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# Research Investigator Manual

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For Faculty, Residents, Medical Students, and Staff

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University of Tennessee College of Medicine Chattanooga

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Note: Format and selected content of this manual were adapted from *A Research Manual for Mayo Internal Medicine Residents, Mayo Foundation, 2005*, and were used with permission of the Department of Internal Medicine, Mayo Medical School, Rochester, MN and the NIH training.com Principles and Practice of Clinical Research Course.

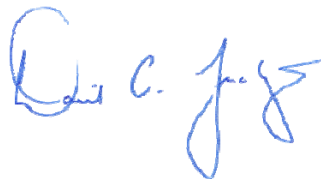
## PREFACE FROM THE DEAN

The University of Tennessee College of Medicine Chattanooga (UTCOCMC), as part of the statewide Health Science Center, supports the efforts of faculty, residents, students and staff to promote research and scholarly activity.

The unique relationships between the UTCOCMC, Erlanger Health Systems, and the University of Tennessee at Chattanooga provide many opportunities for interdisciplinary initiatives. In addition, the city of Chattanooga is home to several large health care insurers (including Blue Cross Blue Shield of Tennessee and The Unum Group) who regularly participate in University research activities. The Health Science Center's mission includes continuing relationships with research and healthcare facilities across Tennessee to ensure that both basic science and applied research stay focused on contemporary health topics.

Our goal is to provide mentoring and administrative resources to facilitate ongoing scholarship. The Office of the Dean is responsible for support of the Institutional Review Board, the Scientific Review Committee, and the Office of Research Compliance to assure the responsible conduct of research. We have developed this handbook to help new investigators get started, but also hope that experienced researchers will find it useful. It is designed to guide you through the first steps of designing and implementing a research project and on to writing and presenting your results.

We look forward to working with you to promote our mission of blending the art and science of medicine to reduce the burden of human illness and suffering.



David C. Seaberg, MD, FACEP  
Dean and Professor, UT College of Medicine Chattanooga

# CHAPTER 1. GETTING STARTED

## ARE YOU ENGAGED IN RESEARCH?

The Department of Health and Human Services (DHHS) has defined research as “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.” Therefore, if you are collecting data (including, for example, interview, review of medical records, screening laboratory results) with the intent of publication, presentation (orally or on a poster), that is considered research and contributing to generalizable knowledge. This can include case studies presented outside the University. (Note: this definition does not include quality assurance review done within a physician’s practice or institution.) The person responsible for the conduct of research is the investigator. If the research is conducted by a team of individuals the investigator is the responsible leader of the team and may be called the principal investigator. Only one person may be principal investigator on any research.

## IS TRAINING REQUIRED?

Investigators and key personnel must complete the online Collaborative Institutional Training Initiative (CITI) human subjects online training program prior to starting any research. The CITI site can be accessed at <http://www.citiprogram.org/>. This training is valid for a three-year period, after which a refresher CITI course must be completed. All key members of a research team are required to complete this training. The Institutional Review Board will not grant approval for protocols in which investigators have not completed training. In addition, there are regularly scheduled training opportunities; see the UTCOMC website (Continuing Medical Education, IRB, and Research Compliance pages) for details.

## WHO CAN HELP?

To work effectively within the university research environment, you will interact with academic, university, and professional groups whose regulatory approvals and support are required for a successful research career. UTCOMC policy does not allow a resident to submit to the Scientific Review Committee or to the Institutional Review Board as a principal investigator; you will require a faculty mentor to serve as PI (see Chapter 8 for addition SRC and IRB information).

The academic departments and residency programs at the UTCOMC each have a key research mentor; you should start by checking within your department or program (department-specific contacts are listed at [Research Contacts - University of Tennessee: College of Medicine Chattanooga](#)). The College of Medicine Chattanooga also maintains a list of resources that are available through the University and the community. This list is updated annually and can be viewed on the UTCOMC [IRB research resources webpage](#).

## USE OF ELECTIVE TIME FOR RESEARCH

Residents in some programs may use scheduled elective time to fulfill their requirement for productive research and scholarly activity. The time and scheduling vary depending on the residents program.

Residents wishing to use elective time for research must fulfill the following:

1. Residents must apply to use elective time for research two months prior to the start of the elective time period.
2. Residents must have written prior approval from their program director or department chair. This approval is contingent on receipt of:
  - a. A project proposal plan (see Chapters 3-5);
  - b. The proposal must have been approved by the appropriate divisional research committee and, if appropriate, the Scientific Review Committee or the Institutional Review Board;
  - c. A description of the resident's involvement and actual activities related to the project for this time period (ie, what will you actually do, how much time will it take, what will be accomplished);
  - d. A letter from your staff mentor listing the title of your joint project, his/her support for your project, and agreement to be your mentor for the specified time period.

## CHAPTER 2. MENTORS

### WHAT IS A RESEARCH MENTOR?

One of the most important hurdles for you to overcome is the identification of both a project and a mentor. Mentors are willing to commit time, resources, and effort toward your project. Your job is to find a mentor with whom you share a research interest. All of the consultants are quite approachable and will be happy to have you call to set up a time when you can discuss the possibilities of a research idea or project.

UTCOCM policy does not allow a resident to submit to the Scientific Review Committee (SRC) or to the Institutional Review Board (IRB) as a principal investigator (PI); you will require a faculty mentor to serve as PI (see Chapter 8 for addition SRC and IRB information).

The function of a mentor is:

1. To facilitate the development and structure of a relevant, achievable research proposal;
2. To sponsor and guide the resident through the appropriate research committees and, when necessary, the SRC and the IRB;
3. To help acquire support, equipment, space, and budgetary resources needed to complete your project;
4. To guide and aid the resident in:
  - a. Critically evaluating relevant scientific literature;
  - b. Gathering and organizing data;
  - c. Involving appropriate support services (statistical, editorial and graphic services);
  - d. Identifying potential sources of grant support or monies, where needed;
  - e. Preparing an abstract, poster, oral presentation, and/or manuscript, to supervise the project in an ongoing way, and to monitor your progress to maintain the suggested timetable for completion.

### WHAT ARE A TRAINEE'S RESPONSIBILITIES?

The trainee (or resident) is responsible to:

- Conduct themselves in a mature, professional, and civil manner in all interactions with faculty and staff.
- Recognize that the faculty advisor provides the intellectual and instructional environment in which advisee conducts research, and may, through access to teaching and research funds, also provide the trainee with financial support.
- Recognize that the faculty advisor is responsible for approving a research plan and for monitoring the progress of the research. Careful, well-conceived research reflects favorably on the trainee, the faculty advisor, and the University.
- Exercise the highest integrity in academic pursuits and in collecting, analyzing, and presenting research data.

- Acknowledge the contributions of the faculty advisor and other members of the research team to the trainee's work in all publications and conference presentations.
- Maintain the confidentiality of the faculty advisor's professional activities and research prior to presentation or publication, in accordance with existing practices and policies of the discipline.
- Take primary responsibility to inform themselves of regulations and policies governing their studies.
- Be aware of time constraints and other demands imposed on faculty members and program staff.
- Take the initiative in asking questions that promote understanding of the academic subjects that are presented by the faculty.
- Communicate regularly with faculty advisors in matters related to research and progress within the program.

