FDA Webinar

Informed Consent:

More Than Just Another Document to Sign?

November 8, 2024

Informed Consent

A Patient's Experience

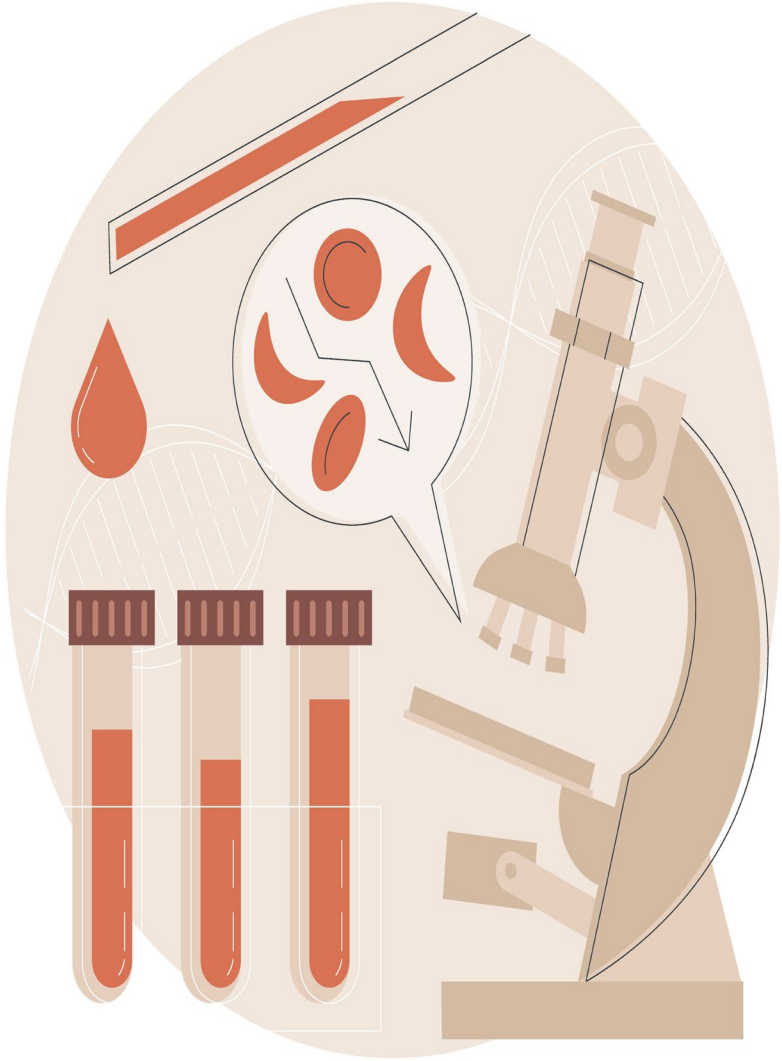
By Lana Maria Escamilla

Disclosures

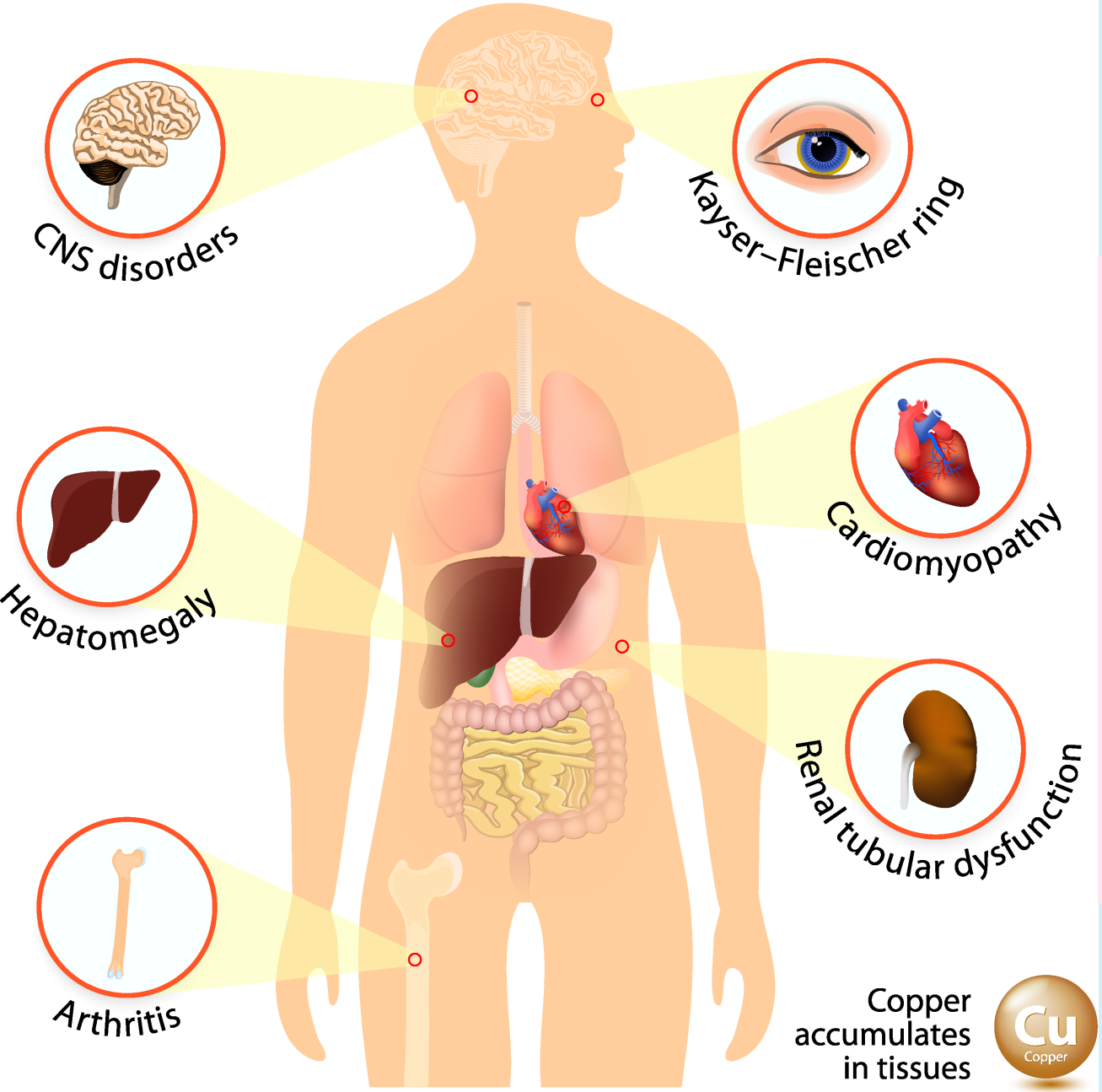
Wilson Disease Association Board Member

Enrolled in a gene therapy clinical trial which was recently terminated by the sponsor – participating in termination visit on November 25, 2024

This presentation is based solely on my personal experiences with informed consent from my participation in 3 clinical trials as a result of my diagnosis of Wilson Disease.



WILSON'S DISEASE



Diagnosed by 22

Wilson Disease is a Genetic Disorder that is fatal unless detected and treated before serious illness from copper poisoning develops.

It is an autosomal recessive disorder resulting from mutations in the copper-transporter ATP7B Gene, which results in the body's inability to excrete copper.

First Clinical Trial – October 2000

Double Blind Study Completed

Second Clinical Trial – May 2021

Investigational study for once daily medication for the treatment of Wilson Disease

Completed study, but study terminated before others completed

Third Clinical Trial – 2024

Gene therapy for Wilson Disease

Terminated approximately 4 months after gene therapy infusion

Questions for Informed Consent

1. Outpatient or inpatient?
2. Is the study double-blind/is everyone receiving treatment?
3. How long does the study last?
4. What are potential adverse effects?
5. How should I expect to feel?
6. Will I miss work?
7. Will I need a caretaker?
8. What are my time obligations?
9. What happens if the study is terminated?
10. Is the study covering my expenses?
11. If the study is terminated and I have an adverse effect because of the study, what happens? Who covers associated health costs?
12. What protocols are in place to protect my safety and privacy?

Thank you all for allowing me to share my story

Special thanks to all those engaged in research to find better treatment options for rare diseases, especially Dr. Fred Askari for his dedication to Wilson Disease Patients & my family for their support through my journey.

Questions: Lana.Escamilla@gmail.com

To learn more about Wilson Disease, please go to the Wilson Disease Association Website:

https://wilsondisease.org

Informed Consent – More than Just Another Document to Sign?

Ann Meeker-O'Connell, MS
Director
Office of Clinical Policy
Office of the Chief Medical Officer | US FDA

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Office of Clinical Policy
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November 8, 2024

Disclaimers

- The views and opinions presented here represent those of the speaker and should not be considered to represent advice or guidance from the Food and Drug Administration (FDA) or the Department of Health and Human Services (HHS).

- No disclosures

Presentation Overview

- What is Informed Consent?
- FDA's Expectations for Informed Consent
- Improving Understanding in Informed Consent
- Joint Draft Guidance – Key Information and Facilitating Understanding in Informed Consent
- Main Takeaway Messages

What is Informed Consent

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

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.

