Re-consent and Subject Notification: Expectations and Flexibilities for Complying with the Common Rule

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Background

“Legally Effective Informed Consent”

- Applies to non-exempt research unless the IRB finds and documents that informed consent can be waived (45 CFR 46.116(f)(1-3))
- Obtained from the subject or the subject’s legally authorized representative in a manner that is consistent with the “Common Rule” in the HHS Protection of Human Subjects Regulations (45 CFR 46.116) and applicable laws of the jurisdiction in which the research is conducted
- Must be sought prospectively
- Conducted only under circumstances that provide the prospective subject sufficient opportunity to consider whether to participate and that minimize the possibility of coercion or undue influence

“Legally Effective Informed Consent”, cont.

- Information is provided in a language that is understandable to the subject
- Cannot include language requiring (or implying) that the subject waive any legal rights
- Usually involves a written consent form
  - Provides extensive and key information as part of the decision-making process and for future reference
  - Proof of the involvement of the subject and the investigator in the consent process
- Documented (i.e., obtaining a signature), as required under HHS regulations at 45 CFR 46.117 and the FDA regulations at 21 CFR part 50
- Note: Obtaining a signed consent form alone does not mean that the consent process was adequate nor does it mean that the consent process is complete

The Informed Consent Process

- Involves three key features:

  (1) disclosure of all the information needed to help potential subjects make an informed decision about participating in the research;

  (2) facilitating the understanding of that information; and

  (3) promoting the voluntariness of their decision to participate or not

- An ongoing exchange of information between the investigator and the subject (or legally authorized representative) throughout a study
  - Subjects should be provided with an opportunity to have their questions and concerns addressed
  - Include the provision of new information as it becomes available and until the subject's participation is complete

Re-Consent

Meaning of the Term “Re-Consent”

- Request for authorization or agreement from an existing subject to continue to participate in an IRB-approved research study
  - This term does not apply to consenting **past** subjects to a new protocol, e.g., secondary research
- Most often re-consent is used to communicate changes to the study or new findings that relate to the research
- In most cases, the investigator actively obtains confirmation from the subject to continue in the research, i.e., either by obtaining a written signature or a verbal affirmation
- Could result in a subject deciding to withdraw from the research

Concept of Re-Consent in the Regulations

- The concept of “re-consent” is not described or defined in the regulations
- The regulations also do not:
  - address all the circumstances that might require repeating or supplementing information previously provided as part of the informed consent process
  - designate a threshold for the significance of the information that should be shared
  - describe mechanisms for how new information should be provided

Concept of Re-Consent in the Regulations, cont.

- The “Common Rule” does require that potential subjects be provided with “significant new findings developed during the course of the research *which may relate to the subject’s willingness to continue participation*” (45 CFR 46.115(a)(7))
  - This requirement does not explicitly address asking subjects to review new information about the study and re-affirm their willingness to continue their participation
- If the protocol design, risks, etc. have changed, it is necessary to ensure that the subjects still wish to participate in the research in order to ensure that their consent remains legally effective

Reasons to Re-Consent Subjects

- Information about new research-related risks or potential benefits becomes available, including a change to the risk/benefit ratio
- Increase in the frequency or magnitude of previously described risks
- Decrease in expected benefits to participation (e.g., related to the efficacy of the investigational therapy)
  - This might also lead to termination of the study.
- Information about an unanticipated problem that exposes subjects to new risks

Reasons to Re-Consent Subjects, cont.

- Availability of new alternative therapies
- New information about the effect of participation on future use of alternative therapies (e.g., investigational agent reduces effectiveness of alternatives or precludes future treatment with standard of care therapy)
- New procedures or other changes to the research design that may increase burden/discomfort
- New research activities that may require prospective consent (e.g., whole genome sequencing or whole exome sequencing)
- Increasing the frequency of visits, adding more required visits, or extending follow up
- Errors or deficiencies in the information included in the original consent

Additional Reasons for Re-Consent

- A substantial period of time has elapsed between the time consent was first obtained and the first study visit
  - For example, the subject may no longer be interested in participating; may no longer meet the eligibility criteria; may no longer find the risks acceptable; or may no longer have the time to complete all the required procedures.

