The Obtaining of the Informed Consent – Skill Development –

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Disclosure:

No conflict of interest with this presentation
Objectives:

1. Describe the essential skills necessary to ensure an adequate informed consent process

2. Identify unique challenges to the informed consent process and summarize potential solutions to those challenges
Outline:

1. What is Informed Consent
2. Ethical basis: Why?
3. The consent process
4. What is required to obtain a valid Informed Consent?
5. Elements of informed consent
6. Special situations
7. Conclusions
Definition

“Informed consent is a vital part of the research process, and as such entails more than obtaining a signature on a form. Investigators must educate potential subjects to ensure that they can reach a truly informed decision about whether or not to participate in the research. Their informed consent must be given freely, without coercion, and must be based on a clear understanding of what participation involves.”*

The documentation of informed consent (i.e., signing of the consent form) is also a vital part of the research process.

*Partners Healthcare: Founded by Brigham & Women’s Hospital & Massachusetts General Hospital
The Consent Process: It’s More Than Just a Form

- Ongoing
- Interactive process
- Different for every subject
- Different for every study
- Essential for study success
- IRB approved
- Providing clear definition between where standard-of-care leaves off and research begins
- Allows re-education
- Requires re-assessment of subject understanding with each visit
The Consent process:

- Information provided
- Information understood
- Decision made
- Comprehension monitored and maintained
What is the consent document?

- A document that provides a summary of the research and explains the subjects rights as a participant

- It is designed to outline and be a reference regarding what is expected of the participant
Valid informed consent requires:

- Disclosure of relevant information to prospective subjects about the research
- Their comprehension of the information.
- Their voluntary agreement, free of coercion and undue influence, to research participation.
The Informed Consent Process - What

8 Required Elements of Informed Consent:

1. **Research** – statement that study involves research, its purpose, duration, procedures, & identification of experimental procedures.
2. **Risks** - or discomforts, that are reasonably foreseeable.
3. **Benefits** – to subject or others, that are reasonably expected.
4. **Alternative** - procedures or treatments available, if any.
5. **Confidentiality** - of records identifying subject, though may be inspected by authorized entities (i.e., FDA, IRB, Sponsor).
6. **Research-Related Injury** – available treatment & compensation (if study is greater than minimal risk).
7. **Contact** – person for questions regarding the study, subject’s rights, or research-related injury.
8. **Voluntary** – no penalty or loss of benefits for choosing not to participate & may discontinue at any time.

FDA 21 CFR 50.25 & 45 CFR 46.116
The Informed Consent Process - What

Additional Elements of Informed Consent:

1. **Unforeseeable Risks** – may be involved.
2. **Participation Termination** – circumstances under which PI may terminate subjects participation without their consent.
3. **Additional Costs** – to subject due to participation.
4. **Withdrawal** – consequences of subject’s decision to withdraw & withdrawal procedures.
5. **Significant New Findings** – subjects will be notified of new findings which develop during the course of research that may relate to their willingness to continue participation.
6. **Subject Numbers** – approximate number involved in study.

The *8 basic* elements are required in all consents. *Additional* elements are used when appropriate and as required by IRBs. They are typically incorporated in the IRB templates with instruction for use.
The Informed Consent Process - Who

Who Must be Consented?
• Potential subjects who are thought to fulfill the inclusion/exclusion criteria for the study.

Who May Obtain Consent?
• Qualified research team members trained in Human Subject Protection & with sufficient knowledge about the specific study. This may include the Principal Investigator (PI), sub-investigators, research coordinators or other research team member approved by the IRB.
• Though the PI may delegate obtaining consent to other team members, proper oversight and execution is always the PI’s responsibility.
The Informed Consent Process - When Informed consent must be obtained:

- **Prior** to conducting any study related tests, procedures, treatments, or questionnaires.

- Using the current IRB approved consent form.

