Overview of the IRB & Strategies for Improving the Informed Consent Process

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Short Course in Clinical Research
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Presentation Goals

- Provide overview of what an IRB is and why they exist
- Discuss one of the primary functions of the IRB - ensuring an adequate informed consent process, including:
  - What constitutes informed consent
  - Regulations governing informed consent
  - Consent challenges
  - Tips for constructing consent documents and processes
UW-Madison IRBs

- There are 4 campus IRBs
  - Health Sciences IRB
    - Primarily reviews clinical trials/research protocols involving medical interventions
  - Health Sciences Minimal Risk IRB
    - Primarily review medical records research, research database and tissue banking projects, survey and interview research, and exemption applications
  - Education IRB
    - Reviews education research (K-12)
  - Social & Behavioral Sciences IRB
    - Reviews social, behavioral, and non-medical health research
What is an IRB?

- The primary function of the IRB is to protect the rights and welfare of human subjects
  - IRBs are only one part of a system that the institution has in place to protect human subjects
- Human subjects research cannot begin at UW-Madison without prior IRB approval or exemption of the study
- IRBs can require modifications to protocols in order for a research team to secure IRB approval
- IRBs can suspend or terminate research
Why do IRBs exist?

- Historical atrocities
- Federal requirements
- Reduce the potential for researchers to lose sight of individual rights and welfare because of a focus on advancing science/knowledge
What does IRB review concentrate on?

- Ensuring it is as safe as possible for people to take part in a study
- If there are serious risks, ensuring they are as low as possible and the right kind of monitoring is in place to prevent adverse effects or identify adverse outcomes as soon as possible
- Ensuring the subject population is the appropriate population to answer the study question
- Ensuring the study design is acceptable so that
  - the question posed can be answered by the research
  - the right number of people will be enrolled (not too many or too few) so that as few people are exposed to risk as possible
- Ensuring the information given to potential research participants is sufficient to allow them to make an informed choice about whether they want to take part in the research study
Informed Consent
Principle of informed consent: Robert Levine’s view

- The requirement for informed consent is designed to uphold the ethical principle of *respect for persons*.
- Through informed consent clinical researchers make operational their duty to respect the rights of others to be left alone or make free choices.
- Professionals who intervene in the lives of others are held to higher standards.
Elements of Adequate Informed Consent

- Subject has the capacity to provide informed consent
  - Ability to appreciate the nature of the situation and its likely consequences
  - Ability to reason with the information and weigh options logically
  - Ability to communicate the choice
- Subject provided with all relevant information to make the decision
- Subject comprehends the information provided
- Subject’s decision to participate free of undue influence, coercion
General Common Rule Requirements [45 CFR 46.116]

- Must be “legally effective”
- Must have “sufficient opportunity” to consider participation in research
- Must “minimize possibility of coercion or undue influence”
- Must be in a “language understandable” to subject/subject’s representative
- Cannot contain “exculpatory language”
Specific regulations

- Common Rule, 45 CFR 46
- FDA Regulations
- VA Regulations
- ICH requirements
Federally Required Elements of Consent
Element 1

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental
Element 2

- a description of any reasonably foreseeable risks or discomforts to the subject
Element 3

- a description of any benefits to the subject or to others which may reasonably be expected from the research
Element 4

- a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
Element 5

- a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
Element 6

- for research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained
Element 7

- an explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
Element 8

- a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled
Additional Elements that May Be Required

- a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable
- anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent
- any additional costs to the subject that may result from participation in the research
- the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject
- A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject
- the approximate number of subjects involved in the study
Additional Language

- Institutional requirements
- Required HIPAA Privacy Rule elements sometimes embedded within consent form
- Sponsor-specific language also frequently added
Some of the challenges to informing subjects

- Legal requirements of the consent documents
- Sponsor requirements
- Complexity of the research/low scientific literacy
- Variation in learning styles
- Intrusion of therapeutic misconception
Some of the challenges affecting comprehension

- Type of disease, procedures required
- Severity of illness
- Low literacy of the US population
- Low to no understanding of English
- Presence of cognitive impairment
- Age: Old and young
- Preconceptions about clinical treatment & therapeutic misconception
- Shortcomings of the informed consent process
Frequent confusions subjects have about clinical research

