involved in Category 3 research**

Wards of state may only be involved in Category 3 research if:
- The research is related to their status as Wards, or
- The research is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved in the research as subjects are not Wards.

---

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<table>
<thead>
<tr>
<th>Parental Permission Criteria:</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minimal Risk (Category 1: 404 / 51)</strong></td>
<td></td>
</tr>
<tr>
<td>The research makes adequate provisions for soliciting the permission of the children's parents or guardians</td>
<td>□ YES □ NO</td>
</tr>
<tr>
<td>Choose one:</td>
<td></td>
</tr>
<tr>
<td>□ The permission of one parent is sufficient even if the other parent is alive, known, competent, reasonably available, and shared legal responsibility for the care and custody of the child.</td>
<td></td>
</tr>
<tr>
<td>□ The permission of both parents is required 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.</td>
<td></td>
</tr>
<tr>
<td>The research makes adequate provisions for soliciting the assent of the children</td>
<td>□ YES □ NO</td>
</tr>
<tr>
<td><strong>OR</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Greater than Minimal Risk with the Prospect of Direct Benefit (Category 2: 405 / 52)</strong></td>
<td></td>
</tr>
<tr>
<td>The research makes adequate provisions for soliciting the permission of the children's parents or guardians</td>
<td>□ YES □ NO</td>
</tr>
<tr>
<td>Choose one:</td>
<td></td>
</tr>
<tr>
<td>□ The permission of one parent is sufficient even if the other parent is alive, known, competent, reasonably available, and shared legal responsibility for the care and custody of the child.</td>
<td></td>
</tr>
<tr>
<td>□ The permission of both parents is required 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.</td>
<td></td>
</tr>
<tr>
<td>The research makes adequate provisions for soliciting the assent of the children</td>
<td>□ YES □ NO</td>
</tr>
<tr>
<td><strong>OR</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Greater than Minimal Risk without the Prospect of Direct Benefit (Category 3: 406 / 53)</strong></td>
<td></td>
</tr>
<tr>
<td>The research makes adequate provisions for soliciting the permission of the children's parents or guardians</td>
<td>□ YES □ NO</td>
</tr>
<tr>
<td>□ The permission of both parents is required 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.</td>
<td></td>
</tr>
<tr>
<td>The research makes adequate provisions for soliciting the assent of the children</td>
<td>□ YES □ NO</td>
</tr>
</tbody>
</table>
### Assent of Children Criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>As a rule of thumb: a &quot;no&quot; from a child overrides a &quot;yes&quot; from a parent, but a &quot;yes&quot; from a child does not override a &quot;no&quot; from a parent (unless the IRB has waived the requirements for parental permission).</td>
<td></td>
</tr>
<tr>
<td>Assent is required by all of the children</td>
<td>□ YES □ NO</td>
</tr>
<tr>
<td>Assent is required by some of the children</td>
<td>□ YES □ NO</td>
</tr>
<tr>
<td>□ Some of the children are not capable of providing assent based on their age, maturity, or psychological state.</td>
<td></td>
</tr>
<tr>
<td>Assent is required by none of the children</td>
<td>□ YES □ NO</td>
</tr>
<tr>
<td>□ The capability of the children is so limited that they cannot reasonably be consulted</td>
<td></td>
</tr>
<tr>
<td>□ 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.</td>
<td></td>
</tr>
<tr>
<td>Assent can be waived using the criteria for waiver of the consent process.</td>
<td>□ YES □ NO</td>
</tr>
<tr>
<td>– The research involves no more than minimal risk to the subjects</td>
<td></td>
</tr>
<tr>
<td>– The waiver will not adversely affect the rights and welfare of subjects</td>
<td></td>
</tr>
<tr>
<td>– The research could not practically be carried out without the waiver or alteration</td>
<td></td>
</tr>
<tr>
<td>– Whenever appropriate, the subjects will be provided with additional pertinent information after participation in the study</td>
<td></td>
</tr>
</tbody>
</table>

For children who are pregnant, assent and permission are obtained in accordance with the regulations.