- Re-consent is required if there is new information that would effect the subjects willingness to continue participation or as directed by the IRB.
The Informed Consent Process - How

• Identify potential study participants based on study criteria.
• Describe the study verbally, as outlined in the approved consent, using non-technical language. An interpreter should be involved if necessary.
• Invite questions and ensure all are answered satisfactorily.
• Allow time to review the consent alone or with physician, family or friends if desired.
• Assess understanding of the major elements of the consent.
• If there is voluntarily agreement to participate, obtain signature, initials where indicated, and date from the subject.
• Consenter must also sign and date, as must the PI if there is a PI signature line on the consent form.
• Provide a copy to the subject and maintain the original in the subject’s study file.
• Complete the Consent Process Documentation form & file.
We are all responsible

• Although the regulations place the burden of responsibility on the PI, the protection of human research subjects is a shared responsibility among all research professionals involved in the conduct of the study.

• Members of a research team have a moral obligation to uphold the ethical and regulatory standards by which human subjects research is conducted.
Investigator responsibilities in involving subjects in research:

- Ultimate protector of the subject’s rights and safety
- Be personally certain that each subject is adequately informed and freely consents to participate in the investigator’s research
- Assure that every reasonable precaution is taken to reduce risk to a minimum for the subject
- The investigator is responsible for whom he delegates authority to
- Follow the protocol
What is the PI/Designee’s Role in the Consent Process?

- Obtain consent before initiating ANY study-specific procedures
- Provide a quiet, comfortable, and private setting
- Explain the consent procedures and process to the subject
- Ensure sufficient time to consider all options
- Access the subject's reading abilities, cognitive status now and throughout study
- Requires accessing subjects understanding
What is the PI/Desigee’s Role in the Consent Process?

- Ensure the subject is the one who wants to participate, free from coercion or other undue influence
- Consistent with IRB approved process
- Provide additional safeguards as required
- Provide new information promptly
- Provide a copy of the consent document and each revised consent document to the subject
- Document process and response from patient
Ways to facilitate the two way conversation and enhance understanding.

- Establish a relationship with the subject
- Provide privacy
- Assess views on research vs. standard of care
- Keep the subject in the center of the process
- Be an active listener
- Ask open-ended questions
- Be aware of non-verbal messages
- Empathize with the subject’s concerns
- Be a teacher by educating the subject and verifying his understanding of the research study
- Assure withdrawal is possible at ANY time
- Inform other options are available
- Be available anytime for any question
- Do not rush the process or the subject
Therapeutic misconception:

“the belief that the purpose of a clinical trial is to benefit the individual patient rather than to gather data for the purpose of contributing to scientific knowledge”

• The subject believes that his medical needs will determine his assignment to a treatment group or the PI will modify the protocol to serve his own medical need.

• The subject has unreasonable expectations about the likelihood of benefit from study participation. In this example the subject believes the PI will not administer treatment that might harm them, but rather, will provide interventions that only help them.
The Plan

- Identify obstacles to participation in study and ways to overcome obstacles
- Identify words subject may not understand
- Compile “Frequently Asked Question” list
- Decide who will do consent discussion
- Decide where consent discussion will be held
- Provide adequate time to explain study to subject
- Provide adequate time for subject to read and consider and for questions to be answered
Consent Process Plan

Decide who will conduct consent discussion

- Investigator may obtain consent
- Investigator may delegate responsibility to a knowledgeable person.
- Investigator is ultimately responsible for assuring informed consent has been appropriately obtained
Consent Process Plan

Decide where consent discussion will be held

- Conduct in a quiet area when possible
- Subject should have adequate uninterrupted time
- Easy access to a study doctor
- Provide space for family members or friends to be present during the consent discussion
Consent Process Plan

Provide adequate time to explain the study and study procedures to the subject

- Create a visual description when possible to foster understanding
- Use patient education tools / brochures to assist in discussion
- Explain the responsibilities of study participation
Consent Process Plan

• Provide adequate time for subject to read and consider
  - No undue influence or coercion
  - Allow subject to take consent home to discuss with families or friends

• Provide time for questions to be answered
Consent Process Plan

Use open-ended questions to assess if subject has received adequate information to make an informed decision

“How frequently will you need to come to the clinic during the study?”

