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Re-consenting human subjects: ethical, legal and practical issues

D B Resnik

Informed consent is one of the foundational ethical and legal requirements of research with human subjects. The Nuremberg Code, the Helsinki Declaration, the Belmont Report, the Common Rule and many other laws and codes require that research subjects (or the subject's legal representative) make a voluntary, informed choice to participate in research.[1-5] Informed consent is based on the moral principle of respect for autonomy, which holds that rational individuals have a right to make decisions and take actions that reflect their values and preferences.[6] Whereas most guidelines and codes also require that informed consent be properly documented, informed consent is much more than signing a piece of paper: It is a continuous process of communication between the investigator and the research subject.[7] Because the body of knowledge impacting a study frequently changes, subjects should receive information from investigators after they have enrolled in a study, such as significant new findings that may affect their decision to participate in research or clinically useful tests results.[8-10] In large studies, some investigators use newsletters to update subjects on the progress of research and other developments.[11]

Most of the ongoing communications between investigators and subjects (or their representatives) involve little more than information sharing, without revisiting the decision to participate in research or signing any additional documents. Sometimes, however, it may be necessary for subjects to reaffirm their decision to participate, to re-consent, or to sign or re-sign a document.[8] Re-consent can be defined as an action in which a subject (or representative) makes the decision to participate in research once again. Re-consent is different from reaffirming a commitment to participate in a study, because in re-consent one actually reconsiders the information necessary to make decision, whereas in reaffirmation one simply expresses a willingness to abide by a decision one has already made. Re-consent is similar to renewing one's wedding vows, whereas reaffirmation is akin to continuing to express loyalty to one's spouse. Research subjects (or their representatives) usually sign a legal document that indicates their decision to participate in research, but signing the document is not the same as providing consent, because a person can sign a document without having sufficient knowledge or understanding to make an informed choice. Re-signing a document is not the same as re-consenting, because a person can sign a document once again without ever reconsidering their decision.

Revisiting the consent decision often does not always involve re-consent: sometimes reaffirmation is all that is required. Reaffirmation may be appropriate when considerable time has passed between the original expression of willingness to participate in a study and the present situation, such that subjects may have changed their minds about participation. Reaffirmation may involve little more than sending subjects a letter thanking them for their

Correspondence to: Dr D B Resnik, NIEHS/NIH, Box 12233, Research Triangle Park, NC 27709, USA; resnikd@niehs.nih.gov.
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participation and reminding them that they are free to withdraw at any time. Subjects do not need to sign a new consent document.[8]

Re-consent may be appropriate when the original consent was invalid or there has been a substantial change to the research or the subject's condition since the time of the original consent, such that research participation may no longer be consistent with the subject's preferences and interests and the subject may need to reconsider the decision.[8] Some examples of situations that might warrant re-consent include:

- Failing to inform the subject about important risks related to the study.
- Conducting the consent when the subject's decision-making capacity was compromised or the subject was under duress.
- Using an improper representative for a subject who is not capable of making an informed choice.
- Significant changes in the research procedures, risks, potential benefits, or alternatives.
- The subject's medical condition worsens or does not respond to treatment.[8]
- Research in which paediatric subjects will reach adulthood while the study is still in progress, such as a longitudinal, prospective cohort study that follows children from birth through adulthood.

Re-consent may be considered appropriate when children reach adulthood so that research participation reflects their own choices, rather than the choices of their parents or guardians.[12]

To re-consent subjects, investigators may contact them in person, by phone, mail, or e-mail, depending on the circumstances of the research project. Investigators should explain the need for re-consent and give subjects an opportunity to ask questions. Investigators may also ask subjects to sign a document affirming their willingness to continue participating in the study. In complex and risky studies it may be wise to ask subjects to sign a new consent form, with the assistance of research staff and possibly a witness.[9]

Whereas re-consent is important for respecting the subject's autonomy and possibly protecting the subject from risks, it must be balanced against other concerns, such as the need to avoid harming research subjects and implementation issues. Re-consent can produce anxiety or confusion in some subjects and may make some feel that their privacy has been violated, if they did not give permission to be re-contacted.[89] Re-consent may be difficult to implement, due to problems with re-contacting subjects (such as missing or incorrect contact information) or resource constraints (such as insufficient time, staffing, or money).

Re-signing a consent form may be appropriate when re-consent is required, or when re-consent is not necessary but there was a legal problem with the documentation of the original consent. The Common Rule and many other guidelines require that informed consent be legally effective and properly documented.[45] Some examples of improperly documented consents include:

- A subject did not sign the consent form.
- An inappropriate legal representative signed for the subject.
- The consent form was not translated into the subject's or representative's language.
- The study's approval had expired during the time when the subject consented.

- The consent document contained some legally invalid language, such as a waiver of the subject's legal rights.
- An outdated version of the consent form was used.

Procedures for dealing with these legal problems vary from case to case, depending on the nature and complexity of the issues. In some situations, such as failure to sign the consent form, all that may be needed is to send the subject a letter explaining the problem and asking him/her to sign a form affirming his or her desire to participate in the study. In other situations, such as an outdated version of the form being used, it may be necessary to send the subject a letter explaining the problem and a new consent form to sign if the outdated consent form was missing important information. In the worst cases, such as an improperly translated consent document, it may be necessary to redo the entire consent process, to ensure that it meets appropriate legal requirements.

One might object to asking subjects to re-sign consent forms if they have already affirmed their willingness to participate in research and re-consent is not required because re-signing consent forms can be difficult and costly to implement and may cause some subjects anxiety. Re-signing consent forms should be reserved for ethically compelling reasons, such as protecting human subjects from harm or promoting their autonomy.

Legally defective consent documents can raise ethical concerns and can have an impact on research subjects, however. If samples or data have been obtained from a subject via a consent process that was not properly documented, then the samples or data cannot be used, because there would be insufficient evidence that they were obtained legally. The subject will also need to be withdrawn from the study until proper documentation of consent can be obtained. Withdrawal from a study could negatively impact the subject's welfare, if the study has medical benefits. Furthermore, not using the data/samples might undermine the subject's pursuit of his or her goals, if the subject participated in the study in order to make a contribution to research. In addition, not using the data/samples would waste time and resources.[13]

As some research subjects may decide to withdraw from a study if they are asked to re-consent, reaffirm their willingness to participate, or re-sign a consent form, investigators have an incentive to avoid discussing these topics with subjects, because too many withdrawals could adversely impact a study's recruitment goals and statistical power. To manage this potential conflict of interest, committees that review research with human subjects, such as institutional review boards (IRB), should oversee the re-consent, reaffirmation and re-signing of consent forms. IRB should determine when it is necessary to re-consent subjects, ask subjects to reaffirm their commitment to research, or re-sign a consent form. IRB should provide investigators with guidance for these procedures.

Because informed consent is an essential part of ethical research involving human subjects, it is important that it be done correctly. To ensure that informed consent is ethically and legally valid, it is sometimes necessary to ask human subjects to re-consent, reaffirm their willingness to participate, or re-sign a consent form. Although these procedures generate their own issues, it is better to deal with these problems than to ignore them.

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