February 16, 2011

NIH Proposals: Write To Win!

The Human Subjects Protection Section

Protection of Human Subjects

"Although it is understandable to focus on goals, our society values the rights and welfare of individuals. **It is not considered ethical behavior to use individuals solely as means to an end.**"*

* Introductory slide of the DHHS "Protecting Human Research Participants" online training program. Accessed February 8, 2011.

Today's Agenda

- Human Subjects Protection
  - NIH Grant Process
  - Human Subjects Protection- Background
  - A Quiz
  - Defining Human Subjects Protection
  - Writing a Winning HSP Section
  - Q&A
- Conclusion & Evaluation

NIH Institutes & Centers

NIH Grant Application Process

- Standardized process for all 27 NIH institutes
- www.grants.gov- electronic filing process
- Standard Format for all applications
  - Adobe B
  - Adobe B1

Elements of Grant Success

- Good Ideas

- Good Timing

- Good Reviewers

- Good Grantsmanship

- Good Presentations

- Good Luck

NIH Proposals

- Approximately 65,000 applications for grants are received each year by NIH.

- Only 1:4 applications are awarded or 25%

NIH Proposals

- Center for Scientific Research is the first to read and score an NIH application, based on scientific merit.

REVIEW CRITERIA:

- **Significance- Does the study address an important problem? How will scientific knowledge be advanced?**
- **Approach- Are design and methods well-developed and appropriate? Are problem areas addressed?🡐 *"Code" for "Did you write an adequate Human Subjects Protection section?"***
- **Innovation- Are there novel concepts or approaches? Are the aims original and innovative?**
- **Investigator- Is the investigator appropriately trained?**
- **Environment- Does the scientific environment contribute to the probability of success? Are there unique features of the scientific environment?**

Human Subjects Protection

SOME BACKGROUND…

Tuskegee Syphilis Study

From 1932 until 1972, the United States Government was conducting research on syphilis using African men, without their consent or knowledge at the University of Tuskegee, Alabama

Although two-thirds had syphilis- the topic of the study- one-third did not. None of the men were asked for their consent to participate or ever given the opportunity to drop out. When it was learned that penicillin could easily cure the disease in 1947, the men were left untreated.

Only after an Associated Press story questioned the ethics of the study, the there was large public outcry, did the US Government close the study. This case, and other famous cases of research studies that did not take into consideration the respect of humankind, is an example of how laws formed to protect individuals from being forced into participating in experiments or research using human participants.

The Three Basic Principles of Human Subjects Protection

1. **Respect for Persons***
   - Individuals should be treated as ***autonomous agents;***
   - Persons with ***diminished autonomy*** are entitled to additional protections.

2. **Beneficence**
   - Treat individuals in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being.

3. **Justice**
   - Requires that individuals and groups be treated fairly and equitably in terms of bearing the burdens and receiving the benefits of research

* **http://ohsr.od.nih.gov/guidelines/belmont.html** Accessed on Feb. 4, 2011.

NIH Definition of a Human Subject

A human subject is a living person about whom an investigator conducting research obtains:

- Data through intervention or interaction with the individual, or
- Identifiable private information.

Definition of a Human Subject (cont'd.)

Intervention=

- Physical procedures by which data are gathered;
- Manipulation of the subject or subject's environment performed for research purposes.

Interaction= Communication or interpersonal contact between investigator and subject .

Private Information= Information about behavior that occurs in a context that an individual can assume no recording or observation is taking place; and information provided by the subject that the subject expects will not be made public.

Human Subjects Protection

When writing a grant the NIH wants to know that:

- → **Any person** asked to participate in a research study **understands the study** and its risks and **gives his/her full prior consent** for involvement or for use of their data or specimens.
- → The **benefits of the research outweigh the risks*** involved in conducting the research.
- → All information about a study involving human subjects, their specimens or their personal **data is protected.**
- → **Protection against risks are well thought out** and adequate for the proposed research project.
- → Human participants know and acknowledge that they have the **right to opt out** of the study at any time.
- → **Investigators** working with human subjects **are qualified** and applicable to the research proposed.
- → The **investigator can justify their decisions on human subject participation**, including age, gender and ethnic/racial choices.

*** "Risks" include the possibility of physical, psychological, or social injury resulting from research.**

Human Subjects Protection

So, how do you know if the research project an investigator is proposing involves human subjects or not?

It seems basic, but it can get quite complicated, really. Here is a Quiz to check your knowledge…

Human Subjects Involvement - QUIZ

Does the proposed research in each scenario involve human subjects?

1. Dr. Yee is conducting research on cadavers at BMC.
2. Dr. Smith is studying the accuracy of medication reconciliation of 100 diabetes patient records from BMC that have all been coded.
3. Dr. Black is proposing to conduct research on biological specimens from 1,000 cancer patients from BMC.

Human Subjects Protection- QUIZ

4. Dr. Wu is planning on conducting a clinical trial on the efficacy of two different radiology methods on breast cancer patients.
5. Dr. Brown wrote a proposal that will test the success of using Induced Pluripotent Cells in humans to reproduce lung cells. However, he noted in the application that he doesn't yet know exactly when the tests will take place.
6. Dr. Svensen proposes to research prostate cancer in men over 60, which obviously excludes all women and children from the study.

Human Subjects Protection- Categories

All research proposals must address the protection of Human Subjects.

The NIH provides specific instructions on what you need to write for this subject, categorized by research scenario.

It has identified six different scenarios under which all research studies fall. They are:

1. No human subjects research (HSR)
2. Non-exempt HSR
3. Exempt HSR
4. Delayed-onset HSR
5. HSR involving a clinical trial
6. HSR involving an NIH-defined Phase III Clinical Trial

Writing the HSP Section of an NIH Research Proposal

No matter which scenario your proposal falls under, you should include the following headings in your Human Subjects Protection Section of your NIH proposal:

1. Risk to Human Subjects;
2. Adequacy of Protection Against Risks;
3. Potential Benefits of the Proposed Research to Human Subjects and Others;
4. Importance of the Knowledge to be Gained.

