# *Research Manual for Faculty, Residents, and Medical Students*

# *University of Tennessee College of Medicine Chattanooga*

***The following research manual is an electronic manual and not intended to be downloaded as a unit. Many of the respective components are independent PDF files or Powerpoint presentations. These can be opened with a single or double click and then downloaded for printing and storage purposes. Please appropriately acknowledge the use of these materials when reproducing or presenting as part of an educational and/or training activity.***

**TABLE OF CONTENTS**

**Note**: Format and selected content of this manual adapted from *A Research Manual for Mayo Internal Medicine Residents. Mayo Foundation, 2005.* Courtesy of the Department of Internal Medicine, Mayo Medical School, Rochester, MN

## Preface From the Dean

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

The unique relationship between the UTCOMC, Erlanger Health Systems, and the University of Tennessee at Chattanooga provides 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 mentorship and administrative resources to facilitate ongoing scholarship. The Office of the Dean is responsible for support of the Research Office, Institutional Review Board, the Institutional Animal Care and Use Committee, review and updating of federal and local policies, and 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 also find it useful. If you find there is information missing that should be added, please let us know through email at gregory-heath@utc.edu.

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

**Preface from Residency Programs**

**LINKS TO ACADEMIC DEPARTMENTS AND RESIDENCY PROGRAMS**

**Family Medicine and Geriatrics: http://www.utcomchatt.org/Dept/FM/fm.asp**

**Internal Medicine: http://www.utcomchatt.org/Dept/Intmed/intmed.asp**

**OB/GYN: http://www.utcomchatt.org/Dept/OBGYN/obgyn.asp**

**Orthopaedic Surgery: http://www.utcomchatt.org/Dept/Orthopaedic/Orthopaedic.asp**

**Pediatrics: http://www.utcomchatt.org/Dept/Pediatrics/Pediatrics.asp**

**Plastic Surgery: http://www.utcomchatt.org/Dept/Plastic/plastic.asp**

**Surgery, Surgical Critical Care and Vascular Surgery:**
**http://www.utcomchatt.org/Dept/Surgery/surgery.asp**

**Transitional Year: http://www.utcomchatt.org/Dept/Trans/trans.asp**

## CHAPTER I
## University of Tennessee College of Medicine Chattanooga

### Residency Program Guidelines for Research/Scholarly Activity and Research Resource List

Check with your individual residency program directors for specific scholarly activity requirements in each program.

Click here to access a Research Resource List to identify individuals you may contact for specific areas of expertise or support.:
**http://www.utcomchatt.org/Docs/Research%20Resource%20List.pdf**

## CHAPTER II
## Mentors and Project Approval

One of the most important hurdles for you to overcome is the identification of both a project and a mentor. Mentors all are willing to commit time, resources, and effort toward your project. Your job is to page through the manual and find a project or mentor with whom you are interested in working. All of the consultants are quite approachable and would be quite happy to have you call them to set up a time when you can discuss the possibilities of a research idea or project. Residents generally have extensive contact with subspecialty fellows and can work with them on research projects.

The function of the mentor is:

1) To facilitate the development and structure of a relevant, accomplishable research proposal

2) To sponsor and guide the resident through the appropriate research committees and, where necessary, the Institutional Review Board

3) To make available secretarial, 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 personnel and services, i.e. Epidemiology, Biostatistics, Editorial, and Medical Graphic Services (through the mentor's budget as needed)

   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 so as to maintain the suggested. timetable for project completion

Mentors should be sufficiently involved in the project to be co-authors on all manuscripts and publications. As such, your mentors will be highly interested in guiding you toward the completion of the project. Use your mentors! They are all readily available to you and anxious to help and be involved in a significant way.

Once you have decided on a mentor and a project, you will need to do the following:

1) Construct a concise and succinct project proposal plan utilizing the format provided in Chapter III.

2) Fill out a project approval form. It is important that you complete this step as it is the only way we have to keep track of resident projects.

3) Through your mentor, and depending on the type of project, you may need the approval of your mentor's research committee, and the Institutional Review Board. All of these committees have certain specifications and deadlines which must be met. Please ask your mentor about the mechanics of this process.

## CHAPTER III
## Project Proposal Format

Note: each section should be a separate page, double-spaced throughout

1. Title of the project

2. Investigators (your name, mentor's name and any co-investigators). List departmental/institutional affiliations.

3. Abstract brief description of project

4. Specific Aims of Proposed Research. Clearly delineate the intent of the study. Enumerate, in the order of importance, the specific objectives or hypotheses you wish to study.

5. Background and Significance. Briefly sketch the background to your proposal, initially evaluating existing knowledge and specifically identifying the gaps in knowledge which the project is intended to fill. State concisely the importance of the research described in the proposal.

6. Preliminary Studies. This section is a review of work already completed by the investigators. Most of you will leave this section blank.

7. Experimental Design and Methods. Discuss the experimental design and procedures to be used to accomplish the specific aims of the project. Describe the protocol to be used and include the means by which the data will be analyzed and interpreted. Include entry/exclusion criteria and an informed consent form for patients to sign, if applicable. Please note that this should be as brief and succinct as possible, while still providing the information necessary to evaluate the protocol for someone who would not be intimately familiar with the field.

The project proposal plan may be as brief as 2-3 typewritten pages (review paper, case report), or as lengthy as needed. The above format is sufficient for submission to the various research committees, who ultimately grant approval.

Project Approval Form

Date: _____

Name: _____

Mentor: _____

Department: _____

Project Title:

Brief Description of Project (attach a copy of your project proposal):

_____

_____

_____

_____

_____

_____

_____

- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -

OFFICE USE ONLY

Mentor Approved _____ Approve _____ Clarify _____ Date _____

Scientific Review Committee _____ IRB _____

Poster or Oral Presentation _____

Published _____
Award _____

## CHAPTER IV
## Starting Your Research Project

The foremost task you face in beginning your research project is identifying an area of interest, and 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 a "critical" attitude.

In particular, important questions arise in your every day clinical practice of medicine, but you must firstly be aware of the question, and secondly have some idea of how to go about answering it, and 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 fast 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 have similar patients presented for medical care? What has been the morbidity/mortality here at Erlanger? How has the treatment changed and what effects has this had?

Answers to these types of questions are immensely facilitated by our 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 whose answers (inevitably) lead to new questions. You must be attuned and attentive to this process. Additionally, this manual contains hundreds of research ideas from mentors willing to share of their expertise, time, and enthusiasm. Take your pick!

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.

- Feasible
    - Adequate number of subjects, adequate technical expertise
- Interesting to the investigator
- Novel
    - Confirms or reflects previous findings
    - Extends previous findings
    - Provides new findings
- Ethical
- Relevant
    - To scientific knowledge
    - To clinical and health policy
    - To future research directions

The discipline of applying the above points to your research idea/question is invaluable, and

in itself promotes critical thinking in the framing, planning, and execution of the projection.

Some suggestions:

- Be explicit in what you wish to accomplish. Your hypothesis/question and the expected outcome should be stated in 2-4 succinct sentences. The more specific and definite, the better! Try to focus on a single question.

- Expand the above sentences into a written 1-3 page project proposal. This should have a format similar to the project approval form (Chapter III). Several revisions are needed to be specific and to lessen ambiguity of your exact project goals and methods of study. Utilize the experience of your mentor in constructing the proposal. This is a crucial step - time spent in protocol development now can save hundreds of hours of time later, and avoid costly delays or even the shelving of an entire project or its conclusions. Being explicit, direct, and concise should be your goal.

- Consult experts in the field, epidemiologists, and/or biostatisticians in finalizing the methods and design component of your project proposal. This ensures that the proper techniques are used in selecting the study variables, choosing the study population, and analyzing the data to yield valid conclusions.