## WHAT ARE A MENTOR'S RESPONSIBILITIES?

The mentor is responsible to:

- Serve as mentor without regard to the race, gender, sexual orientation, or national origin of the trainee.
- Interact with trainees in a professional and civil manner in accordance with University policies governing non-discrimination and sexual harassment.
- Excuse themselves from serving as mentor when there is a relationship that could result in a conflict of interest.
- Acknowledge the trainee's contributions to research presented at conferences and in professional publications.
- Create an atmosphere which stimulates and encourages trainees to learn creatively and independently.
- Have a clear understanding with the trainee about their specific research responsibilities, including timelines for completion of research.
- Discuss authorship policy in advance of entering into collaborative projects.
- Be familiar with university, college, and departmental policies.
- Provide clear timetables for meeting requirements.
- Evaluate trainee progress and performance in regular and informative ways.
- Assist trainees in developing grant writing skills as appropriate.
- Encourage and provide support for trainees to participate in professional meetings.

## CHAPTER 3. STARTING YOUR RESEARCH PROJECT

### ASKING THE RIGHT QUESTION

The foremost task you face in beginning your research is identifying an area of interest and then asking an appropriate question worthy of further investigation. Anyone with a curious and critical attitude will daily come across questions pertinent to the art and science of patient care. But, notice the two key ingredients: curiosity and critical attitude.

In particular, important questions arise in your everyday clinical practice of medicine, but you must first be aware of the question, and second, have some idea of how to go about answering it. You will need the resources necessary to generate data and reach a conclusion or, more often, a new hypothesis. For example, what is the value of ESR in screening patients? What are the operating characteristics of the first strep screens? What routine laboratory and diagnostic tests should be obtained in hospitalized patients? In outpatients? In chronic fatigue patients? How effective is a patient education program on weight reduction? On angina? On rheumatoid arthritis? The resident who admits a patient with a rare or unusual disease process might legitimately wonder how similar patients presented for medical care. What has been the morbidity/mortality at Erlanger? How has the treatment changed and what effects has this had?

Answers to these types of questions are immensely facilitated by record keeping, storage and retrieval practices. Often these questions will arise after a perusal of the current literature stimulated by a discussion during teaching rounds. For the curious, receptive, and creative mind, a plethora of interesting questions exist from which answers (inevitably) lead to new questions. You must be attuned and attentive to this process.

### RESEARCH CRITERIA

One group of investigators has coined the mnemonic FINER for the characteristics of a good research idea. Before embarking on any project, ask yourself whether your study can fulfill each of these criteria:

1. Feasible
  - a. Adequate number of subjects?
  - b. Adequate technical expertise?
  - c. Affordable in time and money?
2. Interesting
  - a. To the investigator?
  - b. To possible funders?
  - c. To reviewers?
3. Novel?
  - a. Confirms or reflects previous findings?
  - b. Extends previous findings?

- c. Provides new findings?
- 4. Ethical
  - a. Potential harm to patients?
  - b. Potential breach of confidentiality?
  - c. Potential conflict of interest?
- 5. Relevant
  - a. To scientific knowledge?
  - b. To patient management?
  - c. To clinical and health policy?
  - d. To future research directions?

The discipline of applying these points to your research idea/question is invaluable, and in itself promotes critical thinking in the framing, planning, and execution of the project.

#### MENTOR REVIEW AND APPROVAL TO START

- Start by submitting a brief document to your mentor for project approval. This should include:
  - Your hypothesis/question and the expected outcome should be stated in 2-4 sentences. The more specific and definite, the better! Try to focus on a single question. Be specific in what you wish to accomplish.
  - Investigators (your name, mentor's name and any other co-investigators and their department/affiliation).
- Once your mentor and department have approved your project, you will be ready to expand the above sentences into a written 1-3 page project proposal, which will be described in detail in Chapter 4.
- Question accepted medical practices and knowledge—great ideas frequently arise from a questioning, critical attitude.

## CHAPTER 4. WRITING A RESEARCH PROPOSAL

### WHAT'S IN A PROPOSAL?

A research proposal is a written document that describes a research protocol and the administrative support required to successfully complete the planned research. The research proposal is an essential part of every research project. A concise written proposal must be prepared before starting the research.

The research proposal has several purposes. It clarifies the investigator's thinking and assists in formulating specific aims and hypotheses which can be tested. It can also be used to request funding for the research.

The process of writing the proposal helps the investigator to clarify ideas and frame the study questions as testable hypotheses. Problems that may arise are anticipated and solutions designed in advance. Prior work in an area is critically evaluated to identify gaps in our current knowledge, controversies that are to be resolved, or observations that are to be confirmed or examined in other settings or with other methods.

In addition to clarifying the investigator's ideas, the research proposal identifies a specific plan of work and indicates how the research will be accomplished. The research proposal contains a timetable and indicates when the important individual steps will be completed. This helps the investigator determine whether the time allocated is appropriate. During the research, the timetable assists in evaluating progress and allows timely changes to make maximum use of available time and resources.

The research proposal also serves to identify the resources needed to successfully complete the research plan. These can include:

- The investigator's time;
- Time for other personnel;
- Clerical support;
- Potential subjects (which may include patients and volunteers and possibly animals)
- Equipment needed to carry out the research including laboratory equipment and computers;
- Other supplies;
- Space (office, laboratory, other).

A research proposal can also assist others in the evaluation of the investigator's achievements and future potential for research contributions.

### WRITING A PROPOSAL

In writing the research proposal, the investigator should answer these four questions:

- What do you intend to do?

- Why is this important
- What has already been done?
- How are you going to do the work?

Many investigators have found writing a research proposal to be the single most important step in their research. They are continually written, rewritten, and revised as ideas are conceived, modified, rejected, and clarified. Although there is no single best way to write a research proposal the following suggestions may be useful.

- Begin now!
- Review your interests and experiences.
- Review the medical literature.
- Work from an outline.
- Revise, rewrite, and revise.
- Test your ideas by obtaining constructive criticism from colleagues and mentors.
- Revise, rewrite, and revise.
- Collect some preliminary data.
- Revise, rewrite, and revise.

#### RECOMMENDED FORMAT FOR A RESEARCH PROPOSAL (AS REQUIRED BY THE UTCOMC SCIENTIFIC REVIEW COMMITTEE)

1. Title page
  - a. Title of project
  - b. Name of principal investigator, institution, department affiliation
  - c. Co-investigators, institutions, department affiliations
2. Abstract/project summary
  - a. Should be  $\leq 350$  words
  - b. Should contain most critical background and methodology information
3. Hypothesis/specific aims
  - a. State hypothesis to be tested
  - b. List specific aims in decreasing order of importance
  - c. Specific aims can be subdivided into primary and secondary aims, if necessary
4. Background/Significance
  - a. Should be thorough and clearly cover the current literature in the area to be studied
  - b. References are required for all work cited
  - c. This section should end with a description of how the proposed study will add to the current body of knowledge
5. Preliminary work
  - a. Describe any preliminary work done by the current investigators relevant to this study
  - b. Many investigators will leave this section blank for a new area of study
6. Methods
  - a. Study design