- In Virginia, to enroll a pregnant minor and her newborn:
  - the minor’s parent(s) must consent for her participation
  - the minor must assent for her own participation, and
  - the minor must consent for her newborn’s participation

### Override of Assent of Children Criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>In general, a child’s dissent to participation should be respected. When a disagreement between parent(s) and the child arises concerning the choice to take part in research, it may be because the child is depressed, the parents have unrealistic hopes, the child may have different goals and outcomes from the parents, or the real prospects of direct benefit present in the research may have been misunderstood. The IRB may determine that the parent’s choice to participate prevails over the child’s dissent to participate in research that offers the child the possibility of direct benefit important to his/her own health (Category 2) and is available only through research.</td>
<td></td>
</tr>
<tr>
<td>Has the protocol been assessed as Greater than Minimal Risk with Prospect of Direct Benefit (Category 2: 405/52)</td>
<td>□ YES □ NO</td>
</tr>
<tr>
<td>□ If yes, is it appropriate to Override a child’s dissent?</td>
<td>□ YES □ NO</td>
</tr>
</tbody>
</table>
Were the 32 CFR 219.111 criteria for approval met?

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Risks to subjects are minimized:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Selection of subjects is equitable.</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 32 CFR 219.116?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• If no, has a Waiver of Informed Consent approved by the IRB?</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Informed consent will be appropriately documented, in accordance with, and to the extent required by 32 CFR 219.117?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• If no, has a Waiver of Documentation of Informed Consent approved by the IRB?</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Are there adequate protections for the confidentiality of data?</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects. (Applicable if study involves pregnant women/fetuses, children, prisoners, mentally disabled persons, economically/educationally disadvantaged persons, deployed active duty personnel.)</td>
<td></td>
</tr>
</tbody>
</table>

IRB Action:

- [ ] Full Board Review
- [ ] Expedited Review

Date Reviewed: __________ Review Cycle: __________ Risk Level: [ ] Minimal Risk [ ] Greater than Minimal Risk

Recommendation to IRB:

- [ ] Approve as submitted
- [ ] Approve pending requirements
- [ ] Do not have any conflict of interest regarding this study

Printed Name of IRB Reviewer/Chair/Vice Chair: __________________________ Signature: __________________________ Date: __________________________
**BASIC STUDY INFORMATION**

<table>
<thead>
<tr>
<th>Protocol Title:</th>
<th>Reader:</th>
<th>BUMED code:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Adults who have impaired decision-making capacity may be involved in research if all of the following criteria are met:**

1. Only incompetent persons or persons with impaired decision-making capacity are suitable as subjects; **AND**

2. Competent persons are not suitable for the proposed research; **AND**

3. The investigator must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects; **AND**
   a. Incompetent persons or persons with impaired decision-making capacity are not being proposed as subjects simply because they are readily available; **AND**
   b. The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the subject; **AND**
   c. The research does not impose a risk of injury, unless the research is intended to benefit that subject and the probability of benefit is greater than the probability of harm; **AND**

4. Procedures are devised to ensure that subjects' legally authorized representatives are well-informed regarding their roles and obligations to protect incompetent participants or persons with impaired decision-making capacity; **AND**

