Issues of Informed Consent

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PART I

Regulatory Requirements

Defining Consent

- Informed consent is a process and not just a document
- Informed consent is ongoing
- Informed consent….

  - **START:**
    "FDA considers direct advertising for study subjects to be the start of the informed consent"*
  - **END:**
    When participation ends? When the study ends? After the study ends?

* **Citation:** *Recruiting Study Subjects – Information Sheet*, FDA Guidance for Institutional Review Boards and Clinical Investigators, 1998.

IRB Review

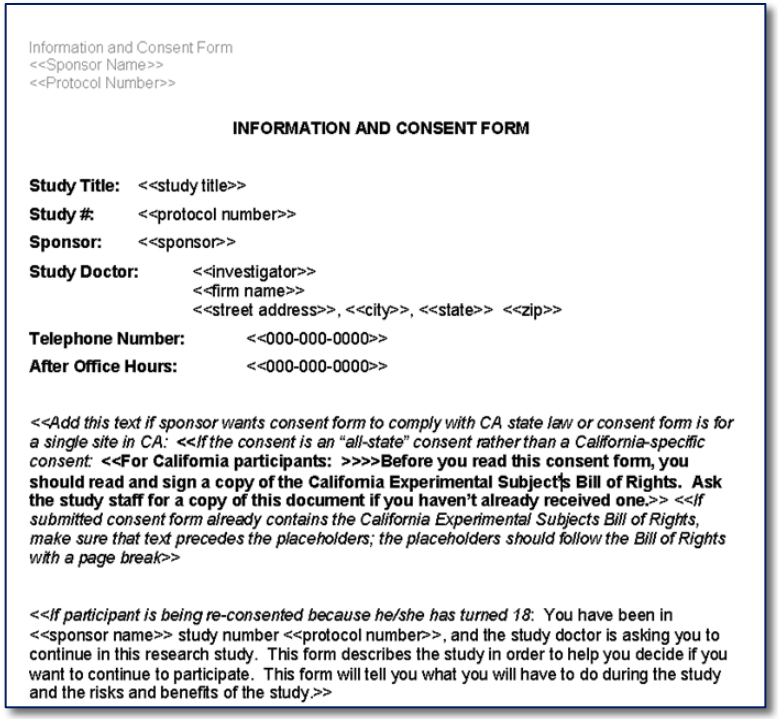
- "An IRB shall require that information given to subjects as part of **informed consent** is in accordance with [the general requirements of informed consent]."

- "…the IRB may require that information, in addition to that specifically mentioned in [the regulations] be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects."

*** Citation:** 21 CFR 56.109(b); 45 CFR 46.109(b)

IRB Review

- The IRB… "is the final authority on the content of the **consent** documents… presented to the prospective study subjects."



Information and Consent Form
<<Sponsor Name>>
<<Protocol Number>>

INFORMATION AND CONSENT FORM

Study Title: <<study title>>
Study #: <<protocol number>>
Sponsor: <<sponsor>>
Study Doctor: <<investigator>>
<<firm name>>
<<street address>>, <<city>>, <<state>> <<zip>>
Telephone Number: <<000-000-0000>>
After Office Hours: <<000-000-0000>>

<<Add this text if sponsor wants consent form to comply with CA state law or consent form is for a single site in CA: <<If the consent is an "all-state" consent rather than a California-specific consent: **<<For California participants: >>>>Before you read this consent form, you should read and sign a copy of the California Experimental Subject's Bill of Rights. Ask the study staff for a copy of this document if you haven't already received one.**>> *<<If submitted consent form already contains the California Experimental Subjects Bill of Rights, make sure that text precedes the placeholders; the placeholders should follow the Bill of Rights with a page break>>*

<<If participant is being re-consented because he/she has turned 18: You have been in <<sponsor name>> study number <<protocol number>>, and the study doctor is asking you to continue in this research study. This form describes the study in order to help you decide if you want to continue to participate. This form will tell you what you will have to do during the study and the risks and benefits of the study.>>

*** Citation:** A Guide to Informed Consent – Information Sheet, FDA, available at: http://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm, Updated 08/09/2011.

Basic Elements of Consent

1. Explanation of Research (purpose; duration; procedures)
2. Risks or Discomforts
3. Benefits
4. Alternatives
5. Confidentiality
6. Compensation and treatment information for research injury
7. Contact information (for research, rights, and injury questions)
8. Explanation of voluntariness

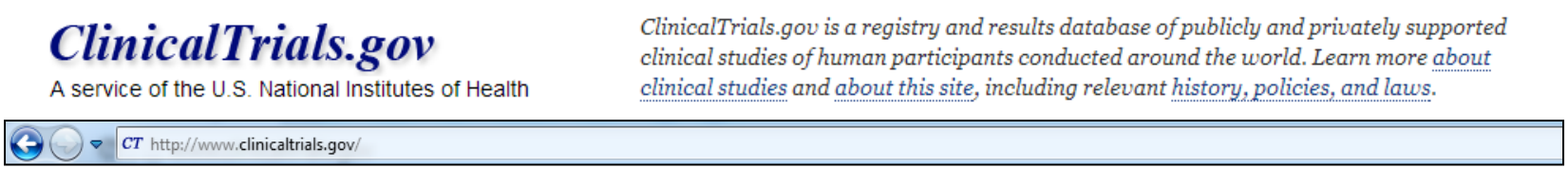
*** Citation:** 21 CFR 50.25(a); 45 CFR 46.116(a)

Additional Elements of Consent

1. Unforeseen risks (including risks to an embryo or fetus)
2. Involuntary termination of participation
3. Costs
4. Consequences of and procedures for withdrawing participation
5. Significant new findings
6. Number of participants

*** Citation:** 21 CFR 50.25(b); 45 CFR 46.116(b)

Clinical Trial Registry (Element of Consent)



- (1) When seeking informed consent for applicable clinical trials, as defined in **42 U.S.C. 282(j)(1)(A)**, the following statement shall be provided to each clinical trial subject in informed consent documents and processes. This will notify the clinical trial subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank under paragraph (j) of section 402 of the **Public Health Service Act**. The statement is:
    - *"A description of this clinical trial will be available on **http://www.ClinicalTrials.gov**, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."*

