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## Part 1: What is Informed Consent?



When most people hear the phrase “informed consent,” they think of the legal document that explains the study and contains the required dated signatures. However, informed consent is first and foremost a continuing process. This includes a person voluntarily agreeing to participate in a research study after being fully informed about it via verbal discussion with study staff, followed by documentation in a written, signed, and dated informed consent form. A participant’s consent will be continually sought during the course of the study, and the participant will be notified of any changes to the study, along with any other pertinent information that may influence their decision to remain in the study.

While documentation of informed consent is required in most clinical studies, there are occasions when a waiver or alteration of written informed consent is obtained from the Institutional Review Board (IRB) for some or all study participants. The fundamental criteria for waivers and alterations of informed consent are located in 45 CFR 46.116(c) and 45 CFR 46.116(d). Please consult the local IRB for determining when it is appropriate to waive the requirement for written consent.

The informed consent document should contain all of the information that the person needs to make an informed decision about taking part in the study. Many research teams use the consent document to guide the verbal explanation of the study to potential participants.

The participant must sign and date the informed consent document before taking part in any study procedures. Signing the consent form is NOT the final step in the informed consent process. The participant may withdraw consent and decline to participate in the study at any time before or after signing the consent document until their participation in the study is completed.

The general requirements for informed consent in federally funded research are spelled out in [45 CFR 46.116](#) and [21 CFR 50.20](#). Some states have enacted requirements for informed consent that go beyond federal regulations. This module reviews the requirements for informed consent that are set out in federal regulations and in the Good Clinical Practice guidelines of the International Council for Harmonization (ICH GCP 4.8.10). It is the principal investigator’s responsibility to know and abide by any additional state requirements.

All researchers must ensure that the process of obtaining informed consent from study participants not only conforms to federal, state, and local regulations but also respects each individual’s right to make a voluntary, informed decision.

Part 2 of this module deals with the informed consent document. Part 4 deals with the informed consent

process.

## Part 2: The Informed Consent Document

### 1. Study Purpose



The consent document must state ([ICH GCP 4.8.10](#)):

- That the trial involves research.
- The purpose of the trial.

### 2. Study Treatment and Randomization

The consent document must state ([ICH GCP 4.8.10](#)):

- The trial treatment(s) and the probability for random assignment to each treatment (if a randomized clinical trial).

### 3. Study Procedures

The consent document must state ([ICH GCP 4.8.10](#)):

- The trial procedures to be followed, including all invasive procedures.
- The participant's responsibilities.
- Those aspects of the trial that are experimental.
- The expected duration of the participant's involvement in the trial.

### 4. Risks of Taking Part in the Study

The consent document must state ([ICH GCP 4.8.10](#)):

- The reasonably foreseeable risks or inconveniences to the participant and, when applicable, to an embryo, fetus, or nursing infant.

### 5. Benefits of Taking Part in the Study

# BENEFITS



The consent document must state ([ICH GCP 4.8.10](#)):

- The reasonably expected benefits. When there is no intended clinical benefit to the participant, the participant should be made aware of this.

## 6. Alternatives to Taking Part in the Study

The consent document must state ([ICH GCP 4.8.10](#)):

- The alternative procedure(s) or course(s) of treatment that may be available to the participant, and their important potential benefits and risks.

**Points to note:** IRBs often want the informed consent document to list other therapies available for the condition under treatment in addition to other treatment options at the facility where the study is being conducted.

## 7. Costs of Participation and Compensation in the Event of Injury

The consent document must state ([ICH GCP 4.8.10](#)):

- The compensation and/or treatment available to the participant in the event of trial-related injury.
- The anticipated expenses, if any, to the participant for participating in the trial.

**Points to note:** When research involves more than minimal risk to the participant, the consent document must describe the treatment and compensation that will be provided in the event that a participant sustains a research-related injury. The language in the consent cannot appear to limit the participant's rights in seeking damages related to injury in a trial.

Federal regulations do not limit the definition of “injury” to a physical injury. An injury may be psychological, social, financial, or of another nature.

## 8. Payment for Taking Part in the Study

The consent document must state ([ICH GCP 4.8.10](#)):

- The anticipated prorated payment, if any, to the participant for participating in the trial.

**Points to note:** Payment to participants for their participation in a research study must never be coercive in either amount or method of distribution.

## **9. Voluntary Nature of Study**

The consent document must state ([ICH GCP 4.8.10](#)):

- That the participant's participation in the trial is voluntary and that the participant may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the participant is otherwise entitled.
- The foreseeable circumstances and/or reasons under which the participant's participation in the trial may be terminated.

## **10. Confidentiality of Personal Information**



The consent document must state ([ICH GCP 4.8.10](#)):

- That the monitor(s), the auditor(s), the IRB, and the regulatory authority(ies) will be granted direct access to the participant's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the participant or the participant's legal representative is authorizing such access.
- That records identifying the participant will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the participant's identity will remain confidential.

**Points to note:** Certificates of Confidentiality are issued by the National Institutes of Health (NIH) to prevent investigators from having to release (e.g., via a subpoena) names or other identifying information about research participants.

