

## Protocol Development

Sponsored by  
Center for Cancer Research  
National Cancer Institute



## Objectives

The clinical trial protocol is the heart of any research project. It is a "recipe" for ensuring that the procedures/measures outlined in the research study are carried out in a consistent, reproducible manner. One of the major roles of the research nurse is to ensure that protocols are adhered to which requires an in-depth knowledge of all components included in the protocol document. This module will review how to plan a protocol, describe the essential elements of a protocol, and briefly review important parts of a protocol.

At the conclusion of this module, you will be able to:

- Describe characteristics of a good research questions
- Describe measurement tools specific to oncology clinical trial endpoints
- Discuss the purpose of a written protocol in clinical trials

## Planning a Clinical Trial



- Formulate the Research Question
- Develop the Study Design
- Define the Study Population
- Select the Measurement Tools/Endpoints
- Determine Sample Size and Statistical Analysis
- Data Collection and Storage

## Formulate the Research Question

- Define Objective(s) clearly and precisely
- Objective(s) need to be tied to measurable study endpoints
- Primary objective of the study must be identified
- May have several secondary objectives

## Characteristics of a Good Research Question – "FINER"<sup>1</sup>

- Feasible
  - Adequate number of subjects
  - Adequate technical expertise
  - Affordable in time and money
  - Manageable in scope
- Interesting
- Novel
  - Confirms or refutes previous findings
  - Extends previous findings
  - Provides new findings
- Ethical
- Relevant
  - To scientific knowledge
  - To clinical and health policy
  - To future research directions



NCI1

<sup>1</sup> Hulley, S.B., Cummings, S.R., Browner, W.S., Grady, D., Hearst, N., Newman, T.B. (2001). *Designing Clinical Research* (2nd Ed.). Philadelphia: Lippincott Williams & Wilkins.

## Select the Study Design

Selection of the study design is based on:

- study question
- ethical considerations
- resources



**See Trial Design Module for details**

## Slide 5

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**NCI1** add pop up for this one - see separate attachment  
Nesse, 1/5/2010

## Study Subject Selection

- Subjects who may benefit
- Subjects who may be at greater risk
- Subject's ability to comply
- Subject's concurrent conditions
- Inclusion criteria
- Exclusion criteria



## Measurement Tools/Endpoints

- Toxicity
  - Common Terminology Criteria for Adverse Events (CTCAE v.4.0)
- Response
  - May use standard disease specific response criteria (e.g., *Response Evaluation Criteria In Solid Tumors – RECIST 1.1*)
- Time to Progression (TTP)
- Survival
- QOL/Patient Reported Outcomes (PRO)
  - Various survey tools (e.g.: FACT)
- Biological Endpoints and Surrogate Markers

## Determine Sample Size

- Get statistician involved early
- Estimate the appropriate number of subjects for a given study design
- Test the hypothesis
- How to handle dropouts/withdrawals?
- For interventional studies:
  - How large a difference between treatment groups is medically important
  - Include enough participants to get a statistically significant results



## Determine Statistical Analysis

- Get statistician involved early
- Analysis plan appropriate for objectives and design
- How endpoints will be measured
- Statistical methods to be used
- How will common problems be addressed
- Management of safety data

## Data Collection & Storage

- Identify critical data elements to be collected
- Develop case report forms (may be required for IRB or FDA submission)
- Safe and secure mechanism for data storage
- Anticipate audits of clinical data
- Length of time for storage
  - Know [FDA regulations](#)
  - Know [institutional policies](#) as appropriate



## THE PROTOCOL



## Clinical Research Protocol

A written, detailed action plan that:

- Provides background about the trial
- Specifies trial objectives
- Describes trial's design and organization
- **Ensures that trial procedures are consistently carried out**

*Please note: Each IRB or Sponsor will have their own Protocol template.*

## Reading a Protocol



How you read a protocol and where you begin will depend on your role on the research team.

### Examples:

Research Nurse may begin with Informed Consent Document (ICD) to familiarize him/herself to protocol and then begin with the eligibility section, study implementation, appendices, etc.

Data manager may begin with ICD and then focus on study implementation and the data/time points to be collected including the case report forms to be used.

Pharmacist may begin with the Pharmaceutical section.

Treatment nurse may begin with Pharmaceutical section to see how drug(s) will need to be administered.

## CCR Protocol Template

There are 3 options for protocol templates in the CCR:

- [NCI IRB template](#)
- [CTEP Template](#)
  - *If using the CTEP template, please remember to include required NCI CCR sections such as Human Subjects Protections and NCI IRB AE reporting requirements.*
- Industry Sponsor Template
  - *NCI IRB will accept an industry sponsored formatted template but an NCI Appendix is required.*

## NCI Appendix

- If a CCR Investigator is not the author of the study, then an NCI Appendix is required and should include:
  - Face Sheet
  - Précis
  - Registration Information
  - NIH Definitions of Violation, Deviation
  - NCI-IRB Reporting requirements
  - Human Subjects Protection Section (if not in protocol)
  - NCI Multi-Center Guidelines
  - Sample storage, tracking and disposition information pertinent to CCR

## iRIS

- Integrated Research Information System (iRIS) is a web-based application to help create, manage and process research protocols.
- It can be accessed from any computer that has a connection to the NIH internal network.
- Information about iRIS is located on the CCR IRB Website: <http://home.ccr.cancer.gov/IRB/>
  - Training is required: see website above for details
  - Recommend to review [user manual](#)
- iRIS url: <https://iris.nci.nih.gov/imedris/>

## References

- Hulley, S.,B., Cummings, S.R., Browner, W.S., Grady, D., Hearst, N., Newman, T.B. (2001). *Designing Clinical Research* (2nd Ed.), Philadelphia: Lippincott Williams & Wilkins.
- Emanuel E, R. Crouch, J. Arras, J. Moreno, and C. Grady. (2003). *Ethical and Regulatory Aspects of Clinical Research: Readings and Commentary*. Baltimore: Johns Hopkins University Press.

## Evaluation

Please complete the [evaluation form](#) and fax to Elizabeth Ness at 301-496-9020.



For questions, please contact Elizabeth Ness  
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