

Informed Consent: Federal Regulations, Institutional Policy & Good Practice

Kelly Unsworth, MS, CCRC
RSRB Specialist Board 05

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Belmont Report

“...respect for persons demands that subjects enter into the research voluntarily and with adequate information.”

- Nuremberg Code; Declaration of Helsinki
- HHS: 45 CFR 46.116 (a) 1-8 & (b) 1-6
- FDA: 21 CFR 50.25 (a) 1-8 & (b) 1-6
- ICH Guideline for Good Clinical Practice: 4.8

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Consent

- A process of information exchange that takes place between the prospective subject and the investigator, before, during and sometimes after the study
 - Written materials (consent form, letters, brochure)
 - Verbal instructions/explanations
 - Q & A
 - Periodic reaffirmation/re-consent

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Key Components

- To be ethically valid, the consent needs to be:
 - *Informed*: Contains the information needed for a reasonable person to make a decision
 - *Understood*: Provided in understandable language
 - *Voluntary*: Free from coercion
- Distinguish clinical practice from research

Required Elements

- Introduction*
- Purpose
- Description of Study Procedures
- Risks/Discomforts
- Benefits
- Alternatives to Participation
- Compensation for Injury*
- Confidentiality of Records and/or HIPAA Authorization*
- Statement re: ClinicalTrials.gov*
- Contact Persons*
- Voluntary Participation Statement*
- Statement that subjects will receive a signed copy*

* See RSRB Consent Document Templates & Investigator Guidance

Additional Elements

- Unforeseeable Risks
 - Subject; Embryo/Fetus
- Circumstances for Withdrawal (by PI)
- Consequences of Withdrawal
- Payment
- Costs
- New Findings
- Number of Subjects
- Probability of Random Assignment
- Funding
- Conflict of Interest
- Elements required by NYS (HIV, Genetic Testing)

* See RSRB Consent Document Templates & Investigator Guidance

Consent Issues In Research Involving Minors

- Combination of assent (agreement) of child and permission of the parent or legal guardian
- If either refuses, the child cannot be enrolled

Consent Issues In Research Involving Minors – Federal Requirements

- IRB shall determine that adequate provisions are made for soliciting the assent of the child
 - Age, maturity and psychological state
- IRB shall determine that adequate provisions are made for soliciting the permission of each child's parent/guardian
 - IRB may find that permission of one parent is sufficient based on risk level assigned to study

Consent Issues In Research Involving Minors – Federal Requirements

Risk Level	Definition	Consent Requirements
46.404	Research not involving greater than minimal risk	Parent permission (1 parent) & Assent of the Child
46.405	Research involving greater than minim but presenting the prospect of direct benefit to the individual subject	Parent permission (1 parent) & Assent of the Child
46.406	Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition	Parent Permission (both parents) & Assent of the Child
46.407	Research not otherwise approvable which present an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of a child...("All other research")	Parent Permission (both parents) & Assent of the Child ** FEDERAL APPROVAL

Consent Issues In Research Involving Minors – Federal Requirements

406 & 407 -

Both parents must give permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child

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Consent Issues In Research Involving Minors – UR Guidelines

- 7 and under
 - Parent Permission; No assent required
- 8-12 year olds
 - Parent Permission & Verbal Assent
- 13-17 year olds
 - Parent Permission & Written Assent

** Assent permits subjects to opt out if parent(s) opt in

* See RSRB Consent Document Templates & Investigator Guidance

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Consent Issues In Research Involving Minors – UR Guidelines

- Assent of child may not be necessary if the RSRB determines that:
 - Capability of some or all of the children is so limited that they cannot reasonably be consulted
- OR
- The intervention or procedures involved in the research holds out a prospect of direct benefit that is important to the health or well being of the children and is available only in the context of the research

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Consent Issues In Research Involving Adult Subjects with Decisional Impairment

RSRB accepts consent to research given by an authorized representative for:

- 1) Minimal risk studies
- 2) Research that poses greater than minimal risk but offers a possibility of direct benefit
- 3) Research involving slightly greater than minimal risk and offers a possibility of benefit to the class of subjects

** Appendix 1 – RSRB Investigator Guidance

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Alterations of the Consent Process