- Tend to not understand the difference between personalized clinical care and the impersonal, more global goals of clinical research
- Do not understand the concept of clinical equipoise (i.e., think we know answer already)
- Tend to not understand the concept of randomization
- Frequently overestimate the benefits of clinical research, underestimate the risks
  - Difficulty understanding percentages, probability statements
Therapeutic Misconception

- Defined as “when clinical research subjects fail to recognize the ways in which research participation may involve the sacrifice of some degree of personal care” [Appelbaum, Lidz, Grisso 2004]
  - Feel their physician would not suggest unless good for them
  - Risks must be low because their physician would not recruit them for the study otherwise
- Of subjects in a variety of clinical research trials that were studied [Appelbaum, Lidz, Grisso 2004]:
  - 31.1% had inaccurate beliefs about individualization of their treatment
  - 51.1% manifested an unreasonable belief in nature or likelihood of benefit
  - 61.8% deemed to manifest therapeutic misconception
Providing the Information
Discussions with Potential Subjects

- Provide oral summaries in addition to more detailed written reference information
  - Highly detailed information not associated with better understanding
  - Don’t just read the consent form to potential subjects

- Interactive discussions important
  - Someone with patient education background highly helpful
  - Consider use of videotapes, CD-ROMs
Presenting information using multimedia

- **Examples:** videos, computer-assisted programs, audio

- **Benefits**
  - Very effective for some populations
  - Can share with relatives/friends more easily

- **Drawbacks**
  - Can be costly and time-consuming to develop
  - Efficacy may depend on subject, condition, and/or study procedures
  - Some forms difficult to update
Participant Brochure

- Provide general information to potential research subjects about
  - The nature of research
  - What to expect if they decide to take part in a clinical research study
  - Where to find additional information
Addressing Therapeutic Misconception

- Involve someone who perceives their role as a patient advocate/educator in the consent process
- Consent Forms
  - Use of jarring language
    - “Subject” rather than “patient”, “volunteer”, “participant”
    - Phase 1: “This research study is not intended to treat your disease. Instead the purpose of this research study is to find out how much of an experimental drug can be given to people without causing side effects that are unacceptable.”
  - Use of terms to describe drugs/procedures
    - “experiment” and “experimental” rather than “research drug”, “study treatment”, “study drug”, “clinical trial”
  - Provide separate lists of research and standard procedures
  - Restraint with benefits language, particularly with Phase 1 and 2 studies
    - E.g., “This research study is not intended to benefit you. The hope is that future patients will benefit.”
Presentation of Written Information

- Provide summary page
- 6th to 8th grade reading level
- Short sentences and paragraphs
- Increase font size
- Use of Question & Answer format
- Use of bold, italics, color
- Use of bullet points
- Cite major risks, append others
- Use of tables for risks
- Use graphics
Summary Page

- Snapshot of the study
- Major procedures
- Number of visits
- Major risks (what you would tell a patient as his/her physician)
- Time commitment
- Hochhauser example
## Hochhauser Model: The Basic Eight

<table>
<thead>
<tr>
<th>What’s the purpose of this research study?</th>
<th>This is an experiment to compare two different drugs on your type of breast cancer.</th>
</tr>
</thead>
<tbody>
<tr>
<td>What’s the procedure?</td>
<td>You’ll get Drug A or Drug B, blood tests, and physical exams for 6 months.</td>
</tr>
<tr>
<td>What are the risks of being in the study?</td>
<td>Side effects of nausea, fever, weakness, loss of appetite. Your cancer might not get better.</td>
</tr>
<tr>
<td>What are the benefits of being in this study?</td>
<td>You probably won’t benefit. But your involvement might help others.</td>
</tr>
<tr>
<td>Can I choose alternative treatments?</td>
<td>Yes. You can choose standard treatment with existing cancer drugs.</td>
</tr>
<tr>
<td>Is information about me kept confidential?</td>
<td>Yes. Your name will not appear in any publications or talks at conferences.</td>
</tr>
<tr>
<td>Who should I call if I have any questions?</td>
<td>Dr. Smith at 555-123-4567 or Dr. Jones at 555-987-6543 for questions about your rights.</td>
</tr>
<tr>
<td>Is my participation voluntary?</td>
<td>Yes. You may leave the study at any time without losing any of your health benefits or legal rights.</td>
</tr>
</tbody>
</table>
### Hochhauser Model: The Additional Elements