- i. Describe the study design
    - ii. Give rationale for choosing the study design
  - b. Study subjects
    - i. Describe the process of subject selection
    - ii. Inclusion criteria
    - iii. Exclusion criteria
    - iv. Process of control selection, if using controls
  - c. Sample size
    - i. Explain total number of subjects to be tested
    - ii. Include statistical methods used to determine adequate sample size
    - iii. If local subject numbers are insufficient, describe plan to address suboptimal sample size (partnership with other researchers, increased recruitment area, etc.)
  - d. Data collection
    - i. Define data points to be collected
    - ii. Describe which data points represent study outcome variables
    - iii. Include any forms to be given directly to subjects exactly as will be used in the study
    - iv. Include form to be used for investigator collection of data
    - v. If laboratory techniques are to be used, describe in detail
  - e. Data handling
    - i. Describe how data will be collected and stored
    - ii. Explain steps taken to assure accurate and complete data collection
    - iii. Describe steps taken to ensure security of any confidential information to be collected during study
  - f. Data analysis
    - i. Explain detailed plan for analysis of data
    - ii. Describe statistics to be used
    - iii. How will analysis performed test study hypotheses?
    - iv. Expected formats for presenting results
  - g. Time frame
    - i. Detailed and realistic time frame for subject recruitment and participation
    - ii. Time frame for completion of entire study (including analysis)
  - h. Strengths/Innovation
    - i. Describe the strengths of the study proposed
    - ii. Describe specifically how this study will enhance the current body of knowledge
  - i. Limitations
    - i. Describe potential problems that may arise and plans to address these problems
    - ii. Describe potential confounding variables in the study and plans to account for the confounders
- 7. Risks and benefits to human subjects, animals, use of hazardous materials

- a. Risks to study subjects
  - b. Direct benefits to study subjects
  - c. Benefits to society
  - d. If animals are to be used, provide detailed plans, describing number of animals, plans for the care and disposal of the animals
  - e. If hazardous materials to be used, describe detailed plans for safe use, storage, and disposal of materials
  - f. Discuss ethical concerns involved in conduct of the proposed study
8. Budget/research environment (facilities, clinical space, etc.)
- a. List total cost to be incurred to complete study
  - b. Identify source of funding for study conduct
  - c. If multiple areas of cost to study, itemize budget as appropriate
9. References
- a. List relevant literature to the proposed study
  - b. Make every attempt to cite the most recent and relevant literature in the area to be studied
10. Appendices
- a. Data collection form
  - b. Any survey or measurement tool to be given directly to the subjects
  - c. Previous publications of preliminary work, if any
  - d. Consent form, if applicable

## CHAPTER 5. WRITING A RESEARCH PROTOCOL

Depending on the content and methodology described in your research proposal, you may need to write a separate research protocol. Your mentor can advise you on the need for a protocol. A protocol contains a study plan on which a clinical trial is based, most often involving testing of a pharmaceutical product or medical device. It describes what types of people may participate in the trial, the schedule of tests, procedures, medications, and dosages, and the length of the study. It enables the investigator to perform the study in a consistent and accurate manner, documenting the duties and responsibilities for the trial. The trial design and methodology may be more detailed in a protocol than a research proposal.

In addition to the information provided in a research proposal, [\*Good Clinical Practice Guidelines\*](#) require that a clinical trial protocol also include the following:

- Protocol title, IRB approval number, date
- Name and address of the sponsor (if applicable)
- Background information
- Trial objectives and purpose
- Trial design
  - A specific statement of primary endpoints and secondary endpoints, if any, to be measured during the trial
  - A description of the design of trial (eg, double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures and stages
- A description of measures taken to minimize/avoid bias
- Trial treatments, dosage and regimen of investigational products
- Expected duration of subject participation, sequence and duration of all trial periods, including follow-up, if any
- A description of stopping rules or discontinuation criteria for individual subjects, parts of trial and entire trial
- Maintenance of trial treatment randomization codes and procedures for breaking codes
- Identification of any data to be recorded directly on the clinical report forms
- Treatment of subjects
  - The treatment to be administered include the name(s) of all products, doses, schedule, route, and treatment period
  - Medications permitted (including rescue medication) and not permitted before and/or during trial
  - Procedures for monitoring subject compliance
  - Adverse event reporting

Additional information is available on requirements for a clinical trial protocol at the [FDA Guidance website](#).

## CHAPTER 6. COMMUNICATING SCIENTIFIC RESULTS

You will note that this chapter builds on Chapter 4: Writing a Research Proposal. Time spent up-front on the proposal, and input from your mentor and other specialists, will save you frustration and extra work later. As you will see, development of a good study proposal allows large portions of subsequent scientific communications to be easily done.

### SCIENTIFIC PAPERS

The biggest mistakes made by new researchers in writing a scientific paper include:

- **Delay in writing the paper (lack of perseverance).** This is a common error and leads to much frustration and wasted time. On the other hand, it is often hard to know the right time to publish (with preliminary results, after a portion of the study has been completed, or at the point of an exciting new discover, etc). Remember that once you have written a study proposal and struggled with conducting the study, you should be as reasonably conversant with the literature in that area as you are going to be. Don't delay! Waiting often means having to go back and spend precious time re-reviewing collected papers, results, etc.
- **Delay in editing.** Don't delay after writing a first draft of a manuscript; keep writing and refining the paper with the input of your co-authors. Delay only increases the time and effort needed to complete the paper.
- **Failure to write a detailed outline of the paper's structure and content.** This is a definite must, unless you have a gift of total mental organization and an incredible memory. Write a detailed outline for each section of the paper, and then proceed with small sections of writing at a time. This approach, while time-consuming and requiring self-discipline at the beginning, will save you much frustration and time in the long run.
- **Writing the paper in illogical order.** Start writing the introduction section of your paper as soon as you start the study. The introduction can be written after writing the study proposal since you have already reviewed the pertinent information. Part 1 of your paper is already done, and you are on your way to completion! A typical pattern for writing scientific papers is as follows:
  - Introduction (soon after writing the study protocol)
  - Methods (you've already done this in your study protocol)
  - Tables and figures (take the data analysis and construct data and figures of the data; this will help you clarify the intent of the paper and the point(s) you want to make)
  - Results
  - Discussion
  - Conclusion or summary
  - References (done continually once you first begin writing; will largely come out of your study protocol)
  - Title
  - Revise, rewrite, and revise

### *STRUCTURED ABSTRACT*

This is different than an abstract used as a preliminary description of important data submitted to a scientific meeting for review (see *Scientific Abstracts* below). A structured abstract for a manuscript is a brief description of the study and its results. Obviously a structured abstract in the format below pertains only to a clinical study, and not to the results of laboratory research or a case review. No references are included in this section. Pertinent subsections of a structured abstract include:

- Background
- Purpose of study
- Study setting
- Description of study subjects
- Methods
- Results (only key results)
- Conclusion(s)

### *INTRODUCTION*

This section should be brief and get to the point. In general, avoid more than three paragraphs.

- Paragraph 1: general introductory statements on the topic;
- Paragraph 2: specific background pertinent to the conduct of the study;
- Paragraph 3: the reasons for the study, the hypothesis to be tested.

### *METHODS*

This section will include several subsections, including:

- Description of study subjects and study setting (essential clinical characteristics, unique epidemiological characteristics, etc.);
- Experimental design (literally taken from your study protocol; a summary of techniques used, study design methodology, etc);
- Statistical methods and analysis (taken from your study protocol which has already been developed, usually with help from a statistician).

### *RESULTS*

This section requires relatively little writing. The majority of the data is best displayed in concise, logical tables and/or figures. Any text is then an explanation or clarification of the presented data. Common mistakes include re-explaining the data that are already present in tables and figures, or including material which belongs in the Methods or Discussion sections of the paper.

### *DISCUSSION*

This section is always the toughest part of the paper to write. There are many dangers. The goal is to accomplish the following:

- Precisely state the most important finding(s) of the study;
- Put the findings of your work into context with the previous results of others;

- Discussion of the limitations of your work, as well as that of previous papers and findings;
- Do NOT overstate the importance of your findings or make broad generalizations about the applicability of your study findings;
- Anticipate the major criticisms of reviewers and answer them up front in this section.

