A One-Way Trip through the IRB

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Tips to Get Your Protocol
through Human Subjects Protection Review Efficiently

Challenges to HSP Review from Investigator's Perspective

- Lack of investigator experience
- Developing a good study design
- The collaborator curse
- Tethered to a template
- In need of a good editor
- Effective management review
- Poor and/or late communication with HSP & IRB staff
- Too many IRB reviews
- Delays in review processes

Conducting Human Subject Research is a Trade

- You are not taught how to do this in medical, nursing or graduate school

- We have <u>limited</u> formal training programs

- This is a trade learned by apprenticeship from a "knowledgeable" MENTOR

Refining Your Idea
The Protocol Synopsis

- *The essence of your protocol should be <5 pages and a schedule of events*

- Work that with your colleagues, funding agency, and consultants until you have a solid plan

- Then, <u>and only then</u>, write your protocol

The Collaborator Curse

- Collaborators are <u>critical to the success</u> of many studies… and nearly mandated now by large granting organizations.

- Multiple institutions bring:
  - Multiple HSP Assurances
  - Unique institutional requirements
  - ? Multiple IRBs
  - Differing ethics standards or HSP laws

- This complexity must be aggressively managed by the PI and built into the protocol

Templates are a TOOL…
not a product

- Your protocol is your <u>contract</u> with the Sponsor/Institution and IRB on how the study will be conducted

- All protocols are different…one, even five, template designs will NOT fit all studies

- Design your protocol to meet your needs NOT to fit into a template
  - include correct DoD reporting language/clauses

Writing the Protocol

- Who: investigator vs. science writer?

- What: format or template?
     A protocol is not a grant/funding proposal

- When: after peer-reviewed study synopsis

- Where: know your study site
              know your collaborators

- Why: to end up with a solid protocol for rapid
         approval

Planning Ahead

- Your protocol should address not only the instruction for execution of the study, but also:

    – Desire to store specimens for future use
      - Respect for volunteers – consent for future use
    – Plans for storage of specimens for future use
      - Coding systems and active management of links
      - Maintain confidentiality
    – Plans to store data and documents
      - Where and how long?

Finding an Editor

- Almost all manuscripts are reviewed by all authors and often an outside reviewer before submission to a journal

- *What is good for manuscripts is good for protocols*

- If someone who is unfamiliar with the project cannot follow the protocol, it is <u>NOT ready</u> for review

Management needs to… Manage

- Managers of investigators engaged in human subjects research need to:
  - Be trained in human subjects protection

  - Be familiar with the project
  - Review and approve collaborators
  - Ensure adequate resources are assigned for success
  - Assign a mentor to junior investigators
  - Assure the editing has occurred before review

I have a good protocol!

…but that's not the end of your planning

Talk *Early and Often* to the Human Subjects Protection Staff

- Early discussions:
  - Ethical ramifications of specific study design
  - State or host nation laws, ethics guidelines or human subjects protection guidance
  - Review of Institutional requirements
  - Sponsor-specific reporting language
  - Managing collaborative reviews

Ethical ramifications of specific study design

- Knowing the study population
  - Identify vulnerable populations

- Consent process
  - When or how to use a test of understanding
  - How to handle consent for volunteers not literate in the primary language

- Managing links to study volunteers

Defining the Human Context of Your Study

- Describe the study population
  - Recruiting contacts
  - Language and barriers to consent
  - Impact of the study on their daily lives
  - Vulnerable populations
  - Why was this population chosen

- Describe study location
  - Physical location
  - Health care available

International Population Information

USAMRMC Office of Research Protections Human Research Protection Office
International Research Study Information Form

The following information is required by the Human Research Protection Office in order to obtain information about the host nation's research site and the local context within which it will be conducted. The form should be completed by the Principal Investigator in conjunction with the investigator(s) in the host nation.

If information requested in this form is described within the protocol, the corresponding page number(s) where the information is located in the protocol may be entered instead.

Country and city in which study is to be conducted: _____

A. Explain the rationale for conducting research in this host country.

B. Explain how this research relates to the current health care needs of the community. For example evaluation of malaria treatments/vaccines in a malaria endemic area and not in an area where malaria is not commonly present.

C. Provide current (within one year) signed and dated CVs for the PI and the investigator(s) who will conduct the research in the host country.