*** Citation:** 21 CFR 50.25(c)

PART II

Key Considerations

Understandability

- Regulations
  - "The information that is given to the subject or the representative shall be in language understandable to the subject or the representative"

- July 2014 Draft Guidance!
  - "Understandable means the information presented to potential subjects is in a language **and** at a level the subjects can comprehend (including an explanation of scientific and medical terms)"

*** Citation:** 21 CFR 50.20; 45 CFR 46.116; FDA Draft Guidance: Informed Consent Information Sheet, July 2014, available at: http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM405006.pdf

Understandability

- 32 million adults in the U.S. cannot read
- 77 million adults have basic or below basic health literacy
- Need to comply with the current regulatory and legal requirements while still making consent forms and the consent process understandable and meaningful

*** Citation:** *The U.S. Illiteracy Rate Hasn't Changed in 10 Years*, Huffington Post, posted 09/06/2013, accessed 07/10/2013 at http://www.huffingtonpost.com/2013/09/06/illiteracy-rate_n_3880355.html, citing: research conducted by the U.S. Department of Education and the National Institute of Literacy in April 2013. FDA Draft Guidance: Informed Consent Information Sheet, July 2014.

Understandability

- **Define acronyms and terms the FIRST time they are used**
- **Use of Second vs. First Person**
- **Use Tables, Diagrams, Pictures to describe procedures***
- **Boilerplate or "template" language**
  With simple explanations of common procedures, study designs, sample storage, medical concepts, and other research specific concepts.
- **Consistent Terminology Throughout**
- **Reading level software/analysis**

* **Citation:** See FDA Draft Guidance: Informed Consent Information Sheet, July 2014.

Therapeutic Misconception

- Therapeutic misconception =
  - The assumption of research subjects that decisions about their care are being made solely with their benefit in mind

*** Citation:** FDA Draft Guidance: Informed Consent Information Sheet, July 2014, Citing: Appelbaum, PS, Roth, LH, and Lidz, C, "The Therapeutic Misconception: Informed Consent in Psychiatric Research," International Journal of Law and Psychiatry Vol. 5, (1982): 319-329.

Therapeutic Misconception

Research is NOT Treatment

- **Scientific Purpose:** Research is designed to produce generalizable knowledge
- **Study Procedures:** Research may involve products, procedures, and tests that are only intended to generate scientific knowledge and are not for patient care
- **Uncertainty:** There is less knowledge and more uncertainty about the intervention than with standard care
- **Adherence to Protocol:** Interventions are based on strict adherence to a protocol
- **Clinician as Investigator:** Clinicians in health care settings provide treatment and in research settings they investigate safety and efficacy

* **Citation:** *Clinical Trials and Medical Care: Defining the Therapeutic Misconception*. PLoS Med. Nov 2007; 4(11): e324.

Therapeutic Misconception

Terminology

- "Careful wording is needed in order to avoid…a subject's therapeutic misconception." Examples:

 *Treatment* or *patient*

 *Doctor*

 *Closely monitor*

 *"For your health"*

*** Citation:** See FDA Draft Guidance: Informed Consent Information Sheet, July 2014.

What Information is "Important"

- IRB members, researchers and research participants were asked to review a consent form for a bio-bank and highlight sentences that contain information important to a participant

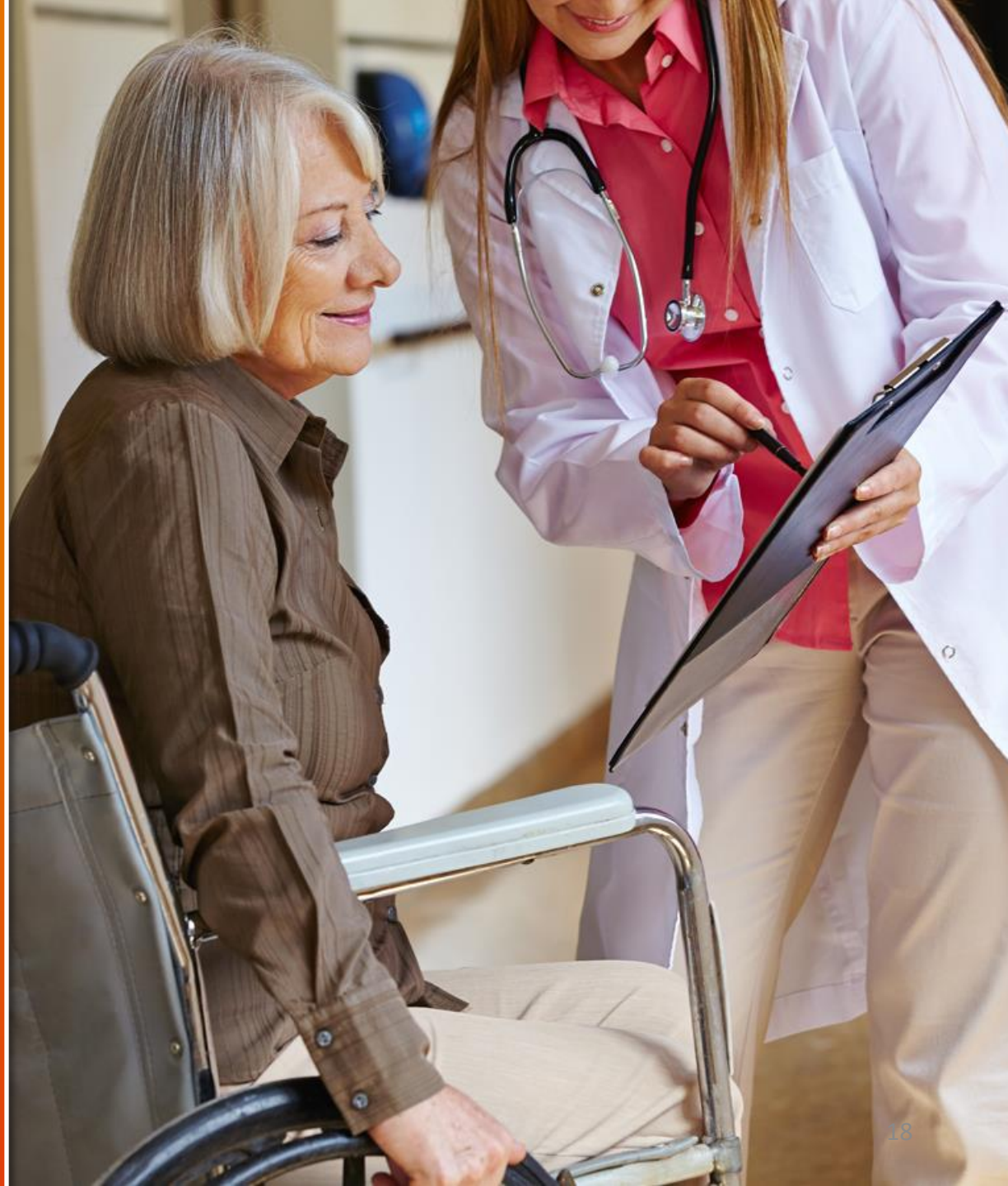
- Mean selected out of 207 sentences:

