Main Line Health®

Informed Consent: Special Populations and Exceptions

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AGENDA

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Purpose

- Researchers are expected to follow consent processes that ensure all information about a study is completely disclosed, and that prospective subjects adequately understand this information so that they can make an informed decision about their participation. However, there are times when researchers may be presented with unique circumstances that do not follow the typical consent format.
- This training will help researchers better understand these unique circumstances and ensure an effective consent process takes place.

What is Informed Consent

- Informed Consent is a process in which researchers provide potential subjects with the information about a study, allowing them to make voluntary decisions regarding their involvement.
- The informed consent process should be an active process of sharing information between the investigator/researcher and the potential subject.
- Three Key features:
  - Disclosing to potential research subjects' information needed to make an informed decision
  - Facilitating the understanding of what has been disclosed
  - Promoting the voluntariness of the decision about whether or not to participate in the research

Belmont Principles

- Three core ethical principles for conducting research involv ing human subjects. They are applied throughout the research process.
  - Respect for Persons
  - Beneficence
  - Justice
- Respect for Persons can be applied when consenting subjects to research.
  - Requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them.

Elements of Informed Consent

- Health and Human Services(HHS) regulations at 45 CFR 46.116(a) require that the following information be conveyed to each subject:
  - A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental
  - A description of any reasonably foreseeable risks or discomforts to the subject
  - A description of any benefits to the subject or to others which may reasonably be expected from the research;
  - A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject

Elements of Informed Consent

- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
- For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained
- An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Consent of adult capable of making decisions for oneself

- Follow this method when:
  - Consenting an autonomous individual

  - Autonomous individual
    - An individual capable of deliberation about personal goals and of acting under the direction of such deliberation
    - An individual who can
      make choices and govern their own life without undue external influence or coercion

Consent of adult capable of making decisions for oneself

- Who signs the consent form:
  - The autonomous individual and the PI/Researcher

- How should the PI/Researcher document consent:
  - Document after explaining the research and answering subject questions
  - Ensure currently approved and stamped consent form is being utilized
  - Subject signs and dates the consent form
  - PI/Researcher will also sign and date the consent form
  - Give the subject a signed copy and keep the original for your records

When to reconsent a subject capable of making decisions for oneself

- Re-consent may be appropriate when the original consent was invalid or there has been a change to the research or the subject's condition since the time of the original consent.
- Examples:
  - Failing to inform the subject about important risks related to the study.
  - Changes in procedures and or safety risks or adverse events were identified.
  - There have been changes to the study protocol that may affect the subject's willingness to participate.

Legally Authorized Representative and consent/reconsent

- Follow this method when:
  - When a prospective subject is unable to provide informed consent due to cognitive impairment, lack of decision-making capacity, or serious or life-threatening diseases and conditions.

- Who signs the consent form:
  - The LAR
  - The PI/Researcher

Legally Authorized Representative and consent/reconsent

- How should the PI/Researcher document consent
  - Document after explaining the research and answering questions
  - Ensure currently approved and stamped consent form is being utilized
  - LAR signs and dates the consent form
  - PI/Researcher will also sign and date the consent form
  - Give the LAR and subject a signed copy and keep the original for your records

- Using a LAR must be approved by the IRB in advance

Consent/Assent of Minors

- Children are “persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted”
- Minor(PA) - under the age of 18
- The IRB must determine, that adequate provisions are made for requesting the assent of the children, when in the judgment of the IRB the children are capable of providing assent, as well as the permission of the parents.

Consent/Assent of Minors

- Documentation of Assent
  - The IRB should require child assent unless it can be appropriately waived, or if the child is not capable of providing assent.

- HHS determines three circumstances where the IRB may determine that waiver of children's assent is appropriate:
  - if the capability of some or all of the children is so limited that they cannot reasonably be consulted
  - if the intervention or procedure involved in the research holds out the prospect of direct benefit to the health or well-being of the children and is available only in the context of the research.
  - if the research meets the same conditions as those for waiver or alteration of informed consent in research involving adults

Consent/Assent of Minors

- Follow this method when:
  - Consenting a minor or a child as defined previously

- Who typically signs the consent form
  - Parent(s) or guardian
    - Both parents are required to sign the consent form unless one parent is deceased, unknown, incompetent, not reasonably available or one parent has sole custody.

Consent/Assent of Minors

- How should the PI/Researcher document consent
  - Parent(s) or guardian sign and date the approved current consent form
  - PI/Researcher also signs and dates approved current consent form
  - If applicable obtain and document child/minor assent
    - Children aged 6 - 13 years, by investigator verification of explanation
    - Children aged 14 - 17 years, will read and sign the standard informed consent document prior to participating as a subject in the research and the investigator will sign the verification of explanation

Consent/Assent of Minors

Verification of Explanation

I certify that I have thoroughly explained the nature and purpose of this research including any discomforts and inconveniences which may occur to_____. He/she has had an opportunity to discuss it with me, to ask any questions and raise concerns. I have answered his/her questions and concerns and he/she has assented (affirmatively agreed) to participate in this research.