D. Provide the name and contact information for the investigator who will conduct the research in the host country.

Host country site investigator: _____
Address: _____
_____
Phone number: _____
E-mail address: _____

E. Regulatory Information

1. List the regulations governing human subjects research in this host country: (e.g. ICH, CIOMS): _____

_____

2. Name of study site's ethical review committee:
_____

_____

Point of contact: _____

Contact information (phone number, email address, etc): _____
_____

3. Does the protocol require review by other Host Nation institutions, offices, departments, Scientific Committees (e.g. Ministry of Public Health) or by a Host Country Drug and/or Device oversight agency?   ___ Yes ___ No

If yes, provide the following information:

Name of Committee	Date of Review	Point of Contact	Phone Number	Email

International Population Information Form

- Host nation selection and context
- Local IRB and ethics policies
- Site information
- Study population
- Local Community Information
- Medical Care
- Unique Site Consent Processes
- Specimen and Data Management

Know your host nation laws and guidelines

International Compilation of Human Research Protections

2008 Edition

Compiled By:
Office for Human Research Protections
U.S. Department of Health and Human Services

- Over 900 guidelines from 84 countries

http://www.hhs.gov/ohrp/international/HSPCompilation.pdf

Institutional Human Subjects Protection Guidance

- We all start with the Common Rule (32CFR219)

- DoD specific guidance (e.g. DoDD 3216.02)
- Component specific regulations (e.g. AR70-25)
- Command specific regulations, e.g. USAMRMC
- Institutional guidelines in your HRPP

- The same is true for your collaborators!!

Other Institutional Requirements

- Early review with your human subjects protection office can also identify need for:
  - an IND/IDE submission to FDA; import permit
  - CRADA/MOU for study execution
  - Clinical Trials Agreement for study execution
  - Material Transfer Agreement for specimen transfer
  - Data Use Agreement for data sharing

Reporting to the 'sponsor' vs. the IRB

- The <u>responsible executive authority</u> for your study may be:
  - The principal investigator
  - Someone in management at your institution
  - A pharma company or USAMMDA (FDA regulated research)

- Reporting protocol lifecycle events to this 'sponsor' authority is different than the IRB
  - separate reporting requirements in your protocol

Managing Collaborative Reviews

- *Juggling is sometimes called the art of controlling patterns, controlling patterns in time and space.*
    - Ronald Graham, mathematician

- Minimizing IRB reviews
    - Should rarely have more than one DoD review
    - Try to avoid more than 2 IRB reviews

- Use of: IRB Authorization Agreements
                   Individual Investigator Agreements

Informed Consent Documents

- *Protocols are written for physicians, nurses and PhDs… consent forms are written for 8th graders or below*

- Consider having a writer other than the protocol writer author the consent

- Consider an information sheet and shorter consent

- Include all required DoD/Component elements in consent

Submitting a Complete Protocol Packet

- A major source of delays

  – *Pay attention to your IRB submission requirements*

- Some items are critical for review initiation; others for recommendation of approval

  – Talk to IRB and set timelines for pending documents

Insist on Talking to an IRB Member before or at the IRB meeting

- 80% of issues can be resolved immediately with effective dialog

- Written communications (pre-review, IRB comments) never convey the nuances of the spoken word
  - *Don't settle for less!!*

- It is OK to rebut the IRB decisions

Respond Promptly to IRB Communications

- Often lengthy delays in reply to the IRB office
  - Loss of momentum works to your disadvantage
    - Lost familiarity with the protocol or stipulations
    - New staff assigned to the review

  - If there is a delay, communicate regularly on progress

- *Journal editors set 30 days limits to reply… so should you!!!*

Version Control,
Version Control,
Version Control

- All protocol documents need a version # and date
- The IRB will approve a version and date

- ***Any change is a new version number and date*** (and requires a new approval)

- Submit the changed document with tracked changes and a clean copy
  - Consider a change management document - 'was-is'

Pearls in Protocol Prep

- Define your 'responsible executive authority'
- Define your funding, to include grant #
- Investigators vs. Consultants
  - Define everyone's roles and responsibilities
- Engage a statistician to help on sample size and design issues
- Describe the test articles (non-IND studies)
- Describe your test procedures and lab assays

Pearls in Protocol Prep

- Careful editorial review before IRB submission
  - Synopsis = body of protocol = consent document

- Separate reporting language for 'sponsor' and for IRBs

- Set your bar for quality oversight appropriately.
  - Good Clinical Practices (ICH E6) does not apply to non-IND studies..

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