21 CFR 50.20

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 participation
  - Assures participation is voluntary
  - Assures continued agreement and understanding throughout participation
- Documentation 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

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

Key Proposed Revisions to 21 CFR Part 50

The proposed rule would, if finalized as proposed, revise the content, organization, and presentation of information included in the informed consent form and process to facilitate a prospective subject's decision about whether to participate in the research

Key Information

- Proposed 50.20 (d) and (e)

Mandatory 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

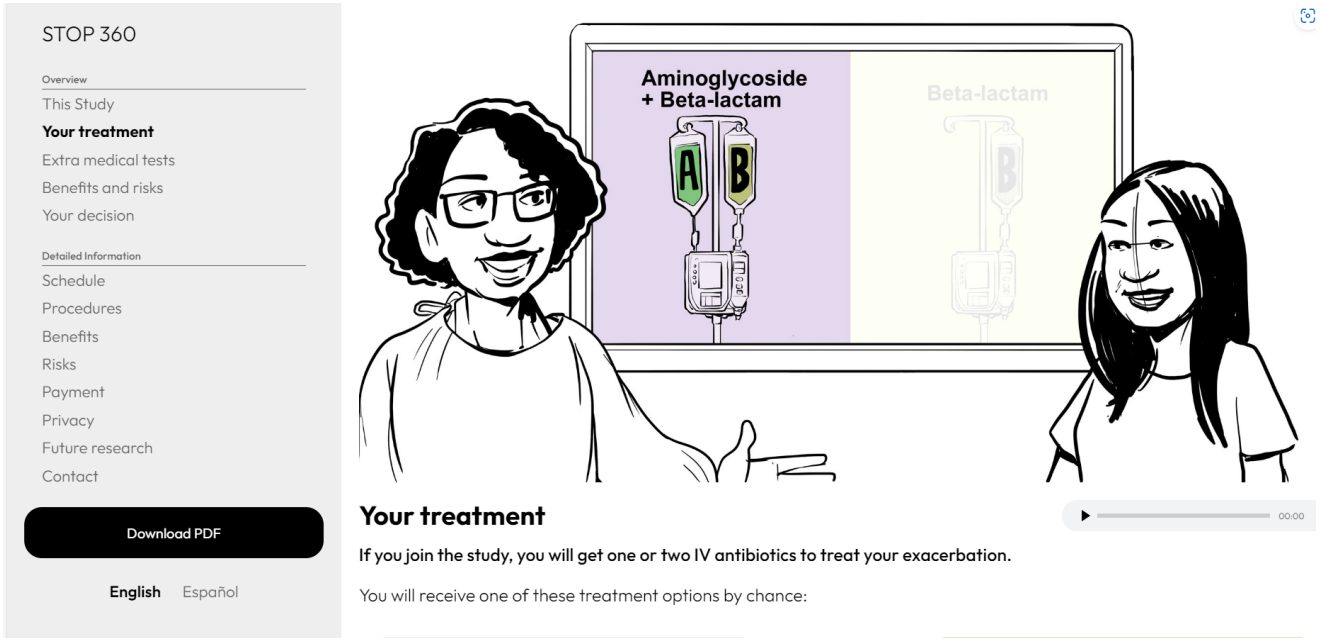
Informed Consent Development

- IRBs, clinical investigators, and sponsors share responsibility for ensuring that the informed consent form and process is adequate and meets FDA's regulatory requirements.
- The regulatory requirements represent the minimum information to be provided to prospective participants for informed consent.

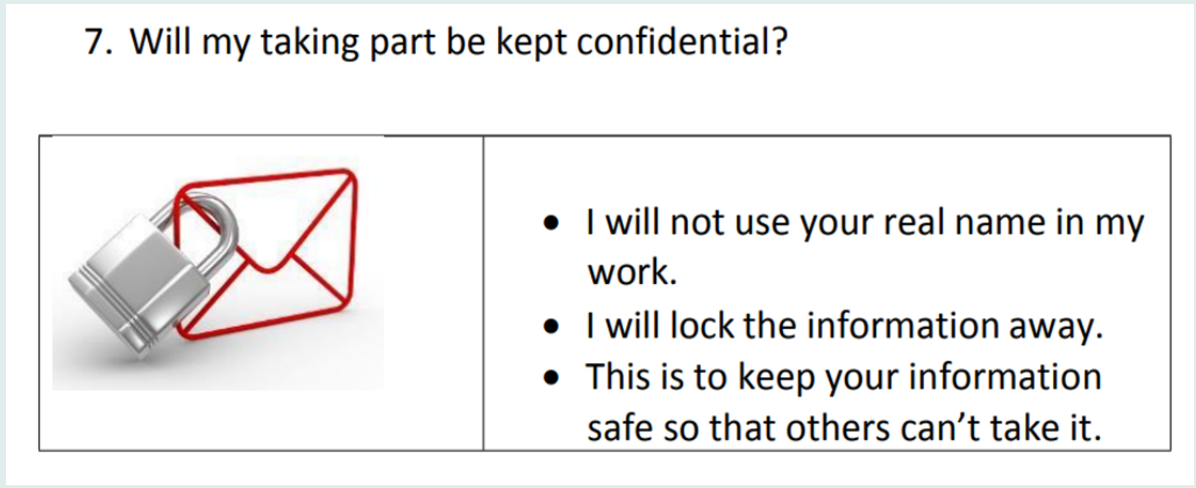
-Courtesy of Christine Lee, Deputy Director, FDA Office of Minority Health and Health Equity (OMHHE)