5. Legally authorized representatives are told that their obligation is to try to determine what the prospective subject would do if competent, or if the prospective subject's wishes could not be determined, what they think is in the incompetent person's best interest.
<table>
<thead>
<tr>
<th>Autonomy in adults of impaired decision-making capacity</th>
<th>Y</th>
<th>N</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Are there reasonable procedures proposed for evaluating the mental status of prospective subjects to determine whether they are capable of consenting?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Is it reasonable to expect that, during the course of the study, subjects may lose their capacity to consent or their ability to withdraw?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Yes</td>
<td>If yes, what provisions have been made to protect the subject's rights (e.g., consenting a caregiver, as well as the subject, etc.)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• No</td>
<td>If no, skip to 3.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Does the Principal Investigator have a reasonable procedure to identify persons authorized to give legally valid consent on behalf of any person(s) judged incapable of consenting on their own behalf to participate in research?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Will the Principal Investigator obtain legal documentation of the person(s) legally authorized to give legal consent on behalf of the person?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. As a means for respecting the autonomy of the individual with impaired decision-making capacity, does the PI have a reasonable procedure to obtain assent for participation?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Will the subject's decision to withdraw from the study at any time be honored?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Is the research likely to interfere with ongoing therapy or regimens?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Are additional safeguards needed to protect the subject's rights and welfare?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Were the 32 CFR 219.111 criteria for approval met?</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>---</td>
<td>-------------------------------------------------</td>
<td>-----</td>
<td>----</td>
</tr>
<tr>
<td>1</td>
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<td></td>
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<td>• Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.</td>
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<td>Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.</td>
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<td>3</td>
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</tr>
<tr>
<td>4</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>• If no, has a Waiver of Informed Consent approved by the IRB?</td>
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<td>5</td>
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<td></td>
<td>• If no, has a Waiver of Documentation of Informed Consent approved by the IRB?</td>
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<td></td>
</tr>
<tr>
<td>6</td>
<td>When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.</td>
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<td></td>
</tr>
<tr>
<td>7</td>
<td>When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.</td>
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<td></td>
</tr>
<tr>
<td>8</td>
<td>Are there adequate protections for the confidentiality of data?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects.</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>(Applicable if study involves pregnant women/fetuses, children, prisoners, mentally disabled persons, economically/educationally disadvantaged persons, deployed active duty personnel.)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**IRB Action:**
- [ ] Full Board Review
- [ ] Expedited Review

**Date Reviewed:**

**Review Cycle:**

**Risk Level:**
- [ ] Minimal Risk
- [ ] Greater than Minimal Risk

**Recommendation to IRB:**
- [ ] Approve as submitted
- [ ] Approve pending requirements
- [ ] I do not have any conflict of interest regarding this study.

**Printed Name of IRB Reviewer/Chair/Vice Chair**

**Signature**

**Date**
APPENDIX H – RESEARCH COMPLIANCE PROGRAM CHECKLISTS

Compliance Assist Visit (CAV) Checklist
Consent Process Observation Checklist
Signed Consent Form Review Checklist
Signed Consent Form Review Guidance
NMCP Research Training
## Compliance Assist Visit Checklist

### Research Compliance – NMCP CID

#### STUDY CHARACTERISTICS

<table>
<thead>
<tr>
<th>Option</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Board</td>
<td>Initial IRB Approval</td>
</tr>
<tr>
<td>Expedited</td>
<td>CO Approval</td>
</tr>
<tr>
<td>Exempt</td>
<td>Current Expiration Date</td>
</tr>
<tr>
<td>Enrollment</td>
<td>Active Subjects □ Retrospective/Prospective Records Review</td>
</tr>
<tr>
<td></td>
<td>Open □ Closed</td>
</tr>
<tr>
<td>Consent</td>
<td>Signed Consents □ Waiver of consent □ Waiver of PHI</td>
</tr>
<tr>
<td></td>
<td>Minimal Risk □ Greater than Minimal Risk</td>
</tr>
<tr>
<td>Vulnerable Population</td>
<td>Newborns □ Minors □ Pregnant/Women/Fetuses</td>
</tr>
<tr>
<td></td>
<td>Decisionally Impaired □ Other:</td>
</tr>
<tr>
<td>Population</td>
<td>Military □ Civilian □ Both</td>
</tr>
<tr>
<td>Multi-Center Trial</td>
<td>YES: □ NO</td>
</tr>
<tr>
<td>CRADA/MOU</td>
<td>YES: □ NO</td>
</tr>
</tbody>
</table>

#### ENROLLMENT ACTIVITY

<table>
<thead>
<tr>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Subjects IRB Approved this Site</td>
</tr>
<tr>
<td>Total Subjects Enrolled Since Initiation</td>
</tr>
<tr>
<td>Total Subjects Withdrawn/Lost to Follow-Up Since Initiation</td>
</tr>
<tr>
<td>Total Subjects Enrolled at Last Continuing Review</td>
</tr>
</tbody>
</table>

