What is a protocol?

The protocol is the blueprint for how the study will be conducted. All the details of the study are described in the protocol. The principal investigator and other research staff must follow the protocol. If the protocol is not followed, the results of the research study may not be useful enough to answer the questions the research is trying to answer.

Suggested Guidelines for Writing a Research Protocol

Cover Sheet

- Display protocol title, protocol identifying number, and date. Amendments should be numbered and dated.
- Display the name and address of both the sponsor and the monitor (if someone other than the sponsor).
- Display the name and title of the investigator responsible for conducting the research, and the address and telephone number(s) of the research site(s).

Purpose of the study and background

- **Purpose of the study:** State the specific scientific objective(s) of the research.
- **Background:** Provide background material which supports the purpose of the research, and which is detailed enough to allow someone who is not an expert in the field to understand the context of the question, and the study design. References may be cited in the Background section.

Criteria For Subject Selection

- **Number of subjects:** State the total number of subjects expected to participate. For multi-center protocols, this should include both the overall total and the number of subjects to be enrolled at each site.
- **Gender of Subjects.** Describe the intended gender distribution of the subjects. If there are any gender-based enrollment restrictions, explain the nature of the restriction(s) and provide justification. Equitable inclusion of both men and women in research is important to ensure that both receive a proportionate share of the benefits of research and that neither bears a disproportionate burden. Therefore, subjects of both genders should be included in the research unless there are appropriate medical or scientific reasons. Women of childbearing potential may not be routinely excluded from participating in research; however, pregnant women should be excluded unless there is clear justification why they should be included. A clear statement whether pregnant women are included or excluded is required, along with the justification and whether a pregnancy test is

required and/or the women are using appropriate birth control methods or are unable to conceive.

- **Age of Subjects.** State the age range of the subjects. Provide the rationale for selecting this age range. Participation of adult subjects in research should not be age-restricted unless there is scientific or medical justification. Check the age of majority in the jurisdiction where the study is to be conducted and whether special considerations apply to research with minors. Additional restrictions may apply to research involving minors.
- **Racial and Ethnic Origin.** Describe the intended racial and ethnic distribution of the subjects. If there are any enrollment restrictions based upon race or ethnic origin, explain the nature of the restrictions and provide justification. Within the limitations imposed by the population of the study site(s), research should include sufficient enrollment of persons of diverse racial/ethnic backgrounds to ensure that the benefits and burdens of research participation are distributed in an equitable manner.
- **Inclusion Criteria.** List the inclusion criteria. These should be based on the scientific rationale and safety considerations, and should define who will be eligible as a subject.
- **Exclusion Criteria.** List the exclusion criteria. These should be scientifically valid and help further define the subject population. Subjects at particular risk from the study interventions or procedures should be excluded. Be sure to account for warnings, precautions, and contraindications listed in current product labeling.
- **Vulnerable Subjects.** If vulnerable subjects are included, justify their inclusion. Children, pregnant women, nursing home residents or other institutionalized persons, students, employees, fetuses, prisoners, and persons with decisional incapacity are examples of vulnerable subjects who may be in need of greater protection. Additional restrictions or requirements may apply to research involving vulnerable subjects.

Methods and Procedures

- **Methods and Procedures.** Summarize the research design and sequentially identify all procedures to be used to accomplish the specific aims of the project. Clearly identify and distinguish procedures that are considered experimental, procedures that are performed exclusively for research purposes (including extra routine tests), and procedures that would occur regardless of the research (i.e., standard of care). Point out any procedures, situations, or materials that may be hazardous, and the precautions to be exercised to maintain subject safety.
- **Data Analysis and Data Monitoring.** Describe the statistical or analytical methods to be used. For research involving intervention that entails potential serious risk to subjects, compares blinded treatments over a long time period, or which may call for stopping rules for certain endpoints, a data monitoring committee may be required to protect the safety or

welfare of subjects. A detailed description of its operation (e.g., membership, function, frequency of review, stopping rules) should be included.

- **Data Storage and Confidentiality.** Describe where the research data will be stored during and after the study and how it will be secured. The investigator must take necessary steps to maintain confidentiality of data. This includes coding data and choosing an appropriate and secure data storage mechanism preventing unauthorized access to data. State who will have access to the data and 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 (e.g., routine verification of case report forms).
- **Transition from Research Participation.** If applicable, describe how subjects terminating their participation in the research will be returned to their usual care (e.g. taper study medication and resume usual medication, return to primary care provider).