- A subject has not participated in a study visit in a long time, or the study takes place over many years or is particularly complex
  - Periodic repetition of the consent process or affirmation of consent should be considered

Subject Notification/ Provision of New Information

Meaning of the Term “Subject Notification”

- Only applicable to existing enrolled subjects on the research study
- Typically used when the information being shared *does not change* what is expected of the subject or the research plan
- Does not require the subject to agree to anything nor would the information affect their decision to continue in the research
  - No response, acknowledgement or signature required

Reasons for a Subject Notification

- Subjects should be notified that:
  - The PI has changed
  - The study coordinator/other contact has changed or has new contact info
  - The study is being put on hold or will be ending early, i.e., study visits will conclude
  - Certain events have occurred, e.g., a loss of specimens or data, or a breach of subjects' PII

- Subjects might be notified about:
  - The results of the research

Re-Consent vs. Subject Notification

Is Re-Consent More Appropriate?

- Does the information include new or increased risks associated with the procedures or the intervention?
- Does the information include changes to the study design, procedures, or intervention, that increase duration or other burdens to subjects?
- Does the new information represent a change to the content in the signed consent form, and directly affect the rights or protections provided to subjects?
- Does the subject need to agree to the information that is being shared in order to continue in the study?

IF THE ANSWER IS YES TO ANY OF THE QUESTIONS ABOVE, RE-CONSENT IS LIKELY MORE APPROPRIATE.

Is Subject Notification More Appropriate?

- Does the information represent a change of the PI or other staff, or their contact information, listed in the consent form?
- Is a study ending earlier than planned (for reasons other than a change in risk to subjects)?
- Is subjects' involvement in the research complete?
- Does the investigator wish to share preliminary findings of the research with subjects?

IF THE ANSWER IS YES TO ANY OF THE QUESTIONS ABOVE, SUBJECT NOTIFICATION IS LIKELY MORE APPROPRIATE.

Plans for Re-Consent or Subject Notification

Developing a Plan

- When deciding how to re-consent and/or notify subjects about new information, the investigator should take into account:
  - The nature of the study (type of study, Natural History vs. Interventional Study, types of procedures, etc.)
  - The nature and urgency of the new information
  - The appropriate timeline for re-consent or notification
    - For example, if urgent, subjects may need to be called initially, with a follow up re-consent process at the next visit
  - The status of subjects who will be contacted, e.g., in screening phase, receiving an intervention/procedures, long term-follow-up, etc.

Developing a Plan, cont.

Remember: The delivery of new information should provide subjects with an opportunity to exercise their right to continue their participation or withdraw from the study

Mechanisms for Re-consent

- Repeat the informed consent process using **a revised long form consent** with subject signature
- Present new information using **a consent addendum** to the original consent document with subject signature or using **an information sheet**
  - The expectation is this would also involve a discussion with a subject.
- Orally communicate the new information using **a verbal script** (communicated either face-to-face, over the telephone or via video-conferencing)
- Use of **a revised web-based consent form** (usually applicable when the original IRB-approved consent process was web-based)
- *All should include documenting the re-consent process in the subject's medical record/research record*

Considerations When Picking the Mechanism for Re-Consent

- Number of changes to the study/consent form
- Length or complexity of the information that must be shared
- Number of subjects affected by the changes
- Whether the change is major or minor
- Whether the change affects the risk/benefit ratio
- Status of the research

When Re-Consent with the Revised Long Form May Be Best....

- When changes are more numerous, lengthy, complex, constitute major vs. minor changes, affect the risk/benefit ratio, **and/or** affect many or all subjects
- If the changes may affect a subject's understanding of the study or may affect a subject's willingness to continue to participate
- The process should almost always involve a verbal conversation

Mechanisms for Notifying Subjects about New Information

- Mailing an information letter which addresses the new information to the subject's home
- All of the mechanisms, which may be used for re-consent, could also be used for a subject notification

Consent Addendum*/Information Sheet

- Should only be used for subjects who have already signed the original consent form and are enrolled in the IRB-reviewed study
- When just a subset of subjects need to be informed of new findings that may impact their willingness to continue in the study
- When just a subset of subjects need to be informed of specific minor changes, e.g., a change in a planned procedure, or when follow up will be extended