Certificates of Confidentiality provide additional protection for participants who are enrolled in studies in which information is being collected that, if disclosed, could have adverse consequences for participants or could damage their financial standing, employability, insurability, or reputation.

See related material from the [Confidentiality and Privacy module](#) for a summary of confidentiality requirements in research involving human participants.

## 11. New Information that may Affect Study Participation

The consent document must state ([ICH GCP 4.8.10](#)):

- That the participant or the participant's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the participant's willingness to continue participation in the trial.

## 12. Study Contacts



The consent document must state ([ICH GCP 4.8.10](#)):

- The person(s) to contact for further information regarding the trial and the rights of trial participants in the event of trial-related injury.

## 13. Duration of Participation and Number of People Taking Part in the Study

The consent document must state ([ICH GCP 4.8.10](#)):

- The expected duration of the participant's participation in the trial.
- The approximate number of participants involved in the trial.

**Points to note:** A consent form should be written in non-technical language that participants would understand. Also, it should be written in language consistent with the participants educational level, cultural views, and familiarity with research.

## Part 3: Special Requirements Concerning Consent

The information that must be provided in an informed consent document is specified in [45 CFR 46.116](#), [21 CFR 50.20](#), and [ICH E6 GCP 4.8.10](#). In the following sections, we will take a closer look at how this information is presented in a sample informed consent document.

The consent document should include the following:

- State that the study involves research.
- Briefly explain the purpose of the research, the reason(s) why the person is being invited to participate, and the expected duration of the person's participation in the study.
- Describe the procedures or interventions to be carried out, identifying which procedures are investigational and which might be provided as standard care in another setting.
- Explain the use of research methods such as randomization and placebo controls.
- Describe any foreseeable risks or discomforts to the participant. Estimate how likely it is that these risks and discomforts will occur.
- Describe the steps that will be taken to prevent or minimize risks or discomforts to the participant.
- Acknowledge that participation in the study may pose unknown and unforeseeable risks.
- Describe any benefits to the participant or to others that the research may reasonably be expected to produce. Estimate how likely it is that these benefits will occur.
- Disclose any appropriate alternative procedures or courses of treatment that may benefit the participant.
- Describe the extent to which records will be kept confidential and provide examples of people or organizations that may have access to research records (e.g., hospital personnel, study sponsors, staff of the U.S. Food and Drug Administration).
- For research that involves more than minimal risk, explain and describe any compensation and any medical treatments that are available if participants are injured as a result of participation in the study, where further information can be obtained, and who should be contacted in the event of a research-related injury.
- Explain who should be contacted for answers to questions about the research and the participant's rights (including the name and phone number of the principal investigator).
- State that participation in the study is voluntary and that declining to participate or deciding to withdraw at any time will involve no penalty or loss of benefits to which the participant is otherwise entitled.
- State that the participant's signature will indicate that he or she has decided to participate in the study, having read and discussed the information presented to him or her about the research.
- Provide any other information that prospective participants might need to make an informed decision about whether or not to participate in the research study, such as any recently obtained information about the investigational drug's toxicity in animals.

### Informed Consent of Trial Participants (ICH GCP 4.8.10)

Both the informed consent discussion and the written informed consent form and any other written information to be provided to participants should include explanations of the following:

1. That the trial involves research.
2. The purpose of the trial.
3. The trial treatment(s) and the probability for random assignment to each treatment.
4. The trial procedures to be followed, including all invasive procedures.
5. The participant's responsibilities.
6. Those aspects of the trial that are experimental.



7. The reasonably foreseeable risks or inconveniences to the participant and, when applicable, to an embryo, fetus, or nursing infant.
8. The reasonably expected benefits. When there is no intended clinical benefit to the participant, the participant should be made aware of this.
9. The alternative procedure(s) or course(s) of treatment that may be available to the participant, and their important potential benefits and risks.
10. The compensation and/or treatment available to the participant in the event of trial-related injury.
11. The anticipated prorated payment, if any, to the participant for participating in the trial.
12. The anticipated expenses, if any, to the participant for participating in the trial.
13. That the participant's participation in the trial is voluntary and that the participant may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the participant is otherwise entitled.
14. That the monitor(s), the auditor(s), the IRB, and the regulatory authorities will be granted direct access to the participant's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the participant or the participant's legally acceptable representative is authorizing such access.
15. That records identifying the participant will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the participant's identity will remain confidential.
16. That the participant or the participant's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the participant's willingness to continue participation in the trial.
17. The person(s) to contact for further information regarding the trial and the rights of trial participants, and whom to contact in the event of trial-related injury.
18. The foreseeable circumstances and/or reasons under which the participant's participation in the trial may be terminated.
19. The expected duration of the participant's participation in the trial.
20. The approximate number of participants involved in the trial.



## **Special Requirements Concerning the Consent of Pregnant Women**

When a research activity involves pregnant women as participants:

- Both mother and father must be informed about any potential impact of the research on the fetus.

