

• Informed Consent –

It's not just a document



Emory University, Office of
Research Compliance

Presentation Overview

- Consent = Process + Documentation
- Participants in Informed Consent Process
- Logistics of Informed Consent





Informed consent is not just a document....

Informed consent is also a
PROCESS



PROCESS + DOCUMENTATION

Informed consent is more than just a signature on a form.

Informed Consent is a process of information exchange that may include, in addition to reading and signing the informed consent document, subject recruitment materials, verbal instructions, question/answer sessions and measures of subject understanding.

Documentation that the consent process has been handled correctly is crucial.

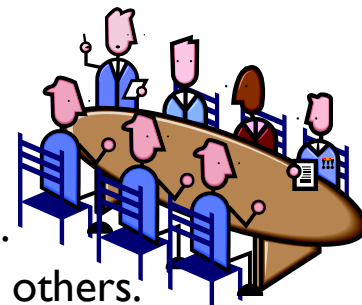
Participants in Informed Consent Process: IRB

- “Institutional Review Boards (IRBs), *clinical investigators*, and research sponsors all share responsibility for ensuring that the informed consent *process* is adequate.”
- “Rather than an endpoint, the consent document should be the basis for a meaningful exchange between the investigator and the subject.”

FDA IRB Information Sheets – “A Guide to Informed Consent”

Participants in Informed Consent: IRB

- IRB is responsible for ensuring that all elements of informed consent are covered in ICF.
- Elements:
 - Statement that study is research and purpose of study.
 - Duration of participation; description of procedures.
 - Description of reasonably foreseeable risks or discomforts.
 - Description of reasonably expected benefits to subjects or others.
 - Disclosure of alternative treatments or courses of action.
 - Description of how confidentiality of records will be maintained.
 - More than Minimal Risk – description of any compensation for injury and explanation of trtmt. available if injury occurs and person to contact if injury occurs.
 - Description of whom to contact with questions about the research or subject rights.
 - Statement that participation is voluntary; refusal to participate will not result in loss of benefits to which subject is otherwise entitled; and subject may discontinue participation at any time without penalty.
 - For FDA research – statement that FDA may inspect records.



FDA WARNING LETTER 4/14/2009 (Coast IRB)

- **The IRB failed to ensure that basic elements of informed consent are included in the IRB-approved consent form. [21 CFR §§ 50.25(a)(2), 56.109(b)].**
- “Under 21 CFR § 56.109(b), the IRB shall require that information given to subjects as part of informed consent is in accordance with 21 CFR § 50.25. One of the basic elements of informed consent, required under 21 CFR § 50.25(a)(2), is a description of any reasonably foreseeable risks or discomforts to the subject. As discussed above, Coast IRB did not have sufficient information to identify any reasonably foreseeable risks to subjects. Coast IRB did not have a complete device description or results from the preclinical and clinical testing referenced in the background section of the protocol (pp. 2-3). Under the heading "What are the possible risks or discomforts involved with being in the study?" the consent form approved by Coast IRB states, "There are no known side effects or discomforts associated with ADHESIABLOC® Gel, but there may be uncommon or previously unknown risks" (p.3). Because Coast IRB approved this consent form without having sufficient information to identify foreseeable risks to subjects, it did not meet its obligation under 21 CFR § 56.109(b) to require that the information provided to subjects as part of informed consent include a description of any foreseeable risks or discomforts.“
- <http://tiny.cc/qOaIC>

Participants in Informed Consent: Physician, Nurse, CRA



- Check study requirements to determine who needs to conduct informed consent process. Person should be trained regarding informed consent process and be knowledgeable about study.
- **EXAMPLE: ECOG Requirements:**
 - “Legally, it is the physician’s responsibility to discuss the study with the patient and obtain the written consent.”
 - “After an initial discussion it may be the physician, nurse, or CRA who provides further details to the patient.”

7.2.6 “Presenting the Consent Form to the Patient,” *ECOG Protocol Management*

- **FDA Requirements:** IRB must know who will conduct consent process. FDA does not require that the PI personally conduct the consent process, but the PI is always responsible for ensuring process is completed correctly.

