
IRB APPLICATION GUIDANCE

This is not an IRB application form. The actual application is a separate document and is located on IRBNet (Forms/Template Library). Please do not return these instructions with your application. If you have questions, please contact the Clinical Investigation Department (CID) at 953-5939.

IRB APPLICATION

You must review IRB review categories in the RSPD SOPs to determine which application is most appropriate to your research activity: Exempt, Expedited, or Full Board.

Page 1 is a checklist. Please complete this when your application is ready for submission to confirm that all required items are included.

Principal Investigator: Enter your Rank, First and Last Name, and degree (MD, DO, PhD, etc.) in the appropriate field.

Study Title: Be certain that your study title matches across all documents and is identical to the title entered into IRBNet.

Command: Identify your Command.

Department: Identify your Department.

Phone/Pager: Identify the best phone number/ pager number to reach you.

Email Address: Identify the best email address to reach you. This will be the same email address used to register in IRBNet.

PRD: Identify the month and year of your Projected Rotation Date. Enter N/A as appropriate.

CITI: Identify the date of completion of your CITI training in month / day/ year format.

CV: Check to indicate that CV is “Linked to the Package” in IRBNet.

Associate Investigators: Identify other members of your Research Team following the guidance above.

Research Monitor: Identify your Research Monitor (mandatory for Full Board protocols only).

Proposed Start Date: When do you propose to begin your project? Remember to allow for at least 60-90 days to gain IRB approval.

Protocol Duration (Years): How long do you anticipate that it will take for you to complete your project?

Collaboration with other institutions: List collaborating institutions.

CRADA or similar agreement number: Enter the agreement number.

IND, IDE or HDE #: If your project involves use of an experimental drug, device, biologic, or a humanitarian device conducted under the oversight of the FDA, enter the corresponding Investigational New Drug #, Investigational Device Exemption #, or the Humanitarian Device Exemption #. Enter N/A as appropriate.

Command where research will take place: Identify where the research activities that this PI is responsible for (subject and/or data interaction) will occur.

SUBJECT POPULATION INFORMATION

Age of Subjects: Identify your age range. Children are aged 0-17; Adults are 18 and older. For HIPAA compliance, all subjects aged 90 and above must be identified in aggregate. (18-89, 90 and above).

Vulnerable Population: Studies may include vulnerable populations, but should only mark this section if vulnerable populations are specifically targeted for participation in the study. Pediatric studies will enroll minors and may enroll newborns, depending on the protocol. Labor and Delivery studies will enroll pregnant women/fetuses and may enroll newborns, depending on the protocol. Alzheimer's, mental health, or PTSD studies may enroll decisionally impaired persons, depending on the protocol. For studies enrolling prisoners, please contact the CID for assistance prior to submission. You are strongly urged to review the RSPD SOPs on IRBNET for additional guidance on conducting research with vulnerable populations.

Population: Identify if your subjects will be Active Duty Military members, beneficiaries, or both.

NUMBER OF SUBJECTS

Total: Identify the total number of subjects to be enrolled. A subject is considered enrolled on a study when they have signed consent, even if they screen fail out prior to randomization or intervention. Be certain to account for subject loss when identifying the total number to be enrolled. (You may need to enroll 30 subjects for 15 to complete the study). If medical records are to be queried, identify the total number of records to be examined, not the number of records expected to meet inclusion/exclusion criteria. (You may choose to query an entire database of more than 10 million records to locate 300 which meet your selection criteria). Do not include a range for enrollment.

Control: Identify how many of the subjects to be enrolled will be controls.

Experimental: Identify how many of the subjects to be enrolled will be experimental.

BRIEF ABSTRACT

Provide a brief overview of the project, describing the purpose, objectives, design, and site of the research in straightforward non-technical language. Limit your abstract to one page.

PROTOCOL APPROVAL SIGNATURE PAGE

The Principal Investigator must sign, attesting that he/she has read and understood the NAVMEDCENTPTSINST and, for the outlying commands, any local research instructions related to the conduct of human subjects research.