- Both mother and father must consent to the woman's participation in the research. However, the father's consent is not required in the following circumstances:
  - The purpose of the research is to meet the health needs of the mother.
  - The father's identity or whereabouts cannot be determined.
  - The father is not reasonably available.
  - The pregnancy resulted from rape.
- If either parent is unable to consent because of availability, incompetence, or temporary incapacity, the informed consent of one parent will suffice provided the criteria in the previous bullet points are not met.
- Consent of a legally acceptable representative of either or both parents does not suffice for informed consent.

Additional protections for pregnant women involved as participants in research are set forth in [45 CFR 46 Subpart B](#).

## Special Requirements Concerning the Consent of Children

The CFR defines *children* as:

“...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.” (45 CFR 46.402)

The legal age for consent in most states is 18; persons under age 18 are considered minors. However, in some jurisdictions, persons under age 18 can consent to treatment for substance abuse or dependence.

Additional protections for children and minors involved as participants in research are set forth in [45 CFR 46 Subpart D](#).

When children or minors are involved in research, both the *assent* of the child or minor and the *permission* of his or her parent(s) are usually required.

*Permission* means the agreement of parent(s) or a legal guardian to the participation of their child or ward in research.

*Assent* means a child's agreement to participate in research. Failure to object is not assent.

In most cases, both parents must give their permission for their child or minor's participation in research. However, [exceptions](#) to this requirement are permitted in certain circumstances. An exception is also permitted in the case of an [emancipated minor](#).

Although children may be legally incapable of giving informed consent, they may nevertheless be able to assent to or dissent from participation in research.

Out of respect for children as developing persons, children should be asked whether or not they wish to participate in the research, particularly if:

- The research does not involve interventions that are likely to benefit the participants, and
- The child can understand what it means to be a volunteer for the benefit of others.

A child's assent should be sought when the child is capable of providing such assent, taking into account his or her age, maturity, and psychological state. The age that a child needs to attain to give assent varies from state to state. In [certain circumstances](#), the IRB may determine that research can proceed without the assent of the children involved.

# Special Requirements Concerning the Consent of Prisoners



Because of their incarceration, prisoners may be under constraints that potentially affect their ability to make a truly voluntary decision about whether or not to participate in a study.

[45 CFR 46.303](#) defines a *prisoner* as:

“Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.”

Additional safeguards for the protection of prisoners involved in research (set forth in [45 CFR 46 Subpart C](#)) include the following:

- The IRB must approve the study as prisoner research.
- The IRB that reviews and approves the study must include a prisoner or prisoner advocate in its membership.
- A majority of the IRB members (exclusive of prisoner members) must have no association with the prison(s) involved in the research, apart from their membership on the IRB.
- The study must present no more than minimal risk to the participants.
- The proposed research must involve the study of:
  - The possible causes, effects, and processes of incarceration and criminal behavior.
  - Prisons as institutional structures or prisoners as incarcerated persons.
  - Conditions that particularly affect prisoners (e.g., vaccine trials; research on hepatitis, which is more prevalent in prisons than elsewhere; research on social and psychological problems such as alcoholism, drug addiction and sexual assault).
  - Practices intended to improve the health or well-being of the participants.

## Part 4: The Informed Consent Process



### Elements of the Informed Consent Process

Part 1 of this module examined the informed consent document in detail. Part 4 will examine the process of obtaining informed consent from potential study participants.

To be valid, informed consent must be based on the following:

#### Capacity to Give Informed Consent

Before the informed consent process can begin, the potential participant must be deemed capable of understanding his or her actions and making a reasoned decision. If the person lacks capacity because he or she is a minor, is ill, or for any other reason, special provisions must apply (such as a life-threatening emergency), or the person may not be included in the study.

A person who has a court-appointed legal guardian or who has been determined by a court to be legally incompetent cannot sign an Informed Consent Form even if he or she has the capacity to make a decision. This determination is made by the legal system and not by clinicians.

#### Disclosure of all Relevant Information

The research team must disclose all relevant information about the study to the potential participant. The information disclosed must be sufficient to enable the potential participant to make an informed reasoned decision about whether to participate. This information generally includes:

- The purpose of the study.
- The nature of the procedure or intervention that is being studied.
- Reasonable alternatives to participation in the study.
- The potential risks and benefits as well as the uncertainties of study participation.
- The participants obligations for the duration of the study.

#### Comprehension by the Participant

The potential participant must understand the information disclosed to him or her about the research study. The participant is free to ask questions to the study team as well as take additional time to make a decision regarding participation. The research team must be able to evaluate the potential participant's ability to understand what his or her participation in the study would involve. The informed consent document might include a quiz or other documented assessment to assess whether the participant truly understands the study.

## **Voluntary Agreement by the Participant**

The participant must agree to participate in the research study and his or her agreement must be voluntary and free from coercion or undue influence.

## **Right to Withdraw**

The participant must be informed that he or she has a right to withdraw from the study at any time and for any reason, without penalty or loss of benefits that he or she would otherwise be entitled to receive.

If a participant wishes to withdraw from a study in which an experimental drug is being tested, he or she must be informed of any procedures that are recommended to ensure safe withdrawal from the study drug. The participant must also be advised of any consequences of withdrawal, such as the inability to continue taking the study medication. No further data will be collected on the participant, but the participant will be informed that data already collected can be used for study analysis.