Participants in Informed Consent Process: Witness

- Some consent forms may require the use of a witness, e.g. VA studies.
- Know what the purpose of witness is – witness signature vs. witness consent process.
- Example: VA requires witness to subject's signature. Witness does not have to be present for entire consent process, but must see subject sign. Witness must be impartial, i.e., not a member of the study team listed with the IRB.

Participants in Informed Consent: Translators

- Informed Consent must be presented in a language understandable to the subject. [45 CFR 46.116 & .117]
- If a non-English speaking population is expected to enroll in a study, then consent documents should be in their language.
 - Discrimination claims
- Translated form should be approved by IRB.

Participants in Informed Consent: Translators

- Use of Short Form – 45 CFR 46.117(b)(2), 21 CFR 50.27(b)(2)
 - Oral presentation of informed consent in subject's language.
 - Short form in subject's language documents oral presentation.
 - IRB must approve short form and written summary of what will be said – i.e., English version of the informed consent.
 - Must have a witness to the oral presentation; witness may be the translator.
 - Short form should be signed by subject or LAR.
 - Witness shall sign short form and copy of summary (i.e., English version of informed consent).
 - Person obtaining consent shall sign summary too.
 - Copy of summary and short form should be given to subject.
 - Translator should be qualified.

Participants in Informed Consent: Participant



Participant must be given sufficient time to consider participation in the study.

Federal Regulations:

“An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.” 45 CFR 46.116; 21 CFR 50.20.

FDA WARNING LETTER 2/2/2009 (Dr. H. Neurological Assoc. of Albany)

- FDA's regulations at 21 CFR 50.20 state that except as provided in 21 CFR 50.23 and 21 CFR 50.24, no investigator may involve a human being as a subject in research covered by the regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. The regulation specifies that an investigator shall seek such consent only under circumstances that provide the prospective subject or the subject's representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. Section 50.27 of FDA's regulations further provides that informed consent shall be documented by the use of a written consent document, which is to be signed by the subject or subject's representative only after the subject or the subject's representative is given adequate opportunity to read the document.
- <http://tiny.cc/5a9oi>

FDA WARNING LETTER 2/2/2009 (Dr. H., Neurological Assoc. of Albany)

- A. For Protocol **[(b)(4)]**, we were unable to determine from your site records if subjects gave informed consent prior to participation in the study and/or if subjects were given sufficient opportunity to consider whether or not to participate in the study. Specifically, we note that your site routinely used sign-in sheets to document the date and time of arrival of subjects.
- Based on the times recorded for appointment time, sign-in, and the commencement of protocol procedures, it does not appear possible that you obtained legally effective informed consent from the subjects in the chart below, in compliance with 21 CFR 50.20 and 50.27. This is because either 1) study-related procedures are listed as having taken place prior to the scheduled appointment time and/or prior to the time the subject signed in, or 2) based on the study records, the time between the appointment time, the time the subject signed in and/or the commencement of the procedure(s) did not provide adequate opportunity for the subjects to read the informed consent document, and to consider whether or not to participate in the study, before signing the informed consent form. For example, Subject **[(b)(6)]** was enrolled into the study on March 25, 2006. The sign in sheet notes that Subject **[(b)(6)]** arrived at your site at 9:00 a.m. However, source documents showed that study related procedures were performed prior to the subject's arrival (i.e., a blood sample was drawn at 8:50 a.m. In addition, as detailed below
- <http://tiny.cc/5a9oi>

Logistics of Informed Consent: Contents of Informed Consent Form (ICF)

- ICF should correctly document that how and when informed consent process took place.
- ICF should correctly document who was involved in the process.



Logistics of Informed Consent: Patient Signature

Informed Consent Document must be signed by:

Subject; or

Subject's Legally Authorized Representative; or

In the case of a child, the parent(s) or legal guardian of the child.

45 CFR 46.117(a) & 45 46.408(d); 21 CFR 50.27 & 50.55.

FDA Warning Letter 3/2/2009 (Dr. C., Mass. General Hosp.)