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 (e.g., images, videos, technology) that can facilitate understanding
- More work is needed to fulfill the promise of truly participant-centered and participant-partnered informed consent



https://stop360main.wpenginepowered.com/



Courtesy of Nancy Kass, Johns Hopkins Berman Institute of Bioethics

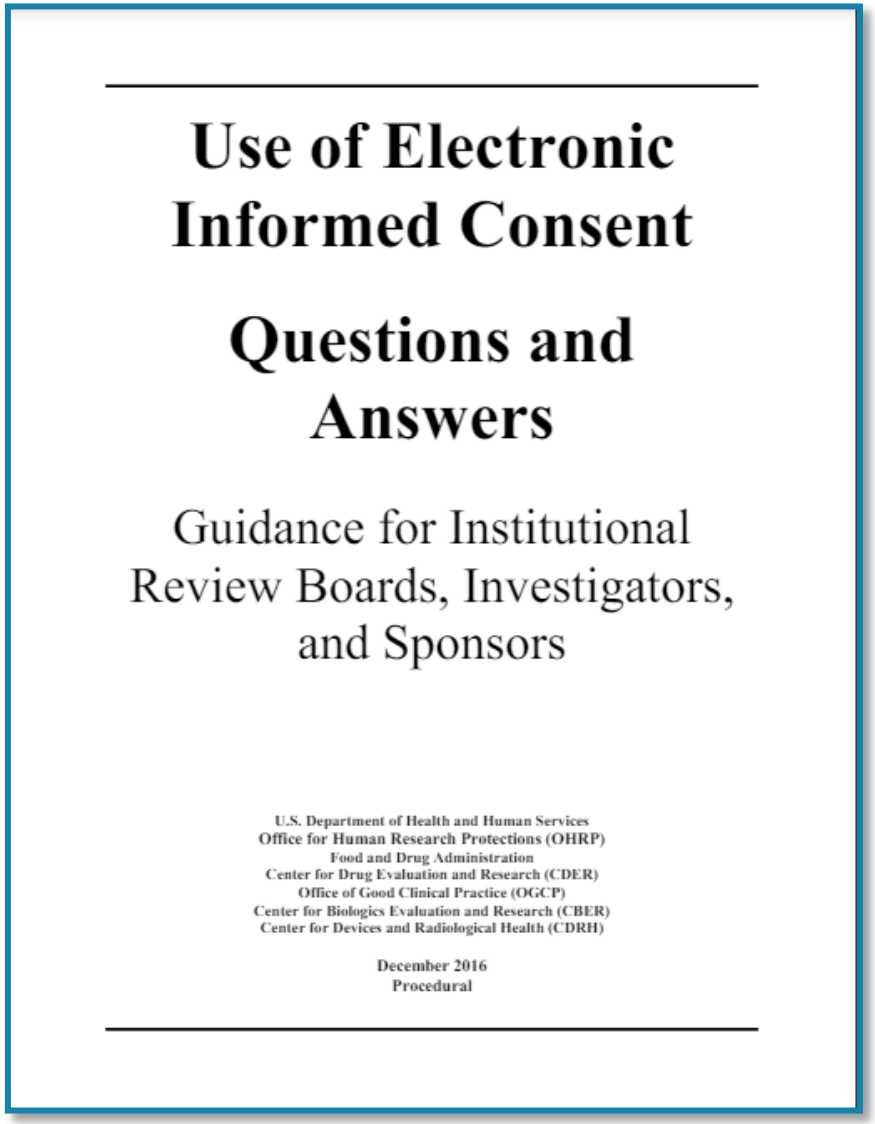
Examples of visual presentation

Improving Understanding

Representative Existing Resources	Ongoing Work
• 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)	• 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 and other techniques 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)



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

Engaging Patients and Communities

Announcing the 2024 Patient Engagement Advisory Committee Meeting

U.S. Food and Drug Administration sent this bulletin at 08/28/2024 01:06 PM EDT

If your email program has trouble displaying this email, view as a webpage.

FDA U.S. FOOD & DRUG ADMINISTRATION

Center for Devices and Radiological Health

SHARE

Patient Engagement Advisory Committee Meeting: Patient-Centered Informed Consent in Clinical Study of FDA-Regulated Medical Products

The U.S. Food and Drug Administration (FDA) is announcing the Patient Engagement Advisory Committee (PEAC) meeting will be held virtually on October 30, 2024.

During this meeting, PEAC will discuss and make recommendations on patient-centered informed consent in clinical study of FDA-regulated medical products. The topics for discussion include:

- The informed consent process, and
- Factors to consider when communicating informed consent to clinical study participants to increase the likelihood of participants understanding the key elements of research.

- Recommendations on the informed consent process and the areas of focus of the informed consent.
- Recommendations on factors to consider when communicating informed consent to clinical study participants to increase the likelihood of participants understanding the key elements of research.