*See the **NIH Consent Addendum Template** in the **Additional Resources** section of this presentation

Consent Addendum/Information Sheet

- Should be used to facilitate discussion with subjects since the changes/new findings are the focus of the document
- A consent addendum involves capturing a signature while an information sheet would not
  - If the information sheet is used, the investigator should be sure to document the communication in the subject's medical record/research record
- If the research team has a question about the appropriateness of a consent addendum, please contact the IRBO

Verbal Script

- A verbal script may be a suitable tool when the new information involves one simple point
- It might also be appropriate when the PI wants to notify the subject about a change or new information that the subject needs to know but does not significantly affect their participation in the study
- If the investigator is calling the subject or doing an in-person oral process as part of a re-consent process, there is an expectation that he/she will get verbal consent
  - As with the original consent process, the investigator should document the communication in the subject's medical record/research record
- Might also be appropriate when the information should be shared right away, but the investigator intends to follow with a face-to-face consent process using the revised long form later

Information Letter

- Most appropriate for subject notification, i.e., sharing information with subjects that the investigator wants them to have--not information that will in any way affect their ongoing participation in the study
- Not typically considered an appropriate mechanism for *re-consent*
  - No way to determine whether the subject received the letter or read it
  - The use of an opt-in or opt-out checkboxes are not considered equivalent to re-consent
  - Does not allow the subject to get questions answered in real-time
  - Does not allow the investigator to make an assessment about the subject's understanding of the information
- Is also a practical approach to share information urgently, when the investigator intends to conduct a face-to-face, re-consent process using the revised consent form in the future

Using Multiple Mechanisms to Communicate the Same Information

- Consider the type of the information being shared and the study status of the various subsets of subjects when deciding how information will be communicated, e.g., future subjects, subjects undergoing the intervention or research procedures, subjects in long-term follow up vs. subjects are off study
- For example, it may make sense to communicate the same change via a consent addendum to subjects who are still undergoing research procedures; via an information letter to subjects who are in long-term follow up or off study; and via a revised long form consent to new subjects.

SACHRP'S Information Scenarios and Suggested Options*

*See **SACHRP, Attachment A2, Reconsent Appendix 2** in the **Additional Resources** section of this presentation

Information is:	Study status is:	Information represents a minor change (likely would not change the individual risk/benefit calculus or an individual's willingness to participate):	Information represents a significant change (some possibility that the individual risk /benefit calculus will be changed or an individual's willingness to participate):	Information represents a major change (changes the overall risk/benefit and is likely to affect an individual's willingness to participate):
Not time-sensitive	**Not yet recruiting**	Full consent form	Full consent form	Full consent form
	Recruitment started and still open	Verbal communication with documentation in the study record	[1]Information sheet/addendum with signature for existing participants*, full consent for new participants	Full consent form
	Recruitment complete: intervention ongoing	Verbal communication with documentation in the study record	Information sheet/addendum with signature	Information sheet/addendum with signature
	Recruitment complete: intervention complete**	Verbal communication with documentation in the study record	Verbal communication with documentation in the study record	Verbal communication with documentation in the study record

[1] This cell with a red background is a situation in which two versions of the consent form would be created.
* For studies that have been transitioned to the updated Common Rule, information sheets or addenda would not be "consent forms" considered to be subject to the new §116 requirements.
** There may be interventions that cannot be considered "complete" (e.g. implantable devices). In such circumstances, the judgement of the study team and IRB should dictate whether participants are asked to reaffirm their participation by signing a new information sheet or addendum.