#### CURRENT DOCUMENTATION

<table>
<thead>
<tr>
<th>Document</th>
<th>Identifier/Dates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Plan</td>
<td></td>
</tr>
<tr>
<td>Consent</td>
<td></td>
</tr>
<tr>
<td>Amendment</td>
<td></td>
</tr>
<tr>
<td>Amendment</td>
<td></td>
</tr>
<tr>
<td>Amendment</td>
<td></td>
</tr>
<tr>
<td>Lapse in IRB approvals?</td>
<td>Yes □ No</td>
</tr>
</tbody>
</table>

---

Research Compliance/NMCP/CID/January 2018

Page 1 of 2
## RESEARCH RECORD REVIEW

<table>
<thead>
<tr>
<th>Item</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research team training current</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regulatory binder complete and current</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial IRB submission and approval filed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Research Plan filed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Approved version of consent form filed and being used</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Approved data collection tools (DCTs) and questionnaires currently being used</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## IRB NOTIFICATIONS

<table>
<thead>
<tr>
<th>Item</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol violations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAEs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## SIGNED CONSENT FORM REVIEW

<table>
<thead>
<tr>
<th>Item</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of consent forms corresponds with documentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number consent logged in binder with subject ID (including screen fails/withdraws)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current IRB approved version used for consent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All pages/signatures/dates present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consent process observed/scheduled</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
DATA/SOURCE DOCUMENTATION REVIEW

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirm eligibility/DCT forms are current approved versions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Review source documentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirm de-identification of data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Review data security procedures</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SUBJECT SOURCE DOCUMENT REVIEW

<table>
<thead>
<tr>
<th>Subject</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject</td>
</tr>
<tr>
<td>Subject</td>
</tr>
<tr>
<td>Subject</td>
</tr>
<tr>
<td>Subject</td>
</tr>
</tbody>
</table>
## Consent Process Observation Checklist

**INFORMED CONSENT PROCESS**

<table>
<thead>
<tr>
<th>Description</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consent obtained prior to study procedures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subject informed the study was research</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Purpose and duration of study participation covered</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summary of study procedures explained</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risks and benefits explained</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consenting location appropriately private</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subject provided all of the information in a language understandable to him/her</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subject questions addressed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subject appeared to understand information provided</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subject did not appear to be under pressure or otherwise coerced</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subject given enough time to decide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subject offered copy of the consent form</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOCUMENTATION**

<table>
<thead>
<tr>
<th>Description</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current IRB stamped consent form</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consenting investigator approved investigator</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signatures dates correct</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signed consent documents secure and separate from other research documents</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Signed Consent Form Review Checklist
Research Compliance – NMCP CID

**CONSENT FORM REVIEW**

<table>
<thead>
<tr>
<th>Description</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of consents for reporting period (enrolled subjects)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consent forms reflect current IRB approved version</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Consenting investigator approved on study</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>All pages of consent form present</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>All signature dates correct</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>All signatures present:</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Subject/Investigator</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assent applicable/properly documented</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Check against submitted CR include screen fails.
SIGNED CONSENT FORM REVIEW GUIDANCE

At the time of Continuing Review, all signed consent forms are reviewed by the CID Research Compliance Advisor (RCA). Consent forms should be submitted electronically directly to the RCA. Consent forms are evaluated based on the following requirements:

- Consent forms reflect current IRB stamped and approved version
- All pages of consent form present
- Subject/Investigator signatures present
- Signatures reflect subject enrollment date
- Number of consents corresponds with Subject Identifier Log (include screen fail consent forms)
- Assent/Waiver of Assent signature (if applicable); assent is required for subjects who are 8-17 years of age; if the PI determines assent is waived, this should be documented as a Waiver of Assent on the consent form

Any findings will be communicated via email to the PI. If review reflects issues of non-compliance, a corrective and preventative action plan or protocol deviation/violation may be required and forwarded to the IRB for review. Following review, subject signed consent forms are then electronically archived at CID.