### *CONCLUSION OR SUMMARY*

In the conclusion, you should:

- Recapitulate the major findings of the study;
- Discuss the implications of your findings;
- Discuss what new questions must now be answered, or what new lines of investigation are appropriate.

### SCIENTIFIC ABSTRACTS

Each society has its own rules regarding abstracts. There seems to be no coordination among national and international societies. Therefore, the best advice is to carefully read the abstract rules for each submission. FOLLOW THE INSTRUCTIONS! Failure to follow simple rules (and it happens every year to someone) may disqualify your abstract and the months/years of work it took to produce. You will have very limited space in which to write your abstract.

Write your abstract with the attitude that you are a reviewer. What would make it interesting? What would make it stand out compared to the other fifty submissions? What would a reviewer be likely to criticize? Do the methods clearly explain what was done and what techniques were used? Are the results clearly demonstrated? Are the conclusions clearly supported by the results?

With this in mind, some useful suggestions:

- Pick the right category for your topic;
- Remember that a reviewer will be reading many, many other abstracts;
- Make your abstract as clear and as interesting as possible;
- Make your abstract stand out;
- Choose an interesting and informative title;
- Avoid abbreviation-mania, both in the title and within the body of the abstract (it makes reading a chore);
- Use a readable font of 11 point or greater;
- Use a word processing program that allows you to adjust the margins; print the abstract, and make sure it fits in the designated space. THEN actually print it on the original form;
- Some societies only allow you to submit abstracts on original (not copied) forms. Think ahead and order extra forms if needed before the deadline.
- A useful format for an abstract:
  - Background (2-4 sentences);
  - Methods (5-12 sentences);

- Results (succinct and informative; you won't have room for every piece of interesting data; if allowed, use tables);
- Conclusion(s)(clearly state important findings and nothing more).

## SCIENTIFIC POSTERS

The great advantage of posters is the face-to-face communication that is promoted with other scientists working in your area. The biggest mistake is the desire to put too much information on the poster. Remember, the purpose is to communicate preliminary information on the major finding of a study. It is NOT to give every detail, just the basics.

The cost of preparing your poster (both in time and in money) is much less with the advent of PC's and word processing programs. You can create an individual poster on a computer with a word processing program which places a border around the edge, print the board with a laser printer using a high quality, thick laser paper. The cost is minimal, it can be done quickly, and allows for changes and corrections.

If you will be working with John Stroud, the UTCOMC Computer Graphic Specialist, you will need to put your information in Powerpoint format (see Chapter 11). A useful organization for your poster is as follows:

- Abstract (1 slide);
- Background (1-2 slides);
- Purpose of study (1 slide);
- Methods (2-4 slides);
- Results (2-4 slides, display data in figures, tables or photos when possible);
- Conclusions (1 slide);
- Limitations (optional, 1 slide).

Be sure to read submit your work with the Computer Graphics Request Form available on the [UTCOMC website](#). Additional suggestions:

- Read the poster information provided by meeting organizers. Most poster boards are 4 feet tall and 8 feet wide, but double-check! When in doubt, edit out.
- Keep your poster presentation as uncluttered as possible. If you don't, it will NOT be read.
- Keep text to the absolute minimum;
- Spend time to align the poster boards properly and space the information proportionately.
- Use neutral background colors with bold printing;
- As a general rule, if the poster cannot be easily read from a 5 foot distance, it won't be read.

## PRESENTATIONS

Every scientific meeting allows different amounts of time for oral presentations. NEVER, NEVER use more than the allotted time. Double-check the time you have been given and consider whether it includes time for questions and answers. You must practice and time the talk repeatedly, with at

least one practice in front of some who can critique your style, presentation, and data. Your mentor can help you with this.

Most scientific meetings allow 10 minutes for presentation and 5 minutes for discussion. Most presentations are done using software (eg, Powerpoint). Some useful tips to consider before you present include:

- Arrive early to see the layout of the room;
- Know how to use the projector, advance mechanism, and pointer (they vary, do not assume it will work like the one you used before);
- Always run through your presentation with a projector before the talk;
- Always check the compatibility of technology;
- Do not create crowded, unreadable slides. Each slide should have a maximum of 20-30 words, with 6-8 lines of text. If your slides are difficult to read you will lose the audience.
- Your slides should be readable from the back of a large auditorium;
- Opinions are divided on whether it is better to memorize a talk or ready from notes. If you are very familiar with the material and its details, memorize. If you are uncomfortable or nervous, prepare a copy of your spoken comments and practice, practice, practice.
- Look at your audience and try to make eye contact with each person, or each section of the auditorium.
- Speak loudly and into the microphone. Vary the tonality and range of your voice for emphasis, and to increase interest and attention among your listeners.
- Be very, very careful with humor. Ask an objective person (your mentor?) if it is funny and/or appropriate for your audience. Nothing is worse than a dud, and it will ruin your self-confidence.
- Only use a pointer when you need it; don't let it wander all over the screen (which is very distracting). Because you are likely to be nervous, use two hands or the side of the podium to steady the pointer light.
- Anticipate the really tough questions you are likely to get from the audience and practice your answers. Always repeat a question from the podium so the audience hears it before you give your answer.

# CHAPTER 7. RESEARCH ETHICS

## GENERAL STATEMENT OF PRINCIPLES

Research, education, and clinical practice are inextricably intertwined. Quality in research is predicated upon both sound scientific principles and unimpeachable integrity. Here are key ethical principles to guide you in the scientific enterprise:

- Science and fraud are incompatible;
- Fraud in biomedical research is an indictment of UTCOMC research and clinical credentials;
- Fraud degrades the entire institution;
- Ethically sound research welcomes and requires continued scientific challenge of data and conclusions;
- All research is to be conducted in a manner respectful to all research subjects;
- It is important to remember that error, however undesirable, must not be confused with fraud.

The University of Tennessee defines misconduct as fabrication, falsification, or other serious unethical or illegal deviations from accepted practices in proposing, conducting, or reporting results of research and service activities. It does not include honest error or honest differences in interpretations or judgments of data.

Any individual who has reason to believe that he/she has knowledge of an act of misconduct by any University of Tennessee faculty, staff, volunteer or student is responsible for communicating this information to a supervisor, appropriate administrator, or mentor. That person will refer the allegation to the administration of the campus where the misconduct is alleged to have occurred. The University will make every reasonable effort to protect the confidentiality of an individual who in good faith makes an allegation of misconduct and also protect the individual from retaliation by any University official. However, if the allegation is later shown to have been made maliciously and falsely, the University may take appropriate disciplinary action against the individual who made the allegation.

If an allegation of misconduct is not substantiated by an investigation, the chief administrator of the campus will undertake diligent efforts to give notice of that fact to all persons involved. If an allegation is substantiated the appropriate administrator shall initiate disciplinary procedures according to UT policy and procedures.

## AUTHORSHIP

The UTCOMC endorses the principle stated in “Uniform Requirements for Manuscripts Submitted to Biomedical Journals” (Ann Int Med 108:258-265, 1988) that all persons designated as authors should qualify for authorship. To qualify for authorship, each author should have participated sufficiently in the work to make public responsibility for the content. Specifically, authors should have made a substantial contribution to:

- Abstract or manuscript writing; and
- Final approval of the abstract or manuscript:

Plus at least one of the following:

- Conception of idea and study design;
- Provision of study material or patients;
- Collection and/or assembly of data;
- Data analysis and interpretation;
- Other (e.g., financial and administrative support).