_____ _____

Principal/Sub-investigator signature Date

Consent/Assent of Minors

- When the child or minor turns 18 while enrolled in the study
  - Unless the IRB determines that the requirements for obtaining informed consent can be waived, legally effective informed consent needs to obtained for the now adult subject.

- If the research does not involve any ongoing interactions or interventions with the subjects, but continues to meet the regulatory definition of human subjects research (example, involves continued analysis of specimens or data for which the subject's identity is readily identifiable to the investigator(s))
  - Legally effective informed consent will still need to be obtained from the now adult subject.

Consent and low English proficiency

- Department of Health and Human Services require that informed consent information be presented "in language understandable to the subject" and, in most situations, that informed consent be documented in writing

- The written consent document should embody, in language understandable to the subject, all the elements necessary for legally effective informed consent.

- Subjects who do not speak English should be presented with a consent document written in a language understandable to them.

Consent and low English proficiency/Short form

MLH Fully Translated Consent form process:

- A medical interpreter or bilingual person obtaining consent must be present during the consent discussion.
  - A telephone or video interpreter is acceptable.

- The note which documents the consent meeting should indicate that an interpreter was present.

- A witness is not required, if the subject is able to read.

- If the subject is unable to read in their preferred language, then a witness must be present during the entire consent discussion.

Consent and low English proficiency/Short form

- The consent form must be translated in full into the subject's preferred language. The translation from the English must be certified in writing by an independent third party.
- The translated consent form and translation certification letter must be reviewed and approved by the IRB of record before use.
- A separate HIPAA Authorization Form is required, if the consent form does not already incorporate HIPAA language. The HIPAA Authorization must be translated and the translation certified, whenever possible.
- The consent form is signed by the person obtaining consent and the subject. If the subject is unable to read, the witness also signs the consent form.

Consent and low English proficiency/Short form

MLH Short Form Consent Process:

- A medical interpreter or bilingual person obtaining consent must be present during the consent discussion. A witness must be present during the consent discussion. The interpreter may serve as the witness, unless the interpreter is the person obtaining consent
- If using a telephone or video interpreter, then the interpreter may not serve as the witness, as the consent documents require signature by the witness.
- Investigators conducting research within MLH facilities must follow MLH policy requiring use of MLH interpreter service.

Consent and low English proficiency/Short form

MLH Short Form Consent Process:

- The following forms are required:
  - Full English IRB approved consent form
  - Study summary
  - Short form consent form
  - HIPAA Authorization Form, if the consent form does not already incorporate HIPAA language.
- Required Signatures:
  - English consent Form – The person obtaining consent and the subject
  - Study summary – The person obtaining consent and witness
  - Short form consent form – The subject and witness sign
  - HIPAA Authorization (if applicable) – The subject and person obtaining consent sign.

Emergency use of an Investigational drug/device and consent

- Follow this method when:
  - Use of an investigational drug or biologic or unapproved medical device for a patient in a life-threatening situation for which no standard acceptable treatment is available when there is not sufficient time to obtain IRB approval.

- Who typically signs the consent form and how to document:
  - For emergency use of a drug, biologic or device, the treating physician is required to obtain written informed consent of the patient or the patient's legally authorized representative.

Emergency use of a drug/device and consent

- Written informed consent does not have to be obtained if both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:
  - The subject is confronted by a life-threatening situation necessitating the use of the test article
  - Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from the subject

Emergency use of a drug/device and consent

- Time is not sufficient to obtain consent from the subject's legal representative.
- No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life

Emergency use of a drug/device and consent

- If time permits prior to the procedure, notify the IRB of the emergency use

  - Investigators/treating physician will contact the IRB Chair, or the Office of Research Protections (ORP) via phone or email. The following information should be provided:

    - Explanation of the life-threatening situation necessitating the emergency use

Emergency use of a drug/device and consent

- Description of standard treatment(s) previously used and/or why available options are not acceptable
- Investigational drug or biologic or unapproved medical device to be used
- If available, IND or IDE number of the drug, biologic, or device.

Expanded access to unapproved drug and consent

- Expanded access, also called "compassionate use," is the use outside of a clinical trial of an investigational medical product not approved by the FDA for the indication it is being used for.

- Prior IRB approval is required

Expanded access to unapproved drug and consent

- The patient must understand the nature of the investigational product, the intended use, the potential benefits, and the known and potential risks

- Obtain informed consent consistent with requirements and as discussed previously in this presentation.

Use of a HUD and Consent

- FDA describes a Humanitarian use Device (HUD) as a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in no more than 8,000 individuals in the United States per year

- The use of a HUD is not considered research and a research protocol is not required for use of a HUD.