The Department Head must sign, documenting that he/she believes the PI is qualified to conduct the research; that the Director has been made aware that this research will occur in the Department; and that accountability for and continuity of ongoing research will be maintained in the event that the PI detaches from the Command. If the Department Head is an investigator on the study, then he/she may not approve as the Department Head, but the next person up the chain of command must be approached to obtain approval.

Scientific Review is obtained by CID. Once scientific review is complete, the study is assigned to an IRB for review. For outlying commands, this review is handled locally by an equivalent review committee (e.g. Research Quality Council).

IRB Chair/Vice Chair approval is obtained by CID.

Command approval is obtained by CID. All agreements associated with a protocol must be finalized before an IRB-approved study may be presented to the CO for approval. In the absence of the CO, the XO serving as “Acting CO” may sign if appropriate training has been completed and approval authority has been granted. **No research activity may occur before CO/XO approval is given.** For research conducted at extramural commands (NHCL, NHJX, NHPC, NMOTC, etc.), approval by the local CO/XO replaces approval by the NMCP CO/XO. Make sure your application includes the signature block for your current Commanding Officer.

Please make an effort to obtain all signatures on a single hard copy for uploading as a PDF into IRBNet, rather than a single sheet for each signature.

HUMAN USE ASSURANCE, INFORMED CONSENT, AND PRIVACY ACT STATEMENTS

The PI and all AIs on a study must be identified by Rank, First Name, Last Name, Degree; contact number, and Department.

Role: Identify the investigator’s role for this project: PI or AI.

Status: Identify the investigator’s status: Staff, Resident, Intern, Student, GS, Contractor, etc.

All listed personnel must sign in the space provided.

Please make an effort to obtain all signatures on a single hard copy for uploading as a PDF into IRBNet, rather than a single sheet for each signature.

CONFLICT OF INTEREST DECLARATION

All members of the Research Team must initial to indicate if they do or do not have a conflict of interest with the protocol. If a conflict is identified, a management plan must be submitted. See the RSPD SOPs on IRBNET for additional guidance on the evaluation and management of conflicts of interest.

Please make an effort to obtain all signatures on a single hard copy for uploading as a PDF into IRBNet, rather than a single sheet for each signature.

SUPPORT STATEMENT

Identify any support activities critical to the conduct of your project that will be performed by patient care departments. The signature of the impacted Department Head must be obtained.

Please make an effort to obtain all signatures on a single hard copy for uploading as a PDF into IRBNet, rather than a single sheet for each signature.

RESEARCH MONITOR

The Research Monitor must sign, documenting their understanding of the responsibilities they are undertaking and their willingness to serve in this capacity.

The Printed Name; Signature; Date of Signature; Department; Data of completion of Research Ethics CITI training, and Projected Rotation Date must be identified.

RESEARCH PLAN

The following outline is a guide to the preparation of your research plan. In part, it is based on the Research Plan Guidance developed by NIH to guide investigators with submission of grant applications. This is not intended as a form page to be filled out with short answers. Do not type answers on this outline. Your research plan should include each of the terms below as the heading for each section with your own description/wording underneath each heading.

1. OBJECTIVES/SPECIFIC AIMS

Incorporate brief statements, using lay language stating:

- 1) The problem area or issue addressed by the protocol and your long-term objectives.*
- 2) Your working hypothesis (es); that is, the research idea that you want to test.*
- 3) Specific aims. State concisely and without references or elaboration, the tests or procedures that you will do to support your hypothesis. It is recommended that you limit these between 1-3 specific aims and that you use only 3-4 sentences to describe each of them. You can keep sentences short by not citing references to published articles here. You will have an opportunity in the next sections to elaborate on each of these.*

2. BACKGROUND AND SIGNIFICANCE

Use this section to support the previous objectives and specific aims by citing relevant background material published in the literature. List these references in the Literature Cited section. Use this section to expand your hypotheses or research ideas and to show logically how your research will support and test them. Use published literature to show the rationale for your ideas. Educate the reader by providing him/her with the knowledge necessary to understand what you intend to do. Avoid jargon and do not assume that reviewers are familiar with your discipline or specialty. Explain how your expected results will support your hypotheses. Explain why this research is important medically, scientifically, or to the Navy, or all three.