- Question “accepted” medical practices and knowledge—great ideas frequently arise from a questioning, critical attitude.

## CHAPTER V
## Writing a Research 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 and a concise written proposal should be prepared before starting the research. The research protocol is an explicit description of the planned research. It should specify the type of research project, the specific aims of the research, the significance of the research, and the methods that will be used to achieve the goals of the research project.

The research proposal has several purposes. In addition to requesting funding for the research, it clarifies the investigator's thinking and assists in formulating specific aims and hypotheses which can be tested.

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 work will be accomplished. The research proposal contains a timetable for the work and indicates when the important individual steps in the research will be completed. This helps the investigator to determine whether the time allocated to complete the research 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. The resources include: the investigator's time and time of other research personnel, secretarial support, the subjects of the research study including. patients, volunteers, or laboratory animals, equipment needed to carry out the research including laboratory equipment and computers, and other supplies, and the space needed to perform the research. The research proposal assists others in the evaluation of the investigators achievements and future potential for research contributions.

**An Outline for a Research Proposal**

The research proposal is an essential document for the investigators and reviewers who have a responsibility for providing resources for the research project. A research proposal should be concise and clear in indicating the investigator's plan for research and resources needed to successfully complete the research. The decision to allocate services for research proposals are made by reviewers. They must base their decisions on the proposal. Accordingly, the research proposal should follow a standard format and be as concise as possible.

**A recommended format for a research proposal follows:**

1. Title

2. Investigators
   List all investigators and advisors

3. Summary
   A concise one paragraph summary

4. Specific Aims
   Describe specific aims of the study and hypotheses to be tested.

5. Significance
   Several paragraph description of importance of research, current knowledge, and gaps in our knowledge and how the research will fill gaps in knowledge or extend our knowledge.

6. Preliminary Work
   Describe any preliminary work or previous studies by the investigator, or the research team, that are relevant to the proposed research.

7. Methods
   a. Designs
      Describe the study design and rationale for choosing the study design.

   b. Study Subjects
      Describe how study subjects will be selected. List eligibility and exclusion criteria.

   c. Sample Size
      Explain how many subjects will be studied and whether sufficient subjects will be available based on statistical tests of hypotheses.

   d. Data Collection
      Describe the data to be collected and any laboratory techniques that will be used.

e. Data Handling
Explain how data will be prepared for analysis. Will data be entered into computer analysis? Explain steps taken to assure accurate and complete data collection. Describe data storage and archiving.

f. Data Analysis
Explain details of data analysis, descriptive statistics, tests of hypothesis, and expected formats for presenting results.

g. Time Frame
Describe a realistic time frame for completing the work.

h. Strengths
Describe the strengths of the proposal study.

i. Limitations
Describe of problems that may arise and plans to resolve any potential difficulties.

8. Human Subjects, Animal Care and Use, Biohazardous Materials
Address issues of risks and benefits, number of animals to be use (if applicable), confidentiality, laboratory and storage requirements, and ethical concerns.

9. References
List only relevant and recent literature.

10. Appendices
Include such items as data forms, previous publications, curriculum vitae of investigators, and other relevant material.

**Writing the Research Proposal**

The research proposal is a written document that explicitly outlines the research plan and resources needed to successfully complete the plan. The research proposal should be brief and concise. In writing the research proposal, the investigator should plan to 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. Research proposals are continually written, re-written, 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, re-write, and revise.
- Test your ideas by obtaining constructive criticism from colleagues and mentors.
- Revise, re-write, and revise.
- Collect some preliminary data.
- Revise, re-write, and revise.

# CHAPTER VI
# Communicating Scientific Results:
# Scientific Papers, Abstracts, Posters, and Presentations

You will note that this chapter builds on Chapter V (Writing a Research Proposal). The most important work you must first do is to write your research proposal. MUCH time should be put into describing and organizing exactly what you plan to do. This will require the help of your consultant-mentor, and often input from an epidemiologist and/or biostatistician. Time spent "up-front" in this task will save you frustration and more work later! As you will see, development of a good study protocol allows large portions of subsequent scientific communications to be easily done.

## I. Scientific Papers

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

*Delay in writing the paper (lack of perserverance)*

This is a common error, and leads to much in the way of frustration and wasted time. On the other hand, it is often hard to know when the "right" time to publish a paper is, i.e., preliminary results, after a portion of the study has been completed, or at the point of an exciting new discovery, etc. Remember that once you have written a study protocol and struggled with conducting the study, you probably are as reasonably conversant with the literature in that topical area as you are going to be. Don't delay! Begin writing your paper. Waiting often means having to go back and spend precious time re-reviewing collected papers, results, etc.

Likewise, 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 eventually complete the paper.

*Failing to write out a detailed outline of the paper's structure and content.*

This is a definite must, unless you have the gift of total mental organization and an incredible memory! My advice is to write out a detailed outline for each section of the paper, and then to proceed with small "sections" of writing at a time. This approach, while taking self-discipline and time-consuming at the beginning, will save you much frustration and time in the long run.

*Writing the paper in an illogical order.*

Start with writing the introduction section of your paper first, as soon as you start the study. The introduction section can be written after writing the study protocol itself, as you have already reviewed the pertinent necessary information. Part 1 of your paper is already done, and you are on your way to completion!

A typical pattern or template for writing scientific papers is as follows:

1. Write the Introduction (soon after writing the study protocol)
2. Write the Methods section (you've already done this in your study protocol for the most part)
3. Take the data analysis and construct pertinent tables and figures of the data (this will help you to clarify what the specific intent of the paper really is, and the point(s) you want to make)
4. Write the Results
5. Write the Discussion
6. Conclusion or Summary
7. Add in References (this should be done on an ongoing basis when you first begin writing, and will largely come out of your study protocol)
8. Write a structured Abstract (see below)
9. Determine an appropriate Title
10. Polish it up! (spell-check, grammar-check, co-author review, expert outside review, etc.)

*Structured Abstract*

This is different than an "abstract", which is the term frequently used to denote a preliminary description of important data, which is submitted to a scientific meeting for review (see below). An "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 a laboratory or case review study. Each journal generally has "Instructions for Authors" printed within the journal, with the specific format specified - follow the instructions! No references are included in this section. Pertinent subsections of a structured abstract include:

- Background
- Purpose of the Study
- Study Setting
- Description of Study Subjects
- Methods Utilized
- Results (only key results)
- Conclusion(s)

*Introduction*

This section should be brief and get right to the point. In general, more than three paragraphs should be avoided. A useful guide is the following:

- Paragraph one: general introductory statements on the topical area
- Paragraph two: specific background pertinent to the conduct of the study
- Paragraph three: the reason for this study; the hypothesis to be tested

*Methods*

This section will generally consist of several sections as listed below:

- Description of study subjects and study setting (essential clinical characteristics, unique epidemiological characteristics, etc.)
- Experimental design (this is literally taken from your study protocol, and is a summary of techniques used, study design methodology, etc.)
- Statistical methods and analysis (taken from your study protocol, and which has already been thought out and described, usually with the aid of a statistician)

*Results*

This section involves 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 is already present in tables and figures, or including material which belongs in either the Methods or Discussion sections of the paper.