- **You failed to obtain legally effective informed consent [21 CFR part 50 and 21 CFR 312.60]**
 - “Except as provided in 21 CFR 50.23 and 21 CFR 50.24, no investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative [21 CFR 50.20]. Informed consent must be documented by the use of a written consent form approved by the institutional review board (IRB) and signed and dated by the subject or the subject's legally authorized representative at the time of consent [21 CFR 50.27(a)]. You also failed to obtain proper assent as determined to be appropriate by the IRB [21 CFR § 50.55].”
- <http://tiny.cc/5Ds8O>

FDA Warning Letter 3/2/2009 (Dr. C.)

- “Fabricated signatures of the subject's legally authorized representative were found on the consent forms for subjects 114403 and 114601, who were enrolled in protocol [(b)(4)], and subject 124402, who was enrolled in protocol [(b)(4)]. We note that you discovered the fabricated signatures through your own internal audit, and that you sent letters dated September 10, 2007 to the parents of subjects 114403 and 114601, and a letter dated December 11, 2007 to the representatives of subject 124402, requesting that the informed consent documents be signed again. In addition, you promptly reported the findings to the IRB. In your May 22, 2008 response to the Form FDA 483, you stated that you asked the study coordinator to ensure that copies of the original, signed consent forms were placed in the subjects' medical records, according to institutional policy, but you did not confirm this action. You stated that had this occurred, you would have been able to retrieve a copy of the original consent forms. You stated that it is presumed that your former research nurse (study coordinator) apparently falsified the signatures after she lost the original, signed consent forms. You also stated that you reported these findings to the Board of Registration in Nursing. As the clinical investigator, you are responsible for oversight of study activities delegated to study staff.” <http://tiny.cc/5Ds8O>

Logistics of Informed Consent: Legally Authorized Representatives

- LAR = Individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to subject's participation in research.
 - 45 CFR 46.402.

Informed Consent Logistics: LAR

- Must consider applicable state law.
- Ga. Law. –
 - Research that involved medical treatment vs. research that does not involve medical treatment.
 - Look at whether research involves “lawful surgical or medical treatment which may be recommended, prescribed or directed by a duly licensed physician.”

Informed Consent Logistics: LAR

- Research involving medical treatment:
 - Is the person an adult or minor?
 - If minor, is minor emancipated, or does research involve type of procedure to which minor can consent.
 - For example:
- **Research Involving Medical Treatment for *Pregnancy, Childbirth, Pregnancy Prevention***
- **Research Involving Treatment for *Drug Abuse or Certain Venereal Disease***

Informed Consent Logistics: LAR

- Research involving medical treatment:
 - If adult, look at whether person is of sound mind and body; is conscious, mentally unimpaired and physically able to read and/or hear and understand; and has not been declared to be legally incompetent.
 - If adult does not meet requirements above, then the following persons can consent:
 - Another adult, per legal document, e.g., advanced directive.
 - Adult child for parent.
 - Parent for adult child.
 - Adult for his/her brother/sister.
 - Grandparent for grandchild.

Informed Consent Logistics: LAR

- Research does not involve medical treatment, then:
 - If adult cannot consent for himself/herself, another adult may consent if he/she has been legally delegated authority to do so by appropriate legal document, e.g. , power of attorney.

Logistics of Informed Consent: Subjects Who Cannot Read

- Person obtaining consent should read aloud entire consent document to subject.
- Document that subject cannot read.
- Provide adequate time to discuss and answer questions.
- Impartial person (person not on study team) should witness consent process and document that process took place; subject understands research and consent process; and subject consented to participant.
- For persons who cannot write, “making their mark” is sufficient.

Logistics of Informed Consent:

Date

- OHRP – Signatures not required to be dated, but it is advisable to get date to show consent was signed prior to participation.
- FDA:
 - “In addition to signing the consent, the **subject** should enter the **date** of signature on the consent document, to permit verification that consent was actually obtained before the subject began participation in the study.”
 - “If consent is obtained the same day that the subject's involvement in the study begins, the subject's medical records/case report form **should document that consent was obtained prior to participation in the research.**”



FDA IRB Information Sheets – “A Guide to Informed Consent”

Logistics of Informed Consent: Date

- ***Neither the PI nor the Research Coordinator should enter a “date” for the subject’s signature. Only the subject or the subject’s legal representative should enter a date for the subject’s or representative’s signature.***

See FDA IRB Information Sheet, A Guide to Informed Consent

FDA Warning Letter 4/9/2009 (Dr. B., Snellville, GA)