The research team or principal investigator may terminate participation in a study if it is in the best interest of the participant.

## Part 5: Inviting Potential Participants to Enroll in a Research Study

Written documentation of [Institutional Review Board](#) approval of the study, consent document(s) and recruitment materials (where appropriate) must be obtained and provided to the sponsor. NIDA and the CTN Lead Investigator must give their approval before recruitment can begin at a study site.

Members of the research team may find it helpful to keep the following questions in mind as they go through the process of recruiting participants for a study:

### Is the participant capable of understanding information about the study and giving informed consent voluntarily?



Adults have the capacity to consent when they possess sufficient mental capability to:

- Understand information given to them.
- Appreciate the relevance of the information to their circumstances.
- Make a reasoned decision about whether or not to participate in a particular study.

Capacity to consent may be affected by several factors, including:

- Age.
- Cognitive (mental) impairment.
- Illness.
- Treatments.

Capacity to consent is study-specific. A person may have sufficient capacity to carry out daily activities and make personal decisions, but he or she may not have sufficient capacity to appreciate the relevance of a given research study to his or her circumstances. On the other hand, a person may be incapacitated in daily activities but still have the capacity to consent to study participation.

For some participants or groups of participants, the investigator or the IRB may decide to obtain an independent capacity assessment. This may involve consulting a psychiatrist or neurologist for a determination of an individual's cognitive ability and ability to understand the details and implications of a study protocol.

If a person is unable to provide informed consent, a legal representative may give permission for the

individual to participate in research in some circumstances. A legal representative may be:

- A parent (for minors only).
- A legal guardian, as determined by state law, who can make health care decisions for a person who is unable to consent.
- An individual who holds a valid durable power of attorney for health care. Because of variability in legal opinions about the authority of the holder of a durable power of attorney for health care, the investigator should clarify whether institutional and IRB policies permit the holder of a durable power of attorney for health care to give informed consent for participation in research on behalf of a study participant.

### **Has the participant been given sufficient, accurate information about the study?**

To be informed means to have thorough knowledge of a matter. To be able to give informed consent, participants must have sufficient, accurate information about a study. This means that participants should be able to answer the following questions:

- What is the purpose of the research?
- Does the study involve an experimental treatment or procedure?
- Does the study involve random assignment to one treatment or another?
- What must I do as a study participant?
- What are the anticipated risks and benefits of participation in the study?
- What alternative treatments or procedures are available?
- Will participants in the study receive any compensation?
- Will I have any expenses for participating in the study?
- How long will my participation in the study last?
- Will my study records be kept confidential?
- Will I be informed in a timely manner about any issues that might affect my willingness to continue taking part in the study?
- Who is in charge of the study?
- Will I receive treatment whether I participate in the study or not?
- May I withdraw from the study at any time if I change my mind and no longer wish to take part?

To ensure that a participant has been given sufficient, accurate information about a study, a member of the research team should:

- Talk with the participant about the study's purpose and requirements.
- Provide fliers or brochures that describe the study or provide general information about clinical research, if available.
- Invite the participant to ask questions and respond to questions asked by the participant.
- Give the participant plenty of time to read the informed consent document and ask questions about it.
- Give the participant a copy of the informed consent document to take home and read before signing it. Additionally, give the participant a copy of the consent form after he or she has signed it.
- Invite the participant to call with questions later and provide the names and phone numbers of people to call.

Potential study participants may have difficulty focusing for an extended period of time for various reasons. For example, in some study populations (e.g., substance use disorders), such difficulty could be related to co-occurring illness, chronic pain, or withdrawal from substance use. Information must be presented in a language they can understand, at a pace they can keep up with, and in a manner that invites questions.

Sometimes information about a study may be presented to a group of potential participants. In this situation, it is important to meet with participants individually, ensuring that each person has the opportunity

to ask questions in private.

### **Does the participant understand the information he or she has been given about the study?**

The research team must be satisfied that the participant understands what he or she has been told about the study. Participants who are in withdrawal, depressed, manic, or otherwise psychiatrically or cognitively impaired may not be able to give informed consent.

The best way to be sure that the participant understands the information he or she has been given about the study is to review the consent document with the participant, line-by-line. Then, ask the participant questions about the study to ascertain what information he or she has absorbed.

It may be helpful to prepare a quiz to test the participant's understanding of the study. Such a quiz would have to be prepared in advance and submitted to the IRB for review and approval along with the other consent documents.

There are instances when it is challenging to assess that participants understand the information they have been given. Consider the following conditions.

### **A Participant has Limited Speaking Ability in English**

[45 CFR 46.116](#) requires that:

“the information given to the participant or the representative shall be in language understandable to the participant or the representative.” In practice, most IRBs require the informed consent document to be translated for potential participants who have limited or no understanding of spoken English. Researchers must follow the procedure approved by the IRB for obtaining consent from these participants.

It is also important to be aware of specific language differences that may be confusing to participants who are not fluent in English. For example, in Spanish, the word “once” means the number 11. An instruction to “take this medication once daily” might be confusing to a Spanish-speaking participant.