All authors should approve the version to be published. Participation solely in the acquisition of funding or the collection of data does not justify authorship. General supervision of the research group is not sufficient for authorship. Any part of an article critical to its main conclusions must be the responsibility of at least one author.

A paper with corporate (collective) authorship must specify the key person(s) responsible for the article; others contributing to the work should be recognized separately under acknowledgements. Many journals today (eg, JAMA) require authors to sign a statement document the section of the manuscript for which they were responsible.

## PLAGIARISM

According to the UTHSC Faculty Handbook, plagiarism is a form of academic misconduct. Faculty members and all other scholars must give full and fair recognition to the contributors to that enterprise, both for substance and for the formulation of their findings and interpretations. Even within the academic community, however, there are complexities and shades of difference. But none of these situations diminishes the central certainty: taking over the ideas, methods, or written words of another, without acknowledgment and with the intention that they be taken as the work of the deceiver, is plagiarism.

## CONFLICTS OF INTEREST

The UTCOMC requires all salaried faculty members to disclose potential conflicts of interests between their duties and responsibilities as employees and their interests outside the scope of their University employment. The policies and procedures used by the UTCOMC with regard to conflict of interest and compensated services are in the [UTHSC Faculty Handbook](#) and are also available at the [UTCOMC website](#).

## CONCLUSION

All persons involved in research at the UTCOMC are expected to conduct themselves in accordance with the highest of personal, moral, and ethical standards. Through example, these standards should be passed on to clinical and laboratory research personnel.

You should take an active role in the education of key personnel regarding research ethics. You should encourage appropriate conduct and communication which enhance professional relationships while encouraging both honesty and differences of opinion. Promote accuracy in the interpretation of results and maintenance of records and be truly accountable for the performance of your studies. The ultimate responsibility for conduct of ethical research resides with the faculty and staff of the UTCOMC.

## CHAPTER 8. SCIENTIFIC REVIEW COMMITTEE/INSTITUTIONAL REVIEW BOARD

Once your project is written, it will need to be reviewed by the UTCOMC Scientific Review Committee (SRC) as well as the UTCOMC/EHS Institutional Review Board (IRB) ([see flow chart](#)). The purpose of the SRC is to ensure that the scientific question being asked is relevant and that the design of a study is appropriate to answer that question. All investigator-generated research is reviewed by this committee prior to review by the IRB. The IRB is charged to protect the rights and welfare of human subjects.

Your department/program mentor can assist you in submissions to these committees. Investigators are expected to present their proposal and be prepared to answer questions at both the SRC and the IRB meetings. Stacey Hendricks is the administrator for the SRC and the IRB and can advise you on which forms to use (only one is required which is used by both committees); they are listed on the [IRB website](#). She is also responsible for scheduling investigators' presentations at each meeting and notifying investigators of the SRC's and IRB's decisions.

### SCIENTIFIC REVIEW COMMITTEE

The SRC is composed of a minimum of eight voting members, to include a representative from each department/program. The SRC/IRB Administrator is an ex-officio (non-voting) member. There should be one liaison member to the Institutional Review Board.

The SRC meets the second Wednesday of each month at noon in the College of Medicine conference room 100. Submission deadlines are available on the [SRC website](#). The format for submission is also available on the website (see Chapter 4).

The SRC will primarily focus on the elements of good scientific study design. Proposals will be evaluated for the following criteria:

- Clarity of the research question;
- Appropriateness and efficiency of design to maximize internal and external validity;
- Rigor and feasibility of methods;
- Qualifications and expertise of the research team;
- Scholarship and pertinence of background material and rationale;
- Adequacy of sample size and relevance of controls;
- Validity of the statistical analysis plan.

In addition, the SRC may comment on the proposal's scientific relevance or compelling ethical or patient safety issues. The SRC will submit a summary of their evaluation to the Institutional Review Board (IRB) and report their final recommendation as:

- Approved as written for submission to the UTCOMC IRB;

- Tentatively approved for submission to UTCOMC IRB pending receipt of requested revisions;
- Revisions required with re-review by full UTCOMC Scientific Review Committee;
- Disapproved, no re-review of this project in current form.

## INSTITUTIONAL REVIEW BOARD

The UTCOMC and Erlanger Health Systems (EHS) both have established a Federal Wide Assurance (FWA) with the Office of Human Research Protections of the Department of Health and Human Services. Under the terms of the Assurance, all of the institution's human subjects research activities, regardless of whether the research is subject to federal regulations, must be guided by the ethical principles in The Belmont Report and other appropriate ethical standards recognized by federal departments and agencies. A similar requirement for IRB review derives from regulations of the Food and Drug Administration (FDA). The three basic principles as set forth in the Belmont Report are:

- Respect for persons; recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy;
- Beneficence: obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm; and
- Justice: fairness in the distribution of research benefits and burdens.

The IRB meets the fourth Wednesday of each month in the College of Medicine conference room 100. Submission deadlines are available on the [IRB website](#). Submission forms are also available there.

The IRB has the authority to approve, require modifications in, and disapprove research based on consideration of human subject protection, including the authority to:

- Require IRB approval prior to the initiation of an investigation and recruitment of subjects;
- Require progress reports from the investigator(s) and oversee the conduct of the study;
- Investigate complaints or reports of noncompliance or protocol deviations;
- Suspend or terminate approval(s) or place restrictions on a study;
- Evaluate the risk/benefit status of studies;
- Ensure the adequacy of the informed consent process and the informed consent documentation;
- Manage potential conflicts of interest in the research; and
- Ensure that the research has adequate mechanisms to protect human subjects, including the auditing of sites and monitoring of the informed consent process by using third party monitors.

## WHAT RESEARCH REQUIRES IRB REVIEW?

**The IRB cannot grant retroactive approval. Always ask first!**

All forms and a corresponding explanation for what the requirements are for each form are listed on the UTCOMC website at <http://www.utcomchatt.org/subpage.php?pageId=833>.

### *CASE STUDIES*

The use of a single subject in research activity (n=1) can constitute research that is subject to IRB review and approval when there is a clear intent before recruiting or interaction with the subject (or a subject's medical record) to use systematically collected data that would not ordinarily be collected in the course of daily life in reporting and publishing a case study. As a general rule, when a series of subject observations are compiled in such a way as to allow possible extrapolation or generalization of the results from the reported case, that activity constitutes research that must be reviewed by the IRB. Additionally, this type of activity must always be reviewed by the IRB when there is intent to publish or disseminate data or findings. Even when a case study is not considered to be research subject to IRB review (because it is not intended to contribute to generalizable knowledge or otherwise does not meet the definition of research), these projects should follow the same guidelines for the protection of people's privacy, dignity, and welfare as if they required IRB review and approval.

### *STANDARD DIAGNOSTIC OR THERAPEUTIC PROCEDURES*

The distinction between research and treatment can become blurred in patient care settings, as well as in some educational and training settings.

- An established and accepted diagnostic or therapeutic procedure that is performed only for the benefit of patient or a student is generally not subject to IRB review.
- However, collection of data about a series of such procedures or treatments for dissemination or generalization (eg, a poster, a presentation, a journal submission) does constitute research that requires IRB review.
- If patient care or assignment to an intervention is altered for research purposes in any way, the activity must be submitted for IRB review.
- A diagnostic procedure for research purposes that is added to a standard treatment requires IRB review.