- **You failed to maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual [21 CFR 312.62(b)].**
 - “For subjects 8202, 8203, and 8205, the dates next to the subjects' signatures on the consent forms were initially dated 6/8/06 and then changed to 6/15/06. For subject 8202, the date was then revised back to 6/8/06 and multiple date changes were made to most of the pages in the Screening Visit Source Documents for these subjects. No documentation was provided to explain these changes.”
- **You failed to obtain informed consent in accordance with the provisions of 21 CFR Part 50 [21 CFR 312.60 and 21 CFR 50].**
 - “**Subject 8210 was randomized to protocol [(b)(4)] on June 12, 2006.** You did not obtain informed consent from this subject until June 26, 2006.”
- <http://tiny.cc/ZTRvP>

FDA WARNING LETTER 3/2/2009 (Dr. C., Massachusetts General Hosp.)

- **You failed to obtain legally effective informed consent [21 CFR part 50 and 21 CFR 312.60].**
 - “Informed consent documents were dated by study personnel rather than the legally authorized representative for subjects 114302, 114401, and 114504 enrolled in protocol [(b)(4)], and subject 124601 enrolled in protocol [(b)(4)]. In your May 22, 2008 response to the Form FDA 483, you acknowledged that it was your routine practice to insert the date yourself, prior to the parents’ signatures, in order to simplify the process. You stated that you now know that subjects and parents must date the consent forms themselves. We acknowledge your assurance that corrective actions have been taken to ensure that this finding is not repeated in any future studies.”

Informed Consent Logistics: Copy of Consent

- “A copy of the consent document must be provided to the subject and the original signed consent document should be retained in the study records.”
- “Note that the FDA regulations do not require the subject's copy to be a signed copy, although a photocopy with signature(s) is preferred.”

FDA IRB Information Sheets – “A Guide to Informed Consent”



Informed Consent Logistics: Copy of Consent

- It is a federal requirement that the patient be given a copy of the signed consent form.
- **21 CFR 50.27 Documentation of informed consent.**
- **“(a) Except as provided in 56.109(c) informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. At the time of consent. A copy shall be given to the person signing the form.”**

Informed Consent Logistics: Copy of Consent

- Emory IRB Policy and *Emory Guidelines for the Responsible Conduct of Research and Scholarship* (<http://policies.emory.edu/7.9>) require a copy of the informed consent to be placed in patient's medical record unless IRB determines otherwise.

Informed Consent: Source Documentation

- Informed Consent Form + Source Documentation of Consent Process = No Audit Findings
 - Remember to include in research and/or medical record a contemporaneous note describing consent process and statement that subject received a copy of the signed consent.

Consent v. HIPAA Authorization

- Informed consent document may or may not have all elements necessary for HIPAA Authorization.
- If HIPAA Authorization is to be included in informed consent form, remember to check to make sure that all Authorization Elements are included.

HIPAA Authorization Elements

- Must be in writing unless otherwise approved by IRB.
- Must be signed by the patient or patient's personal representative and dated.
- Must state what PHI will be used or disclosed and purposes of use/disclosure.
- Must state who may disclose PHI and to whom it may be disclosed.
- Must state that if PHI is re-disclosed it may not be subject to HIPAA.
- Must have an expiration date or event, or state that there is "none" because it is for research.

References

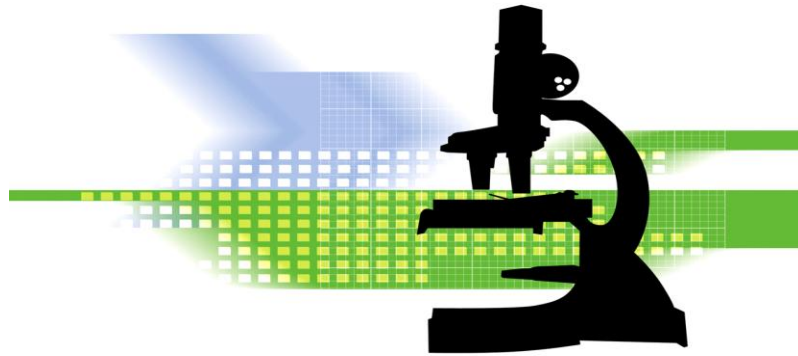
- Common Rule – 45 CFR Part 46
- FDA -- 45 CFR Parts 50 and 56
- Office of Human Research Protections (OHRP) Guidance --
<http://www.hhs.gov/ohrp/policy/index.html>
- FDA Guidance --
<http://www.fda.gov/cder/about/smallbiz/humans.htm> (Guidance for IRBs) and
<http://www.fda.gov/oc/gcp/default.htm> (Guidance on GCP)
- IRB P&Ps <http://tiny.cc/TEJAd> . #41- 46 and 48 – 53.