*Discussion:* This is always the toughest part of the paper to write. The dangers are many. The basic logic behind this section is to accomplish the following:

- Precisely state the most important finding(s) of the study
- Put into context the findings of your work with the previous results of others
- Discussion the limitations of your work, as well as that of previous papers and Findings
- DON'T 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* should include the following:

- 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

## II. 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 society. 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! In general, you will have very limited space within which to write your abstract. With this in mind, some useful suggestions (based on having written many, many abstracts and having reviewed hundreds of abstracts for national meetings) include:

- Pick the right category for your topic
- Remember that a reviewer will be reading through 30-100 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 the abstract a chore
- Use a readable font of at least 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 more forms if needed before the abstract deadline

Structured abstracts are the most readable and informative. For clinical research, a useful format is:

- Background (generally 2-4 sentences)
- Methods (clear, succinct and informative, generally 5-12 sentences)
- Results (clear, succinct and informative. You probably don't have room for every piece of your interesting data! Use tables for better presentation style)
- Conclusion(s) (clearly stated important findings and nothing more)

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

## III. Scientific Posters

The great advantage of posters is the face-to-face communication that is promoted with other scientists working in your topical area. The biggest mistake with preparation of the poster presentation is the desire to put TOO MUCH information into the poster. Remember that the purpose of the poster is to communicate preliminary information on the major finding in a study. It is not to give every detail of the entire study you did, just the basics! Remember too that the cost of preparing your poster (both in terms of time and money) is much less with the advent of PC's and word processing programs. I type my individual poster "boards" onto my computer with a word processing program which places a fancy border around the edge, and print the "board" with a laser printer using a high quality, thick laser paper. The cost is minimal, and it allows me to create the poster quickly, and even change any misspellings, errors, etc.

If you will be working with John Stroud, the UTCOMC Computer Graphic Training Specialist, you will need to put your information in Powerpoint Format (See Chapter XI).

Some hints:

- Read the poster information sent to you by the 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 in appearance 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 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!

A useful organization for your poster is as follows:

- Abstract (1 slide)
- Background (1-2 slides)
- Purpose of the Study (1 slide)
- Methods (2-4 slides)
- Results (2-4 slides - best to display data in tables or figures or photos)
- Conclusions (1 slide)
- Limitations (optional, 1 slide)

**IV. Presentations**

Every scientific meeting allows different amounts of time for oral presentations. NEVER, NEVER use more than the allotted time. ALWAYS double-check the amount of time you have been given, and consider whether the designated amount of time also includes time for questions and answers. You should never give a scientific talk without practicing and timing the talk several times, with at least one practice in front of someone 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 today are done using software such as Powerpoint. Some useful tips prior to your presentation:

- Arrive early to see the "lay out" of the room
- Know how to use the slide projector, advance mechanism, and pointer
- Always run through your presenation with a projector before the talk
- Always check the compatibility of technology.
- Never create unreadable, or crowded slides/frames! Each slide should have no more than 20-30 words, with no more than 8-10 lines of text. If your slides are crowded or difficult to read you've already lost your audience.
- Your slides should be able to be read from the back of a large auditorium
- Opinions are divided on whether to memorize your talk, or to read from notes. If you are very familiar with the material and its details, memorize. If you are a bit uncomfortable or nervous, prepare an actual copy of your spoken comments and practice, practice,

practice! Remember to look up at your audience and try to make eye contact with each person, or each section of the lecture hall.

- 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 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 the pointer when you mean to use it, don't let it "wander" all over the screen (it is very distracting). Because you are likely to be nervous, use two hands or the side of the podium to steady the pointer light, otherwise it wavers all over the place and everyone knows you are nervous.
- Anticipate the really tough questions you are likely to get from your audience and practice your answer. If someone asks a question, repeat it for the audience to hear before you give your answer.

## CHAPTER VII
## Principles of Research Ethics

I. Ethics Awareness

*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 (human and non-human).
- 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 the 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 or 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.

## II. 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 take public responsibility for the content. Specifically, authors should have made a substantial contribution to:

(a) conception and design, or analysis and interpretation of data and
(b) drafting the article or revising it critically for important intellectual content.

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 persons responsible for the article; others contributing to the work should be recognized separate under acknowledgements. Many journals today (e.g., JAMA) require authors to sign a statement regarding what portions of the manuscript/paper they participated in.

## III. 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. In addition, investigators should take an active role in the education of key personnel regarding research ethics. They should encourage appropriate conduct and communication which enhance professional relationships while encouraging both honesty and differences of opinion. They should promote accuracy in the interpretation of results and the maintenance of records which allows them to be truly accountable for the performance of their studies. The ultimate responsibility for conduct of ethical research resides with the faculty and staff of UTCOMC.

## CHAPTER VIII
## Collaborative Research

If you wish to inquire further about the possibility of collaborative research, please email or call one of the following staff:

**Research Office:** **Director: Gregory Heath, DHSc, MPH (423-425-4432)**
**Technical Writer: Kristi Strode (778-4566)**
**Grants Manager: Nancy Geren (778-8102)**

**Family Medicine:** **J. Mack Worthington, M.D. (778-2957)**
**Stephen M. Adams, MD (778-2957)**
**John Standridge, M.D. (778-2957)**

**Internal Medicine:** **Mukta Panda, M.D. (778-6672)**
**Gregory W. Heath, D.H.Sc., M.P.H. (425-4432)**

**OB/GYN:** **Shawn Stallings, MD (778-5192)**
**Stephen DePasquale, MD (698-2050)**

**Orthopaedic Surgery:** **Thomas W. Currey, M.D. (778-9008)**
**Joe Rudd, R.N., Ph.D., (778-6027)**

**Pediatrics:** **Marvin Hall, M.D., (778-6217)**
**Billy S. Arant, Jr., M.D. (778-4448)**

**Plastic Surgery:** **Larry A. Sargent, M.D. (778-9047)**

**Surgery:** **Chris LeSar, M.D. (778-7695)**
**Pat Lewis, R.N., (778-7695)**

**Transitional Year:** **Mukta Panda, M.D. (778-6672)**

## CHAPTER IX
## Collaborative Clinical Projects with the University of Tennessee at Chattanooga (UTC)

A number of departments at UTC are open to opportunities for research collaboration between UTCOMC faculty and residents and UTC faculty and graduate students. The guidelines and review process are listed below.

Guidelines

- The research topic must be of significance to care of patients and/or their families, as well as to the disciplines of UTC and UTCOMC.

- The project should be completed within the time available to the collaborating members.

- Costs should be funded through available funding sources in either department or the institution.

- Collaboration should include the member from a UTC department as a co-investigator. The majority of faculty/students are not available for "free" data collection due to federal labor guidelines.

## CHAPTER X
## Library Resources for Medical Research

I. General Information

Erlanger Health System maintains an excellent Medical Library with more than 10,000 book volumes and 500 journal titles, three major medical indexes on CD-ROM and a small collection of videos and audiotapes. 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, and residents and medical students will appreciate the convenience of 24-hour access.

Located on the 2nd Floor of Erlanger Health System, the following services are available at no charge to residents and medical students:

- computerized bibliographic searches,
- the complete MEDLINE on CD-ROM for those who prefer to perform their own searches
- interlibrary loans
- unlimited photocopying
- nine computer workstations with CD-ROM and printers (some with ZIP drives)
- access to the UTHSC in Memphis for journals not available through Erlanger

Click here to go the actual Medical Library Home Page in 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 databases 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 page by going to http://library.main.erlanger.org/**

II. Library Policies

- Journals may not be checked out.
- Reference Books may be checked out for 3 days -- one renewal.
- Certain Reference Books do not circulate at all - they are marked as such in the back.
- General circulating books may be checked out for 3 weeks - one renewal.
- Fines are $1 per day for circulating books, $5 per day for Reference Books, and $10 maximum. There is a grace period for fines; have the book back within a week of its due date and you owe no penalty. It is far more important to have the book back than it is to collect fines.
- Overdue notices are mailed once a month.
- Renewals are taken in person or via telephone - dial 7246.
- In the case of a lost book, you will be charged the replacement cost for a new copy.

