



**U.S. FOOD & DRUG
ADMINISTRATION**

Informed Consent: More than just a document

Ann Meeker-O'Connell, M.S.

Director, Office of Clinical Policy
Office of the Chief Medical Officer
Office of the Commissioner | US FDA

Clinical Investigator Training – December 2024

Learning Objectives

- Understand FDA's expectations for informed consent
- Examine approaches to facilitating participant understanding in Informed Consent
- Learn about FDA's Draft Guidance – Key Information and Facilitating Understanding in Informed Consent

What is Informed Consent

FDA



- Informed consent (IC) is **not** just a signature or a document.
- Ensures patients have enough information to make an informed decision about participating in clinical research.

50.20 General Requirements for Informed Consent



- FDA regulations require investigators, with limited exceptions, to obtain informed consent from individuals before these individuals can participate in clinical investigations of FDA-regulated medical products.
- Informed consent must be prospective, understandable, and not include exculpatory language.
- The consent process must also not create undue influence or coercion.

Informed Consent Process

- Begins with recruitment materials to the end of the study
- Involves providing a potential participant with relevant information, in a way that:
 - Facilitates understanding
 - Allows sufficient opportunity to ask questions and consider participation
 - Assures continued agreement and understanding throughout participation
- Documentation of informed consent at the start is only part of the process

Elements of Informed Consent



a) Basic Elements (paraphrased)

1. A statement that the study involves research
 - Explanation of the purpose / expected duration
 - Description of procedures/research interventions
2. Reasonably foreseeable risks or discomforts
3. Reasonably expected benefits to the subject or to others
4. Disclosure of appropriate alternatives
5. Confidentiality/FDA may inspect
6. Compensation and research-related injuries
7. Point of contact for questions
8. Participation is voluntary

Elements of Informed Consent



b) Additional Elements (When Appropriate – paraphrased)

1. A statement that the particular treatment or procedure may involve unforeseeable risk to the subject (or embryo or fetus)
2. Circumstances of study termination
3. Costs to the subject
4. Consequences of withdrawal
5. A statement that significant new findings relating to the subject's willingness to continue will be communicated
6. Approximate number of subjects in the study

c) Mandatory verbatim statement related to ClinicalTrials.gov

Key Proposed Revisions to 21 CFR Part 50



Key Information

Proposed 50.20 (d) and (e)



Additional Basic Element of Informed Consent

Proposed 50.25(a)(9)



Additional Elements of Informed Consent

Proposed 50.25(b)(7)-(9)

[Federal Register: Protection of Human Subjects and Institutional Review Boards](#)

[fda.gov/cdersbia](#)

Informed Consent Development



- Courtesy of Christine Lee, Deputy Director, FDA OMHHE

- IRBs, clinical investigators, and sponsors share responsibility for informed consent
- The regulatory requirements represent the minimum information to be provided to prospective participants for informed consent.

Opportunities with Informed Consent

- Informed consent documents are often long, complex, and legalistic
- The informed consent process does not take full advantage of appropriate innovations that can facilitate understanding
- More work is needed to fulfill the promise of participant-centered informed consent

Improving Understanding



Representative Existing Resources

- Clinical Trials Transformation Initiative (CTTI) [Tiered Consent Project](#) (2016)
- [Use of Electronic Informed Consent: Questions and Answers](#) (December 2016)
- [Informed Consent Final guidance](#) (August 2023)
- [Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations, Questions and Answers](#) (October 2024)

Ongoing Work

- Protection of Human Subjects and Institutional Review Boards ([Proposed Rule](#), September 2022)
- ICH E6 (R3) Good Clinical Practice (public consultation on draft guideline starting May 2023)
- Key Information and Facilitating Understanding in Informed Consent ([Draft guidance](#), March 2024)

Electronic Informed Consent (eConsent)



- Permits remote consent
- Enables expanded use of graphics, audio et al to improve understanding
- Permits hyperlinks to sites with supplemental information
- Can facilitate tests for understanding
- Can be used to address a variety of sensory impairments

Use of Electronic Informed Consent Questions and Answers

Guidance for Institutional
Review Boards, Investigators,
and Sponsors

U.S. Department of Health and Human Services
Office for Human Research Protections (OHRP)
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Good Clinical Practice (OGCP)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

December 2016
Procedural

Challenge Question #1



Which of the following statements is NOT true?

- A. FDA regulations include eight elements that must be included in all informed consent documents.
- B. Informed consent is an ongoing process.
- C. FDA regulations do not permit the use of images, graphics, or cartoons in informed consent
- D. Informed consent cannot contain exculpatory language.

