Informed Consent Approaches In Human Subjects Research

UMSON Sept 2024 Monthly Research Seminar

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Disclaimer

Opinions are my own. I am not representing any regulatory agency, company, or institution.

No financial or other conflicts of interest to disclose.

Objectives

- Sharpen operational understanding of various consent approaches in human subject research (HSR)
- Learn compliance considerations to apply depending on the IRB approved approach to consent
- Increase awareness of pitfalls to avoid with eConsent and low participant engagement

Note! I will not be discussing IRB decision making around these types of consent, only the approaches themselves and compliance considerations for said approaches.

Why is there a consent process in HSR?

- Belmont Report
  - Research vs. Standard of Care
  - Ethics
    - Respect for persons (informed consent)
    - Beneficence (risk vs benefit)
    - Justice (participant selection)
- Establish trust, promote public trust
- Participant buy-in, scientific contribution
- Reduce "lost-to-follow-up”
- Federal law, 45CFR46 subpart A (Common Rule)
- International guidance, ICH GCP

Consent Process

- From pre-enrollment through the end of the study
- Includes discussion, assessment of comprehension, timely disclosure of new information, etc.
- Investigator should always document the process
- Documented participant agreement when necessary

Consent Approaches Can Vary

Consent is defined by HHS/Common Rule

-application of definition is site/IRB/local law specific

All consenting methods/approaches must:

- be IRB approved
- include a process
- have verifiable documentation that the consent process occurred

Full Consent Form w/ Signature (Participant/LAR; PI/Designee)

Applies to:

- GTMR and MR non-exempt research

Appearance:

- Multiple pages; can be electronic or paper format
- Signature line for participant, PI/designee, witness/Legally Authorized Representative (LAR)- where/when applicable

Considerations:

- Lay language (3rd- 8th grade level); cultural sensitivity; avoid information overload; may require institutional templates; state specific laws around who must sign; etc.
- Assurance of understanding,
- Documentation of consent process
- Make a copy of the consent available to the participant

Examples:

- Phase 1 oncology treatment study
- Implantable device study

Consent with LAR Signature

Applies to:

- GTMR and MR non-exempt research with disabled/cognitively impaired participants

Appearance:

- LAR signature line prompt on consent document

Considerations:

- Assurance of understanding,
- LAR depends on institution/state laws
- Documentation of consent process
- Make a copy of the consent available to the participant/LAR

Examples:

- Dementia research
- Shock Trauma research

Assent with Participant Signature

Applies to:

- Children (Pediatric research)
- Cognitively impaired (any human subjects research)

Appearance:

- Short, simple language
- Signature line
- Accompanies "full form consent" to be signed by LAR

Considerations:

- Age-appropriate language, cultural sensitivity, avoid patronizing, etc.

Examples:

- Pediatric oncology research
- TBI study at shock trauma

Short Form Consent with Participant Signature

Applies to **non-targeted populations** who may be:

- Illiterate/visually disabled
- Non-native speaking

Appearance:

- Short (generic summary) that accompanies the "full consent form"
- Signature (PI/designee, participant, LAR and/or witness)

Considerations:

- Still requires IRB approval
- Participant should NOT sign the full consent form
- Translator/LAR/Witness (as appropriate)

Example:

- Unexpectedly encounter a non-native speaking person who may qualify for a study
- Unexpectedly encounter an illiterate person who may qualify for a study

Waiver of Documentation of Consent

Applies to:

- Studies where the consent is the only documentation of participant identifiers, and the major risk is a breach of confidentiality
- Minimal risk studies whose activities only involve procedures that do not require written permission

Appearance:

- IRB approved consent form/information sheet/script
- No signature line for participant, HOWEVER, PI must document that the consent process occurred!

Considerations:

- Still need to make copy of the consent form available to participant

Examples:

- Sexual practice research in small towns
- Abortion care research in states with strict abortion laws

Note! waiver of documentation of consent is NOT electronic consent!