Contact: Library Manager, 778-7498 (Langhorne Waterhouse, MLS)

## CHAPTER XI
## Audio Visual and Graphics Services

The University 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.

Each residency program office has the software available for the 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 (e.g., Office 2000 and Microsoft PowerPoint). Mr. Stroud also has the technology to prepare professional quality poster presentations using Quark, Photoshop, and Adobe Illustrator.

Mr. Stroud is located on the 1st Floor of the Whitehall Building, just across the street from Erlanger, in Suite 102, the same suite as the Business Office. He can be reached by phone (778-7815) or by email at: John.Stroud@erlanger.org and his office hours are 7 AM - 3 PM, Monday - Friday.

Standard photography and AV equipment services are available via the Audiovisual Office located in the Erlanger Health System complex. This office is staffed by two individuals (Paul Twomey and Mike Morgan) and they can provide services such as medical photography of patients, equipment, and pathology slides, as well as audio and video tape production or reproduction and equipment. Prints as well as slides of these subjects can be provided to faculty, residents, and medical students.

The AV Office is located on the 2nd floor of Erlanger, just off the E Elevator and directly above the Erlanger Post Office. The phone extensions are 778-4183 or 778-4199. Mr. Twomey's email address is: Paul.Twomey@erlanger.org. Mr. Morgan's email address is: Mike.Morgan@erlanger.org.

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

## CHAPTER XII
## Medical Records Research

Use of patient medical records for research purposes requires the same high standard of confidentiality as does use of the record for direct patient care. The UTCOMC Institutional Review Board also serves as the institutional privacy board for revew 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:
http://www.utcomchatt.org/Research/Research.asp?dpage=irb

IRB Forms can be found at: http://www.utcomchatt.org/Research/Research.asp?dpage=irbforms

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

l . Only those individuals with appropriate UTCOMC/Erlanger Health System 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 (i.e. don't 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.

6. The medical record, or any of its parts, is not to be photocopied.

7. Patient names or identifiable patient data or photographs must not be released outside the institution without specific, prior approval of the HIPAA compliance Officer/IRB. 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 Coordinator (stacey.hendricks@erlanger.org, 778-3818).

# Chapter XIII

## Research Advisory Committee
## University of Tennessee College of Medicine Chattanooga

## Mission and Goals Statement

The mission of the Research Advisory Committee (committee) is to advise the University of Tennessee College of Medicine, Chattanooga (UTCOMC) concerning research activities of the departments and affiliates of the UTCOMC. Committee membership is open to all faculty and residents who have research interests or conduct or plan to conduct research at the UTCOMC. Committee membership is also open to interested faculty from the University of Tennessee at Chattanooga (UTC).

The goals of the committee are to provide a forum of research information exchange, facilitate research collaboration, and when asked by a particular program or department of the UTCOMC, to review research project proposals prior to submission to the Scientific Review Committee and Institutional Review Board. The committee will also advise the Dean of the UTCOMC concerning research activities and priorities.

The committee members will participate in designing educational research programs for faculty, residents, and students. The committee will also facilitate collaborative efforts across departments and institutions in conducting research projects, informing faculty and staff concerning potential research projects, and identify funding sources for research activities.

# CHAPTER XIV

CHATTANOOGA
COLLEGE OF MEDICINE

## UT/EHS Scientific Review Committee

The purpose of the Scientific Review Committee (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.

The SRC is composed of a minimum of 8 voting members, to include a surgeon, an internist, a pediatric physician, a biostatistician, and a resident. The SRC/IRB Administrator and the Research Compliance Officer are ex-officio (non-voting) members. There should be one liaison member to the Institutional Review Board. However, additional members are discouraged from simultaneous participation in the IRB.

Members are expected to attend a minimum of 50% of committee meetings in order to remain in good standing.

The SRC meets the 2nd Wednesday of each month at 12:00pm in College of Medicine Conference Room

A quorum of 4 committee members is required in order for the SRC to conduct protocol reviews or other business.

The standard term of appointment is 36 months; however members who choose to continue to participate beyond the end of a 36 month term may do so, subject to approval by the SRC Chair.

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

1. clarity of the research question
2. appropriateness and efficiency of design to maximize internal and external validity
3. rigor and feasibility of methods
4. qualifications and expertise of the research team
5. scholarship and pertinence of background material and rationale
6. adequacy of sample size and relevance of controls
7. validity of the statistical analysis plan.

In addition, the SRC may desire to 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 IRB and report their final recommendation as:

1. Recommend acceptance without amendment
2. Recommend acceptance pending amendment
3. Recommend rejection

The SRC may call upon a consultant if additional expertise is needed to conduct a review. The opinion of the consultant will be taken into consideration, however the consultant will not vote. The fact that a consultant was utilized will be noted in the letter to the IRB.

The IRB requires scientific review for investigator-originated studies that are determined to be beyond the minimal risk level that have not already undergone review by another body.

**SRC Policy and Procedure**
**Subject: SRC Chair**

The SRC Chair and Vice-Chair shall be appointed by the Dean of the UT COMC from the faculty.

The term of appointment of the SRC Chair is 18 months; however the Chair and/or Vice-Chair may continue to serve beyond the end of the 18 month term at the discretion of the Dean.

The Chair is responsible for ensuring that an adequate number of members are appointed to the SRC to allow timely review of submitted protocols.

The Chair is responsible for ensuring that all protocols submitted to the SRC receive timely review; ideally within two weeks.

The Chair is responsible for assigning protocols submitted to the SRC to committee members for review; this responsibility may be delegated to the IRB Administrator by the Chair.

The Chair is responsible for leading and facilitating the discussion at committee meetings of protocols under review by the committee and for calling a vote on protocols which have completed review.

The Chair is responsible for summarizing the Committee's review of a protocol in a letter to the Principal Investigator (PI), indicating that the SRC has either accepted it and forwarded to the IRB, or is returning it to the PI for revision, clarification, or to request PI response to SRC comments (see chart).

The Chair is responsible for reviewing the PI's responses to Committee reviews and determining if administrative approval of a protocol is appropriate.

The Vice-Chair of the SRC shall execute the responsibilities of the Chair in the absence of the Chair, or as delegated by the Chair.

**SRC Policy and Procedures:**
**Subject: SRC/IRB Administrator**

The SRC administrator is responsible for receiving, cataloguing and tracking all new protocols conducted under the auspices of the UT/EHS IRB.

Following receipt of a protocol, the Administrator conducts an initial administrative review to ensure that all requisite components of the protocol are present before enlisting reviewers for the protocol or before forwarding the protocol to the SRC Chair for reviewer assignment.

Following assignment of reviewers, the Administrator contacts the reviewers and forwards to them all relevant materials.

The Administrator performs follow up with reviewers to ensure that the protocols receive a timely review.