Engaging Patients and Communities

- In 2023, FDA's Office of Minority Health and Health Equity established the Racial and Ethnic Minority Acceleration Consortium for Health Equity (REACH).
- REACH is a research consortium of organizations and institutions that aims to timely and efficiently respond to health equity focused research needs.
- In April 2024, REACH members discussed strategies to increase clinical trial participation for diverse communities
- In September 2024, REACH members extended that discussion to focus on informed consent.

Perspective from Patients/Communities

- Leverage existing trusted relationships with people and organizations in the community.
- Obtain feedback from the community about whether the IC process and research plan make sense to them.

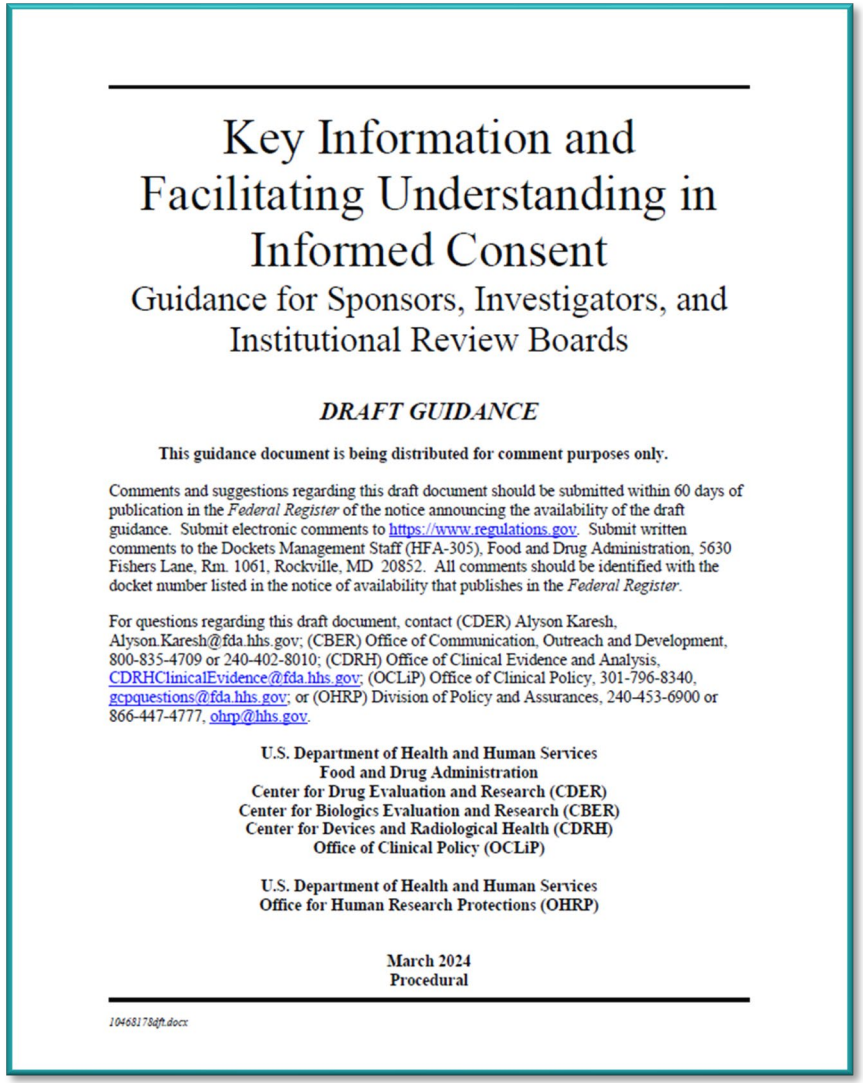
- Use information technology and creativity to develop informed consent materials and processes that can accommodate individuals of different cultures, learning styles, communication styles, and literacy levels.

- Choose research staff who demonstrate empathy, compassion, and caring to participate in the informed consent process.

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



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)