You do not have to provide an exhaustive review of the literature. However, if you cannot provide evidence of a scholarly understanding of published literature (by citing references in the text), the reviewers will assume: (1) you are unprepared to conduct this research; (2) you may be placing subjects at unknown risk; and/or (3) expenditure of Navy resources may be unwarranted.

3. RESEARCH DESIGN/METHODS/SUBJECT JUSTIFICATION

a. General Approach

Provide a brief statement about the type of study design (e.g. prospective, observational, open-label, double-blinded, randomized placebo controlled trial, parallel groups, cross-over, correlational design, etc.). Please be sure to mention if this is a multi-site study, and if so, which DoD sites/Universities, etc. will be participating.

(1) **Research Objective**

State the research objective(s). If employing different experimental practices not shared among all of the objectives, it may be worthwhile to present each objective and the descriptions separately. NOTE: This should mirror the objective(s) stated in the Specific Aims/Objectives section, and stated in lay-language understandable by non-medical personnel.

(2) **Detail How Many Groups or Arms are in the Study and what each Receives.**

Define study groups. Describe the interventions, procedures, assessments, etc. for each group.

(3) **Randomization Procedures**

State the method that will be used to randomly-assign subjects to your experimental and control groups. You may use a system similar to rolling dice, flipping a coin, or using a shuffled deck of cards. You may choose to create a computer generated list with a random number table. The biostatistician can help develop a randomization list. The randomization approach should be designed to reduce selection bias and distribute subjects equally among your groups.

b. Methods and Materials

Identify all procedures, both experimental and standard of care, which will be performed. Describe in detail all screening procedures, interventions, (pre-/post assessments, diagnostics, laboratory tests, study visit procedures [including surgical procedures] and use of instruments or assessment tools [satisfaction surveys, QOL surveys, etc.]). A description of procedures to be undertaken at each study visit is strongly recommended. Identify the expected duration of procedures, and the anticipated results from the procedures. {Diagrams or reference articles may be helpful.} Provide specific information about what procedures each member of the research team performs.

If a study drug will be used, define the dose, route of administration, and who will administer the drug. Specify if drugs to be used are approved for the condition under study, for the population to be enrolled, and at the dose and means of administration to be used in the study. Describe any wash-out periods or escalated dosing regimens that are required.

Describe any new methodology to be used and its advantage over existing methodologies. Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims.

Indicate if this is a multicenter or collaborative study, describe what each collaborator will do, and how data will be collected, combined and shared.

(1) **Experimental Procedure**

Identify all procedures or interventions that are experimental. This includes experimental drugs and/or devices, unapproved treatment procedures, non-standard behavioral and/or educational interventions, and instruments which are not validated. Explain how the experimental procedure tests the hypothesis. Define how outcomes will be measured (physical measurements, performance assessments, questionnaires, perception assessments, etc.).

(2) **Research Material To Be Collected**

- i. *If requesting a Waiver of Authorization for the Use of PHI provide justification and attach the appropriate form (Appendix C).*

Identify sources for specimens, records, and data. Specify if the data or procedures generating data are being performed for research purposes only or are done per standard of care. Specify how identifiers will be maintained, including the coding of data sheets. The description of data to be collected should reflect data fields on data collection tool.

For retrospective chart review studies, describe how records are identified for inclusion and by what means they are collected.