Consent in MR Exempt Research

Applies to:

- Minimal Risk Exempt studies (studies that meet one of the DHHS common rule exemption criteria)

Appearance:

- Short, typically 1 page
- No signature required

Considerations:

- Include certain elements of consent
- Study documentation of consent process still required

Examples:

- Survey study of adults (no children or reputationally sensitive topics)
- Educational research

Waiver of Consent (No Consent)

Applies to:

- studies involving no more than minimal risk to participants **AND**
- could not practicably be carried out without the requested waiver **AND**
- will not adversely affect the rights and welfare of the subjects

Appearance:

- Guess!

Considerations:

- May be partial waiver, so a form must be approved for future use

Examples:

- Shock trauma
- Certain chart review studies

Note! Waiver of consent ≠ waiver of documentation of consent!

Electronic Consent (eConsent)

Applies to:

- GTMR and MR non-exempt research

Considerations:

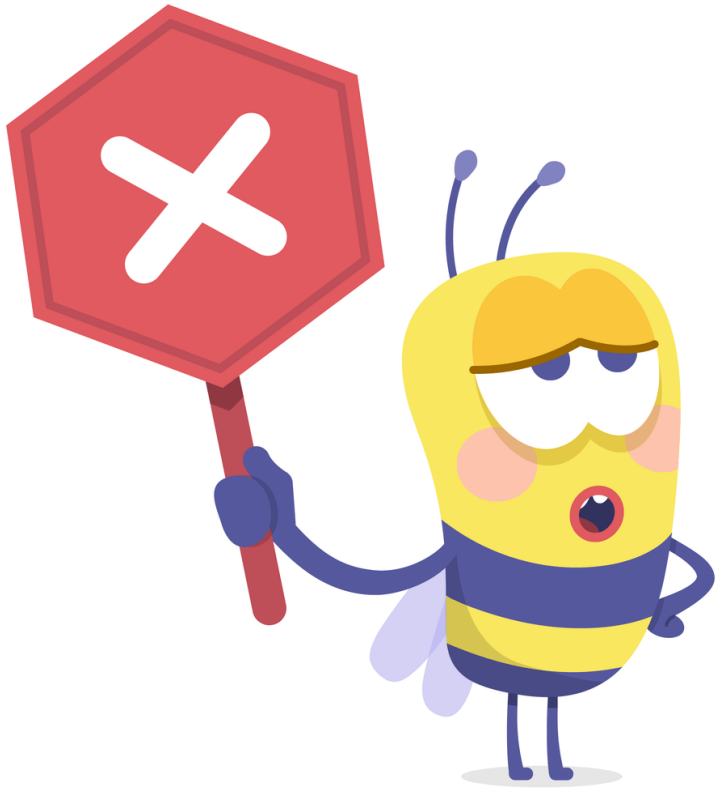
- Platform for obtaining electronic signature must be approved by Sponsor/Institution; capable of providing a verified alternative to wet signature
- Plan involving eConsent must be approved by IRB
- Participant should be able to easily navigate back and forth, take their time
- Consent process documented
- Copy of consent needs to be given

Appearance:

- Varies

Examples:

- Phase 1 oncology treatment study
- Implantable device study



eConsent- what is it not?

- A waiver of documentation of consent (not verbal!)
- Meant for exempt research
- A replacement for the consent process
- A replacement for a study team member

Electronic Signature- what is it?

An electronic alternative to a hand-written wet ink signature

Definition varies according to jurisdiction:

- "OHRP permits electronic signatures if such signatures are legally valid within the jurisdiction where the research is to be conducted." **-DHHS** Q&A

- "IRBs, investigators, and sponsors should consider…how the electronic signature is created… [They] may rely on a statement from the vendor of the electronic system used for obtaining the electronic signature that describes how the signature is created and that the system meets the relevant requirements contained in 21 CFR part 11" **-FDA/DHHS** Q&A

eConsent Considerations

- Regs and Policies
  - Policies (site, sponsor, CRO, etc.)
  - FDA Regs 21CFR11
  - DHHS Regs (45 CFR §46.117 (a))

§ 46.117 Documentation of informed consent.