March 2024
Procedural

10468178dft.docx

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

Provision 1: 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

Key Information Example

Key Information

Voluntary Participation

Purpose

Key Information Example

Risks or Discomforts

Potential Benefits

Key Information Example

Duration and Procedures

Compensation and Treatment for Injuries

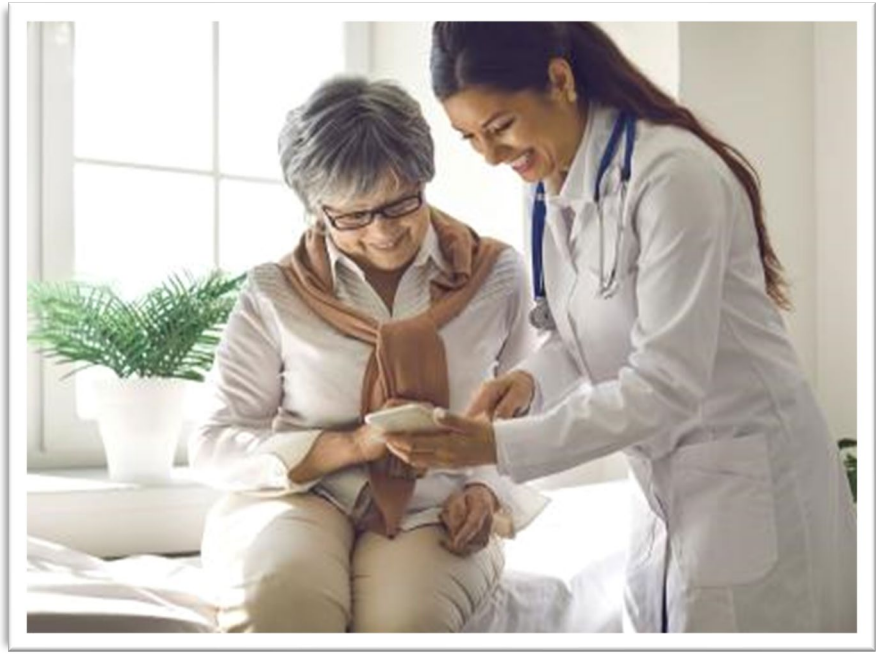
Other Alternatives

Key Information is NOT…

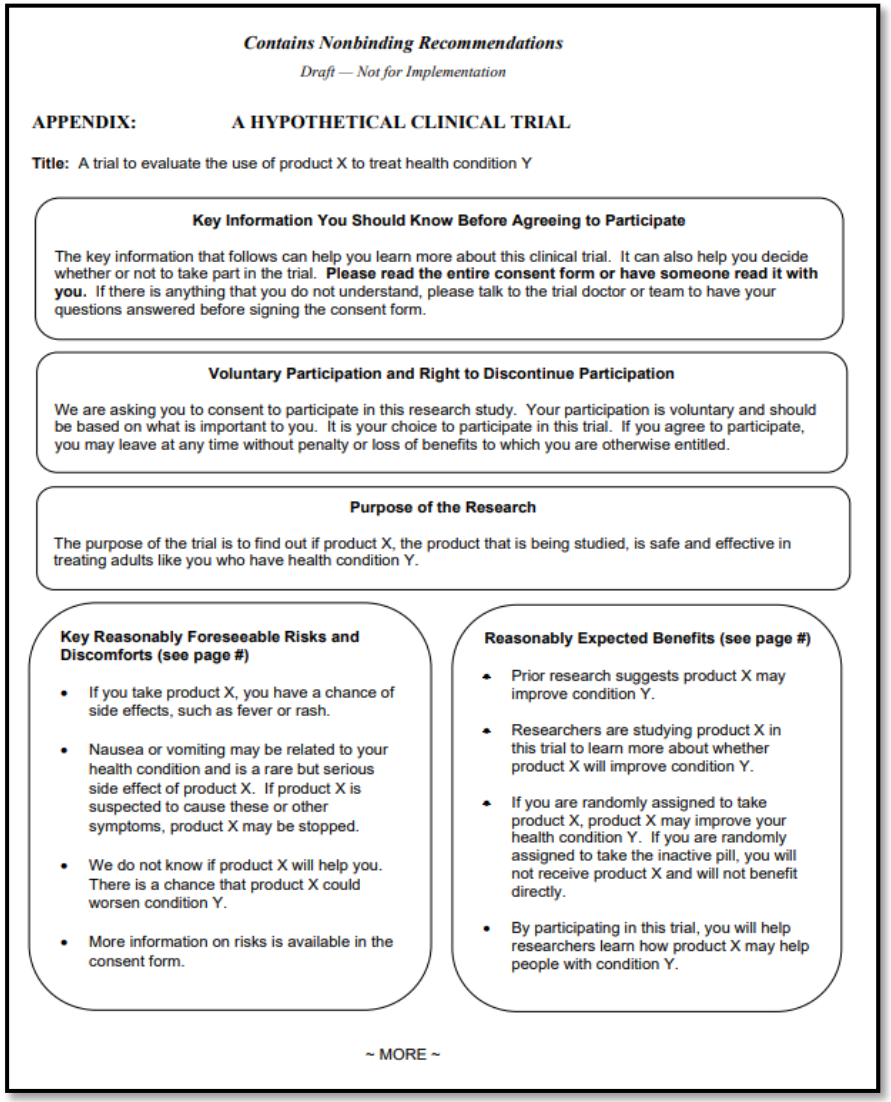
- A substitute for the consent process
- A change in responsibilities
- A "one-size-fits-all" approach for all studies

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



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.