EXAMPLE: “Retrospective chart review study- participants will not be actively recruited by NMCP staff or the assigned Research Coordinator. ICD-9 codes will be searched within S3, CHCS, AHLTA, clinical data mart...to find carpometacarpal fracture-dislocation (815.02, 833.04, 833.05).”

- ii. If requesting a Waiver of Authorization for the Use of PHI, provide justification and attach the appropriate form (Appendix C). State if a Waiver will be requested for a retrospective data review involving existing specimens, records, or data. “Existing data” is defined by the federal regulations as data that exists before the study is proposed to an institutional official or to an IRB. As such, the collection of retrospective data requires that a data window be established stating that data collected for the study is limited to data, documents, records, or pathological specimens in existence prior to DATE OR collected between DATE and DATE OF IRB SUBMISSION. If prospective Waiver of Authorization is requested, then a data window for such data must also be identified. It is possible for a project to involve both retrospective and prospective data windows, although the request for Waiver of Authorization of must be specific to each time period.

(3) Data Collection Tools

List all forms, assessment instruments, questionnaires, subject diaries, data collection sheets, case report forms, screen prints of data spreadsheets, Subject ID Keys, and lab reports or diagnostic readouts, etc. that will be used in obtaining or documenting data. Upload copies of all data collection sheets into IRBNet for IRB review and approval.

(4) Protection and Security of Data and Identifying Information

Explain what measures will be taken to maintain the security and integrity of collected data. Are data both electronic and hard copy? Where will data be stored and under what conditions? Who will have access to data? Outline procedures for coding, recording, transmitting, storing and protecting the data. Any study that involves the accessing or collection of patient information must have this filled in. A “best practice” is to have a master list which links identifying information with a subject ID #. The master list is kept locked in a separate location from any clinical data associated with the subject ID#. Only the investigators should have access to the master list. In this scenario, the data collection sheet will not include identifiers, including initials, SSN last 4, etc.

(5) Disposition of Data and Identifying Information at End of Project

State how the data will be used. If data with subject identifiers will be released, specify the person(s) or agency to whom the information will be released and the purpose of the release (such as, verification of data).

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)). Study documents should be disposed of per Navy instruction at the conclusion of the three years. Explain how study materials will be stored for the three year duration at the conclusion of this project.

(6) Gender and Ethnicity

Identify if the study population will be comprised of a specific gender or of specific ethnicities. Justify why it is appropriate to exclude any group of individuals. If gender or ethnicity is not important to the study design, it should state that neither is a factor for inclusion nor exclusion from the study.

(7) Subject Population

a. Subject Inclusion and Selection Criteria

The criteria for inclusion and selection should be identified in separate paragraphs. A bulleted list of all inclusion criteria is recommended.

EXAMPLE:

Inclusion Criteria:

1. Male or female Active duty (U.S. Army, Navy, Marine Corps, Air Force or U.S. Coast Guard) who is ≥ 18 and < 45 years of age at the time of the screening visit.
2. Meets Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) criteria for MDD, as assessed by the KIDDIE Schedule for Affective Disorder and Schizophrenia – Present and Lifetime Version (K-SADS-PL) and clinical interview.
3. CDRS-R score > 40 .
4. CGI-S score of ≥ 4 .

b. Subject Exclusion

The criteria for exclusion of subjects should be identified in separate paragraphs. A bulleted list of all exclusion criteria is recommended. Dual participation is not forbidden by the IRB and is considered on a case by case basis.

EXAMPLE:

Exclusion Criteria:

1. Any potential subject not in generally healthy medical condition as determined by the investigator.
2. History or current evidence of gastrointestinal disease known to interfere with absorption or excretion of drugs, or a history of surgery known to interfere with absorption or excretion of drugs.
3. Severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or study drug administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the subject inappropriate for entry into this study.

c. Subject Recruiting Methods

Describe how prospective subjects will be identified and recruited. Explain who performs recruitment and in what setting. All recruitment materials, including email text, posters, flyers, videos, telephone scripts, presentations, etc. must be submitted for IRB review. An

advertisement/flier/broadcast can only be used exactly as it was written and for the specific purpose specified as approved by the IRB.