### *INNOVATIVE PROCEDURES OR TREATMENT*

Innovations in diagnosis or therapy are not generally subject to IRB review IF they are applied to a patient for the sole purpose of aiding that individual. Such innovations are governed by the appropriate professional ethics (eg, obtaining informed consent). IRB review is required when a "systematic investigation" of such innovations is considered. For example, if a physician plans to collect information about the innovation for scientific purposes or will repeat the innovation in other patients in order to compare it to standard treatment the physician must receive prior IRB review.

### *EMERGENCY USE OF AN INVESTIGATIONAL DRUG OR DEVICE*

Federal regulations do not permit research activities to be started, even in an emergency, without prior IRB review and approval. When emergency medical care is initiated without prior IRB review and approval, the patient may not be considered a research subject. Nothing in FDA policy is intended to limit the authority of a physician to provide emergency medical care for patients who need such care. Rather, the use of information collected about that treatment for research purposes is prohibited.

#### IRB REVIEW FOLLOWING APPROVAL

It is the investigator's responsibility to inform the IRB of any unanticipated problems involving risks to subjects or adverse events that were serious or unanticipated and resulted in a change to the risk/benefit ratio.

All research must be reviewed by the IRB every year (365 days) or less. The IRB must be notified when a study is closed to new patient accrual and when it is officially closed (ie, all data is reviewed and results are final). (See [UTCOCM/EHS Policies and Procedures](#) for additional information).

## CHAPTER 9. MEDICAL RECORDS RESEARCH

Use of patient medical records for research requires the same high standard of confidentiality as does use of the record for patient care. The UTCOMC Institutional Review Board also serves as the institutional privacy board for review as mandated by HIPAA (the Health Insurance Portability and Accountability Act). If your research involves looking at an individual's medical records (whether living or deceased), you will need authorization or a waiver before you will be given access to records. Further details and corresponding forms are available on the [UTCOMC IRB website](#).

The following institutional rules apply to the use of medical records.

1. Only those individuals with appropriate UTCOMC/Erlanger authorization appointments may view a medical record.
2. Records should be requested only for projects which have been approved by the appropriate committees.
3. Medical records of patients refusing the general authorization are not to be reviewed for research purposes except with specific written consent.
4. The medical record must not be removed from its assigned place without notifying location file. Medical records are NEVER to be removed from the institution at any time for any reason (ie, do NOT take records home). Medical records are never to be locked in a desk or file cabinet.
5. Information found in a medical record is not to be discussed with anyone other than co-investigators. Data collection forms or other patient data should be handled so as to prevent unauthorized review (password protection and encryption are likely to be required; check with the EHS HIPAA Compliance/Security Office for details, 423-778-5827).
6. The medical record, or any of its parts, may not be photocopied.
7. Patient names or identifiable patient data or photographs must not be released outside the institution without specific, prior approval of the IRB (and possibly the HIPAA Compliance Officer). All names must be deleted before copies of abstracts or computer lists can be taken from the institution.
8. Patients, physicians, or institutions must not be identified by name in any specific situation in any publication.

Questions about these requirements may be referred to Stacey Hendricks, the Institutional Review Board Administrator, [Stacey.hendricks@erlangers.org](mailto:Stacey.hendricks@erlangers.org), 778-3818).

## CHAPTER 10. LIBRARY RESOURCES

Erlanger Health System maintains an excellent Medical Library with more than 8,000 book volumes, 300 journal title, and several major medical indexes online. It is the largest health sciences library (and among the oldest health science collections) serving the region bounded by Nashville, Knoxville, and Atlanta. The Medical Library is staffed Monday through Friday, 8:00 am – 4:00 pm.

Located on the second floor of Erlanger Health System, the following services are available at no charge to residents and medical students:

- Computerized literatures searches;
- Over twenty scholarly and general medical databases available online, including PubMed (Medline, The Cochrane Library, and The CINAHL Nursing Index);
- Online book catalogue;
- Online journals
- Eighteen computer workstations with printers and USB ports;
- Access to the UTHSC in Memphis for journals and other resources not available in Chattanooga.

Click [here](#) to go to the Medical Library Home Page on the Erlanger website for more information about the Library.

The Library also has an intranet site for physicians on Erlanger's internal network system. Our residents, students, and faculty have access to a variety of online data bases and resources on computers within Erlanger via the Erlanger intranet. If you are now viewing this page from one of the Erlanger in-house computers, you can access the Intranet Library by clicking [here](#).

For more information, contact the Library Manager at 423-778-7246 (Rachel Bohanon).

## CHAPTER 11. AUDIOVISUAL AND GRAPHICS SERVICES

The UTCOMC provides excellent, state-of-the-art graphic and audiovisual services for medical students, residents, and faculty. John Stroud, Computer Graphic Training Specialist, provides assistance for:

- Computer generated slide presentations in PowerPoint;
- Digital/full-color scanning of slides, photographs, graphs, x-rays, scans, etc.
- Copy stand photography;
- Research poster presentations;
- Brochure layout;
- Digital video editing.

Each residency program office has software available for computer-generated slides. However, Mr. Stroud is also available for guidance to enhance your educational presentations, whether for live lectures or publication submission. The computer graphics equipment supports IBM compatible software (including Windows 98) for production of professional quality teaching slides or computer-driven presentations (eg, Office 200 and Microsoft PowerPoint). Mr Stroud also has the technology to prepare professional quality poster presentations using Quark, Photoshop, and Adobe Illustrator.

Standard photography and AV equipment services are available via the Audiovisual Office. Paul Twomey and Mike Morgan provide services such as medical photography of patients, equipment and pathology slides, as well as audio and video tape production or reproduction. Prints as well as slides of these subjects can be provided to faculty, residents, and medical students.

The AV Office is located on the second floor of Erlanger, just off the E Elevator and directly above the Erlanger Post Office (west wing 2). Mr. Stroud's office is right across the hall, marked by a blue sign that says UT Chattanooga Graphics Services.

**The University does not charge faculty, residents nor medical students for these graphics or AV services if done in conjunction with our educational programs.**

Contact information:

[Mike.Morgan@erlangers.org](mailto:Mike.Morgan@erlangers.org) (423-778-4183)

[John.Stroud@erlangers.org](mailto:John.Stroud@erlangers.org) (423-778-7815)

[Paul.Twomey@erlangers.org](mailto:Paul.Twomey@erlangers.org) (423-778-4199)

## CHAPTER 12. RESEARCH SYMPOSIUM AND RESEARCH WEEK

Since 1998, the UTCOMC Research Office has coordinated a clinical research curriculum for faculty and residents through several educational offerings. A primary program is the annual Nuts and Bolts Research Symposium. This day-long event offers recognized leaders in health science research as guest faculty to promote quality and responsible research. In addition, the UTCOMC, UTC, and other guest faculty provide concurrent sessions on research essentials for the newly arrived resident as well as the seasoned clinical researcher. The research symposium is usually held in the late summer/early fall.

In 1983, the University and Erlanger sponsored Resident Research Day, the first interdepartmental event to highlight research activities at the UTCOMC. Residents were provided the opportunity to present research papers or scholarly case reports to other residents, faculty and hospital staff. Plaques and cash awards were given in categories including Best Research Paper and Best Case Report. This event has been conducted annually since 1983, and in 1998 it was expanded to an entire week. It now includes a poster exhibit as well as oral presentations and awards.

The Research Week awards are named in honor of Robert C. Coddington, MD, the UTCOMC's first associate dean. Each year residents are asked to submit abstracts of either interesting case reports or research projects with which they have been involved during their residency. The Scientific Review Committee reviews these and selects the most outstanding submissions for either poster exhibit or oral presentation. Three judges are named each year to determine the awards presented at an awards dinner, marking the conclusion of Annual Research Week.