### **A Participant has Limited Reading Ability**

[45 CFR 46.117](#) states:

“[the consent] form may be read to the participant or the participant's legally authorized representative, but in any event, the investigator shall give either the participant or the representative adequate opportunity to read it before it is signed.” The participant may take the consent home and return at a later date with a decision.

Both [45 CFR 46.117](#) and [ICH E6 GCP 4.8.9](#) state that if a participant is unable to read, a witness must be present throughout the informed consent discussion and must sign the consent form(s).

### **Is the participant's decision to participate in the study entirely voluntary or has he or she been coerced or influenced in any way (e.g., by circumstances or by other people)?**

Coercion occurs if an individual perceives that he or she could be harmed or punished for refusing to take part in a study, or if he or she feels compelled due to financial circumstances.

Historically, individuals in relationships of dependence or unequal power have been particularly vulnerable to coercion. Coercion occurred in the 1960s at Willowbrook State School when some parents could not admit their child to the school unless they agreed to the child's participation in studies in which children



were deliberately infected with hepatitis.

Blatant coercion such as this, as well as coercive financial incentive, is rare today because of the vigilance of research teams and IRBs. However, in some cases, coercion may occur subtly and unintentionally. This kind of coercion can be more difficult to detect.

**Does the participant understand that signing the informed consent document indicates agreement to participate in the study?**

In most cases, the dated signature of the participant, or his or her legally authorized representative, on the informed consent document indicates that the participant understands the study and is willing to participate. Signing the informed consent document should be the final step in the informed consent process.

A member of the research team must sign the consent form to confirm that:

- To the best of the team member's knowledge, the participant has understood the information given to him or her about the study and is volunteering without coercion.
- The informed consent process followed the procedures authorized by the local IRB.

ICH GCP requires that the person conducting the informed consent discussion sign the form.

The participant should be given a copy of the signed consent document. The original must be kept on file in the research offices per local IRB guidelines.

## Part 6: Quality Control in the Informed Consent Process



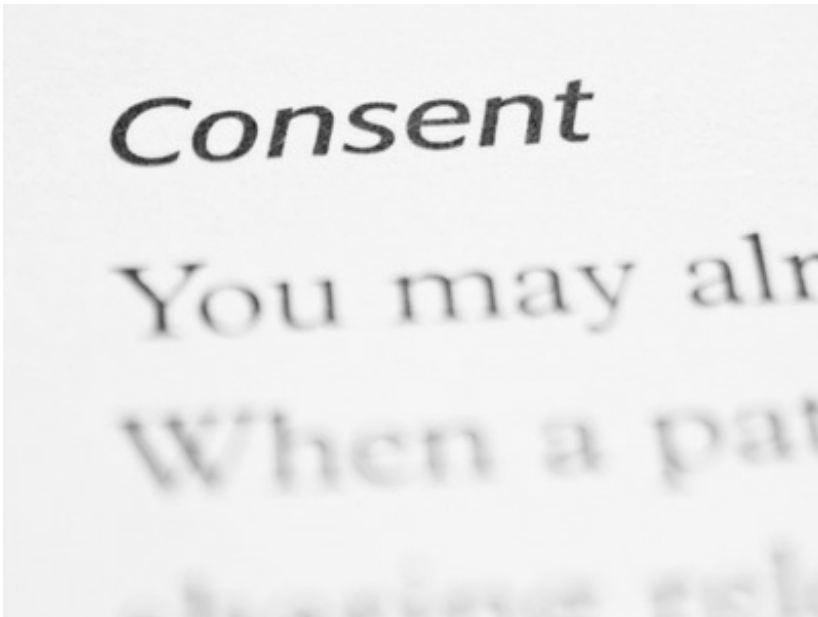
Protection of human research participants is the primary goal of the IRB and the informed consent process. Failure to comply with general requirements for informed consent ([45 CFR 46.116](#)) and documentation of informed consent ([45 CFR 46.117](#)) may result in suspension of a study. Errors in the informed consent process are considered protocol violations and, as such, must be reported to the relevant IRBs, along with a description of the action taken to correct the error and prevent it from occurring again.

If violations of the informed consent process are severe or continuing, penalties may be imposed and the IRB may report the problem to the regulatory authorities. It is therefore important to ensure that the process of obtaining informed consent from participants is carried out carefully and with due attention to every detail. This section describes common errors that can occur in the informed consent process and discusses how they can be prevented.

Remember, mistakes will happen. The most important thing to remember is to deal with them openly and honestly and report them immediately upon identification. The study staff will help you identify methods to prevent them from happening again.

The following are examples of some of the most common errors that can occur in the informed consent process.

## Part 6: Quality Control in the Informed Consent Process



### **The Participant Signs the Informed Consent Form After Study Procedures Have Begun**

#### **How did this happen?**

Some studies may involve clients as they come into the clinic. An eager staff member sees that the person who usually conducts consent interviews is busy and tries to help by having the client “just fill out some forms” while waiting.

Another staff member later assumes, without checking and without seeing the completed forms, that the participant has already completed the informed consent documentation and proceeds to enroll the person into the study.

#### **How can this error be prevented?**

- Never assume anything. Always check that a participant’s informed consent documentation is complete before beginning a study procedure.
- Never perform any study assessments on potential participants before informed consent has been obtained.