***REMINDER*** All original signed consent documents must be maintained by the PI in a secure, locked location. Study files, including subject signed consent forms, will be maintained by the PI according to department record retention policy

Email Submission (less than 10 consent forms)

- Send encrypted email to the RCA ONLY (for data security purposes, do not CC or include anyone else on the email)
- Email should include PI name, IRB#, and study title, and total number of subjects enrolled during the respective Continuing Review period
- Attach up to 10 Signed Consent Forms in one PDF
- Also attach the Subject Identifier Form (Appendix A of Continuing Review submission)
- All signed consent forms must be submitted in their entirety, all pages including subject name and signature (no blocking out subject name)

AMRDEC SAFE Submission (more than 10 consent forms)

AMRDEC SAFE (the U.S. Army Aviation and Missile Research Development and Engineering Center’s Safe Access File Exchange) is an alternative method to transfer large files via a secure, electronic process. AMRDEC permits encryption, is Common Access Card (CAC) enabled, and allows zip files.
RESEARCH COMPLIANCE PROGRAM

- Go to – https://safe.amrdec.army.mil/SAFE/
- Follow the instruction prompts
- Input receiving user's email address (gretchen.a.lenk.ctr@mail.mil)
- Upload Subject Identifier Form (Appendix A of Continuing Review submission)
- Upload PDFs of scanned consent forms (typically up to 10 consents per scan)
- Send RCA an email notification to expect the AMRDEC submission, include in your email:
  - PI name
  - IRB# and study title
  - Total number of subjects enrolled during the respective Continuing Review period

Welcome to the AMRDEC SAFE Web Application

Please contact the Research Compliance Advisor if you have questions.

Gretchen Lenk, MPH
Research Compliance Advisor
Clinical Investigation Department, Naval Medical Center Portsmouth
Phone: 757.953.5473
Email: gretchen.a.lenk.ctr@mail.mil
The following training is required for all research personnel and collaborators conducting research at NMCP:

**QITI Training (no CAC required)**
1. Go to [www.citprogram.org](http://www.citprogram.org)
2. Under "Create an Account," click on "Register."
3. Step 1: Select an Institution – under 'Participating Institution,' select "Department of the Navy." Continue to Step 2.
4. Enter your name and email address (if no work email, use personal email). Continue to Step 3.
5. Create your username and password. Continue to Step 4.
6. Complete Steps 4 and 5.
8. Select the first check box under "What kinds of research are you conducting?"
9. Select "The Biomedical Sciences" under 'What is your research focus?'
10. Select "Investigator and Key Research Personnel" under 'What is your role in biomedical research?'
11. You will now be back at the Main Menu where your course modules are listed and you can begin your training.

*(Animal Protocols: Under "Do you supervise studies that use laboratory animals?" select "Working with the IACUC" and 'Working with (select your specific species, i.e., swine)." Additional species can be added at a later time if necessary.)*

12. Send an email to the NMCP Research Compliance Advisor (gretchen.a.lenk.ctr@mail.mil) attaching required CITI training certificates.

Reminder: Save your CITI certificates for submission with IRB/IACUC applications.

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**Research Integrity Training (CAC dependent)**
1. Go to the CID (Clinical Investigation Department) SharePoint page [https://nmcp.med.navy.mil/CP/Pages/CID.aspx](https://nmcp.med.navy.mil/CP/Pages/CID.aspx)
2. Click "Training" on the homepage
3. Click "Mandatory Integrity Training"
4. Watch "Introduction to Research Ethics" (view time 37mins, 54secs)
5. Read "On Being A Scientist, 3rd Edition"
6. Read BUMED/DOD Instruction PDF document (BUMEDINST 6500.3 and 3910.2, and DODI 32100.7)
7. Once you have completed the training and check all of the boxes, click "Submit"
OR

Research Integrity Training (without CAC)
1. Watch "Introduction to Research Ethics" (view time 37mins, 54secs) available at: https://archive.org/details/RESEARCHETHICSWM9960x54016x9
5. Read DOD INSTRUCTION 32100.7, "Research Integrity and Misconduct" at: https://nmcp.med.navy.mil/CID/Shared%20Documents/DOD%2032100-7.pdf
6. Send an email to the NMCP Research Compliance Advisor (gretchen.a.lenk.ctr@mail.mil) attesting completion of all of above required modules.

Please contact the NMCP Research Compliance Advisor if you have questions regarding training requirements.

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Research Compliance Program/NMCP CID 11Jan16