Additional information on both these events is available on the [UTCOMC website](#).

## APPENDICES

There is a vast resource of research educational materials on the worldwide web, including online training and tools (eg, Collaborative Institutional Training Initiative (CITI), the Office of Human Research Protections, the National Institutes of Health, the Food and Drug Administration, the Association of American Colleges). A few select tools are included in this appendix, but you are encouraged to work with the UTCOMC faculty and staff as well as the Medical Librarians for resources specific to your project.

Remember, for the most current information, you can also access links to policies, educational resources, FAQ's, timelines, tools, and forms on the [UTCOMC research website](#) through the IRB, the SRC, and the research compliance education, guidance and resource and policies pages.

## APPENDIX 1. ASKING THE RESEARCH QUESTION

In the space below, write three research questions that might interest you.

1. \_\_\_\_\_  
\_\_\_\_\_
2. \_\_\_\_\_  
\_\_\_\_\_
3. \_\_\_\_\_  
\_\_\_\_\_

### Research Questions

	Yes	No
<b>Feasible</b>		
Adequate number of patients?		
Adequate technical expertise?		
Affordable in time and money?		
<b>Interesting</b>		
To the investigator?		
To possible funders?		
To reviewers?		
<b>Novel</b>		
Confirms or reflects previous findings?		
Extends previous findings?		
Provides new findings?		
<b>Ethical</b>		
Potential harm to patients?		
Potential breach of confidentiality?		
Potential conflict of interest?		
<b>Relevant</b>		
To scientific knowledge?		
To patient management?		
To clinical and health policy?		
To future research directions?		

### Potential Problems

Vague or inappropriate question	<ul style="list-style-type: none"> <li>• Refine the question</li> <li>• Write a 1-2 pg concept draft (be specific)</li> <li>• Consider more generalizable knowledge</li> <li>• Make measurements more representative of the topic of interest</li> </ul>
Too broad	<ul style="list-style-type: none"> <li>• Specify a smaller number of variables</li> <li>• Narrow the question</li> </ul>
Not enough subjects	<ul style="list-style-type: none"> <li>• Expand the inclusion criteria</li> </ul>

	<ul style="list-style-type: none"> <li>• Narrow the exclusion criteria</li> <li>• Seek additional sources of patients</li> <li>• Collaborate with others</li> <li>• Lengthen the enrollment period</li> <li>• Devise more efficient variables or enrollment schemes</li> </ul>
Methods inadequate	<ul style="list-style-type: none"> <li>• Consult with experts</li> <li>• Review the literature (or re-review!)</li> </ul>
Investigator not qualified	<ul style="list-style-type: none"> <li>• Learn the skills</li> <li>• Collaborate</li> </ul>
Too expensive	<ul style="list-style-type: none"> <li>• Devise less costly methods or study design</li> <li>• Look for grant or scholarship funding</li> <li>• Consider a sponsor</li> </ul>
Questionable ethically	<ul style="list-style-type: none"> <li>• Obtain an ethics consult</li> <li>• Modify the research question to avoid potentially unethical elements</li> </ul>

## APPENDIX 2. DEVELOPING A HYPOTHESIS AND SPECIFIC AIMS

The specific aims and hypotheses are probably the most important part of your proposal. The study aims tell what your study is about. Before this is done, however, you must decide whether the intent of the proposed research is to perform a descriptive study, a hypothesis-generating study, or a hypothesis-testing study.

Relationship between study purpose and study design<sup>1</sup>

Purpose	Example of study design type
Descriptive	Survey study, uses a statistically-derived sample
Hypothesis-generating	<ul style="list-style-type: none"><li>• Cross-sectional survey</li><li>• Cohort study</li><li>• Case-control study</li></ul>
Hypothesis-testing	<ul style="list-style-type: none"><li>• Experiment (clinical trial)</li><li>• Observation study (cohort or case-control design)</li></ul>

After deciding upon the purpose of the study, the following steps should be considered:

1. Write out a list of objectives and establish a priority for each objective.
2. Refine the objectives into a set of written Specific Aims.
3. Rewrite the Specific Aims into written, testable hypotheses.

**Step 1.** The primary reason for investing time into this step is to clarify and record what you wish to accomplish in the study. Explicitly writing the objectives out in formal writing eliminates (or at least reduces) sloppy thinking and confusion. Such a step aids the investigator and in the investigative team to focus on the precise objectives of the study. In turn, all the remaining steps in the design and implementation of the study follow from these objectives.

Additionally, this set of objectives must be prioritized. All objectives will compete for personnel, time, money and other study resources. Prioritizing and deciding (later in protocol development) on a timeline will allow decisions about feasibility to be made.

*Example objective: To study factors that influence measles immunity.*

**Step 2.** Each hypothesis should be stated as a specific aim of the study.

---

<sup>1</sup> Adapted from Pak and Adams, Techniques of Patient-Oriented Research

*Example specific aim: To study factors determining measles immunity by comparing the proportion immune and the mean antibody level in two populations immunized at different ages.*

It is important to realize that the form in which the hypothesis is written drives the entire analysis of the study and determines what statistical analyses are done. As you will see later, if the null hypothesis is written in a non-directional manner, the statistical test of significance will be two-tailed. If it is directional, it will be one-tailed. In turn, this is important because a one-tailed test of significance is more likely to yield a statistically significant result.

**Step 3.** In this step, the previously written set of objectives will be refined into hypotheses. A hypothesis is a prediction of what the outcome of the study will be. Put another way, it is a prediction of what the associations of the measured variables will be after statistical analysis. The hypothesis differs from an objective in that a hypothesis is stated in terms of the actual direction of the associations that will be tested.

The hypothesis is generally written as a null hypothesis. The statistical analysis that is performed on the data gathered in the study then seeks to accept (ie, prove true) or reject (prove untrue) the null hypothesis.

*Example of null hypothesis: Measles antibody seropositivity does not differ by age at vaccine administration or by current age of subjects.*

The hypothesis may also be written in a non-directional manner or a directional manner.

*Example of a non-directional manner: We will test the hypothesis that measles antibody seropositivity differs by age at vaccine administration and by current age of subjects.*

*Example of a directional manner: We will test the hypothesis that measles antibody seropositivity increases with increasing age at vaccine administration and by current age of subjects.*

### APPENDIX 3. CHOOSING THE STUDY SUBJECT

Based upon the purpose of your study, you will need to choose an appropriate study design. All clinical studies involve, at one level or another, human subjects. The choice of these subjects has profound implications for bias/error and generalizability. Therefore, you must understand who they are, where they come from, how they were chosen, and how reflective they are of the broader population. **This cannot be over-emphasized; how you sample subjects determines the validity, generalizability and reliability of your study results.**

Some useful definitions:

**POPULATION:** A complete set of people with a specified set of characteristics. All members “fit” into this grouping.

**TARGET POPULATION:** The set of subjects to whom your study results will be targeted to, or generalized to. Defined by clinical and demographic characteristics.

**INTENDED POPULATION:** The subject of subjects you hope to sample and enroll.

**ACCESSIBLE POPULATION:** The subset of the target population that is available for study. Defined by geographic and temporal factors.

**ACTUAL POPULATION:** The group of subjects who actually end up in your study.

Because the accessible population is too large or too spread out or too expensive to study, most investigators will be forced to sample subjects in some manner. There are two major ways of sampling.