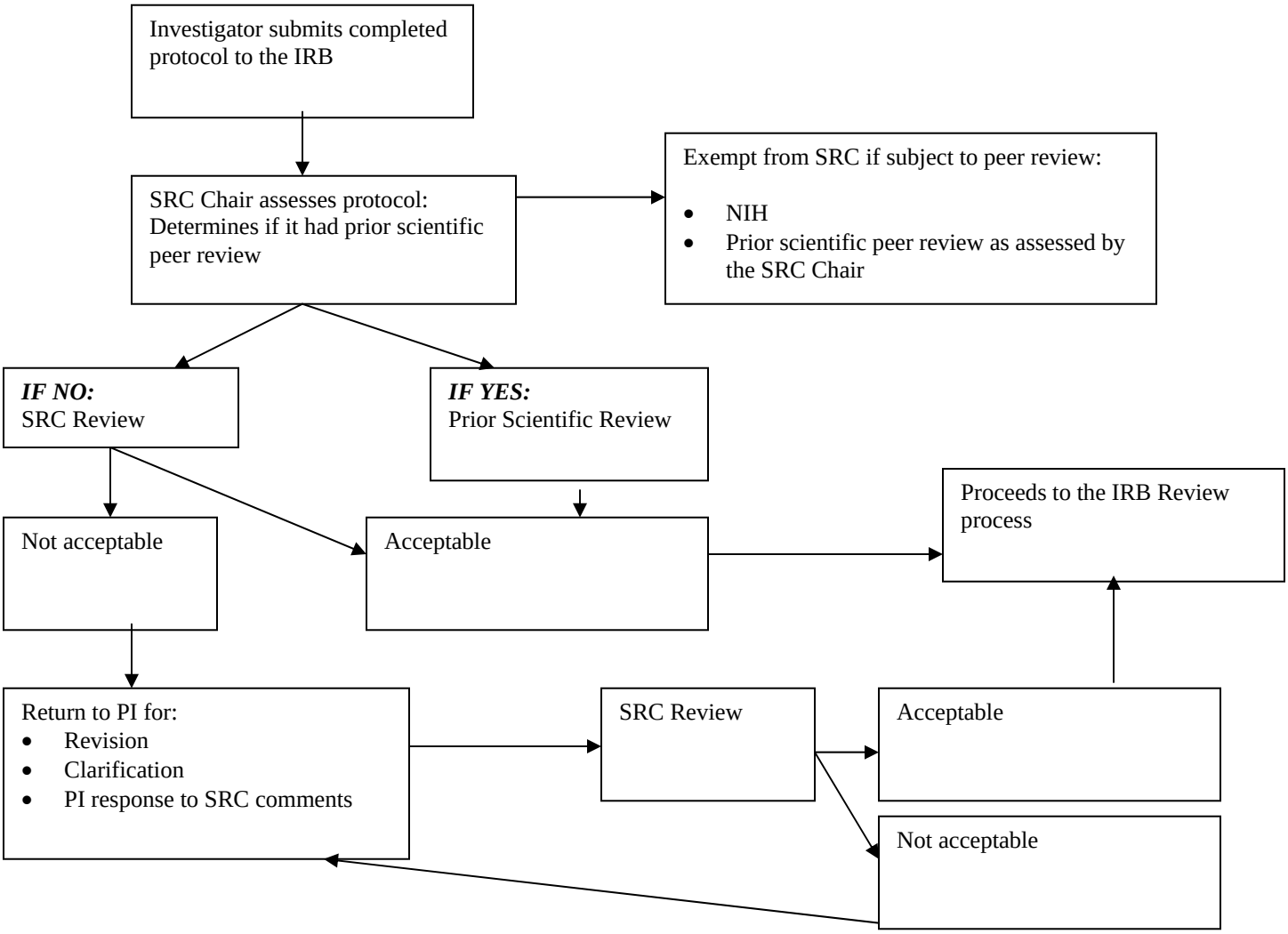
The Administrator schedules SRC meetings and notifies committee members of meeting times.

The Administrator records all minutes and committee votes in written form, and maintains appropriate records and other documentation.

The Administrator manages and oversees all committee correspondence and all committee-related clerical duties.

The Administrator performs other SRC-related business delegated by the Chair.

## Scientific Review Committee Process



## CHAPTER XV
## Fall Research Symposium and Resident Research Week/Awards Banquet

Since 1998 the Research Office at the UTCOMC has coordinated a clinical research curriculum for faculty and residents through several educational channels. A primary channel is through the annual 'Nuts and Bolts' research symposium. This day-long event seeks to bring name-recognized leaders in health science research as guest faculty to highlight specific research topics. In addition, UTCOMC, UTC, and guest faculty provide concurrent sessions on research essentials for the newly arrived resident as well as the seasoned clinical researcher. The research symposium is held early in the fall, usually in late September or early October.

In 1983, the University and Erlanger sponsored the first interdepartmental event to highlight research activities at the Chattanooga Unit: Resident Research Day. 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, was expanded to an entire week and included a Poster Exhibit as well as the final oral presentations and awards. In 2004 the event was expanded to include a poster from one of our medical students rotating from Memphis. We now refer to it as "Annual Research Week."

The Research Week awards are named in honor of the Chattanooga Unit's first Associate Dean, Robert C. Coddington, M.D. Each year residents are asked to submit abstracts of either interesting case reports or research projects with which they have been involved over the past year. Between 20 and 30 abstracts are selected for posters. These are exhibited throughout Research Week and are then judged at a Walking Poster Rounds at the end of the week. The four to six most outstanding abstracts are selected for oral presentations just prior to the awards dinner at the end of the week. Research Week is open to all residency programs and our visiting medical students. This endeavor has encouraged and fostered research efforts to expand, particularly clinical research, at the Chattanooga Unit.

The Director of Research, Dr. Gregory W. Heath, works in conjunction with the Scientific Review Committee to select the best abstracts for presentation (either poster or oral presentations) for the Annual Research Week. Abstracts are reviewed by the committee to determine which ones will be selected for the poster exhibits and oral presentations. Three judges are also named each year by the committee to determine the awards presented at the conclusion of the Annual Resident Research Week.

**Click here to access the 2008 Abtract Form for the Annual Research Week. Be sure to save the Word document to your computer so you can see the boxes on the abstract form:**
**http://www.utcomchatt.org/Docs/F-RWAbs08.doc**

**Click here to view a pdf file with the schedule and deadlines for the 2008 Annual Research Week (April 21 – 25, 2008)**

## CHAPTER XVI
## Use of Elective Time for Research

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

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

1. Residents must apply to use elective time for research 2 months prior to the start of the elective time period.

2. Residents must have written prior approval from their Program Director. This approval is contingent on receipt of the following:

   a. a project proposal plan (see Chapters III through V )

   b. the proposal must have been approved by the appropriate divisional research committee, and if appropriate, the Institutional Review Board or Institutional Animal Care and Use Committee;

   c. a description of the resident's involvement and actual activities related to the project for this time period (i.e. what will you actually do and how much time will it take, what will be accomplished?)

   d. a letter from your staff mentor listing the title of your joint project and his/her support for your project, and agreement to be your mentor for the (specified) one month. time period.

## CHAPTER XVII
## Classnotes and Handouts from the NIH's Principles and Practice of Clinical Research Course
## **LINK TO THE FOLLOWING NIH LINKS :

**http://www.nihtraining.com/cc/ippcr/archive06f/menu.html**

Perhaps the most valuable result of all education is the ability to make yourself do the thing you have to do, when it ought to be done, whether you like it or not.

-- *Walter Bagehot, "Physics and Politics," 1879*

## THE CYCLE OF RESEARCH

- Choosing a research question
- Developing a written protocol
- Pretesting and revising the protocol
- Implementing the study
- Analyzing the findings
- Drawing conclusions
- Communicating the results

## STARTING OUT - HOW DO YOU BEGIN?

1. Study Question. A one sentence analogue of the research question that specifies what the study will actually answer if it is successful.

2. One - two page outline of the elements of the study. Acts as a checklist and reminder. Has an orderly sequence that helps to clarify the investigator's thinking.