Participant	Number of Sentences	Percentage of "Important" Sentences
Research Participant	83.7	40%
Researcher	109.8	53%
IRB Member	149.7	72%

*** Citation:** Beskow, Laura M. *Informed Consent for Biobanking* (March 22, 2012), Duke Institute for Genome Sciences & Policy, slides available online: http://www.niehs.nih.gov/news/assets/docs_f_o/informed_consent_for_biobanking.pdf

PART III

ELEMENTS of Consent



The Consent Form Introduction

A statement that the study involves **research**

*** Citation:** FDA, 21 CFR 50.25(a)(1); DHHS, 45 CFR 46.116(a)(1); ICH, 4.8.10(a)

Study Purpose & Background

"What is the Study About?"

An explanation of the **purpose** of the research

ADVICE:

1. The explanation should reflect the purpose of the research as stated in the "Objectives" or other applicable section of the protocol.
2. In general, the consent form should list primary objectives. However, secondary objectives may be included as well.

*** Citation:** 21 CFR 50.25(a)(1); 45 CFR 46.116(a)(1); ICH, 4.8.10(b)

Study Purpose & Background

"What is the Study About?"

If appropriate, the **approximate number** of subjects involved in the study

ADVICE:

1. If appropriate and known, include the number of subjects in the submission materials to the IRB. Otherwise, the IRB may ask you about the approximate number of subjects in a follow-up correspondence.

*** Citation:** 21 CFR 50.25(b)(6); 45 CFR 46.116(b)(6); ICH, 4.8.10(t)

Alternatives

A list of pertinent **alternative** procedures or treatment

ADVICE:

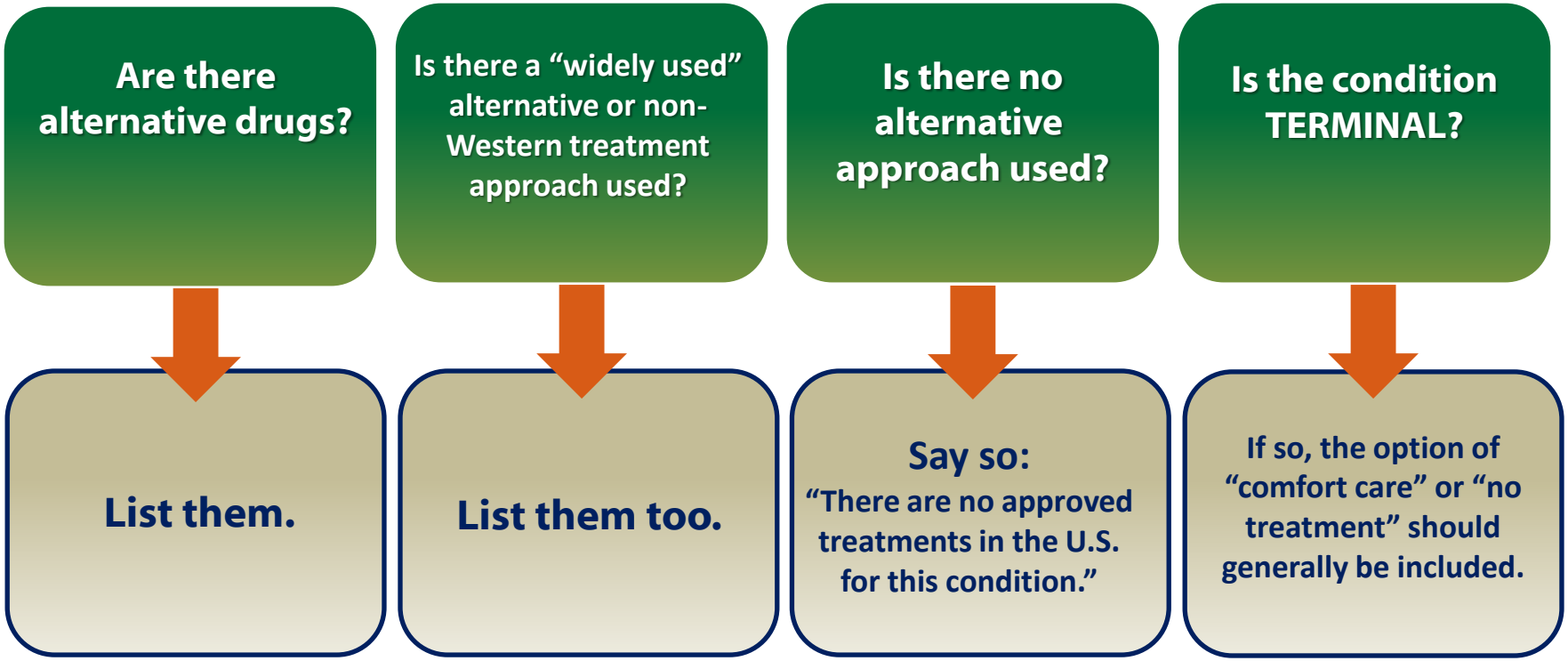
1. July 2014 Draft Guidance! "FDA recommends subjects first be informed of the care a patient would likely receive if not part of the research and then be provided with information about the research."
2. Generally, the list of alternatives will include treatments obtainable outside of the study.
3. In studies in healthy subjects, or in data-collection studies, pertinent alternatives may not exist. The alternatives sections for these studies should communicate that the participant's alternative is to not participate in the study.
4. The consent form should only list supportive-care options if the study will enroll participants who are at end of life, such as participants with late-stage cancer.

