U.S. FOOD & DRUG ADMINISTRATION

Informed Consent, Electronic Informed Consent & Key Information: An Overview

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CDRH Patient Engagement Advisory Committee
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Disclaimer

The views and opinions presented here represent those of the speaker and should not be considered to represent advice or guidance on behalf of the U.S. Food and Drug Administration

Objectives

- Define informed consent and informed consent process
- Describe FDA Regulations for Informed Consent
- Present FDA guidances on Informed Consent and Electronic Informed Consent
- Outline Key Information Guidance

Informed Consent

- Informed consent (IC) is **not** just a signature or a document. Obtaining consent involves:
  - The disclosure of the relevant information to research participants that allows for an informed decision.
  - Creating an environment/process that is conducive to the discussion
  - An ongoing dialogue throughout the conduct of a trial
  - When appropriate, an assessment of the participant's understanding of the research

Informed Consent Process

- Begins with recruitment materials to the end of the study
- Involves providing a potential participant with relevant information to allow for an informed decision in a way that:
  - facilitates understanding
  - allows sufficient opportunity to ask questions and consider whether or not to participate,
  - assures no undue influence or coercion
  - assures participation is voluntary
  - assures continued agreement and understanding throughout the duration of participation
- Documentation of informed consent at the start of the trial is only part of the process

FDA Regulations for Informed Consent

- **21 CFR Part 50, "Protection of Human Subjects"**
  - Subpart A: General Provisions
  - Subpart B: Informed Consent Requirements
  - Subpart D: Additional Safeguards for Children

- Note: Part 50 focuses on informed consent only. Additional protections for participants can be found throughout FDA regulations (e.g., 21 CFR parts 56, 312 & 812)

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.

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

21 CFR 50.25

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 posting on ClinicalTrials.gov

21 CFR 50.25

Informed Consent

Guidance for IRBs, Clinical Investigators, and Sponsors

Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors

U.S. Department of Health and Human Services Food and Drug Administration
Office of Clinical Policy
Center for Drug Evaluation and Research Center for Biologics Evaluation and Research Center for Devices and Radiological Health

August 2023 Good Clinical Practice

Electronic Informed Consent (eConsent): Advantages

- Can use a multimedia approach to include embedded videos, graphics, audio, podcasts and interactive websites to improve understanding
- Permits hyperlinks to sites with supplemental information if needed
- Can facilitate tests for understanding
- Can be used to address a variety of sensory impairments (e.g., enlarge fonts, improved contrast, audio recordings for visually impaired)
- Enables expanded use of graphics, audio and other techniques to improves understanding
- Easier to update than paper documents

eConsent Advantages

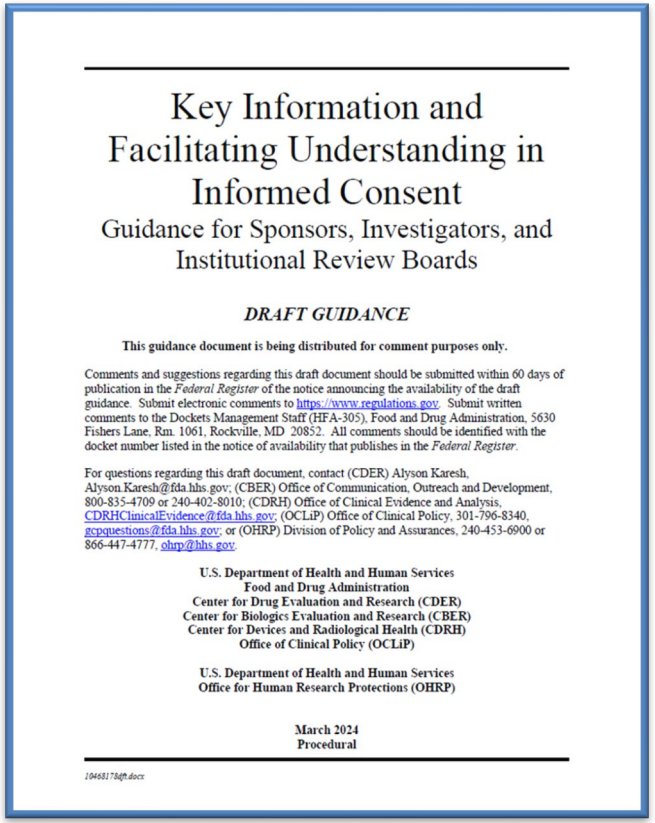
- Can obtain consent remotely
- Offers the opportunity for study participants to review and sign consent document in the comfort of their own home
- Allows for investigators to interact virtually with study participants
- Audio-visual material can show graphically what study procedures involve, what medications look like, what potential adverse events may look like
- Elimination of paper is cost effective, saves time, space and trees

eConsent Guidance: Overview of Recommendations

- Must meet the same requirement as for paper consent
- Must include some method to verify study participant's identity
- Must provide an adequate electronic equivalent of a copy of the informed consent
- Must be secure with restricted access and should include methods to ensure participant confidentiality

New Informed Consent Draft Guidance: Key Information

- Key Information and Facilitating Understanding
- Published March 2024



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 Karesh, Alyson.Karesh@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; (OCLiP) Office of Clinical Policy, 301-796-8340, gcpquestions@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 (OCLiP)

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

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2 Proposed Consent Provisions

Both are intended 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 21 CFR 50.20(e)(1) and (2)

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.

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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.

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.

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.

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.