- The FDA allows the use of HUDs under a Humanitarian Device Exemption (HDE), which does not require the manufacturer to demonstrate the device's effectiveness prior to marketing

Use of a HUD and Consent

- Use of a research consent form is not required unless the use represents a clinical investigation, however the IRB may require that one is used in all cases, and requires that information on the use of the HUD be provided to patients. For example, patient information packet or information.

- The IRB may determine what is required for the use of a specific HUD on a case by case basis.

- Initial IRB approval must be obtained prior to the first use of the HUD and ongoing IRB approval must also be obtained as long as the HUD continues to be used.

Use of a HUD and Consent

- If consent is required by the IRB for the use of the HUD, the subject or LAR and PI/Researcher will need to sign and date an IRB approved consent form as well as give any IRB required information on the use of the HUD to the subject.

Planned emergency use research and consent

- Follow this method when:
  - Research involving an IRB approved protocol with subjects who are in need of emergency medical intervention, but who cannot give informed consent because of their life-threatening medical conditions and who do not have an available legally authorized representative to provide consent.

- Who typically signs the consent form:
  - The IRB may approve emergency research without requiring that informed consent is obtained from subjects or their LAR only if the IRB finds and documents that each of the following requirements has been met:

Planned emergency use research and consent

1. The human subjects are in a life threatening situation.
    - Available treatments are unproven or unsatisfactory.
    - The relative risks and benefits of the proposed intervention are unknown or thought to be equivalent, or better, compared to standard therapy.

2. The collection of valid scientific evidence, including evidence from randomized, placebo-controlled studies, is necessary to determine the safety and efficacy of the intervention

Planned emergency use research and consent

3. Obtaining informed consent is not feasible because of all of the following:
   - The subjects will not be able to give their informed consent as a result of their medical condition(s)
   - The intervention under investigation must be administered before consent from the subjects' LAR is feasible.
   - There is no reasonable way to prospectively identify the individuals likely to become eligible for participation in the research.

Planned emergency use research and consent

4. Participation in the research holds out the prospect of direct benefit to the subjects because of all of the following:

- Subjects are facing a life-threatening situation that necessitates intervention.
- Appropriate animal and other preclinical studies have been conducted and the information derived from those studies, and related evidence, supports the potential for the intervention to provide a direct benefit to the individual subjects.
- Risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, and what is known about the risks and benefits of the proposed intervention or activity.

Planned emergency use research and consent

5. The research could not practicably be carried out without the IRB approval of a waiver of informed consent.

6. The protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact an LAR for each subject within that window of time and, if feasible, to asking the LAR for consent rather than proceeding without consent

- Investigators will summarize efforts made to contact the LAR and provide this information to the IRB at the time of continuing review.

Planned emergency use research and consent

7. The IRB has reviewed and approved an informed consent process and consent document.

MLH IRB Policy and Procedure Manual

- The approved informed consent procedures and consent document are to be used with subjects or their LAR when feasible.
- The IRB has approved procedures and information to be used when providing an opportunity for a family member to object to the subject's participation, as described below.

Planned emergency use research and consent

8. Additional protections of the rights and welfare of subjects will be provided.

9. A separate IND or IDE is obtained for use of the investigational drug, biologic or device to be studied in a population that includes subjects who are unable to consent.

Planned emergency use research and consent

The IRB will approve procedures to inform the subject, the LAR, or a family member, of the following at the earliest feasible opportunity:

- That the subject was included in the study
- Details of the research and other information contained in the informed consent document.
- That the subject's participation may be discontinued at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Key Takeaways

Following proper consent practices during the consent process is critical to ethical research.

There may be instances where the typical consent process cannot be followed. It is imperative that subjects are still consented effectively in these instances and that researchers know the correct regulations and policies to follow.

The FDA and Health and Human Services(HHS) websites as well as the MLH IRB Policy Manual and Office of Clinical Research have an abundance of helpful resources, linked on the last slide of this presentation.

Policies and Helpful Links

- MLH IRB **Policy No. XII** Subject: INFORMED CONSENT DOCUMENTATION
- MLH IBR **Policy No. VIII** Subject: EMERGENCY/EXPANDED ACCESS USE OF AN INVESTIGATIONAL TEST ARTICLE
- MLH IRB **Policy No. IX** Subject: EXPANDED ACCESS TO FDA-REGULATED INVESTIGATIONAL TEST ARTICLES (formerly, “compassionate use”)
- MLH IRB **Policy No. X** Subject: HUMANITARIAN USE DEVICE/HUMANITARIAN DEVICE EXEMPTION
- MLH IRB **Policy No. XXIV** Subject: DECISIONALLY IMPAIRED TO CONSENT AND SURROGATE CONSENT
- LIMR CRC **Policy 3.0** Informed Consent for Study Participants with Low English Proficiency
- Informed Consent FAQs | HHS.gov
- *Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors

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Thank you!