Risk/Benefit Assessment (a determination as to the risks and benefits of the research to subjects is the responsibility of the IRB; however, the following information is still required in the submitted protocol)

- **Risk Category.** State the risk that the research presents as one of the following: Minimal, or Greater than Minimal. Minimal Risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. A risk is a potential harm associated with the research that a reasonable person would likely consider injurious.
- **Potential Risk.** Describe the potential risks associated with the study. Risks are not only physical, but can be psychological, sociological, economic, and or legal. Risks include any specific toxicities noted in the investigator's brochure. If possible, estimate the probability that a given harm may occur and state its potential reversibility.
- **Protection Against Risks.** Describe how the study design will prevent or minimize any potential risks or discomfort. Potential risks and discomforts must be minimized to the greatest extent possible such as by subject monitoring, appropriate subject withdrawal criteria and adequate follow-up.
- **Potential Benefits to the Subjects.** Describe potential medical benefit(s), if any, for subjects participating in the research. If there are no anticipated benefits, this should be stated.
- **Alternatives to Participation.** This section should include a description of alternative therapies or courses of action which are available should the subject elect not to participate in the study.

Subject Identification, Recruitment and Consent/Assent

- **Method of Subject Identification and Recruitment.** Describe how prospective subjects will be identified and recruited. The identification and recruitment of subjects must protect privacy and be free of undue influence. Recruitment of an investigator's own students, employees and patients is considered coercive in most circumstances. The steps taken to minimize undue influence must be included if these individuals are to be enrolled as subjects.
- **Process of Consent.** Describe or list everyone who is authorized to obtain consent and how the process of informed consent will be structured to be conducive to rational and thoughtful decision making by the subject (or subject's legally authorized representative) without any element of coercion or undue influence. If used, Auditor/Witness roles would be described in this section.
- **Subject Capacity.** If not all subjects will have the capacity to give informed consent, describe how capacity will be assessed and by whom. Describe the anticipated degree of impairment relative to their ability to consent to participate in research. Research with persons who have diminished capacity is allowed only for minimal risk or direct benefit studies.
- **Subject/Representative Comprehension.** All investigators have a legal and ethical obligation to ensure that prospective subjects or subjects' representatives have sufficient knowledge and comprehension of the information represented by the elements of informed consent to enable them to make an informed and enlightened decision whether or not to participate or allow participation in research. In this section, describe how it will be determined that the subject or subject's authorized representative understood the information presented. This section should clearly document that the investigator has an adequate plan in place to assure an acceptable level of comprehension before consent is obtained. If children or decisionally impaired adults will be subjects, this section should also include a specific plan to assess comprehension during assent (the subject's agreement).
- **Debriefing Procedures.** In psychological studies where any information will be purposely withheld from the subject, state the information to be withheld, justify this non-disclosure, and describe the post-study debriefing of the subject.
- **Consent Forms.** Consult IRB consent form guidelines for specific sections required for consent documents. See 21 CFR 50.25 available on the FDA website, or **http://www.fda.gov/oc/ohrt/irbs/informedconsent.html**
- **Documentation of Consent.** The PI is responsible for ensuring that valid consent is obtained and documented for all subjects. If not already addressed above, specifically describe how consent will be documented and how and where documentation will be stored.

- **Costs to the Subject.** Describe and justify any costs that the subject will incur as a result of participating in the study. This section should clarify who (e.g., sponsor, grant, subject) will pay for procedures associated with the study or necessary follow-up. Normally, subjects should not have to pay for research procedures that do not provide direct benefit. No charge may be made to subjects for costs covered by another entity. Subjects may not be charged for investigational drugs without the written permission of the FDA.
- **Payment for Participation.** Describe any reimbursements or payments (e.g. cash, coupons or gift certificates, academic credit) that the subjects will receive for participation. List the prerequisite condition(s) that must be fulfilled by subjects to receive these payments. The amount must be justified and not constitute undue inducement of the subject to participate in the research or to continue beyond where they would have otherwise withdrawn. To protect the subject's right to withdraw without penalty, the IRB requires a prorated system for financial payments. In most circumstances, no more than 50% of the total payment may be withheld till the end of the study. Ideally, payments are accrued as the study progresses and subjects do not have to complete the entire study to be eligible to receive a payment.