EXAMPLE TEXT:

"You should discuss your alternatives to participating in this research with the study doctor or study staff. In addition, you may discuss your options with your regular health care provider."

*** Citation:** *21 CFR 50.25(a)(4); 45 CFR 46.116(a)(4); ICH, 4.8.10(i);* FDA Draft Guidance: Informed Consent Information Sheet, July 2014.

Alternatives



Study Funding & Conflict of Interest

"Who is paying for this study?"

If appropriate, language related to reportable **conflicts of interest**

Example Text:

"The study doctor receives payment from the sponsor, such as for speaking and consulting fees. If you have concerns about this payment, ask the study doctor for more information."

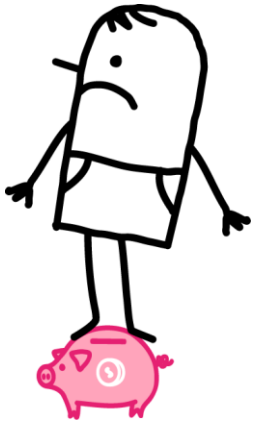
"A study staff member has a significant amount of stock or other ownership in the sponsor of the study. If you have concerns about this ownership, ask the study doctor for more information."

"The study doctor is an employee or executive of the sponsor. If you have concerns about this employment, ask the study doctor for more information."

*** Citation:** See 21 CFR 56.109(b); 45 CFR 46.109(b) (These citations do not specifically address conflicts of interest, but rather the IRB having the ability to add information to consent forms that meaningfully adds to the protection of participants)

Participant Costs

"Will it cost anything to be in this study?"



A statement explaining any additional **costs** to the subject that may result from participation in the research

Advice:

1. Costs may include the test article; rescue medication, other medication or supplements given as part of the study; costs related to procedures; insurance co-pays; etc.

2. The term "free" is allowable but should be used judiciously. For example, the phrase "you will receive free medical treatment" is not allowed. However, the phrase "free of charge" in reference to study procedures and costs is allowable and does not have to be replaced with the phrase "at no cost."

*** Citation:** FDA 21 CFR 50.25(b)(3); 45 CFR 46.116(b)(3); ICH, 4.8.10(l)

Duration

"How long will I be in this study?"

The expected **duration** of the subject's participation – including the number of visits a participant will have as part of the study

Advice:

1. The duration of a subject's participation may include screening periods and follow-up periods. The screening and follow-up periods should therefore be included as part of the total duration of study participation, or the duration of screening/follow up should be noted separately from the duration of the study participation.

2. If applicable, the consent form should include language clarifying that the overall duration of participation is potentially indefinite or variable. For example, participation in oncology protocols is often indefinite or variable.

*** Citation:** 21 CFR 50.25(a)(1); 45 CFR 46.116(a)(1); ICH, 4.8.10(d); ICH, 4.8.10(s)

Duration

"How long will I be in this study?"

The expected **duration** of the subject's participation – including the number of visits a participant will have as part of the study

Example Text:

"If you decide to be in this study and the study doctor says you can be in the study, your participation will last about X <<days, weeks, months or years>>."

"You will be in the study for 10 weeks after the screening period; the screening period may last up to 30 days."

"If study drug dosing is stopped, you may continue your study participation by taking part in the study's follow-up period (described in this form). The follow-up period will not end unless you decide to withdraw from the study, your participation is stopped for any reason, or the study ends."

*** Citation:** 21 CFR 50.25(a)(1); 45 CFR 46.116(a)(1); ICH, 4.8.10(s)

Procedures

"What will happen during this study?"

If the research involves **study groups**:

- A description of the study groups
- The probability for random assignment to each group

Example Text:

Equal randomization: *"You will be assigned by chance (like flipping a coin) to 1 of the following study groups. You have an equal chance of being in <<either, any>> of the study groups."*

Unequal randomization: *"There is a X out of X chance you will get the drug and a X our of X chance you will get placebo."*

*** Citation:** 21 CFR 50.25(a)(1); 45 CFR 46.116(a)(1); ICH, 4.8.10(c)

Procedures

"What will happen during this study?"

If the research involves **blinding** or **randomization**:

- A explanation of the blinding
- Any procedures related solely to selection and randomization

Example Text:

Blinding: *"You will not know and the study doctor or study staff will not know which study group you are in. The study doctor or study staff can find out if it is necessary to know for your health. If this happens, the study doctor or study staff may not be able to tell you which study group you were in until everyone finishes the study (which may be years in some cases)."*

Randomization: *"Neither you nor the study doctor or study staff will be able to pick which study group you are in."*

*** Citation:** 21 CFR 50.25(a)(1); 45 CFR 46.116(a)(1); ICH, 4.8.10(f)

Procedures

"What will happen during this study?"

If the research involves a **placebo**: An explanation of placebo

Advice:

1. Ensure it is clear in the consent form that placebo will be used in the study.
2. A reference to a placebo run-in should NOT be so specific as to reveal when the run-in would occur.

*** Citation:** 21 CFR 50.25(a)(1); 45 CFR 46.116(a)(1); ICH, 4.8.10(f)

Procedures

"What will happen during this study?"

If the research involves a **placebo**: An explanation of placebo

Example Text:

"Placebo is a pill that looks like a drug but has no drug in it."

If placebo is used to maintain the blind: *"Some of the pills you receive may be a placebo. This is so that no one knows what dose you are receiving."*

If all participants receive placebo at some point: *"Everyone in this study will receive placebo during some part of the study."*

Procedures

"What will happen during this study?"