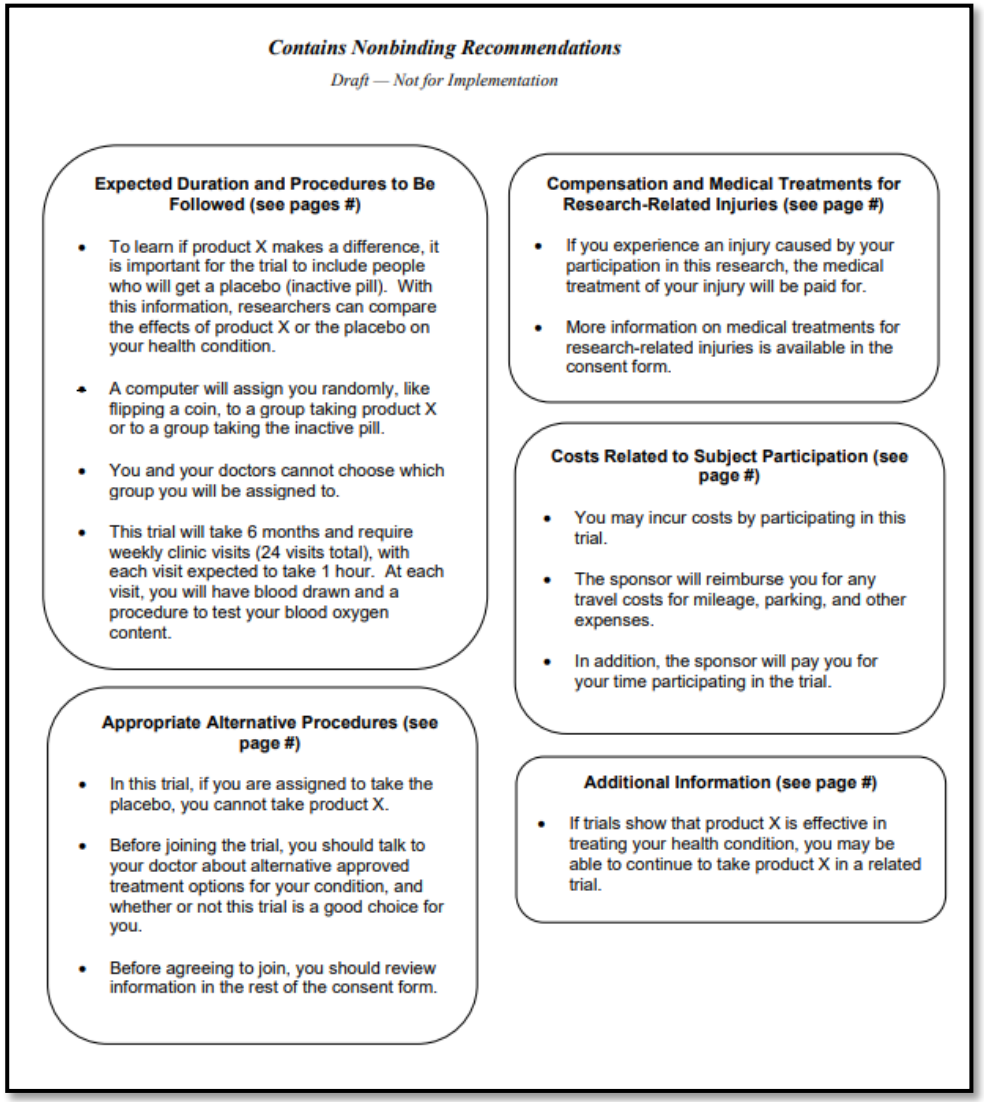
Key Reasonably Foreseeable Risks and Discomforts (see page #)

- 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.

~ MORE ~



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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.

*This is one approach; others are possible.

Study on Design Features

Influence of Patient Medication Information Format on Comprehension and Application of Medication Information: A Randomized, Controlled Experiment

Vanessa Boudewyns, PhD[*,†], Amie C. O'Donoghue, PhD[‡], Bridget Kelly, PhD, MPH[*], Suzanne L. West, PhD, MPH[*], Oluwamurewa Oguntimein, MHS, CHES[‡], Carla M. Bann, PhD[*], Lauren A. McCormack, PhD, MSPH[*]

[*]RTI International

[‡]Center for Drug Evaluation and Research, Food and Drug Administration (FDA)