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Time-sensitive	**Not yet recruiting**	Full consent form	Full consent form	Full consent form
	Recruitment started and still open	Verbal communication with documentation in the study record (no change in full informed consent form for any group)	[1]Information sheet/addendum with signature for existing participants*, full consent for new participants	Full consent form
	Recruitment complete: intervention ongoing	Verbal communication with documentation in the study record	Verbal communication with documentation in the study record, followed by information sheet/addendum with signature	Verbal communication with documentation in the study record, followed by information sheet/addendum with signature
	Recruitment complete: intervention complete**	Verbal communication with documentation in the study record	Verbal communication with documentation in the study record	Verbal communication with documentation in the study record

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Urgent	**Not yet recruiting**	Full consent form	Full consent form	Full consent form
	Recruitment started and still open	Verbal communication with documentation in the study record (no change in full informed consent form for any group)	[1]Verbal communication with documentation in the study record, followed by information sheet/addendum with signature for existing participants*, full consent for new participants	Verbal communication with documentation in the study record, followed by full consent for all participants
	Recruitment complete: intervention ongoing	Verbal communication with documentation in the study record	Verbal communication with documentation in the study record, followed by information sheet/addendum with signature	Verbal communication with documentation in the study record, followed by information sheet/addendum with signature
	Recruitment complete: intervention complete**	Verbal communication with documentation in the study record	Verbal communication with documentation in the study record	Verbal communication with documentation in the study record

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** There may be interventions that cannot be considered "complete" (e.g. implantable devices). In such circumstances, the judgement of the study team and IRB should dictate whether participants are asked to reaffirm their participation by signing a new information sheet or addendum.

Expected Content in Consent Addendums, Information Sheets, Verbal Scripts, & Information Letters

- Minimally should include:
  - Reference to the protocol number, name of the study, and the PI and the fact that the subject is currently/was previously enrolled in the study
  - Detailed description of the new information or change written in plain language, i.e., the expectation is that the language be at an eighth-grade reading level
  - Statement that all other aspects of the study as described in the signed consent form remain the same
  - Contact information in case the subject has questions or wishes to withdraw from the study

Plans to Re-Consent or Notify Subjects: Other Required Information

- Who needs to be re-consented or notified? (Only new subjects? Subjects undergoing procedures? Subjects in follow up? All subjects?)
- Context (in person, over the telephone, videoconferencing, etc.)
- Time Frame (immediately, ASAP, at the time of the next study visit, etc.)
  - Time frame can vary depending on the urgency of relaying the new information, immediate risk to subjects
  - The time of the next study visit may be too late
  - It may be important to share information with subjects that might affect their participation prior to them traveling to campus for their next visit, especially if the changes will affect what will occur at the visit

IRB Approval of Plan to Re-consent/Notify Subjects

Role of the PI

- Submit an amendment and provide the proposed plan for re-consent or subject notification along with describing:
  - Targeted subjects, i.e., who will be re-consented and/or notified
  - Mechanism(s) for re-consent/subject notification (type of document/script that will be used)
  - Context (face-to-face, over the phone, etc.); and
  - Timing (ASAP, within three weeks, at the next planned visit, within 3 – 6 mos., etc.)
- Upload a copy of the document/script that will be used for re-consent or subject notification
  - The NIH IRB wants to see and approve the verbatim information that will be communicated to the subject
- If the PI believes that no re-consent or subject notification is necessary, provide a rationale

Role of the IRB

- Will review and approve the re-consent or notification plan or the justification for not re-consenting or notifying subjects
- Will consider the nature of the new information, and the likelihood that the nature of the new information would be considered important by a reasonable person, such as a significant new risk that has been identified

Role of the IRB, cont.

- Must review and approve any revisions to the consent form or new consent/notification documents and associated procedures, prior to them being utilized.
  - "….Any proposed changes [should be] reviewed and approved by the IRB, **except when necessary to eliminate apparent immediate hazards to subject.**" (45 CFR 46.108(a)(3))

Role of the IRB, cont. (2)

- May disagree with the PI's proposal and instead provide a determination that re-consent or subject notification must occur, as well as require a change in the targeted subjects, mechanism(s) or timing
  - For example, the IRB may require that subjects be brought back for a study visit immediately or that information be provided via telephone
  - The IRB determination will be captured in the IRB amendment approval letter

Compliance with the Approved Re-Consent/ Notification Plan

- The investigators are expected to comply with the IRB's determination regarding the plan for re-consent or subject notification
- Responsibility of the investigators to be aware of the IRB's determination and follow it
- If unable to follow the approved plan, submit a new amendment now to propose a new plan and include a detailed justification
- If the IRB-approved re-consent or notification plan is not followed within the proposed time frame, submit a reportable event form
  - This would be considered non-compliance

Additional Resources

NIH OHSRP Templates, FAQs, Policies, Guidelines, etc.

