Protection of Human Subjects (ICF)

21 CFR 50 and 45 CFR 46

Requirements of: Informed Consent

45 CFR.46
21CFR Part 50

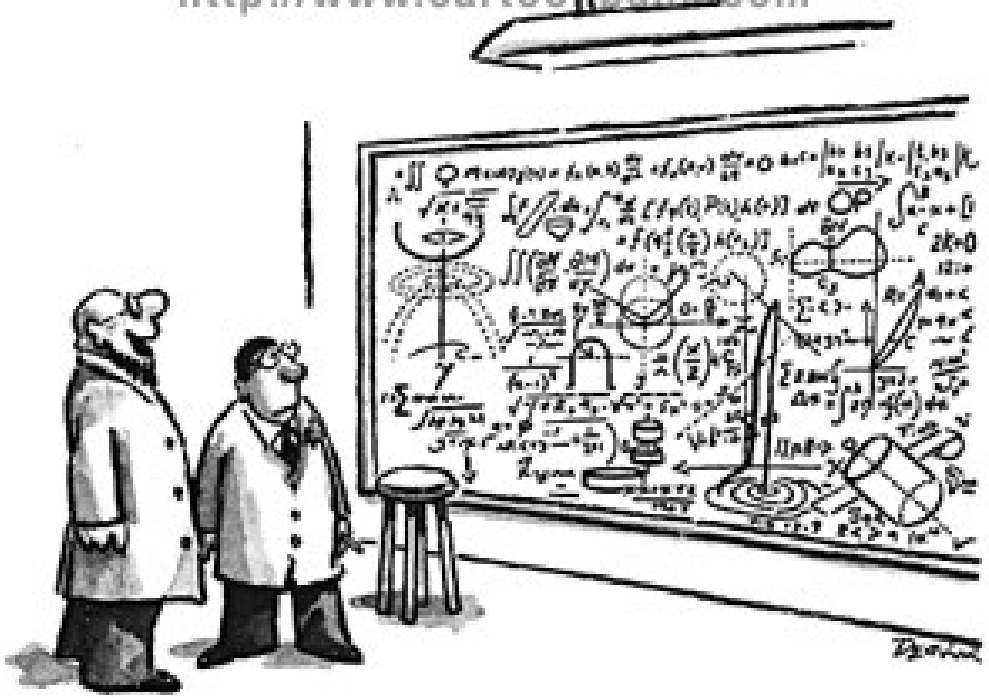
An investigator must obtain (45 CFR.46) the legally effective informed consent of the subject or the subject's legally authorized representative

Consent Process involves:

- giving a subject adequate information concerning the study
- providing adequate opportunity for the subject to consider all options
- responding to the subject's questions
- ensuring that the subject has comprehended this information
- obtaining the subject's voluntary agreement to participate
- continuing to provide information as the subject or situation requires

This is challenging in the acute treatment window

Reading Consents



"Hey, no problem!"

Informed Consent: Christine Grady, Department of Bioethics, NIH Clinical Center

Average Reading Time

of words in ICF

CAPTIVA~8,149

SleepSMART~6,436

SATURN~5,834

FASTEST~4,198

SISTER ~6,078

Table #2: Minutes to read a consent form

Consent Form Length (Words)	Very Slow Reading Speed (100 words/min)	Average Reading Speed (200 - 250 words/ min)	Fast Reading Speed (300 words/ min)
2,000	20 minutes	8 - 10 minutes	7 minutes
3,000	30	12 - 15	10
4,000	40	16 - 20	13
5,000	50	20 - 25	17
6,000	60	24 - 30	20
7,000	70	28 - 35	23
8,000	80	32 - 40	27
9,000	90	36 - 45	30
10,000	100	40 - 50	33
11,000	110	44 - 55	37
12,000	120	48 - 60	40

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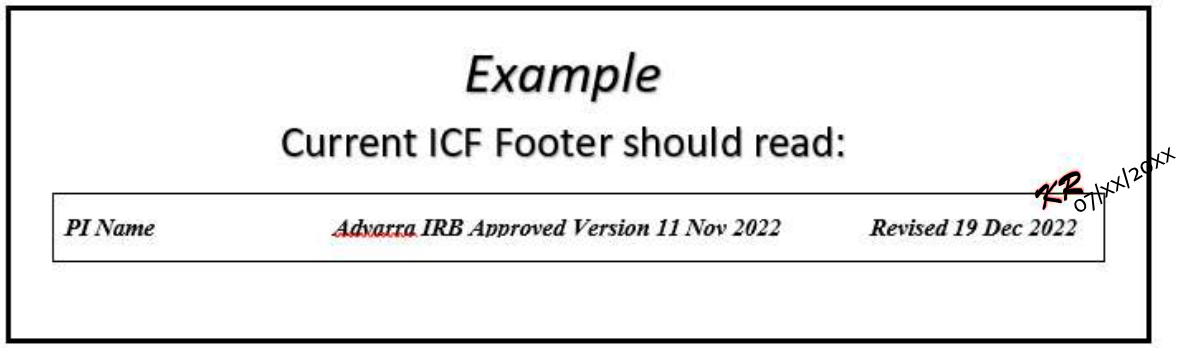
Informed Consent: Christine Grady, Department of Bioethics, NIH Clinical Center