On more thing ...

- ... On a completely different subject.

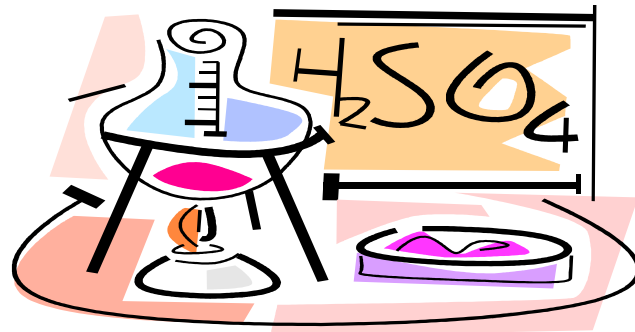
Research Integrity

- Responsibly conducting research.



Research Integrity

- Ensuring accuracy and integrity of data collected from research.
- Process for review of allegations of fraud, falsification or plagiarism.
- Process for review of allegations of violations of other research related regulations.



Terms to Know

- **Fabrication** is making up data or results and recording or reporting them.
- **Falsification** is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- **Plagiarism** is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.
- Emory's Policy on Research Misconduct (Policy 7.8):
 - Allegations of fraud, falsification or plagiarism – reviewed under process for Matters Involving Allegations of Research Misconduct
 - Allegation of violating other research related policies or rules – reviewed under process for Matters involving Other Allegations

Emory's Policy on Research Misconduct

Responsibility to Report Research Misconduct or Regulation/Policy Violations: immediately report any observed or suspected Research Misconduct or Regulation/Policy Violation to your supervisor, the chair or chief administrator of their department, the dean/director of your unit, or directly to the RIO. If an allegation is initially reported to any one other than the RIO, then that person, in turn, should report the allegation to the RIO. Similarly, if the RIO initially receives a report, then s/he should notify the appropriate Administrative Official and any other appropriate administrators and/or University committees or units that may have jurisdiction over the issue.

Policy 7.8 <http://policies.emory.edu/7.8>



Emory's Code of Business Ethics and Conduct Policy

...is to ensure that employees operate in accordance with all applicable U.S. laws and regulations in carrying out all of their job responsibilities, and any responsibilities they have in connection with Federal Research/Contract Activities.

- Adhere to ethical principles
- Follow policies
- Report suspected violations
- Prohibits retaliation

Policy 7.20 <http://policies.emory.edu/7.20>

Research Misconduct Process

- Initial Review by RIO
- Administrative Official
- Inquiry
- Investigation
- Appeal
- Reporting to federal agencies, journals and others.

To establish research misconduct ...

- It must be shown by a preponderance of evidence that:
 - Fraud, falsification or plagiarism occurred.
 - It was committed intentionally, knowingly or recklessly.
 - It was a significant departure from accepted practices of the research community.
 - It did not result from honest error or a difference of opinion.



Questions or Concerns

- If unsure whether or not a particular incident or practice constitutes research misconduct or a regulation/policy violation, you may call the Research Integrity Officer (RIO) to discuss the matter confidentially and obtain guidance.
- Kris West, JD
Research Integrity Officer
Office of Research Compliance
Phone: 404-727-2398
Email: kwest02@emory.edu
- Alternatively, reports or questions may be made anonymously by dialing the Trust Line. More information on the next slide about the Trust Line.

Emory University Trust Line

- Anonymous reports can be made to the Emory University Trust Line at:
 - 1-888-550-8850
- The Trust Line is operated by an independent third party who will maintain the caller's anonymity, while ensuring that the caller's report is routed to the proper individuals within the University.



Questions

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