Key Information and Facilitating Understanding

Draft guidance addresses two proposed provisions to help people decide whether to join a study

- 1) Consent must begin with key information
- 2) The whole consent must be organized and presented to help facilitate understanding

Proposed FDA provisions: 21 CFR 50.20(e)(1) and (2)
Revised Common Rule: 45 CFR 46.116(a)(5)(i) and (ii)

fda.gov/cdersbia



Key Information and Facilitating Understanding in Informed Consent Guidance for Sponsors, Investigators, and Institutional Review Boards

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to <https://www.regulations.gov>. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Alyson Karesch, Alyson.Karesch@fda.hhs.gov; (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010; (CDRH) Office of Clinical Evidence and Analysis, CDRHClinicalEvidence@fda.hhs.gov; (OCLP) Office of Clinical Policy, 301-796-8340, OCPquestions@fda.hhs.gov; or (OHRP) Division of Policy and Assurances, 240-453-6900 or 866-447-4777, ohrp@hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Office of Clinical Policy (OCP)

U.S. Department of Health and Human Services
Office for Human Research Protections (OHRP)

March 2024
Procedural

1046817&ft.docx

Provision 1: What is Key Information?



- Consent must begin with key information
 - Explain the study and reasons someone may want to participate
- Be concise and focused
- Be organized to facilitate comprehension

Example of Organizing Key Information



Contains Nonbinding Recommendations
Draft — Not for Implementation

APPENDIX: A HYPOTHETICAL CLINICAL TRIAL

Title: A trial to evaluate the use of product X to treat health condition Y

Key Information You Should Know Before Agreeing to Participate

The key information that follows can help you learn more about this clinical trial. It can also help you decide whether or not to take part in the trial. **Please read the entire consent form or have someone read it with you.** If there is anything that you do not understand, please talk to the trial doctor or team to have your questions answered before signing the consent form.

Voluntary Participation and Right to Discontinue Participation

We are asking you to consent to participate in this research study. Your participation is voluntary and should be based on what is important to you. It is your choice to participate in this trial. If you agree to participate, you may leave at any time without penalty or loss of benefits to which you are otherwise entitled.

Purpose of the Research

The purpose of the trial is to find out if product X, the product that is being studied, is safe and effective in treating adults like you who have health condition Y.

Key Reasonably Foreseeable Risks and Discomforts (see page #)

- If you take product X, you have a chance of side effects, such as fever or rash.
- Nausea or vomiting may be related to your health condition and is a rare but serious side effect of product X. If product X is suspected to cause these or other symptoms, product X may be stopped.
- We do not know if product X will help you. There is a chance that product X could worsen condition Y.
- More information on risks is available in the consent form.

Reasonably Expected Benefits (see page #)

- Prior research suggests product X may improve condition Y.
- Researchers are studying product X in this trial to learn more about whether product X will improve condition Y.
- If you are randomly assigned to take product X, product X may improve your health condition Y. If you are randomly assigned to take the inactive pill, you will not receive product X and will not benefit directly.
- By participating in this trial, you will help researchers learn how product X may help people with condition Y.

Contains Nonbinding Recommendations
Draft — Not for Implementation

Expected Duration and Procedures to Be Followed (see pages #)

- To learn if product X makes a difference, it is important for the trial to include people who will get a placebo (inactive pill). With this information, researchers can compare the effects of product X or the placebo on your health condition.
- A computer will assign you randomly, like flipping a coin, to a group taking product X or to a group taking the inactive pill.
- You and your doctors cannot choose which group you will be assigned to.
- This trial will take 6 months and require weekly clinic visits (24 visits total), with each visit expected to take 1 hour. At each visit, you will have blood drawn and a procedure to test your blood oxygen content.

Compensation and Medical Treatments for Research-Related Injuries (see page #)

- If you experience an injury caused by your participation in this research, the medical treatment of your injury will be paid for.
- More information on medical treatments for research-related injuries is available in the consent form.

Costs Related to Subject Participation (see page #)

- You may incur costs by participating in this trial.
- The sponsor will reimburse you for any travel costs for mileage, parking, and other expenses.
- In addition, the sponsor will pay you for your time participating in the trial.

Appropriate Alternative Procedures (see page #)

- In this trial, if you are assigned to take the placebo, you cannot take product X.
- Before joining the trial, you should talk to your doctor about alternative approved treatment options for your condition, and whether or not this trial is a good choice for you.
- Before agreeing to join, you should review information in the rest of the consent form.