“When can you decide if you want to discontinue from the study?”

“What medications must you avoid while in the study?”
Consent Process Plan

Avoid closed-ended questions

• “Do you understand?”

• “Do you have any questions?”
Documentation of Informed Consent Process (ICF)

- Check that contact information is complete on ICFs given to subject
- Provide subject with one of the copies of the signed and dated ICF
- File the original signed and dated ICF in the subject file
- Document study participation in medical records of subject
Children’s assent

To use children in research, you must first obtain the permission of the parent(s) and then obtain assent from the child.
What do Auditors/Monitors look for?

- If SOP’s exist are they followed?
- Confirm consent process documentation
- Implementation of changes only after IRB approval
- Correct version non expired consent used
- All options completed by subject
- Consent signed and dated by all parties
- Consent signed prior to ANY procedures
- Consented by trained individuals
Problems observed in the informed consent process.

- Signatures of subject and consenting person on different dates
- Consent and study procedures on same date
- Consent was performed by an untrained or unqualified care provider
- Person consenting is not listed as KSP
- Check boxes within the consent incomplete
- Crossed out sections or white out used in the IRB approved consent
- Unable to locate consent for subject on study
- Subjects not re-consented with revised consent as instructed
- Ineligible subjects enrolled
- Multiple consent documents for same patient with no explanation why
- Person consenting did not state the purpose or procedures of the study
- Consent document left on clip board for subjects to complete and return to nurse if interested
- Person consenting the subject did not sign the form
How can your department avoid deficiencies?

• Confirm all personnel consenting subjects are study personnel
• Document training and qualifications of all study personnel
• Establish one place to retrieve ONLY the latest IRB approved consent
• Conduct random audits of the consent documentation
• Review the FDA Warning Letters and *FDA IRB Information Sheets* – “A Guide to Informed Consent”
• Become familiar with the Regulations, state law, institutional and IRB Policies
FDA Warning Letter 2014

1. You failed to personally conduct or supervise the clinical investigations [21 CFR 312.60].

Specifically, for Protocol (b)(4), you failed to supervise adequately the individuals to whom you delegated study tasks. Your failure to supervise adequately the conduct of Protocol (b)(4) led to many of the violations noted in this letter. These violations include, but are not limited to, enrollment of subjects into the protocol when approval by the Columbia University Medical Center (CUMC) Institutional Review Board (IRB) had lapsed; failure to obtain informed consent from 28 of 50 enrolled subjects; and randomization and administration of investigational drug to 10 subjects before obtaining their informed consent to participate in the study.

As the clinical investigator, it was your ultimate responsibility to ensure that the studies were conducted properly and in compliance with FDA regulations in order to protect the rights, safety, and welfare of study subjects and to ensure the integrity of the study data. Your lack of supervision and oversight over Protocol (b)(4) raises significant concerns about the adequacy of your protection of study subjects enrolled at your site in the studies mentioned above and also raises data integrity concerns generated for Protocol (b)(4).
2. You failed to obtain informed consent in accordance with the provisions of 21 CFR part 50 [21 CFR 312.60 and 21 CFR 50.20].
   a) You failed to obtain informed consent from the following 28 of 50 subjects who were enrolled in Protocol (b)(4): Subjects C1, C4 through C7, C9 through C12, C17, C19, C20, C22, C26, C28, C30, C31, C33, C34, C37 through C42, C45, A3, and A5.
   b) You enrolled 10 subjects into Protocol (b)(4) and gave them investigational drug before each signed the informed consent document.
Summary

• Consent is an ethical obligation governed by federal regulation, which requires the use of current IRB approved consent forms.

• Consent must be informed and voluntary.

• Consent must be completed prior to any study-related activity.

• Documentation of the consent process (by signing the consent form) is required for most studies.

• Obtaining consent may be delegated to trained research team members, but is always the PI’s responsibility.

Consent is a Process – Not just a Form!