**Corrective Action:** Review the study and the consent form with the participant as soon as the failure is identified. Document all steps to correct the situation, attach them to the signed Informed Consent Form and notify your supervisor as soon as possible.

## **Part 6: Quality Control in the Informed Consent Process**

### **The Consent Form is Signed by the Participant But is Missing the Initials or Signature of the Investigator or Witness (if Applicable), or is Not Dated**

#### **How did this happen?**

The investigator may have become distracted. Perhaps the phone rang or another client needed attention. Perhaps the participant asked a question about another aspect of the study and the investigator turned the page, forgetting to sign or initial the form as required or to check that the participant has written the date on the form next to his or her signature.

It is important to remember that the principal investigator (PI) is accountable for the informed consent process. While the PI may delegate the task of reviewing or discussing informed consent to another research staff member, such as the research coordinator or clinician, the PI must provide oversight of the process and ensure that the participant is comfortable with the discussion.

#### **How can this error be prevented?**

- Conduct consent interviews in a quiet, separate room.
- When reviewing a consent form with a participant, focus on that task. Don't answer the phone or respond to distractions unless there is a genuine emergency.
- The person obtaining the participant's consent must be present when the consent form is signed. Having the investigator sign the consent form later is unacceptable. Never backdate a consent form.
- Create and use a checklist to ensure that every detail in the informed consent process is completed.

## **Part 6: Quality Control in the Informed Consent Process**

### **Whiteout is Used to Correct an Error on the Consent Form**

#### **How did this happen?**

Failure to follow Good Clinical Practice or Good Medical Record correction techniques is the only reason for this error. Whiteout should never be used on any research or medical record document.

#### **How can this error be prevented?**

By following good documentation practices. If an error occurs while the consent form is being completed, use Good Clinical Practice or Good Medical Record correction techniques to correct it: Cross out the error without obscuring the original entry, initial and date the crossing-out, and enter the correct information. (See also [Good Medical Record practices to observe when writing progress notes](#) in the [Documentation and Record-Keeping](#) module.)

## Part 6: Quality Control in the Informed Consent Process

### An Out-of-Date Version of the Consent Form is Used

#### How did this happen?

Several versions of an Informed Consent Form may be developed before IRB approval is received. Or, if the study has been in progress for more than 1 year, a new version of the consent form (most likely with a different date stamp) will have been prepared. In either case, a staff member may mistakenly pull out and use an out-of-date version of the form.

#### How can this error be prevented?

- Ensure that the current version of the consent form is readily identifiable (e.g., color coded, marked with a prominent date stamp).
- Keep copies of the current version of the consent form in a different place than older, archived versions. Destroy copies of old, unused consent forms and *mark the old original as obsolete* in the regulatory binder.

**Corrective Action:** When the issue is identified re-consent the participant using the appropriate Informed Consent Form. Attach a memo identifying the issue and the corrective action to the new consent form.

## Part 6: Quality Control in the Informed Consent Process

### A New Consent Form is Required, But Not All Participants Signed It

#### How did this happen?

- Some participants were absent from the clinic during the week when most participants signed new consent forms. When the absent participants returned the following week, the need for them to sign new consent forms was overlooked.
- A staff member assumes that a colleague already had the participant sign a new consent form.

#### How can this error be prevented?

- Again, never assume anything. When a new consent form is required, check on each participant's next clinic visit to ensure that he or she has signed the new form.
- Devise a system for flagging the files of participants who have not yet signed new consent forms.
- Use a tracking spreadsheet.
- Ensure documentation of consent form is in the source notes.

**Corrective Action:** When the issue is identified have the participant review, sign and date the new consent form. Document the reason for the delay and attach it to the new consent form.

## **Part 6: Quality Control in the Informed Consent Process**

### **The Original Consent Form Has Been Lost**

#### **How did this happen?**

- A staff member may mislay a participant's consent form among other papers on his or her desk.
- The form may have been filed incorrectly.
- The original of the consent form may have been given to the participant by mistake.

#### **How can this error be prevented?**

- Devise written procedures for the handling of informed consent documentation and train all staff in the use of these procedures.

**Corrective Action:** Report the loss of a consent form immediately to the IRB and/or the sponsor and get another signed as soon as possible. To avoid the appearance of fraud, carefully document the sequence of events that led to the loss of the first consent form.



## Part 6: Quality Control in the Informed Consent Process

### Informed Consent Activity

Users are instructed to choose the answer that best describes the action to correct the informed consent document as described.

1. As the research coordinator for a study at ABC Treatment Center, you discussed the informed process with the participant and she signed and dated the informed consent form. After re-reviewing the form later that day, you noticed that the study participant signed the informed consent form but added yesterday's date and she has already left the clinic. What should you do? Choose the best answer from the options given below:
  - A. You cross out the wrong date and add the correct date.
  - B. Throw away the old consent form and start a new informed consent form when the participant comes in for the next visit.
  - C. Ask the PI to cross out the wrong date, add the correct date, then initial, and date the informed consent form with the current date.
  - D. On the next visit, ask the participant to cross out the wrong date, add the correct date, then initial, and date the informed consent form with the current date.
  - E. Do nothing. Yesterday's date will suffice.