A statement describing the **dose amount and frequency** of dosing for studies testing drugs, vaccines, or biologic

- Include **total daily dose**, if different from per dose amount
- A statement describing the **frequency** with which the device is used for studies testing devices
- Language noting the **formulation** of the test article (e.g., pill, gel, etc.)

*** Citation:** 21 CFR 50.25(a)(1); 45 CFR 46.116(a)(1); 4.8.10(d)

Procedures

"What will happen during this study?"

A statement regarding a **change in current medications** for the purpose of participating in the study

Advice:

1. A change in current medication could be a
   a) washout (discontinuation) of current medication;
   b) change in dose of current medication; or
   c) change from one medication to another medication.
2. A washout or other change of medication for the study must occur AFTER the consent form is signed.
3. This consent requirement is not referring to medications that are <u>exclusion criteria</u>.

*** Citation:** 21 CFR 50.25(a)(1); 45 CFR 46.116(a)(1); ICH, 4.8.10(d)

Procedures

"What will happen during this study?"

A statement regarding a **change in current medications** for the purpose of participating in the study

Example Text:

"If you decide to be in this study, you might have to <<stop taking, change the dose of>> your regular medication, therapy, supplement>> during the entire study."

Procedures

"What will happen during this study?"

A description of the invasive and non-invasive **procedures** to be conducted

Advice:

1. The procedures subjects will encounter should be outlined in the consent form, or an explanation of the procedures, such as a procedures chart, may be attached to and referenced in the consent form before the signature page.
2. **Contrast dye:** If the protocol mentions contrast dye (such as *gadolinium*) will be used with scans, this should be noted in the consent form.
3. **Sensitive questions:** If there are questionnaires or interviews with potentially sensitive topics, the consent form should note this fact

*** Citation:** 21 CFR 50.25(a)(1); 45 CFR 46.116(a)(1); ICH, 4.8.10(d)

Procedures

"What will happen during this study?"

If the participant will give **blood samples** for communicable disease testing, illegal drug testing, or pregnancy testing during the study:

A statement that the blood samples will be used for testing

Advice:

1. Consider individual state laws regarding reporting.

*** Citation:** 21 CFR 50.25(a)(1); 45 CFR 46.116(a)(1); ICH, 4.8.10(d)

Procedures

"What will happen during this study?"

If the participant will give **blood samples** for communicable disease testing, illegal drug testing, or pregnancy testing during the study:

A statement that the blood samples will be used for such testing

Example Text:

"Some of your blood will be used to test for HIV and other communicable diseases (diseases that can be spread from one person to another). Ask the study doctor or study staff which diseases your blood will be tested for."

"The study doctor or study staff will tell you if the test results are positive. If required by law, the study doctor or study staff may report a positive test result to the local health department."

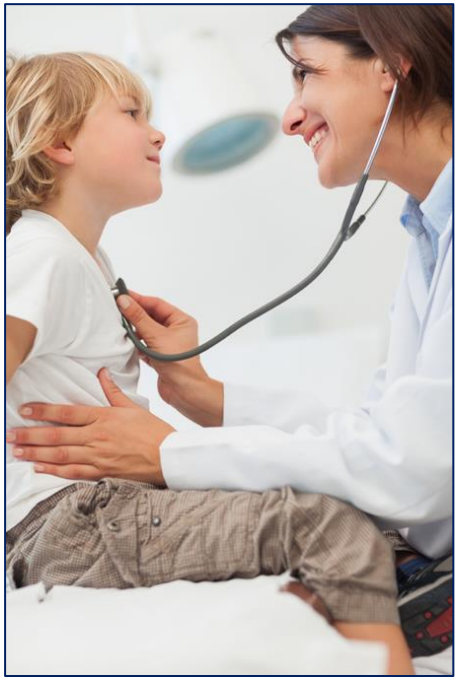
Benefits

"Will being in this study help me?"

A description of any **benefits** to the subject and/or to others which may reasonably be expected from the research

Advice:

1. The description of benefits to the subject should be clear and not overstated.
2. If applicable, a statement that there might be benefits to others should be included.
3. In discussing benefits to the subject, this section should only address potential benefits related to the participant's condition. <u>It should not include participant compensation.</u> In addition, this section should not include reference to free medical care (such as study procedures being provided at no cost).



*** Citation:** 21 CFR 50.25(a)(3); 45 CFR 46.116(a)(3); ICH, 4.8.10(h)

Risks

"What are the risks to me if I am in this study?"

A description of any reasonably foreseeable **risks** or discomforts to the subject

Advice:

1. If the study does not involve physical risk, only confidentiality risk language may apply.

2. Do not minimize risks unless the minimizing language is supported (e.g. *this side effect is rare, occurring in X% of people who have received the study drug*).

*** Citation:** 21 CFR 50.25(a)(2); 45 CFR 46.116(a)(2); ICH, 4.8.10(g)

Risks

"What are the risks to me if I am in this study?"

A description of any reasonably foreseeable **risks** or discomforts to the subject

Advice (Continued):

3. the consent form should not include risk language for standard of care study procedures or approved study products, a surgery the participant must have to qualify to be in the study etc.

4. the consent form should include risks of study procedures relating solely to research (e.g. risks related to infusions/injections, lumbar puncture, MRIs, CT scans, Contrast Dye, X-rays, etc.)

*** Citation:** 21 CFR 50.25(a)(2); 45 CFR 46.116(a)(2); ICH, 4.8.10(g)

Risks

"What are the risks if I or my partner are pregnant or nursing during this study?"

If women of child-bearing potential are included in the study:

A statement that the particular study product or procedure may involve **specific risks to the pregnant subject or to the embryo or fetus**

Advice:

1. Risk language may also include unknown risks related to nursing.

*** Citation:** 21 CFR 50.25(a)(2), (b)(1); 45 CFR 46.116(a)(2), (b)(1); ICH, 4.8.10(g)

Risks

"What are the risks if I or my partner are pregnant or nursing during this study?"