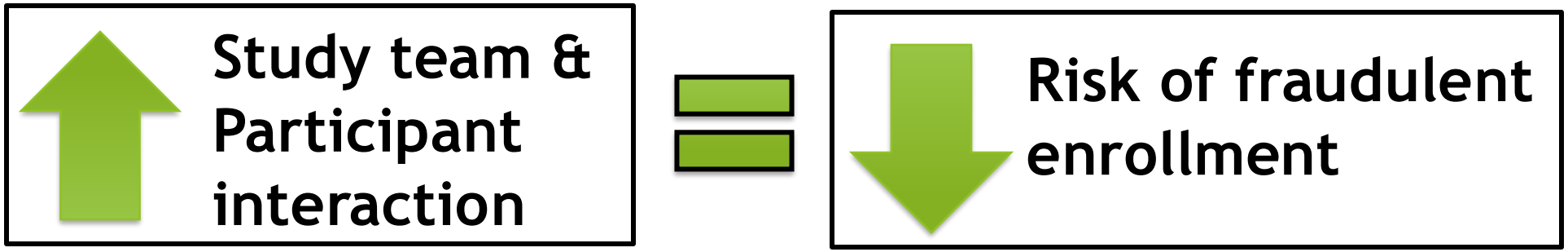
(a) Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written informed consent form approved by the IRB and signed (including in an electronic format) by the subject or the subject's legally authorized representative. A written copy shall be given to the person signing the informed consent form.

- Delivery
- Reporting/Validation
- Logs/Monitoring
- Documentation/Recording/Storage/Retention

eConsent

When to use it	When NOT to use it
Paper option is not feasible	Participant pool has limited electronic resources/skill
Its use is justified	In lieu of low resources
It does not diminish consent process	Without IRB review
It improves consent process	Study has high risk for fraudulent enrollment

eConsent and Recruitment Plan Considerations



- eConsent + incentives + social media recruitment + low interaction= very risky
- How are you assessing eligibility? What is your monitoring plan?
- Quality by design is essential here

Fraudulent Enrollment Example

Threats of Bots and Other Bad Actors to Data Quality Following Research Participant Recruitment Through Social Media: Cross-Sectional Questionnaire

Rachel Pozzar [1]; Marilyn J Hammer [1]; Meghan Underhill-Blazey [1,2]; Alexi A Wright [3]; James A Tulsky [4]; Fangxin Hong [5]; Daniel A Gundersen [6]; Donna L Berry [1,7]

271 surveys completed in 7 hours:

- 94.5 % of responses fraudulent
- 86.7% of responses inconsistently verified
- 16.2% bot automated

https://www.jmir.org/2020/10/e23021/

eConsent does NOT remove eligibility assessment

Conclusion

- Many approaches to informed consent,
  - all of which require:
    - IRB approval
    - Documentation of the process
  - all of which must consider:
    - Verifiability of the participant
    - Participant provision of consent form
    - Intended audience

Remember! If it wasn’t documented, it didn’t happen!

References

- Belmont Report https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html
- 2018 Common Rule https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html
- ICH GCP https://ichgcp.net/4-investigator
- Fraudulent Research Example https://www.jmir.org/2020/10/e23021/
- UT Research Study Flier (slide 22) https://utk.co1.qualtrics.com/jfe/form/SV_6WJRcBNtBeh6yr3?Q_CHL=qr
- Standford Research Study Flier (slide 22) https://med.stanford.edu/rodriguezlab/research/suicide.html
- OHRP Webinar on e-Consent https://www.umaryland.edu/hrp/for-researchers/ohrp-econsent.php
- DHHS Regulations: (45 CFR § 46.117): https://www.law.cornell.edu/cfr/text/45/46.117
- FDA Regulations (21 CFR § 11): https://www.fda.gov/regulatory-information/search-fda-guidance-documents/part-11-electronic-records-electronic-signatures-scope-and-application

Questions?

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