*Feedback: Which do you choose: A, B, C, D, or E? The best answer is: On the next visit, you should ask the participant to cross out the wrong date, add the correct date, then initial, and date the informed consent form with the current date. That would be multiple choice D.*

2. Now that you know how to correct the informed consent form when an error occurs, how could you prevent the problem from occurring again? (*Choose the best answer from the options given below.*)
  - A. Have a list handy of key items to check when reviewing informed consent documents signed by study participants.
  - B. Highlight the initial, signature, and date lines in the actual consent form document so that as the form is discussed, these areas are clearly identified.
  - C. Be sure to review the signed informed consent form before the participant leaves the visit to ensure that all items are marked, signed, and dated appropriately.
  - D. Keep a calendar handy to check today's date against the date provided by the participant in the form.
  - E. All of the above.

*Feedback: Which do you choose: A, B, C, D, or E? The best answer is: All of these strategies would help participants to complete accurately the informed consent form. That would be multiple choice E.*

## Part 7: Requirements for the Documentation of Informed Consent



Requirements for the documentation of informed consent are set forth in [45 CFR 46.117](#), [21 CFR 50.27](#), and [ICH GCP 4.8](#). In brief, these requirements are as follows.

### **Informed Consent Shall be Documented by the Use of a Written Consent Form**

- The IRB must approve the consent form.
- The participant or the participant's legally authorized representative must sign the current version of the IRB approved consent form.
- ICH GCP requires that the consent form should also be signed by the person conducting the informed consent discussion.
- A copy of the form must be given to the person who signs it. The study site must keep the original on file.

### **The Consent Form May Take One of Two Organizational Structures**

- A written document that embodies the elements of informed consent required by [45 CFR 46.116](#). This form may be read to the participant or the participant's representative. The investigator should give the participant or representative ample time to absorb the content of the form before signing it.
- A short-form written document stating that the elements of informed consent were presented orally to the participant or the participant's representative. When the short form document is used:
  - A witness must be present at the oral presentation.
  - The IRB must approve a written summary of what is to be said to the participant or representative.
  - The participant or representative must sign only the short form itself.
  - The witness must sign both the short form and a copy of the summary.
  - The person obtaining the participant's consent must also sign a copy of the summary.
  - A copy of the summary, in addition to a copy of the short form, must be given to the participant or the participant's representative.

## **Researchers Must Not Waive or Appear to Waive Any Legal Rights of Participants**

For example, care must be taken when describing what compensation (beyond the provision of immediate or therapeutic intervention) the institution is voluntarily willing to provide in an event such as a research-related injury.

Participants should understand that, regardless of what the institution may agree to provide as compensation for a research-related injury, they retain the right to take legal action against the institution and/or those responsible for the injury.

## **The Consent Form Must be Revised When New Information Becomes Available that May Be Relevant to the Participant's Consent**

If a new [adverse event](#) appears to be related to the study medication (e.g., a severe allergic reaction that occurs shortly after a medication is given), this risk should be added to a revised consent form.

- The revised consent form must be approved by the IRB.
- The participant must be informed of the new information in a timely manner.
- The communication of the new information to the participant must be documented.

## **Other considerations for the Informed Consent Process**

The investigator must document the informed consent process in the participants' source notes. When new information becomes available which results in a revised informed consent form, the participant must be informed in a timely manner and the communication of this information must be documented in the source notes.

In obtaining and documenting the informed consent, the investigator should comply with ethical principles that have their origin in the Declaration of Helsinki, ICH GCP, CFR and applicable regulatory requirements.

Non-therapeutic trials should be conducted in subjects who are capable of personally giving consent and signing and dating the consent form.(ICH GCP 4.8.13)

Non-therapeutic trials may be conducted with consent from a legal representative if the following conditions are met:

- The objectives of the trial cannot be met by a participant that can personally give consent.
- The foreseeable risks to the participants are low.
- Any negative impact on the participants' well-being is minimized.
- The trial is not prohibited by law.
- The approval of the IRB is expressly sought on the inclusion of such participants and is documented in a written approval letter.

These type of non-therapeutic trials should be conducted in patients having a disease or condition for which the investigational product is intended and they should be closely monitored.

## **Further Information**

- [45 CFR 46.116](#)
- [21 CFR 50.20](#)
- [ICH E6 GCP 4.8](#) — ICH GCP Guidelines
- [45 CFR 46 Subpart B](#) — Research Involving Pregnant Women
- [45 CFR 46.408](#) — Research Involving Children
- [45 CFR 46.303](#) — Research Involving Prisoners

## Part 8: Scenario

The three investigators below are planning clinical trials that involve substance abuse treatment. Read about each of their trials, and then make a decision: **Who did NOT obtain the informed consent necessary for the individual to participate in the trial?** After making your selection, consider the feedback provided.

### Interactive: Informed Consent

**Scenario:** Three investigators are planning clinical trials that involve substance abuse treatment. Read about each of their trials, and then make a decision: Who did NOT obtain the informed consent necessary for the individual to participate in the trial?