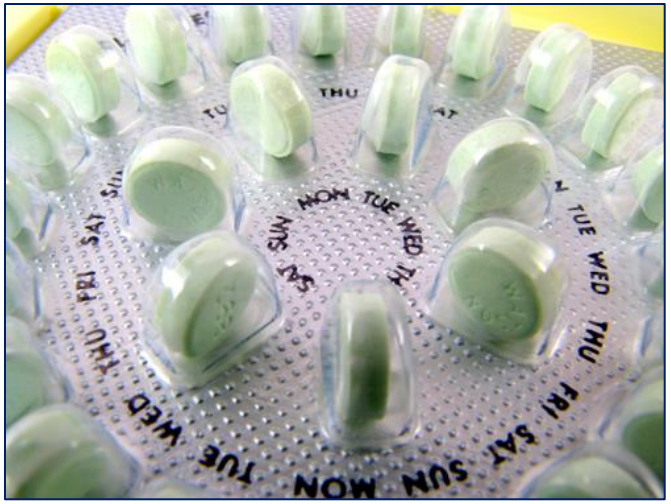
If women of child-bearing potential are included in the study:

Example Text:

1. *For studies requiring use of birth control by female participants: "If you are pregnant or nursing a child while <<taking, receiving, using>> <<study product name(s)>>, there may be risks to your unborn baby or nursing child. Risks include: <<Include relevant risks here.>> Some drugs cause premature (early) birth or birth defects. Nobody knows what all of these risks are right now."*
2. *For studies requiring use of birth control by male participants and/or their female partners: "If you are a man, there may be risks to an unborn baby you father during or after the study. Risks include: <<Include relevant risks here.>> Some drugs cause premature (early) birth or birth defects. Nobody knows what all of these risks are right now."*

Risks

"What are the risks if I or my partner are pregnant or nursing during this study?"



If a **method of birth control** is required:

- A statement that birth control must be used, including the duration of use
- A statement about notifying the study doctor if the participant (or participant's partner is pregnant)
- If the protocol so indicates: A statement that the participant would be removed from the study if a pregnancy occurs. Also, a statement indicating that information about the pregnancy and outcome may be collected and shared with the sponsor

*** Citation:** 21 CFR 50.25(a)(2), (b)(1); 45 CFR 46.116(a)(2), (b)(1); ICH, 4.8.10(g)

Unknown Risks

"Could I have other problems with my health if I am in this study?"

A statement that a particular study article or procedure may involve **risks to the participant which are currently unforeseeable**

Advice:

1. This language is not appropriate for every study (i.e. those studies not involving physical risk).

*** Citation:** 21 CFR 50.25(b)(1); 45 CFR 46.116(b)(1); ICH, 4.8.10(g)

Unknown Risks

"Could I have other problems with my health if I am in this study?"

A statement that a particular study article or procedure may involve **risks to the participant which are currently unforeseeable**

Example Text:

"It is possible that you could have problems and side effects from <<name of drug, device, vaccine, product, etc.>> that nobody knows about yet, which could include your <<condition>> getting worse <<if appropriate: or even death.>>"

New Information

"Will I receive any new information during the study?"

A statement that **new findings** developed during the course of the research which may related to the subject's willingness to continue participation will be provided to the subject

Advice:

1. "New findings" should not be limited simply to findings about the study article. Findings may be any findings (e.g. additional diagnostic procedure added, extended length of visits, high number of reported AEs, etc.).

*** Citation:** 21 CFR 50.25(b)(5); 45 CFR 46.116(b)(5); ICH, 4.8.10(p)

Injury/Illness

"What if I get hurt or sick while in this study?"

The **compensation and treatment available** to the subject in the event of trial-related injury

Advice:

1. This requirement only applies to research involving more than minimal risk.
2. The regulations do not say that compensation is required to be provided; only that information about compensation must be provided.
3. Information about compensation for research related injury should also include information about whether subjects will be billed for the cost of the medical treatment necessary to address the injury.

*** Citation:** 21 CFR 50.25(a)(6); 45 CFR 46.116(a)(6); ICH, 4.8.10(j)

Injury/Illness

"What if I get hurt or sick while in this study?"

Elimination/revision of statements that may suggest the sponsor, investigator, institution, or its agents are not liable for research related injuries

Advice:

1. No informed consent form may include any exculpatory language—language that seems to clear the sponsor of fault or guilt.
2. Prohibitive language is that which actually waives a participant's right (e.g. "You cannot sue the sponsor for any research-related injury") or language that appears to waive a participant's right (e.g. "The sponsor will not pay for any research-related injury").

*** Citation:** 21 CFR 50.20; 45 CFR 46.116; ICH, 4.8.4

Exculpatory Language

Injury/Illness

Examples of exculpatory and acceptable language

I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.

The hospital is not able to offer financial compensation nor to absorb the costs of medical treatment should you be injured as a result of participation in this research.

The hospital makes no commitment to provide free medical care or payment for any unfavorable outcomes resulting from participation in this research. Medical services will be offered at the usual charge.

*** Citation:** "Exculpatory Language" in Informed Consent, Office for Protection from Research Risks (OPRR), November 15, 1996, available at: http://www.hhs.gov/ohrp/policy/exculp.html . See also. Draft: Guidance on Exculpatory Language in Informed Consent, FDA, OHRP, August 19 2011, available at: http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM271036.pdf

Injury/Illness Language (Example 1)

POLL QUESTION:

The sponsor will not pay for injuries caused by the study drug if you did not follow the direction of the study doctor.

A

The sponsor will pay for injuries related to this research if you follow the directions from your study doctor. The sponsor will not pay for injuries caused by the study drug if you did not follow the direction of the study doctor.

B

The sponsor will pay for injuries related to this research if you follow the directions from your study doctor. The sponsor ~~will not pay~~ has no plans to pay for injuries caused by the study drug if you did not follow the direction of the study doctor.

C

The sponsor will pay for injuries related to this research.

Injury/Illness Language (Example 1)

POLL QUESTION:

The sponsor will not pay for injuries caused by the study drug if you did not follow the direction of the study doctor.

A The sponsor will pay for injuries related to this research if you follow the directions from your study doctor. The sponsor will not pay for injuries caused by the study drug if you did not follow the direction of the study doctor.

B The sponsor will pay for injuries related to this research if you follow the directions from your study doctor. The sponsor ~~will not pay~~ has no plans to pay for injuries caused by the study drug if you did not follow the direction of the study doctor.

