Module 4.1 Transcript

Interpretation and Application of ICH E6(R3):

GOOD CLINICAL PRACTICE (GCP)

Welcome to the Interpretation and Application of ICH E6(R3): Good Clinical Practice.

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Module 4 of this training discusses the important features of informed consent. There are two parts in this module, 4.1 and 4.2, that should be taken sequentially.

Key questions you will be able to answer after completing this module include:

- Who is involved in the informed consent process?
- What are the key elements that should be included in the informed consent materials and the informed consent discussion?
- And what are the key considerations of an informed consent process?

This module will also provide some practical considerations for obtaining and documenting informed consent.

As we reviewed in Module 1.2, principle 2 of the E6(R3) Guideline states: “Informed consent is an integral feature of the ethical conduct of a trial. Clinical trial participation should be voluntary and based on a consent process that ensures participants (or their legally acceptable representatives, where applicable) are well informed.”

Principle 2 also highlights the importance of the following:

- Obtaining freely-given informed consent.
- Enabling potential trial participants to evaluate the benefits, risks, and burdens of participation.
- Considering relevant aspects of the trial when designing the informed consent process.
- And, obtaining consent as soon as possible for clinical trials in emergency situations where consent cannot be obtained prior to trial participation.

These subparts will be described in more detail within this module.

The GCP Guideline defines informed consent as: “A process by which a participant or their legally acceptable representative voluntarily confirms their willingness to participate in a trial after having been informed and been provided with the opportunity to discuss all aspects of the trial that are relevant to the participant's decision to participate.”

Varied approaches to the provision of information and the discussion about the trial can be used. This may include, for example, providing text in different formats, images and videos, and using telephone or video conferencing with investigator site staff.

Informed consent is documented by means of a written informed consent form that is signed and dated. The form may be paper or electronic. Obtaining consent remotely may be considered when appropriate.

Freely-given, or voluntarily-given, informed consent from all persons before their trial participation is critical to respecting their rights. To achieve this, all relevant information about the trial should be shared with the potential participant in a way that they can understand.

The potential participant should be given ample time and opportunity to ask questions for them to decide on trial participation. And, the participant should voluntarily decide on trial participation without any undue influence or coercion.

Obtaining informed consent goes beyond collecting a signature on a form.

The process of informed consent should enable each participant to understand and evaluate the potential benefits, risks and burdens of participating in the trial, including the impact of any changes as the trial progresses.

Let's look at the different interested parties who are involved in the informed consent process in different ways: The sponsor, the Institutional Review Board (IRB) or Independent Ethics Committee (IEC), the investigator, and the participant.

Please note that moving forward in this module, an Institutional Review Board or Independent Ethics Committee will be abbreviated as IRB or IEC.

The sponsor generally produces the informed consent materials.

Note that in some regions, the investigator is responsible for the development of the informed consent materials, which may be supported by the sponsor.

When developing informed consent materials, the sponsor should consider inputs from a wide variety of interested parties, including investigators, patients, patient advocates, healthcare professionals, and more. The sponsor should address relevant aspects of the trial, such as the characteristics of the participants, the trial design, the anticipated benefits and risks of medical intervention, and the setting and context. The sponsor may also consider the potential use of technology to support the informed consent process.

The information provided in informed consent materials should be clear and concise to be understandable by potential participants or legally acceptable representatives.

Once the trial begins, updates to informed consent materials should be made as necessary. For example, when relevant safety information emerges.

Both the informed consent materials and the informed consent process (including those for re-consent) will be subject to review and approval by IRB or IEC.

The IRB or IEC reviews all informed consent materials as well as the description of the process of how informed consent is obtained. They review assent materials and the assent process if minors are to be included in the trial.

The IRB or IEC should also review the amount and method of payment to participants if compensation is offered for participation.

The ICH E6(R3) Guideline notes that reasonable reimbursement of participants' expenses, such as for travel and lodging, is not coercive.

Information regarding the method, amount and schedule of payment to trial participants should be explained in the informed consent materials. Local context should be used to determine what is considered reasonable.

In addition, the IRB or IEC should ensure the appropriate consideration is given to trials that intend to recruit vulnerable participants.

Please see the E6(R3) Annex 1, Section 1.2 for more information. You may access the full guideline, including Annex 1 at any time using the Resources tab.

The investigator should ensure that the informed consent materials and process are approved by the IRB or IEC before starting the informed consent process with any potential trial participants.

Submissions and communications with the IRB or IEC are made in some regions by the investigator or institution and in other regions by the sponsor in accordance with applicable regulatory requirements.

Please see the E6(R3) Annex 1 sections 1.1 and 2.8 for more information.

When providing the information, the investigator should use language that is as clear, concise and simple as possible and avoid unnecessary volume and complexity, to ensure that participants or their legally acceptable representatives have an adequate understanding of the clinical trial and can therefore make an informed decision on trial participation.

Trial participants should be given ample time to consider their decision and the opportunity to ask questions about the trial.

Throughout the informed consent process, the investigator or their delegated investigator site staff should not use language that causes the participant to waive legal rights, coerces the participant, or unduly influences someone to participate in the trial.

By signing the consent form, the investigator or delegated investigator site staff attests that the informed consent was freely given by the participant or the participant's legally acceptable representative, and that the consent information was accurately explained to and apparently understood by the participant or the participant's legally acceptable representative.

The requirement for the investigator to sign the informed consent form varies by local regulatory requirements, including whether delegated site staff may sign on the investigator's behalf.

Of course, the most important person in the informed consent process is the participant. Informed consent materials and the informed consent discussion should clearly outline: the objectives of the trial, what is expected of participants during their participation in the trial, the alternative treatments and potential benefits, risks and burdens of participating in the trial.

For example, the informed consent materials should facilitate a participant's understanding of the schedule of trial visits and procedures, what other medications they may or may not take during the trial, and other expectations to comply with the trial protocol.

The informed consent process should make it clear that participants have the right to withdraw from a trial at any time without any penalty. More information about end of participation in a clinical trial can be found in the E6(R3) Guideline at Annex 1, sections 2.8.10 and 2.9.

Let's look more closely at the informed consent materials. Informed consent materials are information sheets, images, videos, interactive websites, or other materials used in the informed consent process to convey information about the trial to potential participants.

The informed consent form itself is also considered an informed consent material.

The E6(R3) GCP Guideline outlines a number of elements that should be included in informed consent materials. Of these, 5 are new or have been modified.

We will briefly discuss each new or modified element here. For a full list of what should be included, please refer to Annex 1, Section 2.8.10.

While it has long been important for informed consent materials to include the reasonably foreseeable risks or inconveniences to the participant, the GCP Guideline now recommends including the reasonably foreseeable risks to the participant's partner, to an embryo, foetus, or nursing infant when applicable.

Additional new elements in the E6(R3) version address:

- The follow-up procedures for participants who stopped taking the investigational product, withdrew from the trial or were discontinued from the trial.
- The process by which the participant’s data will be handled, including in the event of the withdrawal or discontinuation of participation.
- Informing the participant that the trial may be registered on publicly accessible and recognised databases, per applicable regulatory requirements.
- And, informing the participant that trial results and information on participants' actual treatment, if appropriate, will be made available should they desire.

Although there is a lot of important information that should be included in informed consent materials to facilitate understanding and informed decision making, informed consent materials should not be unnecessarily long.

Please navigate to Module 4.2 to learn about the informed consent process.