3. Study Protocol. The main document used to plan the study and to apply for permission(s) and monetary support.

4. Operations manual. The collection of specific procedures used to actually carry out the study.

## OUTLINE OF A STUDY PROTOCOL

| Element | Purpose |
|---|---|
| 1. The research question | what questions are addressed? |
| 2. Background and significance | what are the important issues, what isn't already known, why are these important questions? |
| 2. Study design<br>- Approach<br>- Study time frame | is the study feasible? |
| 3. Research subjects<br>- Selection criteria<br>- Sampling design | who are the subjects - is this reasonable, are biases present, how will subjects be selected? |
| 4. Study Variables<br>- Predictor variables<br>Outcome variables | are they reasonable? Can the research question be answered with this data? |
| 5. Statistical issues and analysis<br>- Sample size<br>- Power<br>- Analytic approach | how large is the study? How will it be analyzed? Will the results be valid? |

## STEPS IN DESIGNING A CLINICAL RESEARCH PROJECT

A. The Planning Steps:

1. Decide what the research question is.
2. Write out the objectives/specific aims.
3. Define the variables.
4. Define the study population.
5. Refine the objectives into written, testable hypotheses.
6. Anticipate error and bias.
7. Develop the study design/method.
8. Estimate sample size and power.
9. Write a protocol.
10. Plan the data collection process.

B. The Implementation Steps:

1. Manage and monitor data collection.
2. Manage the database.
3. Analyze the results by tables and graphs.
4. Test the hypotheses with statistical tests.
5. Generate additional tables and graphs to explain the findings.
6. Publish the results.

## THE TEN COMMANDMENTS FOR PICKING A RESEARCH PROJECT

I. Anticipate the results before doing the first study.

II. Pick an area on the basis of the interest of the outcome.

III. Look for an underoccupied niche that has potential.

IV. Go to talks and read papers outside your area of interest.

V. Build on a theme.

VI. Find a balance between low- and high-risk projects.
VII. Be prepared to pursue a project to any depth necessary.
VIII. Differentiate yourself from your mentor.

IX. Do NOT assume that outstanding clinical research is easier than outstanding basic research.

X. Focus, Focus, FOCUS!

**ASKING THE RESEARCH QUESTION**

In the space below, write three research questions that might interest you. As you continue through this course, you will be refining and clarifying these questions.

1. Is hepatitis B vaccine "X" as efficacious as hepatitis B vaccine "Y"?

2. Do physicians vary in their attitudes toward influenza vaccine and do those attitudes affect behavior with patients?

3. Do patients of Afghani descent significantly vary in their immune response to flu vaccine compared to patients of European descent?

| | **RESEARCH QUESTIONS** | | |
|---|---|---|---|
| | 1 (Yes No) | 2 (Yes No) | 3 (Yes No) |
| **Feasible?** | | | |
| Adequate numbers of patients? | _____ | _____ | _____ |
| Adequate technical expertise? | _____ | _____ | _____ |
| Affordable in time and money? | _____ | _____ | _____ |
| **Interesting?** | | | |
| To the investigator? | _____ | _____ | _____ |
| To possible funders? | _____ | _____ | _____ |
| To reviewers? | _____ | _____ | _____ |
| **Novel?** | | | |
| To the field? | _____ | _____ | _____ |
| Ethical? | _____ | _____ | _____ |
| Potential harm to patients? | _____ | _____ | _____ |
| Potential breech of confidentiality? | _____ | _____ | _____ |
| **Relevant?** | | | |
| To scientific knowledge? | _____ | _____ | _____ |
| To patient management or health/public policy? | _____ | _____ | _____ |

## ASKING THE RESEARCH QUESTION

In the space below, write three research questions that might interest you. As continue through this course, you will be refining and clarifying these questions.

1. _____

_____

2. _____

_____

3. _____

_____

## RESEARCH QUESTIONS

| | 1 (Yes No) | 2 (Yes No) | 3 (Yes No) |
|---|---|---|---|
| **Feasible?** | | | |
| Adequate numbers of patients? | _____ | _____ | _____ |
| Adequate technical expertise? | _____ | _____ | _____ |
| Affordable in time and money? | _____ | _____ | _____ |
| **Interesting?** | | | |
| To the investigator? | _____ | _____ | _____ |
| To possible funders? | _____ | _____ | _____ |
| To reviewers? | _____ | _____ | _____ |
| **Novel?** | | | |
| To the field? | _____ | _____ | _____ |
| Ethical? | _____ | _____ | _____ |
| Potential harm to patients? | _____ | _____ | _____ |
| Potential breech of confidentiality? | _____ | _____ | _____ |
| **Ethical?** | | | |
| Potential harm to patients? | _____ | _____ | _____ |
| Potential breech of confidentiality? | _____ | _____ | _____ |
| **Relevant?** | | | |
| To scientific knowledge? | _____ | _____ | _____ |
| To patient management or health/public policy? | _____ | _____ | _____ |

## ASKING THE RESEARCH QUESTION

| Potential Problems | Solutions |
|---|---|
| 1. Vague or inappropriate question | -refine the question<br>-1-2 page concept draft - explicit<br>-new approaches:<br>-more generalizable<br>-patients more representative<br>-make measurements more representative of the phenomena of interest |
| 2. Not feasible | |
| Too broad | -specify a smaller number of variables -narrow the question |
| Not enough subjects | -expand the inclusion criteria<br>-narrow the exclusion criteria<br>-seek additional sources of patients<br>-collaborate with others<br>-lengthen the enrollment period<br>-devise more efficient variables or enrollment schemes |
| Methods inadequate | -consult experts<br>-review the literature |
| Investigator not skilled | -learn the skills<br>-collaborate |
| Too expensive | -devise less costly methods or study design<br>-find the money |
| 3. Not relevant or novel | -modify the research question |
| 4. Questionable ethically | -ethics consult<br>-modify the research question to avoid potentially unethical elements |

## DEVELOPING A HYPOTHESIS AND SPECIFIC AIMS

The Specific Aims and Hypotheses are probably the most important page of a grant. This may be the only page that a reviewer reads. Think of this as an attorney might: this is the "opening argument" to the jury. In this section you want to generate excitement and enthusiasm for your ideas, and get the reader/reviewer to "read on". The reader MUST finish reading these and have an immediate sense of the importance of the idea and approach, as well as the feasibility of the study. The Specific Aims tell what your study is about, the entire remainder of the grant merely amplifies these aims.

The next major consideration in developing a clinical research protocol is the development of a hypothesis and specific aims. Before this is done however, one 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***

| **Purpose** | **Example of Study Design Type** |
|---|---|
| Descriptive | Survey study, uses a statistically-derived sample |
| Hypothesis-generating | Cross-sectional survey, cohort study, case-control study |
| Hypothesis-testing | Experiment (clinical trial)<br>or<br>Observational study (cohort or case-control design) |

***adapted from Pak and Adams. Techniques of Patient-Oriented Research**

After deciding upon the purpose of the study, as discussed above, the following steps in protocol development should be considered:

**Steps in protocol development:**

**STEP 1:** Write out a list of objectives and establish. a priority for each objective.

**STEP 2:** Refine the objectives into a set of written Specific Aims.

**STEP 3:** Re-write 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 the investigative team in focusing 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:** Finally, each hypothesis should be stated as a Specific Aim of the study.

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 we will see later in this course, if the null hypothesis is written in a nondirectional 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 onetailed 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 (abbreviated H„). The statistical analysis that is performed on the data gathered in the study then seeks to accept (i.e., proved true) or reject (i.e., prove untrue) the null hypothesis.

Example of a null hypothesis: H,: 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 nondirectional manner, or a directional manner.

Example of a nondirectional 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.

# Methods Development: Study Design and Choosing the Study Subject

**Based upon the purpose of your study, you will need to choose an appropriate study design.**

**Relationship between study purpose and design**

| **Purpose** | **Study Design** |
|---|---|
| **Descriptive** | **Survey - using a statistical sample** |
| **Hypothesis-Generating** | **Cross-sectional survey, or "quick and dirty" Cohort or Case-Control study** |
| **Hypothesis- Testing** | **Experiment (clinical trial) or Observational study (cohort or case-control most often)** |

**All clinical studies involve, at one level or another, human subjects. Because how we choose these subjects has profound implications for:**

**a. BIAS/ERROR**

**b. GENERALIZABILITY**

**We 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.**

Therefore, we must define:

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 subset of subjects you hoped 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 ended up in your study.