Example: Key Information Design

Example: Key Information Design

Design Tips

Bubbles

2 pages

Risks/benefits side-x-side first page

Bullet points

Hyperlink to more details

Simple text

White space

2 columns

Contains Nonbinding Recommendations

Draft — Not for Implementation

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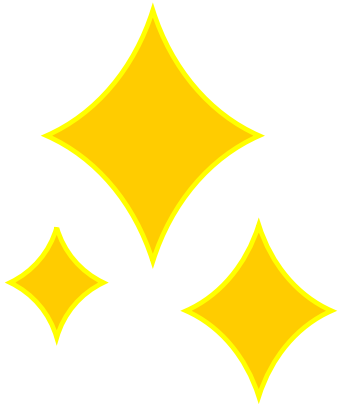
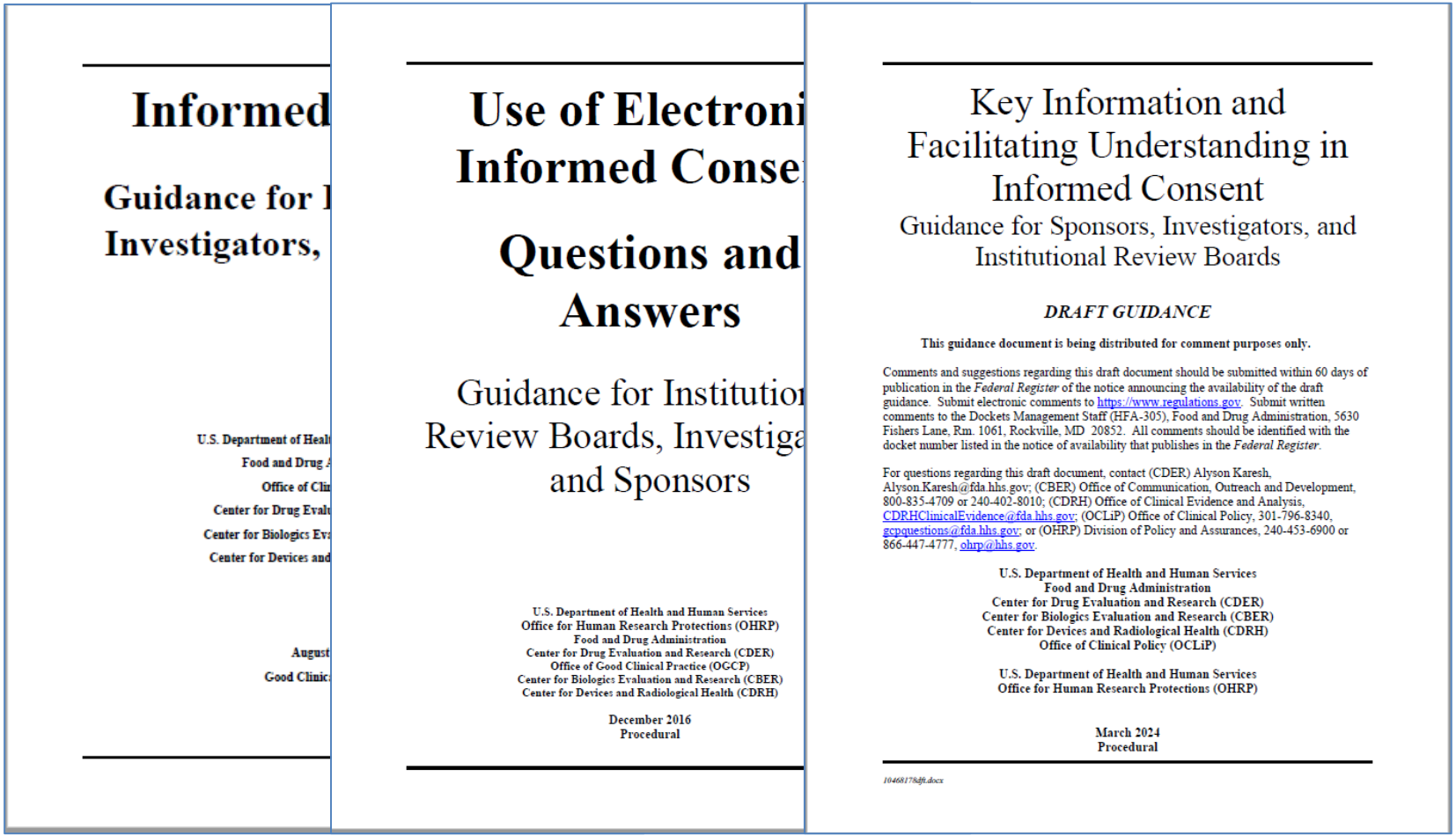
Consider Multiple Approaches

- Be creative and innovative
- Use video, graphics, along with electronic consent
- Consult with patient groups and communities



FDA Guidance Documents



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Call to Action on Informed Consent

- FDA has published guidance documents encouraging approaches that support potential participants in understanding planned research and making an informed decision on whether to participate
- Literature indicates that informed consent processes and documents have changed very little in practice
- Informed consent documents often remain long, complex, and legalistic

Thanks for your attention

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Additional Resources

- FDA Informed Consent Regulations – 21 CFR 50 (https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-50)
- Common Rule regulations – 45 CFR 46 (https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46)
- Clinical Trials Information (https://www.fda.gov/science-research/science-and-research-special-topics/clinical-trials-and-human-subject-protection)
- Clinical Trials: What Patients Need to Know (https://www.fda.gov/patients/clinical-trials-what-patients-need-know)
- FDA Final "**Informed Consent Guidance**", August 2023, available at: https://www.fda.gov/media/88915/download
- FDA Draft Guidance "**Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations: Questions and Answers**", March 2023, available at: https://www.fda.gov/media/166215/download
- FDA Information Sheet Guidance on Payment and Reimbursement to Research Subjects (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/payment-and-reimbursement-research-subjects)