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does this study involve unknown risks to me or my fetus? Can I get pregnant while in this study?</td>
<td>Yes, there may be unknown risks. You must not get pregnant while in the study.</td>
</tr>
<tr>
<td>Can Dr. X take me out of this research study?</td>
<td>Yes, if it’s not in your best interest to continue.</td>
</tr>
<tr>
<td>What happens if I drop out of this research?</td>
<td>We’ll ask you to return for a last follow-up visit to make sure you’re OK.</td>
</tr>
<tr>
<td>Are there any extra costs for being in this research?</td>
<td>Not for routine treatment costs. But you or your insurance company will be billed for any injury-related treatments.</td>
</tr>
<tr>
<td>Will I be told of significant new findings?</td>
<td>Yes.</td>
</tr>
<tr>
<td>How many subjects will be in this study?</td>
<td>About 600 nationally. About 20 at this hospital.</td>
</tr>
</tbody>
</table>
Resources

- Health Sciences IRBs website tips and templates – see *Informed Consent and Subject Recruitment* link on IRB website at [www.medicine.wisc.edu/irb](http://www.medicine.wisc.edu/irb)
  - Consent form wizard tool
  - Templates for a variety of studies
  - Guidance
  - Special consent processes
  - Required institutional language
  - Links to HIPAA forms and requirements
INFORMATION SHEET FOR RESEARCH SUBJECTS

Research Study Title:
Principal Investigator:
How to contact the study staff:

Who to call if you have questions about being a research subject: University of Wisconsin Hospital and Clinics Patient Relations Representative at 608-263-8009

This sheet provides some of the key information you need to know about this research study. Taking part in a research study is voluntary. You do not need to take part in this study to receive care for your condition. You can stop taking part in this study at any time without any penalty. Attached to this summary of the research study is a consent form that will give you in depth information about the procedures it involves, the risks and benefits of the study, other possible procedures or treatments you can receive instead of those in this research study, and how the your study information will be protected. Please feel free to ask the researchers any questions you have about this study.

The purpose of the research study:

Main research procedures:

Number and length of study visits:

Main risks of taking part in this research study:

Possible benefits of taking part in this research study:
Example for a Phase 3 Study

INFORMATION SHEET FOR RESEARCH SUBJECTS

Research Study Title: HS-IRB Protocol 2003-0XXX “A Phase III Study of Experimental Drug X Compared to Approved Drug Y for the Treatment of Condition Z”

Principal Investigator: Jane Doe, MD

How to contact the study staff: (608) 123-4567

Who to call if you have questions about being a research subject: University of Wisconsin Hospital and Clinics Patient Relations Representative at 608-263-8009

This sheet provides some of the key information you need to know about this research study. Taking part in a research study is voluntary. You do not need to take part in this study to receive care for your condition. Attached to this summary of the research study is a consent form that will give you in depth information.

The purpose of the research study: This research study will try to find out if an experimental drug called Drug X is safer and more effective for the treatment of Condition Z than Drug Y. Drug X has not been approved by the US Food and Drug Administration (FDA) for the treatment of Condition Z and can only be given in a research study. Drug Y has been approved by the FDA for the treatment of Condition Z. You will be assigned which drug you will receive by chance. Neither you nor your study doctor will know which drug you will receive through the entire study.

Main research procedures: This study involves giving you one of two drugs, blood tests to check your health, taking blood to see how much of the study drug is in your body, physical exams, and answering questions about how you are feeling. Both drugs are given in pill form.

Number and length of study visits: You will have 12 total visits if you complete all of the study. Visits can be as short as 1 hour and as long as 4 hours.

Main risks of taking part in this research study: The most common risks of Drug X are upset stomach, vomiting, feeling tired, lowering the number of white blood cells you have which can make you more likely to get an infection. The most common risks of Drug Y are upset stomach, vomiting, itchiness, and headaches. A rare but serious risk of both Drugs X and Y is an allergic reaction.

Possible benefits of taking part in this research study: Drug X may turn out to be better than Y. It is possible than Drug X will not treat your condition as well as Drug Y or may have more side effects.
Conclusions

- **Process not a form**
  - Providing information in a digestible format
  - Allowing time for potential subjects to think it over and talk with family, friends
  - Ongoing check throughout the research study
  - Involving individuals who perform patient education functions

- **Provide information in more than one format**
  - Oral and written
  - Reference information and brief summaries
  - Consider multimedia presentations

- **Alter written consent documents to be more reader-friendly**
Questions or need help?

Contact the IRB Office at 608-263-2362

- Email
  AsktheIRB@medicine.wisc.edu

- Set up a consultation with a staff reviewer