- Verbal Consent
- Information Letters
- Consent through Oral Presentation and Short Written Form
 - Non-English speaking subjects
 - Includes attestation, signature line and date for witness
- Deception Studies → consent to procedures & consent to data use

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Recruitment



Cartoonist: Don Mayne (www.researchcartoons.com)

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Recruitment

- Direct advertising considered part of the informed consent process
- Includes: websites, newspaper ads, radio ads, TV ads, flyers, brochures, telephone scripts, recruitment letters
- Must be reviewed by the RSRB
 - Coercive?
 - Imply favorable outcome?
 - Benefits beyond what is outlined in the consent & protocol?
- Initial contact from treatment team
 - No "cold calls"

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Writing Consent Documents

- Must be understandable to the subject population
- Use lay terms
- Information must be consistent with the study protocol and RSRB application
- Write as if you were talking to the subject
 - "You will be asked to..."
- Check to make sure items are in a logical order (start at the beginning; end at the end)
- Use consistent terminology throughout (drug names/abbreviations)


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Writing Consent Documents

- Use subheadings, white space, bullets to improve readability
- Use pictures, graphics, tables, lists or charts to help clarify procedures/schedules
- Use at least a 12 point font
- Aim for nothing higher than an 8th grade reading level
- Keep words to 3 syllables or less
- Don't use "etc"
- HINT: Work off of a previously approved consent for a similar study

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Consent Process



Cartoonist: Don Mayne (www.researchcartoons.com)

→ Recruitment, presentation & provision of additional information

**** THE PAPER IS NOT THE PROCESS****

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Consent Process

- Follow your protocol
 - Who, What, Where, When & How?
- Minimize undue influence, seek consent:
 - In a private setting
 - In advance of the procedure
 - With personal "advisors"
- Don't rush the process
- Consider vulnerable populations
- Use additional aides – videotapes, brochures, etc.
- Answer questions & ask open-ended questions
- Ongoing process → before, during & after

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RSRB Expectations

- University's expectations regarding the consent process are outlined in the RSRB approval letters
 - Comply with the protocol approved by the RSRB
 - Only consents bearing the RSRB watermark may be used
 - Only the most recently approved version of the consent (or recruitment document) may be used
 - Consent forms/recruitment letters must include department letterhead
 - PIs are responsible for maintaining signed consent forms for 3 years after the research is completed (or longer if required by FDA, sponsor, etc.)
- Expectations the same regardless of risk involved in the study

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Documentation of Consent

- Make sure you're using the correct document
 - Consent or Permission; Written Assent or Verbal Assent
 - Control/Experimental Consent
- Signature/Date required from the subject and the person obtaining consent
 - Generally speaking the dates should be the same. If they aren't, document why
- Anyone obtaining consent needs to be listed on the application as personnel
 - Sections 1.5-1.7 or 85.1

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Documentation of Consent

- Make sure any checkboxes are completed
- DON'T sign or date the consent for the subject
- DON'T white out, cross out or otherwise change any part of the approved consent form → Any revisions must be submitted to the RSRB as an amendment and approved prior to implementation
- Make sure to provide the subject with a signed copy of the entire consent
- Keep the original of the entire consent, not just the signature page

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Documentation of Consent

- Witnesses...
 - OHRP & FDA: only when presented orally and short form is used
 - ICH: presented orally; subject or LAR is unable to read
- Most cases – sponsors provide no guidance as to whether a witness signature line is mandatory or optional → should be in protocol
- Witness should be...
 - Someone unaffiliated with the research
 - Who cannot be unfairly influenced by people involved in the trial
 - Who attends the informed consent process & reads the informed consent document & any other written information supplied to subject

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Documentation of Consent

- Document the process (relevant sequence of actions) in the progress note/case history
 - Who?
 - What?
 - Review of study/procedures
 - Questions raised & answers given
 - Time to review document
 - Subject understanding
 - Agreement to participation
 - Where?
 - Date/Sign

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Documentation of Consent

Medical Record Entries

10/15/02 Mr. Jones, a white 36 year-old male, presented in clinic today for possible inclusion in study #RR-1672. No history of ETOH or drug abuse. Smoked 1 pack of cigarettes x 5 years, but stopped x 3 years ago. Patient states history of high blood pressure but has been controlled by medication during the past year. No history of carcinoma or pulmonary disease. Explained study protocol and reviewed informed consent form. Patient states he wants to take informed consent form home to discuss with wife. Scheduled to return tomorrow at 10:00 am.