SAMPLING OF SUBJECTS

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: (explain the difference) .

I. Probability sampling

A. Simple random

B. Systematic

C. Stratified random D. Cluster

E. Two-Stage Cluster

II. Nonprobability sampling

A. Consecutive B. Convenience

C. Judgmental or Purposive

There are two major ways of sampling: (explain the difference)

I. Probability sampling: 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". 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 2 stages in an attempt to efficiently seek to randomly sample clusters of heterogeneity.

II. Nonprobability 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.

**TYPES OF STUDY DESIGNS**

I. 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 outcome are observed and measured as they occur "forward in time"

B. Retrospective: Data on exposures and outcome are observed and measured after they occur "backward in time"

C. Nested Case-Control: A case-control study "nested" within 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 subanalysis of a specific risk factor - just as in a case-control study.. 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.

II. 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.

III. EXPERIMENTS: Have 5 key elements:

1. A concurrent, prospective comparison of 2 or more groups.

2. One or more groups is intentionally exposed to an intervention, while group is not.

3. Study subjects generated from a single, homogenous pool of subjects. Assignment of subjects to groups is random.

4. All study participants (subjects, investigators, technicians, etc) are blinded with respect to group assignment.

5. Control subjects receive an intervention that is indistinguishable from the actual intervention.

| Type of Study | Statistic | Definition |
|---|---|---|
| Cross-sectional | Prevalence | # with disease at one point<br># at risk at one point |
| Cohort | Incidence | # disease cases/time unit<br># people at risk/time unit |

**STEPS IN DESIGNING A CLINICAL RESEARCH PROJECT**

A. The Planning Steps:

1. Decide what the research question is.
2. Write out the objectives/specific aims.
3. Define the variables.
4. Define the study population.
5. Refine the objectives into written, testable hypotheses.
6. Anticipate error and bias.
7. Develop the study design/method.
8. Estimate sample size and power.
9. Write a protocol.
10. Plan the data collection process.

B. The Implementation Steps:

11. Manage and monitor data collection.
12. Manage the database.
13. Analyze the results by tables and graphs.
14. Test the hypotheses with statistical tests.
15. Generate additional tables and graphs to explain the findings.
16. Publish the results.

## PLANNING THE MEASUREMENTS: DATA MANAGEMENT AND ANALYSIS

Appropriate Next Steps in Protocol Development:

1. Move from the conceptual stage (research question) - to the measurement stage.

2. Do this by operationalizing terms. This is simply adding the next level of detail to what has been previously described within the research question.

3. Once the terms are operationally defined, extract the variables from this list.

4. Once the variables are defined, identify possible methodsinstruments to measure these variables.

5. Next, decide the level of data measurement (nominal, ordinal, continuous, etc.).

6. Create a data collection form and codebook with coding rules.

7. Go back and refine the research question!

**External Validity:** How well the variables designed for the study represent the phenomena of interest. (a.k.a. generalizability: are the conclusions appropriate when applied to the universe outside the study)

Internal Validity: How well the actual measurements represent those variables. The degree to which the investigator's conclusions correctly describe what actually happened in the study.

ERROR:

Sampling Error

Measurement Error

- Precision (random error)
- Accuracy (systematic error)

Measurement Scales

- Continuous variables
    - discrete
- Categorical variables
    - dichotomous (limited to 2 values)
    - nominal (no ordering)
    - ordinal (ordered positions)

1. Give examples of above

2. What is the information content and power of each of the above?

## PRECISION AND ACCURACY

- Both have profound influences on the power of a study (the more precise and accurate a measurement, the greater the statistical power at a given sample size)

## PRECISION

- Definition?

- Random error

- Observer variability

- Subject variability

- Instrument variability

Assessment of Precision:

- Standard deviation

- Coefficient of variation (cv = sd/mean)

- Correlation coefficient (degree of concordance among paired measurements)

- Ways to control: standardize measurement methods, train observers, refine the instruments, automate, repetition

## ACCURACY

- Definition?

- A function of systematic error or bias:

    - Observer bias

    - Subject bias

    - Instrument bias

Assessment of Accuracy:

- Compare with "gold standard"

- Make unobstrusive measurements

- Blinding

- Calibration

## DATA MANAGEMENT

You need a "data management system"!

Why?

- Completeness
- 1RB reporting
- Data management - Data analysis
- Follow-up of subjects
- Future use of the database

**Elements of Data Management:**

1. Storage
2. Rules for data entry
3. Coding of variables
4. Editing data
5. Error checks (logical, range)
6. Software

**ANALYZING THE DATA**

- Need a deliberate, planned approach

- Start with descriptive "look" at the data, THEN analytic

- Start with descriptive statistics

  - frequency distributions
  - measures of central tendency (mean, median, sd, etc.)
  - proportions

- Next, analytic statistics

  - purpose is to analyze associations between variables - three steps are involved:

    - detect patterns of association within the sample
    - compute the magnitude of the association in the sample
    - estimate the likelihood that the association observed in the sample also exists in the population from which the sample was drawn (statistical significance)

**EXAMPLE**

Ho: There is no association between level of education and cigarette smoking

- sample: 154 subjects

- initial findings:

  - 82 smoked (82/154 = 53.3%), and 72 never smoked (72/154 = 46.8%)

  - 81 with < 12 years of education (81/154 = 52.5%), and 73 wit. > 12 years of education (73/154 = 47.4%)

- What proportion of the less educated group smoked?

- What proportion of the more educated group smoked?

- What is the magnitude of this association?

- Does the association observed above in this sample exist in the population from which the sample was drawn? How do you test this? How confident are you of these findings?

**AN EXAMPLE ANALYSIS**

Outcome variable: Ever smoked?

| Yes | No |
|---|---|
| 51 | 30 |
| 31 | 42 |

**MEASURING VALIDITY**

| | Disease + | Disease - |
|---|---|---|
| | a | b |
| | c | d |

Sensitivity (PID) = a /a + c = True Positive

Specificity (NIH) = d /b + d = True Negative

Positive Predictive Value (PPD) = a /a + b

Negative Predictive Value (NPD) = d /c + d

Assumptions:

1. Our test has a 90% sensitivity

2. Our test has a 90% specificity

3. Assume prevalence of 9%

## THE ROLE OF STATISTICS: SAMPLE SIZE AND POWER

### Classification of Hypotheses:

1. Null: States there is no association between the predictor and outcome variables. It is THE formal basis for testing statistical significance.

2. 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:

1. 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.

2. Two-tailed: The hypothesis states only that an association exists, it does not specify the direction of the association.

### *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 the hypothesis.

Therefore, the following principles are important:

1. Type I and II errors.

   a. Type I error: A false-positive. One rejects the null hypothesis when it is actually true.

   b. 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!

2. Effect Size. Refers to the magnitude of an association in the target population. The investigator must specify what effect size she/he would like to detect in the sample.

3. Alpha and Beta.

   a. Alpha (also called the level of significance) refers to the probability of committing a Type I error.

b. Beta refers to the probability of committing a Type II error. I - B = Power.

c. Power is the probability of observing/detecting a specified effect size in the sample if one of this magnitude or greater exists.

4. 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-ornone" phenomena.

5. 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, larger sample sizes are required.

Confidence Intervals: Allows the investigator not only to reject or accept a hypothesis within a known degree of uncertainty, but also to estimate the size of the treatment effect together with some measure of the uncertainty in the estimate.

