



## 6 key elements to writing a strong clinical trial protocol synopsis

A clinical research protocol is a roadmap. In order to have a clear roadmap, it is important for the investigator to have a succinct and relevant synopsis that others can review at a glance for a general sense of direction.

In Lewis Carroll's *Alice in Wonderland*, the King says to the White Rabbit, "Begin at the beginning, then go until you reach the end. Then stop." He could have been telling an investigator about the process of crafting a clinical trial protocol. The synopsis is often used when investigators apply for grants or seek to obtain resources and other support to undertake the study.

For medical school residents, a synopsis can be used as a discussion point with an advisor. For investigators seeking grants from pharmaceutical or device companies, the synopsis is a good way to "put out feelers" with potential sponsors.

Sometimes a well-crafted research protocol synopsis can be used in an informal review by IRB members to determine issues that may come up in a more formal review process.

Unfortunately, too many investigators wait to write their synopsis after they have written the entire protocol, using the extensive details they have gathered as a foundation for the two-page document. This means the investigator has already gone through the exhaustive protocol-writing process without the opportunity of vetting the idea for the study to see if it's even feasible or needed.

These are the key elements of a strong synopsis:

### 1. Design a study to achieve your goals

The design of a study is an iterative process, with each step largely influenced by the answer to the previous question. Typically, the first question an investigator must answer is whether the study is a treatment study or an observational study.

As the investigator answers these initial questions, he or she will eventually be guided to one of several designs. Each design approach is better suited to study one over another kind of research question.

### 2. Connect your endpoints to the objectives

The endpoints (or outcomes), determined for each study participant, are the quantitative measurements required by the objectives. "Hard" endpoints are well-defined in the study



protocol, definitive with respect to the disease process, and require no subjectivity. “Soft” endpoints are those that do not relate strongly to the disease process or require subjective assessments by investigators and/or patients.

The FDA says that a primary endpoint should generally not be a measure of something that is not important to the patient. Clinical endpoints, therefore, can include symptom benefits, biomarkers, response rates, or progression-free survival. Clinical trial design is driven by endpoints. Clinical endpoints influence the complexity of a trial. Methods for recruiting and enrolling participants; performing the study; gathering and analyzing the data are all directly related to the endpoints.

### 3. Define measurable objectives

Research objectives should be measurable and directly answer the research question. A common mistake made by inexperienced investigators is overloading the protocol with too many objectives, making data collection difficult or impossible. It's best to focus on a single primary objective.

Often, the objective is too vague. For example, “The objective of this protocol is to determine the safety and efficacy of drug x in disease y” is too vague and has no clear measurement. A better way of stating an objective would be to say, “We want to evaluate if 12 weeks of a specific dose of a drug is superior to placebo.”

### 4. Develop a hypothesis

Once the literature has been thoroughly researched, it is time to make an educated guess and develop a hypothesis. It is important to distinguish the hypothesis from the research question. The hypothesis should be an educated, testable prediction about what will happen in the “experiment.” A well written and defined hypothesis is the key to developing a research protocol. With a strong hypothesis, the investigator can then define specific objectives that will answer the research question.

### 5. Start with a clear research question

Why is the study being done? What is the intent of the research? The research question should be interesting, novel and relevant. Investigators should know the literature to ensure this question has not already been answered. The importance of reviewing the literature cannot be overemphasized. In combing the literature, you may find many studies similar to yours have already been conducted. What you learn from available research and data can help you shape your project and research hypothesis.



## 6. Know your study population

In addition to identifying the number of planned research subjects, you should also include a brief description of the population. This can include their health or disease stage, gender, age, and so on. You should also include inclusion and exclusion criteria for participant enrollment.

Keep these six key elements in mind to have a succinct and relevant synopsis that others can review at a glance for a general sense of direction.