Are you using the correct version of the ICF?

- Informed consents are often revised over the course of a study
- Consenting on the wrong version of the ICF is an FDA audit finding
- How do you prevent this?
  - Use eCONSENT (version is managed centrally)
  - Verify you are using the correct version at time of use

When using a paper ICF the study team personnel should verify the version in hand is correct. (eg. thru central file verification, ClinOne app, etc).

Best Practice Idea: After confirming you are using the correct version of the ICF, initial the date stamp information, to demonstrate this was verified prior to consent.



Informed Consent – Witness

Must a witness observe the entire consent interview or only the signature of the subject?

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FDA does not require the signature of a witness when the subject reads and is capable of understanding the consent document, as outlined in 21 CFR 50.27(b)(1). The intended purpose is to have the witness present during the entire consent interview and to attest to the accuracy of the presentation and the apparent understanding of the subject. If the intent of the regulation were only to attest to the validity of the subject's signature, witnessing would also be required when the subject reads the consent.

21 CFR Part 50

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/institutional-review-boards-frequently-asked-questions#GeneralQuestions
Guidance for Institutional Review Boards and Clinical Investigators (1998 Update)

Informed Consent – Witness

- Attests to the fact informed consent was provided, not that the signature belongs to the subject.
- In the prevention setting where the ICF is often read independently by the subject, or in the hospital setting where you leave the consent for the patient to read, and then you return later to answer questions, a witness is NOT needed
- If the ICF is read to them because they are illiterate, or visually impaired, or physically unable to sign due to limb impairment, a witness is needed.
- A witness needs to be a impartial bystander. Members of the research team do NOT qualify as impartial.

Informed Consent – Witness

How do I know if I need a witness?

Ask yourself: Can the participant/LAR **read** and **sign** the ICD?

Yes – no witness needed

No – witness needed

Reasons a participant/LAR can not read or sign the ICD:

1. They are non-English speaking therefore can not read an English ICD
2. They are illiterate therefore can not read or sign the ICD
3. They are visually impaired therefore can not read the ICD
4. They are physically unable to sign the consent form

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Informed Consent – Witness

Who can be my witness?

- **Impartial Witness** - A person who is independent of the trial, cannot be unduly influenced by the people involved with the trial, who is present during the entire informed consent process and who attests to the adequacy of the consent process and to the participant's/LAR's voluntary consent.
- A **non-research staff member** or the **participant's adult relative** if there is no reasonable concern that the proposed witness is not acting in the best interest of the individual.
  - Sites may have different policy on who can be a witness. Sites should follow any local policy.

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Regaining Capacity to Consent

Initial consent by LAR/surrogate

Consenting is an ongoing process:

- For patients where consent was initially given by an LAR/surrogate, the patient's capacity to provide consent should be assessed at every visit.
- A subject who regains the cognitive ability to consent must be reconsented using standard consenting procedures.

Informed Consent – Documentation

Reminders and Tips

- **DATE**
  - **DO NOT** fill in the dates for subject/LAR/witness.
  - **MUST BE** in same handwriting as signature line
- **DO NOT** leave any lines unaddressed (strike through or write N/A)
- **TIME** (if present on ICF)
  - Ensure consent obtained **PRIOR** to research procedures
- **RECONSENT** – Once a subject regains capacity
- **Medical Record**: Document the consent process in your study note and place a copy of the signed ICF in the patient's medical record.

Best Practices:

- Instead of paper, obtain consent using the REDCap eConsent provided by the study
- If a LAR is used at enrollment, evaluate a patient's capacity to consent daily while hospitalized and at each visit post-discharge; document the outcome of the evaluation in the medical record.

Informed Consent

REMINDER

ALL consents (100%) will be reviewed in:

- Sponsor audits
- IRB audits
- Compliance audits
- OHRP audits
- FDA audits

GET IT RIGHT!!