1. Probability sample: Uses a random process to ensure that each unit of the population has the same, specified chance of selection. Provides a basis with which to estimate whether the phenomena observed in the sample are representative of the entire population.
  - a. Simple random: selecting a sample at random (use a random number table)
  - b. Systematic: selecting by a periodic process, such as “every other one.” Great potential for error or bias.
  - c. Stratified random: dividing the population into “strata” based on a characteristic and taking a random sample from each strata. Used to study disproportionate groups by oversampling.
  - d. Cluster: a random sample of natural groupings in a population; for example, a random sample by race or geographic location or age.
  - e. Two-stage cluster: same as above only in two stages in an attempt to efficiently seek to randomly sample clusters of heterogeneity.
2. Non-probability sampling: More practical (less expensive, easier to accrue, faster enrollment, etc.). Used to imitate a probability sample. GREAT potential for bias/error. Best used when almost any sample will likely be representative.

- a. Consecutive: sampling every subject who meets inclusion/exclusion criteria over a specified period of time.
- b. Convenience: sampling those subjects who are easily available. Best used for pilot studies.
- c. Judgmental or purposive: the investigator hand-picks accessible subjects judged most appropriate for the study.

## APPENDIX 4. TYPES OF STUDY DESIGNS

1. COHORT STUDIES: Study subjects selected on the basis of exposure to a risk factor or treatment and are followed to determine a specified outcome of interest. The outcome is descriptive or analytic (analyze associations).
  - a. Prospective: Data on exposures and outcomes are observed and measured as they occur “forward in time.”
  - b. Retrospective: Data on exposures and outcomes are observed and measured after they occur “backward in time.”
  - c. Nested case-control: A case-control study “nested” with a prospective or retrospective cohort study. Data collected just as in a cohort study, but later the investigator selects from this cohort subjects and controls for sub-analysis of a specific risk factor (primary advantage is lower cost and efficiency).
  - d. Double-cohort: Two distinct samples of subjects with different levels of exposure to a risk factor or treatment.
2. CROSS-SECTIONAL and CASE-CONTROL
  - a. Cross-sectional: All measurements are made at one time with no follow-up. Used to describe variables and their distribution and for examining associations.
  - b. Serial survey: A series of cross-sectional studies observed at several points in time.
  - c. Case-control: Study subjects selected on the basis of whether they have the outcome of interest, and then are studied to determine who had been exposed to a risk factor or treatment. The study design is in the opposite direction from a cohort study.
3. EXPERIMENTS: Have five key elements:
  - a. A concurrent, prospective comparison of two or more groups.
  - b. One or more groups is intentionally exposed to an intervention, while one or more groups is not.
  - c. Study subjects generated from a single, homogenous pool of subjects. Assignment of subjects to groups is random.
  - d. All study participants (subjects, investigators, technicians, etc.) are blinded with respect to group assignment.
  - e. Control subjects receive an intervention that is indistinguishable from the actual intervention.

## APPENDIX 5. THE ROLE OF STATISTICS: SAMPLE SIZE AND POWER

Why do we need statistics?

The best an investigator can do is to draw probability inferences about phenomena in the population from events observed in the sample. You cannot absolutely prove or disprove an hypothesis.

- Classification of hypotheses:
  - Null: States there is no association between the predictor and outcome variables. It is THE formal basis for testing statistical significance.
  - Alternate: States there is an association between the predictor and outcome variables. It CANNOT be directly tested. Rather, it is accepted by exclusion or default if the test of statistical significance rejects the null hypothesis.
- Hypotheses can be one-tailed or two-tailed
  - One-tailed: The hypothesis states the direction of the association between predictor and outcome variables. It has the statistical advantage of requiring a smaller sample size.
  - Two tailed: The hypothesis states only that an association exists, it does not specify the direction of the association.

The following principles are important:

- Type I and II errors
  - Type I error: A false positive. One rejects the null hypothesis when it is actually true.
  - Type II error: A false negative. One fails to reject the null hypothesis even though it is actually false.
  - Both these errors are avoided by having a sufficiently large sample size!
- Effect size
  - Refers to the magnitude of an association in the target population.
  - The investigator must specify what effect size he/she would like to detect in the sample.
- Alpha and Beta
  - Alpha (also called the level of significance) refers to the probability of committing a Type I error
  - Beta refers to the probability of committing a Type II error
  - Power is the probability of observing/detecting a specified effect size in the sample if one of this magnitude or greater exists.
- P-value:
  - Refers to the probability of obtaining the study results by chance if the null hypothesis is true.
  - Statistical significance is NOT an “all or none” phenomena
- Variability

- Refers to the variability or spread in the outcome variable(s) being measured.
- The greater the variability, the more difficult it is to demonstrate differences between groups. Hence, a larger sample is required.
- Confidence intervals
  - Allows the investigator to reject or accept a hypothesis within a known degree of certainty
  - But also allows the investigator to estimate the size of the treatment effect together with some measure of the uncertainty in the estimate.
  - Many misinterpret these intervals, believing they can be confident that the interval contains the true value being estimated.
  - A 95% confidence interval is simply the range of values that would NOT differ from the estimate provided by the study at a statistical level of 0.05.

## APPENDIX 6: ANATOMY OF A RESEARCH BINDER

A research binder contains all vital study documentation and is maintained by the principal investigator or his/her designee. A regulatory binder is required by the FDA for all clinical trials, but its list of contents is useful for organizing records for any study.

The binder should be maintained on a regular basis and items filed in reverse chronological order.

It should include the following items:

- A copy of the proposal and/or protocol
- The IRB-stamped consent form document (all IRB approved and stamped versions)
- IRB approval/correspondence
  - Original IRB application/submission form
  - IRB review response to the investigator
  - Investigator responses to the IRB
  - IRB approval letter
  - All correspondence with the IRB (including emails)
  - You may also want to include SRC correspondence in this section
- Sponsor correspondence (if applicable)
- A signature list of research staff and their roles/responsibilities
- Serious unexpected/adverse event reports
- Monitoring/audit log reports
- Final study reports
- Investigator's brochure or package insert
- Standard operating procedure manual
- FDA Form 1572 (or Investigator's Agreement, if applicable)
- Laboratory certification (if applicable)
- Range of normal laboratory values (if applicable)
- Drug/device accountability documentation (if applicable)
- Tracking and shipping log (if applicable)

This binder may also serve to organize information for local, investigator-initiated (ie, not commercially sponsored) research. Other documents that may apply include:

- All original consent forms (copies go to the IRB, the medical record, the subject)
- Data collection/clinical report forms
- A log of screened subjects
- A log of enrolled subjects

## APPENDIX 7: THE TOP 10 RULES FOR PICKING A RESEARCH PROJECT

1. Anticipate the results before doing the first study.
2. Pick an area on the basis of the interest of the outcome.
3. Look for an under occupied niche that has potential.
4. Go to talks and read papers outside your area of interest.
5. Build on a theme.
6. Find a balance between low- and high-risk projects.
7. Be prepared to pursue a project to any depth necessary.
8. Differentiate yourself from your mentor.
9. Do NOT assume that outstanding clinical research is easier than outstanding basic research.
10. Focus, Focus, Focus

## APPENDIX 8. THE TOP 10 MOST COMMON REASONS FOR PROPOSAL FAILURE

1. Lack of original ideas.
2. Diffuse, unfocused, or superficial research plan
3. Lack of knowledge of published relevant work.
4. Lack of experience in essential methodology.
5. Uncertainty regarding future directions.
6. Questionable reasoning in experimental approach.
7. Absence of acceptable scientific rationale.
8. Unrealistically large amount of work.
9. Lack of sufficient experimental detail.
10. Uncritical approach.