J. Rachel, RN

10/16/02 10:00 am Mr. Jones returned today. He and Dr. Smith further discussed the 1672 study and Dr. Smith answered his questions. Mr. Jones, Dr. Smith, and I signed the ICF; Mr. Jones was given a copy.

J. Rachel, RN

Source: Mathieu, Mark P., ed. Good Clinical Practice A Question & Answer Reference Guide, May 2009. Barnett Educational Services / Chi, 2009. Print.

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Using the Current, RSRB Watermarked Consent

- Only consent the University recognizes as valid
- Each page is watermarked
- Each time the consent is amended, a new watermark is applied
- Each time the study is re-approved, a new watermark is applied

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Need for Re-consent

- Study participation is ongoing and
 - Subject reaches age 18
 - Subject regains competency
- New study information
 - Substantial Amendments
 - Changes in study procedures
 - Changes in risk
 - Changes in subject payment

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Consent Storage

Signed Consents:

- Designate a specific area for all original copies of signed consents for a study
 - Store in chronological order
 - Be consistent with how/where you store
- Link to subject number?
- Departmental custody
- Maintain for at least 3 years after complete

Approved Documents:

- Maintain a copy of all approved consent documents in regulatory file

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RSRB Review of Consent during Continuing Reviews

- Submit a copy of the consent signed by the last subject enrolled (all pages)
- If the study has more than 1 approved consent/permission/assent, submit a copy of the last signed form for **each** type of consent document
- Block out the name & signature of the subject to maintain confidentiality but not the date of consent

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RSRB Review of Consent during Continuing Reviews

SIGNATURES/DATES

I have read (or have had read to me) the contents of this consent form and have been encouraged to ask questions. I have received answers to my questions. I give my consent to participate in this study. I have received (or will receive) a signed copy of this form for my records and future reference.

Study subject: _____ PRINT NAME

Study subject: _____ SIGNATURE *4-29-08* DATE

Person Obtaining Consent

I have read this form to the subject and/or the subject has read this form. I have provided the subject with a signed copy of the form. An explanation of the research was given and questions from the subject were solicited and answered to the subject's satisfaction. In my judgment, the subject has demonstrated comprehension of the information.

Kelly Winslow Health Project Coord. PRINT NAME AND TITLE
Kelly SIGNATURE 4/29/08 DATE

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RSRB Review of Consent during Continuing Reviews

- RSRB will review the following:
 - Signatures & dates provided
 - Person obtaining consent was approved by the RSRB
 - Entire, correct version was used
 - Each page has current watermark
 - First page is on letterhead

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Mistakes Happen...



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Most Common Findings

- Incorrect Form
 - No letterhead, no watermark
 - Expired or not current form
- Study procedures prior to consent
- Consent by staff w/o research training &/or who have not been approved by RSRB
- Cross outs/Additions on consent document

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How do we fix it?

- Reportable Event via ROSS as non-compliance (type 8); Question 5.8 on Progress Report
- Call your RSRB Specialist
- Possible Fixes
 - Re-consent
 - Current version of the document
 - Person obtaining consent does not have to be the one to re-consent
 - Use current date
 - Note to File...Reporting still required
 - Exclude data

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Invalid Consent Forms

- Failure to adhere to federal regulations and University policy = failure to obtain a legally effective informed consent
- May be considered serious non-compliance under federal regulations and repeated failures may be considered continuing non-compliance
 - Reported to federal agencies

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Preventative Action Measures

- Incorporate electronic letterhead on consent forms submitted to RSRB
- Name only PI on consent heading
- Leave out witness signatures & subject initials on each page

Preventative Action Measures

- Have a process for:
 - Maintaining the current approved consent
 - store on shared network drive
 - keep a current file in the clinic
 - designate a consent “gatekeeper”
 - DESTROY OUTDATED COPIES
 - Ensuring the signature page is completed
 - Providing subjects with a signed copy

Questions?
