Elements of Informed Consent
What an IRB Considers When Reviewing Informed Consent Materials
April 9, 2014

Presented by:
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Director of Board Services
Established in 1983
US and Canadian boards fully accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP)
Superior audit history with FDA—five consecutive audits with no findings.
21 CFR Part 11 compliant electronic systems
Compliant with FDA, OHRP and Health Canada requirements
About Schulman Associates IRB

- Full board meetings **five days a week**
- Dedicated **daily expedited review** of qualifying minimal risk protocols
- **Phase I Board** with streamlined processes tailored to Phase I timelines
- **Oncology Review Board** for all phases of oncology research
- Customized services for **institutions and AMCs**
- Experienced primary points of contact for sponsors, CROs, institutions and sites
Clinical Quality Assurance (CQA) and Human Research Protection (HRP) consulting services provided by Provision Research Compliance Services

Provision is a joint venture between Schulman Associates IRB and Falcon Consulting Group
James MacFarlane, BS, CIP
Director of Board Services

- BS in History of Science and Medicine from Northern Kentucky University
- With Schulman since 2008
- Responsible for direct support of board operations, including IRB liaison for informed consent development, safety reporting, and study change management
- Member of PRIM&R and Mensa
In this presentation, we will discuss:

- the purpose of informed consent
- the basic elements of informed consent
- the regulations that affect and shape informed consent
- some contemporary issues surrounding informed consent
What Is Informed Consent?

- The purpose of informed consent is to inform the potential subject of the research’s
  - Purpose
  - Potential risks
  - Potential benefits
Who Makes the Rules, and What Are They?

- Belmont Report
- Federal Regulations (DHHS, FDA)
- ICH (GCP)
Belmont Report – Core Principles of IC

- Core protections for Human Research Subjects
- Part C
  - Information
  - Comprehension
  - Voluntariness
Belmont Report – Core Principles of IC

Core protections for Human Research Subjects

Part C

- Information
- Comprehension
- Voluntariness

“The extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge.”
Belmont Report – Core Principles of IC

- Core protections for Human Research Subjects
- Part C
  - Information
  - Comprehension
  - Voluntariness

“The manner and context in which information is conveyed is as important as the information itself.... it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information.”
Belmont Report – Core Principles of IC

Core protections for Human Research Subjects

Part C

- Information
- Comprehension
- Voluntariness

“An agreement to participate in research constitutes a valid consent only if **voluntarily** given. This element of informed consent requires conditions free of coercion and undue influence.”
Federal Regulations:
Detailed Guidance on Informed Consent Content
Federal Regulations - Basic Elements of Informed Consent

- **DHHS/FDA**
  
  - (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

*Tip:* 

*Divide and Conquer*
Federal Regulations - Basic Elements of Informed Consent

DHHS/FDA

- (2) A description of any reasonably foreseeable risks or discomforts to the subject

Tip:

Cross-reference the IC language with any and all risks presented in the protocol document.
DHHS/FDA

- (3) A description of any benefits to the subject or to others which may reasonably be expected from the research

Example:

You may benefit as a result of your participation in this study. There is, however, no guarantee that you will benefit from your participation in this study. Results from this study may benefit others in the future.
DHHS/FDA

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject

Example:

[For treatment studies] You do not have to be in this study to receive treatment for your [disease type]. Your options include: [Insert relevant options] [List available alternative procedures and the important benefits and risks of the alternative procedures or treatments that may be available to the subject]. The study doctor will discuss with you the risks and benefits of the alternative treatments.
Federal Regulations - Basic Elements of Informed Consent

- **DHHS/FDA**
  - (5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained

**Example:**

Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The study doctor, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified.
DHHS/FDA

(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.

Example:

If you are injured as a result of taking the study drug(s) or from procedures done for the purpose of this study, the sponsor will pay for those medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third party coverage. There are no plans to provide other compensation beyond that which is listed in this informed consent document.
DHHS/FDA

(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

Example:

During the study, if you experience any medical problems, suffer a research-related injury, or have questions concerns or complaints about the study, please contact the study doctor at the telephone number listed on page one of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in a research study being conducted by the study doctor listed on page one of this document.
DHHS/FDA

(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.

Example:

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care.
Additional Elements of IC – DHHS/FDA

- (1) 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.
- (2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
- (3) Any additional costs to the subject that may result from participation in the research.
- (4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
- (5) 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.
- (6) The approximate number of subjects involved in the study.
ICH

- (1) The trial treatment(s) and the probability for random assignment to each treatment
- (2) The subject’s responsibilities
- (3) The anticipated prorated payment, if any, to the subject for participating in the trial
- (4) The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks
- (5) That the monitor(s), the auditor(s), the IRB/IEC, and the regulatory authority(ies) will be granted direct access to the subject’s original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject’s legally acceptable representative is authorizing such access
Federal Regulations – Waiver of IC and Short Form

- Documentation – Written, signed, contain the basic elements, copy provided to the subject, LAR specifically mentioned, adequate time to read.
  - Allows for waivers if IC is only link to subject, and minimal risk.
- Short Form – Allows basic elements to be presented orally. Witness required. IRB must approve a written script. Subject or LAR signs as usual. Witness and person obtaining consent sign script. Summary and short form copy given to subject.
Common Informed Consent Issues
Common Informed Consent Issues

- Most common issues IRBs find in their review of an informed consent:
  - Therapeutic misconception
  - Missing risk text
  - Exculpatory language
  - Understandability of language
Some examples of problematic language

- “Doctor”
- “Patient”
- “Treatment”
(1) 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;
(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
(3) Any additional costs to the subject that may result from participation in the research;
(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
(5) 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; and
(6) The approximate number of subjects involved in the study.

Therapeutic Misconception

Some examples of problematic language

“Study Doctor”
“Subject” or “Participant”
“Study Treatment”
Risk Text and Understandability

➢ Risk text often presents the greatest challenge to understandability.

➢ Using a protocol analysis checklist can help ensure that the IC mirrors the risks presented in the protocol.

➢ Lay Term Conversion Guides are very useful, as is software created specifically to assist in achieving an 8th grade reading level.
Exculpatory Language – What Is It?

- Exculpatory Language: 45 CFR 46.116

  - No informed consent, whether oral or written, may include any exculpatory language through which the subject is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.
Exculpatory Language – Example

By agreeing to this use, you should understand that you will give up all claim to personal benefit from commercial or other use of these substances.
Exculpatory Language – Example

- By agreeing to this use, you should understand that you will give up all claim to personal benefit from commercial or other use of these substances.
Exculpatory Language – Example

- I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all right, title, and interest to said items.
Exculpatory Language – Example

- I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all right, title, and interest to said items.
Exculpatory Language – Example

By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.
Exculpatory Language – Example

➢ By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.
Exculpatory Language – Example

➢ I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.
Exculpatory Language – Example

- I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.
Other Considerations

- Submit a finished document
- Limit site-specific language
- Submit the most recent version of the document
- Multinational trials
- Avoid hidden text, codes and macros
- Give us a call!
- Embedded HIPAAs
- Basis for revisions
Conclusion

➢ Informed consent is

- one of the central protections provided to subjects by the regulations
- a process, not just a document
- a partnership
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