- **NIH Consent Addendum Template:** https://irbo.nih.gov/confluence/download/attachments/67273126/NIH%20Consent%20Addendum%20Template%20for%20CC%20Use%20Only.docx?version=2&modificationDate=1654021710122&api=v2
- **OHSRP FAQs, "Everything You Need To Know about Consent":** https://irbo.nih.gov/confluence/display/ohsrp/Frequently+Asked+Questions#FrequentlyAskedQuestions-FAQConsent
- **NIH HRPP Policy 301 – Informed Consent:** https://policymanual.nih.gov/3014-301
- **QAPAC Informed Consent Questions:** https://irbo.nih.gov/confluence/download/attachments/36241835/QAPAC%20Informed%20Consent%20Questions.ppsx?version=1&modificationDate=1643229715149&api=v2
- **NIH HRPP Policy 303 – Intramural Research Program Telehealth Requirements:** https://policymanual.nih.gov/3014-303
- **OHSRP Obtaining Consent Using a Remote or Other Alternative Process:** https://irbo.nih.gov/confluence/display/ohsrp/Remote+Consent

SACHRP Recommendations

- **Secretary's Advisory Committee on Human Research Protections (SACHRP), Attachment A - New Information Provided to Previously Enrolled Research Subjects (March 11, 2020), Recommendations to the HHS Secretary:** https://www.hhs.gov/ohrp/sachrp-committee/recommendations/april-7-2020-attachment-a/index.html
  - **Attachment A1 – Reconsent Appendix 1:** https://www.hhs.gov/ohrp/sachrp-committee/recommendations/april-7-2020-attachment-a1-reconsent-appendix-1/index.html
  - **Attachment A2 – Reconsent Appendix 2:** https://www.hhs.gov/ohrp/sachrp-committee/recommendations/april-7-2020-attachment-a2-reconsent-appendix-2/index.html

OHRP & FDA FAQs and Tips

- **OHRP Informed Consent FAQs:**
  https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/informed-consent/index.html

- **OHRP Informed Consent Tips:**
  https://www.hhs.gov/ohrp/regulations-and-policy/guidance/informed-consent-tips/index.html

- **FDA Use of Electronic Informed Consent: Questions and Answers:**
  https://www.hhs.gov/ohrp/regulations-and-policy/guidance/use-electronic-informed-consent-questions-and-answers/index.html

OHSRP Presentations

- **OHSRP Education Series, The Informed Consent Process - The Good, the Bad & the Ugly:** https://irbo.nih.gov/confluence/download/attachments/45646144/The_Informed_Consent_Process_OHSRP_Educational_Series_2022_508C.pdf?version=1&modificationDate=1653586312252&api=v2
- **Using and Sharing Existing Specimens and Data for Secondary Research: Expectations for Consent and IRB Approval:** https://irbo.nih.gov/confluence/download/attachments/45646144/Using_and_Sharing_Existing_Specimens_and_Data_for_Secondary_Research_Expectations_for_Consent_and_IRB_Approval_7-OCT-2021_508C.pdf?version=1&modificationDate=1634594191319&api=v2
- **OHSRP Education Series, Informed Consent Procedures in the Era of COVID-19: Beyond the Use of a Standard Written Consent Document:** https://irbo.nih.gov/confluence/download/attachments/45646144/Informed-Consent-Procedures-in-the-Era-of-COVID-19_11_17_20_Final.ppsx?version=1&modificationDate=1607087719970&api=v2
- **OHSRP Education Series, Informed Consent One Year after the 2018 Common Rule Revisions: Updated Information and Processes:** https://irbo.nih.gov/confluence/download/attachments/45646144/Informed%20consent%20PPT%20for%20January%2014%202020%20%28for%20posting%29_FINAL%20%282%29%20%281%29.pdf?version=1&modificationDate=1594816672920&api=v2

?Questions?