Many wrongly misinterpret these intervals, believing that 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.

**SAMPLE SIZE WORKSHEET**

1 . Estimate the number of subjects in your intended population that you think you can recruit in a specified time period, such as one month:

_____

2. After applying your a priori exclusion criteria, what, proportion would still be eligible to enroll in your study?

_____

3. Is your alternate hypothesis:

One-tail_____ Two-tail_____

4. What alpha level do you wish to set?

0.10_____ 0.05_____ 0.01_____ 0.001_____

5. What beta level do you wish to set?

0.10_____ 0.20_____ 0.30_____

6. What difference in effect size do you want to detect? Is this difference clinically significant?

_____

## WRITING A RESEARCH PROPOSAL

### Most Important Factors:

1. Have a method and a format.

    - find a model proposal, collect examples

2. Learn how to write well.

    - take a scientific writing course
    - practice, practice, practice
    - find excellent examples

3. Have someone else read and critique the proposal.

    - ideally someone knowledgeable about the topic
    - include someone who is scientifically knowledgeable, but not expert in your particular topic

4. Clarity and presentation style are **EVERYTHING!**
    - one study of successful proposals finds that the clarity of the presentation was the single most important determinant of success

**Elements of a Proposal:**

1. Title

    - short, concise, descriptive (52 characters) - most memorable part of the study - influences who reviews the proposal

2. Abstract

    - a concise summary of the protocol
    - spend A LOT of time writing this section
    - start with the research question, then set out the design and methods, and finish with a statement of the importance of the potential findings
    - this and the title are the ONLY parts of the proposal-that will be read by many reviewers

3. Budget

    - be honest and fair - don't "pad"
    - justify, justify, justify

4. Biosketches

    - standard format

5. Resources and Environment
    - describes the institutional environment and infrastructure
    - used to demonstrate that all the necessary "tools" are in place to "guarantee success" with the study

6. Specific Aims

    - always put in order of importance (sometimes in chronological order) - concise, clear, interesting, novel

7. Background and Significance

    - stay tuned next week

8. Methods

    - this is THE section of the grant
    - it is the "make or break" section
    - weaknesses in methodology are THE most common reason why proposals are not funded at the NIH
    - acknowledge, then address potential weaknesses
    - usual organization in a clinical study looks like this:

i. overview and rationale
ii. selection of subjects (and controls)
iii. measurements
iv. statistical analysis
v. data management/quality control vi. limitations/anticipated weaknesses

9. Human Subjects

- address ethical concerns and issues

10. Consultant Letters

- have enthusiastic letter of support outlining what consultant will do or provide
- include biosketch

11. References

- up to date
- grantsmanship

12. Appendix

- reprints
- photos, other material that doesn't go into the body of the grant - keep it short

**THE TOP 10 MOST COMMON REASONS FOR PROPOSAL FAILURE AT THE NIH:**

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

**WRITING THE GRANT: A MINI-SYNOPSIS**

1. Good Idea - specific aims and hypotheses

2. Good Science - background, preliminary data

3. Good Application - follow the application requirements, forms, budget, etc.

"To receive a fundable priority score, a research project must be perceived by the reviewers to be important, interesting, and likely to succeed."

**IMPORTANCE:**

Remember that what constitutes importance is NOT what you think is important, but what the study section members think is important.

So, what do they think is important?

1. Applied research is less important than basic research.

2. Phenomenological/descriptive research is much less-important, and is almost never funded.

3. Quantitative research is more important than qualitative research.

4. Disease-related research is more important than studies with little clinical relevance.

5. Hypotheses that are novel, interesting and testable are the most important.

**SIGNIFICANCE AND BACKGROUND:**

Allows you to state concisely the importance of the proposed research. This is where the "big picture" is presented. It should be comprehensive, and yet comprehensible to those not expert in the field.

Goals:

1. relate specific aims/hypotheses to long term scientific objectives

2. demonstrate knowledge of the relevant published literature

3. critically assess key results/papers/methods/findings of others

**Organize in the following manner:**

a. Background - description of the research activities that led to the proposed project. It should make obvious that your proposed work is the logical "next step" in the field.

b. Literature - you demonstrate your qualifications by proving that you are thoroughly familiar with the field, and have a balanced knowledge of it. Point out discrepancies in the literature. Reference the last 20-30 highly pertinent references. Avoid over-referencing.

c. Gaps - identify the gaps that the project is intended to fill.

d. Importance - lay out your case for why the results of the proposed work is important - how will it "advance the field?"

While styles of writing vary, the ability to write well is of the utmost importance in this section. Hints:

1. Be sure there is a logical starting point, a logical flow throughout the section, and a logical end-point.

2. Each paragraph should start with a topic sentence, and end with a transition sentence.

3. There should be a n obvious logical connection from one paragraph to the next.

## PRELIMINARY DATA

Goals:

1. Provides evidence that the hypothesis is reasonable and testable.

2. Demonstrates your ability to successfully use the proposed methodology, i.e. that you are competent in all the proposed procedures.

3. Gives you the opportunity to appropriately and critically interpret your early results, and "make obvious" what the next steps are.

**Hints:**

- Highlight early and published data
- Include photographs or actual data recordings.
- Not all reviewers will have the appendix material.
- The data must be comprehensible and of obvious high quality. Demonstrate new techniques/procedures.

## EIGHT FUNDAMENTAL QUESTIONS USED TO REVIEW A GRANT:

1. Are the aims logical?
2. Are the hypotheses valid?
3. Are the procedures feasible, adequate, and appropriate for the research proposed?
4. Is the research likely to produce new data and concepts, or confirm existing hypotheses?
5. What is the significance and originality of the proposed research?
6. Are the principal investigator and staff qualified to conduct the proposed work?
7. Are the facilities, equipment and other resources adequate for the proposed work?
8. Is the budget appropriate?

## RESEARCH PROTOCOL FORMS

1. NIH or Foundation forms

2. IRB forms

3. Divisional Research forms

4. Financial Disclosure/Conflict of Interest form

5. Animal Use forms

6. Radiation Committee forms

7. System-Wide AIDS Committee forms

8. Health Services Research forms

9. Others

## Chapter XVIII

**RESEARCH PROJECT AND MENTOR CONTACTS:**

**Research Office:** **Director: Gregory Heath, DHSc, MPH (423-425-4432)**
**Technical Writer: Kristi Strode (778-4566)**
**Grants Manager: Nancy Geren (778-8102)**

**Family Medicine:** **J. Mack Worthington, M.D. (778-2957)**
**Stephen M. Adams, MD (778-2957)**
**John Standridge, M.D. (778-2957)**

**Internal Medicine:** **Mukta Panda, M.D. (778-6672)**
**Gregory W. Heath, D.H.Sc., M.P.H. (425-4432)**

**OB/GYN:** **Shawn Stallings, MD (778-5192)**
**Stephen DePasquale, MD (698-2050)**

**Orthopaedic Surgery:** **Thomas W. Currey, M.D. (778-9008)**
**Joe Rudd, R.N., Ph.D., (778-6027)**

**Pediatrics:** **Marvin Hall, M.D., (778-6217)**
**Billy S. Arant, Jr., M.D. (778-4448)**

**Plastic Surgery:** **Larry A. Sargent, M.D. (778-9047)**

**Surgery:** **Chris LeSar, M.D. (778-7695)**
**Pat Lewis, R.N., (778-7695)**

**Transitional Year:** **Mukta Panda, M.D. (778-6672)**

**Click here to access a Research Resource List for further information and contacts:**
**http://www.utcomchatt.org/Docs/Research%20Resource%20List.pdf**