d. Informed Consent Procedures

- i. If requesting a *Waiver of Consent* or *Waiver of Documentation of Consent* provide a justification and attach the appropriate form (See Appendix C)

Describe the process for obtaining consent. Who performs the consent, under what timeline, and in what setting? Are subjects consented individually or in a group? How is consent documented? If minors are being enrolled in a long-term study, will their consent be obtained upon reaching the age of majority? If subjects are unable to consent for themselves due to emergent situations or impaired status, will a Legally Authorized Representative (LAR) be approached? How will decisionally-impaired subjects be assessed to determine if they are competent to consent? Will subjects receive a copy of their consent at the end of the initial interaction? How will ongoing consent be ascertained? Describe how and where signed consent forms will be stored.

- ii. If requesting a *Waiver of Consent* provide an explanation, attach the appropriate form, and justify why it is appropriate to involve individuals in this project without their consent.

d. Justification for Use of this Subject Population

Explain why the population to be studied is appropriate for the project. Describe the characteristics of the subject population, such as the age range, gender, ethnic background, if they are military or civilian, all officers or all enlisted personnel, military health beneficiary status, and health status. Rationale for the use of special classes of subjects, such as pregnant women, children, prisoners, or others who are likely to be vulnerable must be given.

e. Vulnerable Populations

Define vulnerable populations to be recruited into the study, including (but not limited to) children, pregnant women/fetuses, prisoners, decisionally-impaired individuals, economically disadvantaged persons, educationally disadvantaged persons, tribal populations, non-native or ESL speakers, persons in emergency situations, persons with fatal or incurable diseases, persons in hierarchical social structures (such as employees, students, or members of the military), and persons who are marginalized in society (such as the homeless). Some explanation of the need to include such groups, and the special precautions taken will be required here. If you are unsure of what special regulations exist, please consult the RSPD SOP's or contact the Research Subjects Protection Division (RSPD) at CID. If your study doesn't anticipate enrollment of vulnerable populations, state so here.

f. Number of Subjects and Justification

For minimal risk studies involving retrospective chart reviews, identify the number of subject charts to be reviewed and the data window (i.e., 14 Nov 2003 – 15 Dec 2013). For prospective studies involving active subject participation, identify how many subjects you expect to enroll, the number to be enrolled at each site (if multi-centered), and the justification for this number. Remember to consider the anticipated screen failure / lost to follow up rate and how many subjects are needed to complete the protocol when identifying target enrollment goals.

g. Risks

- i. **List and Document Risks**

Describe potential risks to subjects, It is recommended that risks be presented in a "Likely, Less Likely, and Rare" model. Remember that risks may be physical, psychological, social, economic, professional, etc. Identify both the likelihood and

magnitude of potential harm. Differentiate between risks related to standard of care procedures and risks stemming from procedures performed for research purposes only. Describe alternative treatments or procedures that are available to subjects (if any). Remember that even retrospective chart review studies generally involve a risk associated with the accidental release of PHI.

ii. **Justification of Risks**

Discuss WHY the risks to subjects are reasonable in relation to the anticipated benefits to subjects and in relation to the importance of the knowledge that may reasonably be expected to result. For protocols that involve a risk associated with the accidental release of PHI, indicate that it is impossible to completely eliminate the possibility of accidental release of PHI.

iii. **Minimization of Risks**

Describe the procedures for protecting against or minimizing any potential risks, and assess their likely effectiveness. Discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Also, describe the provisions for monitoring the data collected to ensure the safety of subjects. If the only risk associated with participation is the possibility of accidental release of PHI, describe how PHI will be protected during collection and maintenance of the information.

h. **Benefits**

Describe any anticipated benefits to subjects. It is possible that subjects may not receive any benefit from participation. Pay particular attention to the likelihood of benefit to subjects who are enrolled in research through third party consent (children, decisionally-impaired individuals, individuals in emergency situations, etc.). If subjects will be compensated for participation, describe the means of compensation and amount (compensation of \$50 cash for a blood draw; compensation of \$100 by check for time and travel, etc.). Refer to the RSPD SOPs on IRBNET for guidance on subject compensation.

i. **Costs to Subjects**

Describe any anticipated costs to subjects for participation, including expenses for items such as medical supplies and travel. If no costs are expected, state as such.