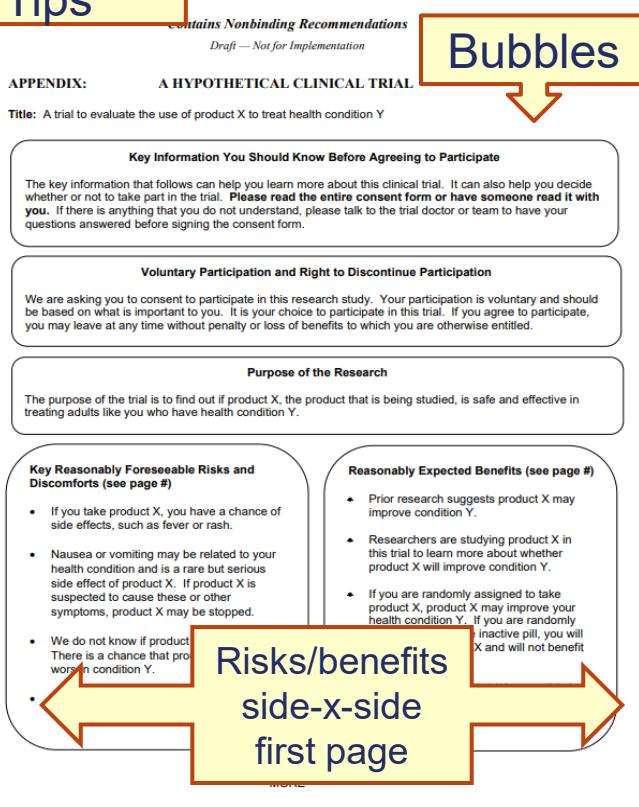
Additional Information (see page #)

- If trials show that product X is effective in treating your health condition, you may be able to continue to take product X in a related trial.

*This is one approach; others are possible.

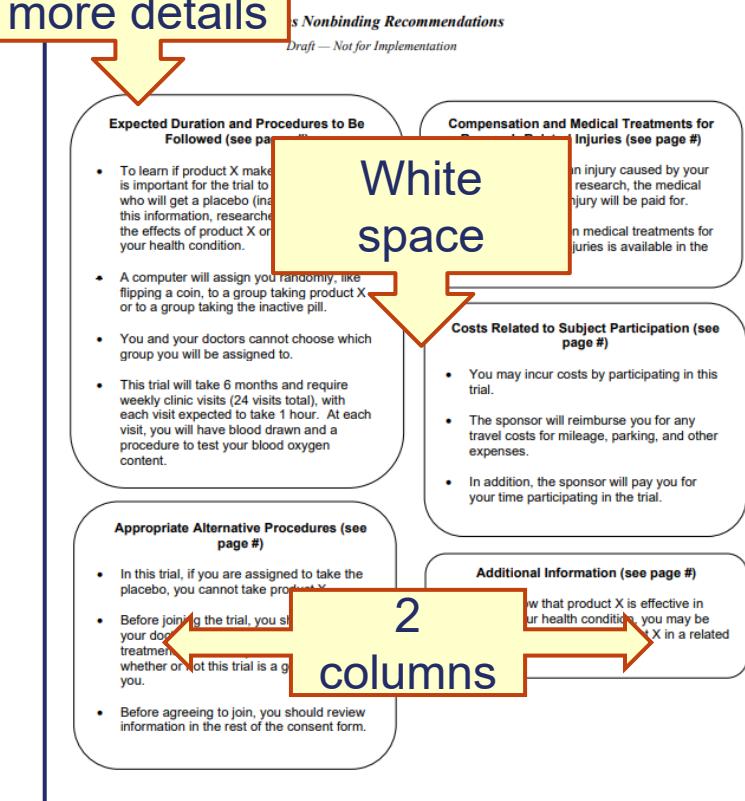
Example of Organizing Key Information

Design Tips



Bubbles

Hyperlink to more details



*This is one approach; others are possible.

A few pages

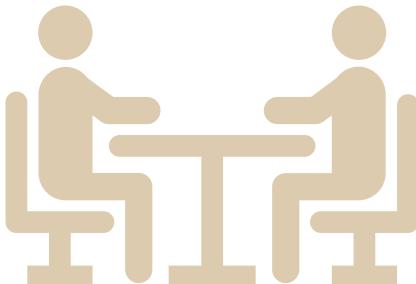
Bullet points

Simple text

Provision 2: Facilitating Understanding



- Applies to the whole consent, which must
 - Provide research information in sufficient detail
 - Be organized and presented in a way to help facilitate the participant's understanding of why someone may want to participate



Consider Multiple Approaches



Be creative and innovative



Use video, graphics, along with electronic consent



Consult with potential research participants and communities



Consider using new design approaches in whole consent form

Challenge Question #2



FDA's proposed key information provisions:

- A. Outline a specific format for presenting key information
- B. Require key information to be presented last
- C. Are intended to replace informed consent
- D. Are intended to facilitate understanding about why an individual might or might not want to participate in a trial

Summary



- Be clear and concise and use plain language
- Engage patients and communities for insights on the informed consent form and process
- Be innovative with content and approaches for informed consent
- Regulatory requirements don't prohibit creativity

Closing Thought



- “They always say time changes things, but **you actually have to change them yourself.**”

– Andy Warhol



**U.S. FOOD & DRUG
ADMINISTRATION**

Questions?

Ann Meeker-O'Connell, M.S.

Director, Office of Clinical Policy
Office of the Chief Medical Officer
Office of the Commissioner | US FDA

gcpquestions@fda.hhs.gov