#### A) Dr. Johnson

Marc has been using cocaine for nearly ten years and is interested in seeking treatment. Dr. Johnson is leading a clinical trial on a pharmacological treatment for cocaine addiction.

After receiving details about the study and having all of his questions answered, Marc decides to think about it for a few days and talk it over with some friends and family members. He comes back later that week, asks Dr. Johnson some additional questions, and after hearing the responses signs and dates his consent to participate in the study, and Dr. Johnson proceeds with enrollment. Did Dr. Johnson obtain the necessary informed consent?

#### B) Dr. Band

Dr. Band is researching the effects of buprenorphine/naloxone (BUP/NX) for participants dependent on prescription opioid analgesics. Alicia— a 38 year old prescription opioid user— is interested in the study.

Dr. Band leaves the consent form for Alicia to read over, but she has a difficult time understanding the medical terms and can't answer any of the consent quiz questions correctly. In the interest of saving time Dr. Band has her sign and date the consent form and enrolls her and promises to review the study procedures in detail at their next visit. Did Dr. Band obtain the necessary informed consent?

#### C) Dr. Hirsch

Ada has been trying to stop her heroin use on her own, but muscle and bone pain, insomnia, vomiting, and other withdrawal symptoms have caused her to repeatedly relapse. Dr. Hirsch is holding a clinical trial combining pharmacological and behavioral interventions for the treatment of heroin. The doctor explains the trial and the possible effects.

Ada asks questions about the study, demonstrates her understanding of the procedures, signs and dates the consent form for the study. Did Dr. Hirsch obtain the necessary informed consent?

**Who did NOT obtain the informed consent necessary for the individual to participate in the trial: A, B, or C? Let's consider the feedback:**

#### A) Dr. Johnson

*Feedback:* Dr. Johnson provides the appropriate information about the study and answers all of Marc's questions. He allows Marc to absorb the information, discuss with others, and be comfortable and confident with his decision before signing the consent form. Sorry, A is not the correct answer. The necessary informed consent was obtained in this case.

**B) Dr. Band**

*Feedback:* Dr. Band leaves the consent for Alicia to read and does not explain any of the information. He enrolls Alicia in the study without her fully understanding the study information, and requests that she sign the consent despite knowing that she does not demonstrate an understanding of the study. A consent form should be written in nontechnical language that potential participants would understand, in language consistent with the proposed participants' educational level, cultural views, and familiarity with research. If you chose B, you are correct. In this case, he did NOT obtain the informed consent necessary for the individual to participate in the trial.

**C) Dr. Hirsch**

*Feedback:* Dr. Hirsch explains the procedures and information regarding the study, answers Ada's questions and asks her questions to ascertain her understanding of the trial. Only then does she sign and date the consent and enroll in the study. Sorry, C is not the correct answer. The necessary informed consent was obtained in this case.

## Part 9: Summary of Key Points

- Informed consent is a process by which a person voluntarily agrees to participate in a research study after being fully informed about it.
- The informed consent document should contain all of the information that the participant needs to make an informed decision about participating in the study.
- The participant's signature on the informed consent document confirms his or her voluntary agreement to take part in the study.
- The general requirements for informed consent in federally funded research are spelled out in 45 CFR 46.116 and 21 CFR 50.20. Some states have enacted requirements for informed consent that go beyond federal regulations.
- All researchers have a responsibility to ensure that the process of obtaining informed consent or assent from study participants not only conforms to federal, state, and local regulations but also respects each individual's right to make an informed decision voluntarily.
- The first step in the process of informed consent is preparing the consent document and supporting documents for presentation to the Institutional Review Board that must review and approve the study and consent document. The IRB must review and approve the consent document before the study can begin.
- Consent documents should be written in nontechnical language that the proposed participants would understand. The language should be consistent with the proposed participants' educational level, cultural views, and familiarity with research.
- The information that must be provided in an informed consent document is specified in 45 CFR 46.116, 21 CFR 50.20, and ICH GCP 4.8.10.
- The legal age for consent in most states is 18; persons under age 18 are considered minors. Additional protections for children involved as participants in research are set forth in 45 CFR 46 Subpart D. In most cases, both parents must provide permission and the child himself or herself must assent to the child's participation in research.
- If a person is unable to provide informed consent, a legal representative may give permission for the individual to participate in research in some circumstances. Only one person gives consent. If the participant is capable and is not court ordered legally incompetent, then he or she should sign. If the participant is not capable or is legally incompetent, then the legal representative or guardian should sign. A child and the parents sign, but minor children assent, parents provide permission, and legal guardians consent.
- Participants must not be coerced or unduly influenced. Coercion occurs if an individual perceives that he or she could be harmed or punished for refusing to take part in a study. In some cases, coercion may occur subtly and unintentionally.
- The value of an incentive for participation in a study should not be so high that it could be considered an undue influence on an individual's decision to participate.
- It is important to ensure that the process of obtaining informed consent from human participants is carried out carefully and with vigilant attention to every detail. Failure to comply with general requirements for informed consent (45 CFR 46.116) and documentation of informed consent (45 CFR 46.117) may result in suspension of a study as well as fines and penalties.