C The sponsor will pay for injuries related to this research.

Injury/Illness Language (Example 2)

POLL QUESTION:

You cannot receive free medical care for injuries related to this research. You will be responsible for paying for care you receive at the XYZ Medical Center.

A

If you are injured you can receive medical care at XYZ Medical Center. ~~You cannot receive~~ The hospital will not offer free medical care for injuries related to this research. You or your insurance company will be billed ~~responsible~~ for paying for care you receive at the XYZ Medical Center.

B

~~You cannot receive~~ The hospital will not offer free medical care for the injuries related to this research. You or your insurance company will not be billed ~~responsible~~ for paying for care you receive at the XYZ Medical Center.

C

~~You cannot receive~~ The hospital will provide free medical care for injuries related to this research. You will not be responsible for paying for care you receive at the XYZ Medical Center.

Injury/Illness Language (Example 2)

POLL QUESTION:

You cannot receive free medical care for injuries related to this research. You will be responsible for paying for care you receive at the XYZ Medical Center.

A

If you are injured you can receive medical care at XYZ Medical Center. ~~You cannot receive~~ The hospital will not offer free medical care for injuries related to this research. You or your insurance company will be billed ~~responsible~~ for paying for care you receive at the XYZ Medical Center.

B

~~You cannot receive~~ The hospital will not offer free medical care for the injuries related to this research. You or your insurance company will not be billed ~~responsible~~ for paying for care you receive at the XYZ Medical Center.

C

~~You cannot receive~~ The hospital will provide free medical care for injuries related to this research. You will not be responsible for paying for care you receive at the XYZ Medical Center.

Injury/Illness Language (Example 3)

POLL QUESTION:

The sponsor will not pay for injuries if:

I. They were caused by your participation in the research and not an underlying condition;

II. You followed the directions of the study doctor; and

III. You promptly contacted the study doctor after the injury.

A

The sponsor has no plans to ~~will not~~ pay for injuries if:

I. They were caused by your participation in the research and not an underlying condition;
II. You followed the directions of the study doctor; and
III. You promptly contacted the study doctor after the injury.

B

The sponsor will not pay for injuries if:

I. They were caused by your participation in the research and not an underlying condition;
II. You followed the directions of the study doctor; and
III. You promptly contacted the study doctor after the injury.

You or your insurance company will be billed for other injuries that the sponsor does not pay for.

Injury/Illness Language (Example 3)

POLL QUESTION:

The sponsor will not pay for injuries if:

I. They were caused by your participation in the research and not an underlying condition;

II. You followed the directions of the study doctor; and

III. You promptly contacted the study doctor after the injury.

A

The sponsor has no plans to ~~will not~~ pay for injuries if:

I. They were caused by your participation in the research and not an underlying condition;
II. You followed the directions of the study doctor; and
III. You promptly contacted the study doctor after the injury.

B

The sponsor will not pay for injuries if:

I. They were caused by your participation in the research and not an underlying condition;
II. You followed the directions of the study doctor; and
III. You promptly contacted the study doctor after the injury.

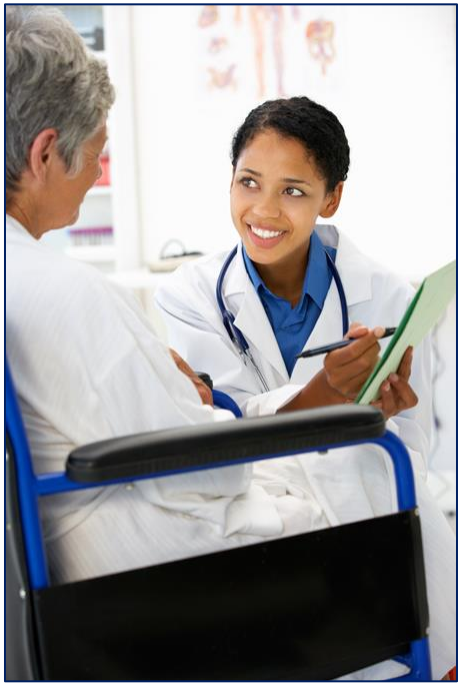
You or your insurance company will be billed for other injuries that the sponsor does not pay for.

Voluntary Participation

"Do I have to be in this study?"

A statement regarding **voluntary participation** that includes all of the following:

- Participation is **voluntary**
- Participant may refuse to participate **without penalty or loss of benefits** to which the participant is otherwise entitled
- Participant may withdraw at any time **without penalty or loss of benefits** to which the participant is otherwise entitled



*** Citation:** 21 CFR 50.25(a)(8); 45 CFR 46.116(a)(8); ICH, 4.8.10(m)

Voluntary Participation

“Do I have to be in this study?”

A statement that **participants may be removed from the study** without their consent and the reasons why

Advice:

1. This statement is <u>not applicable to all studies</u> (e.g. data-collection studies, single blood draw study).

*** Citation:** 21 CFR 50.25(b)(2); 45 CFR 46.116(b)(2); ICH, 4.8.10(r)

Voluntary Participation

"Do I have to be in this study?"

A statement that **participants may be removed from the study** without their consent and the reasons why

Example Text:

"The study doctor or study staff or sponsor can remove you from the study at any time, even if you want to stay in the study. This could happen if:

- *The study doctor or study staff believes it is best for you to stop being in the study;*
- *You do not follow directions about the study; or*
- *The sponsor stops the study for any reason."*

*** Citation:** 21 CFR 50.25(b)(2); 45 CFR 46.116(b)(2); ICH, 4.8.10(r)

Voluntary Participation

"Do I have to be in this study?"

The **consequences of a participant's decision to withdraw** from the research and what will happen if he/she withdraws

Advice:

1. The consent form should explain any withdrawal procedures that are necessary for the subject's safety.
2. If a subject withdraws, the consent form should explain that his/her data that was already collected cannot be removed.
3. If the subjects who withdraw will be asked to permit follow-up of their condition by the researchers, the process and options should be outlined in the consent form. Such outlined information may include information regarding:
    i. Maintenance of privacy and confidentiality; and
    ii. Distinction between follow-up related to study interventions as opposed to clinical outcomes.

