

## **Section 18: Protocol Design**

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All DF/HCC research projects involving human participants must be written as protocols. The OHRS and Clinical Investigator Toolkit sections of the DF/HCC web site provide guidelines for writing minimal risk and greater than minimal risk protocols in the DF/HCC format. Cooperative group trials have their own required format and thus are exempt from the DF/HCC protocol format. Protocols written elsewhere, such as industry sponsored trials need not be placed in DF/HCC format.

### **18.1 The Protocol Document**

The essential elements of the protocol are:

#### **Synopsis of the Protocol**

- The objective(s) of the research protocol
- Current knowledge and relevant literature
- Rationale for the use of the selected study population
- Statistical/qualitative methodology
- Explicit inclusion/exclusion criteria
- How the inclusion/exclusion criteria are assessed and by whom
- Participants' alternatives to participation in the trial
- Consent process or request to waive consent

#### **Risks to Participants**

- Risks (anticipated and potential)
- Risks from trial article/research procedures (i.e., washout risks, placebo assignment)
- Expected frequency, degree of severity, and reversibility
- Possible late effects
- Assessment procedures for the occurrence of adverse events
- For trials with more than minimal risk, or FDA-regulated products/trials, plan for monitoring trial and data

#### **Potential Benefits**

- Potential direct or indirect benefits to the participant

- Potential benefits to the group or class from which the participants are recruited
- Potential benefits to society

### **Risk/Benefit/Alternative Assessments**

- The risk/benefit ratio of participants' participation, including careful consideration of alternative therapy, benefit to the class of patients, and benefits to society

### **Procedures**

- Duration of participants' active participation
- Follow-up after active participation ends
- Number, duration, and nature of trial visits/encounters
- Procedures to be performed solely for the purposes of the research
- All procedures that will be performed to generate data for the research

## **18.2 Protocol Sections**

Sections of a protocol document will often include:

- Title Page
- Outline of current and previous version information
- Table of Contents
- Study Schema
- Summary of the Study
- Background and Significance
- Statistical Considerations
- Study Objectives and Endpoints
- Enrollment and Registration Information
- Eligibility Criteria
- Pre-Therapy Evaluations
- Treatment Plan
- Expected Adverse Events, Dose Modifications and Un-blinding Information
- Drug Information

- Reporting of Adverse Events
- Data Collection & Required Data Tables
- Follow Up Monitoring of Study Participants
- Long-Term Follow Up/Survival Data Collection
- Submission of Collected Research Specimens; Ancillary Studies Information
- References
- Appendices

It is critical that the protocol document be kept as simple as possible and that only necessary requirements and tests be included in each trial. Once a protocol is activated, it must be followed as written (except for emergent safety reasons as described below). All auditors will monitor compliance with the protocol *as it was written and approved*. The more complicated a protocol, the more difficult it is to follow. Consistency and accuracy are critical. Although amendments can correct issues with the protocol, these require increased effort from the investigator and time for appropriate review. Therefore, careful consideration of the trial design, including eligibility requirements, required data elements, and length of follow-up is essential.

Investigators may not improvise on the protocol plan. A protocol must be implemented exactly as it is approved.

Many protocols include follow-up. It is important that the protocol and the consent identify the information and procedures that will be included in follow-up of the participant.

Any changes to be made must be first approved by the IRB, unless the safety of research participants enrolled is at stake.