4. **RESEARCH MONITOR**

Per SECNAV 3900.39D a study which involves greater than minimal risk must have a Research Monitor assigned. The monitor cannot be an investigator on the study.

A research monitor (formerly known as “Medical Monitor”) must be identified for all protocols reviewed as “greater than minimal” risk, and at the discretion of the PI and the IRB for protocols which are “minimal risk”.

A research monitor should have expertise commensurate with the nature of risk(s) identified within the research protocol, and they must be independent of the investigative team, although an individual 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. More information regarding the duties and requirements of research monitors are detailed in the IRB application.

5. ADVERSE EVENT MANAGEMENT AND REPORTING

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 it is considered related to the subject's participation in the research.

Serious adverse events (SAEs) are adverse events (AEs) which meet all of the following three criteria: they must be serious, and unexpected, and related to the research. 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.

Describe how subjects who experience an adverse event will be treated and what reporting mechanism will be implemented to notify study sponsors and the IRB. Be aware of the reporting requirements detailed in the RSPD SOPs.

SAE Reporting requirements:

All local SAEs require notice to CID by telephone or email within one business day of discovery. Events satisfying all three criteria for identification as an SAE (serious, unexpected, and related to participation) require submission of a signed copy of the Report Local SAE form, a report from the Research Monitor, and any other related documents to CID within five business days of the PI and IRB Chair's agreement that the event is an SAE.

Adverse events judged to be SAEs will be reported to the Commanding Officer, to DON HRPP, and presented to the full IRB at the next available meeting.

AEs, but not SAEs:

Local AEs that are obviously not SAEs should be reported to the IRB in summary format at time of continuing review.

Sponsor's criteria for SAE:

A research protocol sponsor may have different criteria than NMCP for defining an SAE. Reporting an event as an SAE to a sponsor does not mean that event will also meet NMCP criteria.

6. STATISTICAL ANALYSIS

NMCP can provide statistical expertise in designing your experiment in order that a proper test of statistical significance, if any, can be made. You may contact the CID Biostatistician for assistance with the completion of this section.

In this section, explain the statistical analysis technique(s) to be used and from what basis the sample size was derived, including statistical power calculations. Ensure that an adequate justification for the number of human subjects to be used is provided. This statistical information should be incorporated as a part of each identifiable sub-study.

Include the means by which the data will be collected, analyzed, and interpreted. Describe what will happen to data from subjects who do not complete the study.

7. SIGNIFICANCE TO NAVY MEDICINE

All research programs are important to graduate medical education and to meeting the academic requirements of staff/faculty. If this research has additional impact on Navy medicine, please state so in this section.

8. PATENT DISCLOSURES/INVENTIONS

Indicate if any patents will be developed in conjunction with this project.

9. POTENTIAL HAZARDS TO THE RESEARCH TEAM

Hazards are potential risks researchers may be exposed to during the conduct of the study. Present information on any toxic substances, radiation or biohazards involved in your study and what protections for researchers are in place. For example, what type of PPE is required for investigators?

10. ANTICIPATED ENROLLMENT TIMELINE

Complete the Table with subject numbers as indicated. Indicate approximately how many subjects will be enrolled per year to reach total subject accrual goals.

11. BIBLIOGRAPHY FOR BACKGROUND SECTION AND RESEARCH PLAN

List complete citations of the publications used to develop this proposal. Be sure that all references cited here are discussed and annotated in the text of the protocol.