4.1 Protection of Human Subjects

4.1.1 Risks to Human Subjects-

a. Human Subjects Involvement, Characteristics, and Design-

You should write this paragraph in your own words, as it pertains to your research. However, using the bullets as a guide, be sure to include the following main points:

- Describe the proposed involvement of human subjects, specimens or data in the work outlined in the research strategy section.
- Describe and justify the characteristics of the subject population, number, age range and health status, if relevant.
- Explain the rationale for involvement of special vulnerable populations, such as fetuses, neonates, pregnant women, children, prisoners, institutionalized individuals, or others.
- If relevant, describe procedures for assignment to a study group and/or describe and justify selection of an intervention's dose, frequency, and administration.
- List all collaborating sites where human subjects will be performed for this study and describe their role in the proposed research. Explain how sites will be obtained, managed, and protected.

4.1 Protection of Human Subjects

4.1.1 **Risks to Human Subjects-**

b. Sources of Materials- In your own words, in narrative format, cover the following topics in this section as they relate to your research topic:

- Describe the research material obtained from living individuals in the form of specimens, records, or data.

- If data will be collected from human subjects, describe how and when it will be collected, and how it will be managed and protected.

- Indicate who will have access to individually identifiable private information about subjects.

4.1 Protection of Human Subjects

4.1.1 **Risks to Human Subjects-**

c. Potential Risks- In this section, in narrative form and in your own words, describe the potential risks facing the Human Subjects, their specimens, or data being used for this project. Include:

- Potential risks to subjects (physical, psychological, financial, legal, or other), and assess their likelihood and seriousness to the human subjects.
- Where appropriate, describe alternative treatments and procedures, including the risks and potential benefits of the alternative treatments and procedures, to participants in the proposed research.

4.1 Human Subjects Protection

4.1.1 **Risks to Human Subjects-**

QUESTIONS?

4.1 Protection of Human Subjects

4.1.2 Adequacy of Protection Against Risks

a. ***Recruitment and Informed Consent-*** *Use this section to describe:*
   a. *plans for the recruitment of subjects (where appropriate)*
   b. *process for obtaining informed consent, including description of circumstances under which consent will be sought and obtained*
   c. *If children are involved (anyone under 21 years old), describe process for meeting parental permission and child assent*
   d. *Describe who will seek consent and how they are qualified*
   e. *If waiver is included, provide justification.*
   f. *Informed consent documents are not necessary unless requested in the RFP guidance.*

4.1 Protection of Human Subjects

4.1.2 Adequacy of Protection Against Risks

b. Protections Against Risk- In your own words, include the following points in this category:

- *Describe planned procedures for protecting against or minimizing potential risks, including risks to privacy of individuals or confidentiality of data; assess their likely effectiveness.*
- *For research that involves vulnerable populations, include information on how you will protect these populations, as outlined in the DHHS and OHRP guidelines, subparts A-D.*
- *Links to additional protections guidelines:*
  - *http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#subpartb*
  - *http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#subpartc*
  - *http://www.hhs.gov/ohrp/policy/index.htm#prisoners*
  - *http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#subpartd*
  - *http://www.hhs.gov/ohrp/children*

4.1 Protection of Human Subjects

4.1.2 Adequacy of Protection Against Risks

b. Protections Against Risk- In your own words, include the following points in this category:

- Where appropriate, write out your plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects.

- Clinical trials proposals must include a general description of the plan for data and safety monitoring of clinical trials and adverse event reporting to the IRB, NIH, and others.

4.1 Protection of Human Subjects

4.1.3 Potential Benefits of the Proposed Research to Human Subjects and Others

- Discuss the potential benefits of the research to the research participants and others.

- Explain why the risks to subjects are reasonable in relation to the anticipated benefits to participants and others.

4.1 Protection of Human Subjects

4.1.4 Importance of the Knowledge to be Gained

- Describe the importance of the knowledge to be gained overall or as a result of the proposed research.
- Explain why the risks to subjects are reasonable in relation to the importance of the knowledge that reasonably may be expected to result.

Note: For test articles, you must name them if they have not yet been approved by the Food and Drug Administration. You must also state in the Research Plan:

- Whether the 30-day interval between submission of applicant certification to the FDA and its response has elapsed or has been waived;
- Whether use of the test article has been withheld or restricted by the FDA,
- The status of requests for an Investigational New Drug or Investigational Device Exemption covering the proposed use of the test article.

Inclusion of Women and Minorities

This section should address the following points:

1. The targeted/planned distribution of subjects by sex/gender and racial/ethnic groups for each proposed study or protocol, using the format in the Targeted/Planned Enrollment Table;
2. A description of the subject selection criteria and rationale for selection of sex/gender and racial/ethnic group members in terms of the scientific objectives and proposed study design.
3. Compelling rational for proposed exclusion of any sex/gender or racial/ethnic group.
4. A description of the proposed outreach programs for recruiting sex/gender and racial/ethnic group members as subjects.

Inclusion of Children

1. This section goes immediately after the Targeted/Planned Enrollment Table
2. A “Child” is a person under age 21.
3. Provide a description of the plans to include children or, if they will be excluded, a strong justification for the exclusion.
4. If children will be included, provide an explanation to justify any age range restrictions, if applicable.
5. Plan must also include a description of the expertise of the investigative team for working with children at the ages included, of the appropriateness of the available facilities to accommodate the children and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of study.

Questions & Answers

QUESTIONS?