*** Citation:** 21 CFR 50.25(b)(4); 45 CFR 46.116(b)(4)

Commercial Issues

"Who owns my study data?"

If proprietary information or information about **ownership** of samples, data, and future discoveries is included, the consent should include an explanation of ownership interests

Advice:

1. It is generally acceptable for consent forms to indicate that the sponsor, study doctor, or other individuals or entities will own data and/or commercial developments, including future discoveries and patents.
2. It is generally not acceptable for consent forms to indicate that participants are waiving rights to their samples.
3. The word "donate" is generally not accepted in reference to samples provided for research. Instances of "donate" should be replaced with a word such as "provide."

*** Citation:** 21 CFR 50.20; 45 CFR 46.116; ICH, 4.8.4

Confidentiality

"How will my information be kept confidential?"

A statement describing the extent to which **confidentiality** of records identifying the participant will be maintained

Advice:

1. A "Medical Release" (a section for participants to give permission to release records held by other entities to the study doctor) is <u>not appropriate</u> in a consent form.

*** Citation:** 21 CFR 50.25(a)(5); 45 CFR 46.116(a)(5); ICH, 4.8.10(n,o)

Confidentiality

"How will my information be kept confidential?"

Language addressing the following:

- What information will be collected about participants and for what **purposes**
- Who has **access** to information collected about the identity of participants (e.g. sponsor, IRB, FDA)
- A description of the anticipated **uses** of the information collected
- Who has a **duty to disclose** information collected (e.g. the study doctor *if required by law*)
- Who may **receive** the information collected (e.g. the sponsor)

*** Citation:** 21 CFR 50.25(a)(5); 45 CFR 46.116(a)(5); ICH 4.8.10(n,o)

Contact Information

"Who can I talk to about this study?"

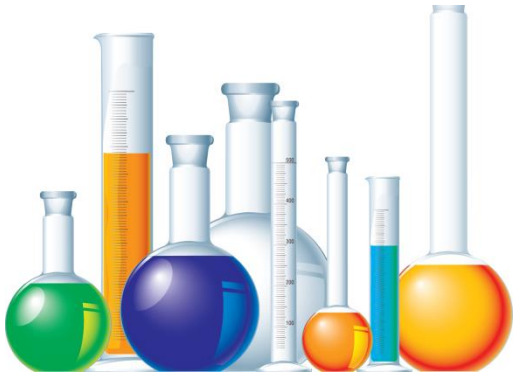
The consent document should provide the name of a specific office or person and the telephone number to **contact** for answers to questions about all of the following:

- The research subjects' rights (contact = IRB)
- Research-related injury (contact = study doctor/staff)
- The research study itself (contact = study doctor/staff)

*** Citation:** 21 CFR 50.25(a)(7); 45 CFR 46.116(a)(7); ICH, 4.8.10(q)

Future or Secondary Research

If the research indicates that a participant's specimens or information may be used for research **outside the scope of the current research**, include information about the general types of research to be conducted. If the general types of research are unknown, this should be stated



*** Citation:** 21 CFR 50.25(a)(1); 45 CFR 46.116(a)(1); ICH, 4.8.10(b)

Future or Secondary Research

This document is helpful to think about when considering describing **future** use in consent forms:

"Under existing interpretations of the Common Rule's informed consent requirements, it is generally permissible to seek subjects' consent to future research so long as the future uses are described in sufficient detail to allow an informed consent. Consent to future uses may be appropriate, for example, where data or biologic materials collected from patients with a certain disease and studied in the course of a primary research study will be stored and studied in the future as additional tests and hypotheses are developed. An IRB reviewing a consent form for such a study may be comfortable that the subjects are adequately informed about the general types of research to be conducted in the future and the privacy protections that will be in place to ensure that the scope of the subjects' consent is honored."

*** Citation:** Per Office for Human Research Protections (OHRP), Secretary's Advisory Committee On Human Research Protections (SACHRP), Appendix D, available at www.hhs.gov/ohrp/sachrp/appendixd.html (last accessed Oct. 13, 2010):

Optional Activities

If the research indicates that the study includes **optional activities** (and there is not a separate consent form addressing the optional activities), the main consent form should include:

- A description of the optional components of the research, generally in the body of the consent form
- Language indicating that the participant may decline to take part in the optional component of the research and still take part in the rest of the study
- A means to consent participants into the optional components of the research

*** Citation:** 21 CFR 50.25(a)(1); 45 CFR 46.116(a)(1); ICH, 4.8.10(b)

Optional Activities

Example Text:

"Some study centers are doing an optional pharmacokinetic (PK) sub-study as part of the main study. You do not have to take part in the PK sub-study to be in the rest of the study. Information about the PK sub-study is included earlier in this form. If you later change your mind about being in the optional PK sub-study, tell the study doctor or study staff.

Initial below beside only one option:

_____ *The study doctor or study staff informed me that my study center is not doing the optional PK sub-study.*

_____*Yes, I agree to be in the optional PK sub-study.*

_____ *No, I do not agree to be in the optional PK sub-study. I can still be in the rest of the study."*

Signature Page

"Consent"

A **signature and date line** for the participant (or participant's legally authorized representative) AND a signature and date line for the person who conducted the informed consent discussion

*** Citation:** 21 CFR 50.27; 45 CFR 46.117; ICH, 4.8.8

Signature Page

“Consent”

If persons to be enrolled cannot read due to illiteracy or vision impairment, an **impartial witness signature and date line**

Advice:

1. If an impartial witness signature line is used, this line must be accompanied by what is called a witness statement (e.g. “As an impartial witness, I attest that the information in the consent form and other written information was accurately explained to the participant.”).

*** Citation:** A Guide To Informed Consent, FDA Information Sheet; ICH, 4.8.9

SUMMARY

- Always consider understandability, therapeutic misconception, and what is important to participants when drafting a consent form or having a consent discussion
- Many factors play into why specific content is included in a consent form, but the federal regulations and ICH contain the specific consent form requirements
- It's important to understand how consent requirements actually translate into consent form language

Questions?

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Issues of Informed Consent

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