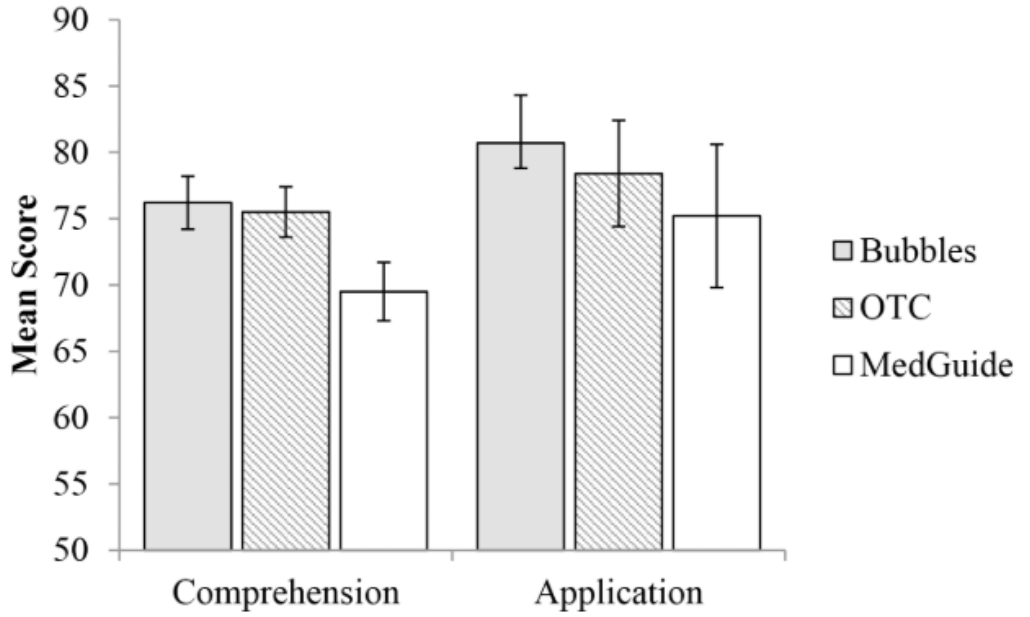


Figure 3.
Effect of Patient Medication Information Handout Format on Comprehension and Application Scores.
Bar graph shows the mean comprehension and application scores for participants in each of the three experimental conditions. Error bars are 95% confidence limits.

Boudewyns, V., et al. Science Direct (2015)
https://doi.org/10.1016/j.pec.2015.07.003

Example of Organizing Key Information

Design Tips

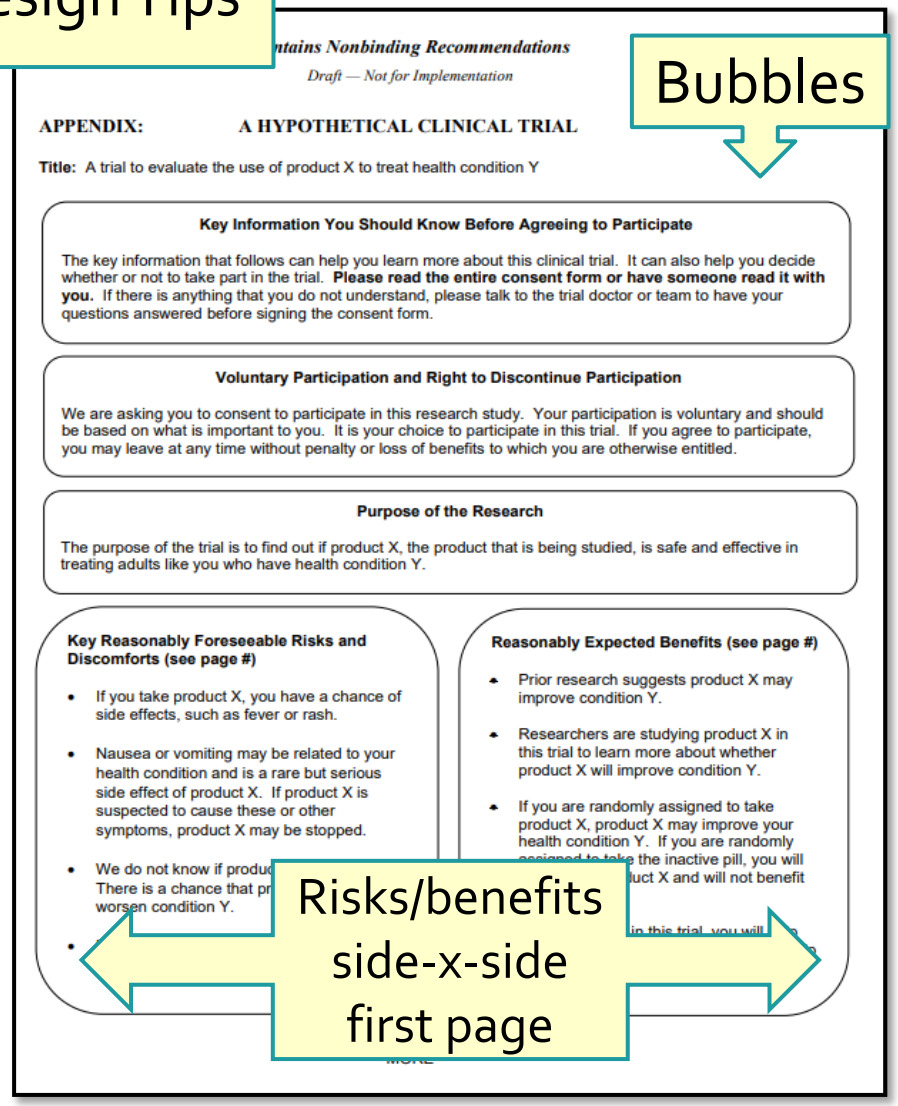
Bubbles

Hyperlink to more details

White space

2 columns

Risks/benefits side-x-side first page



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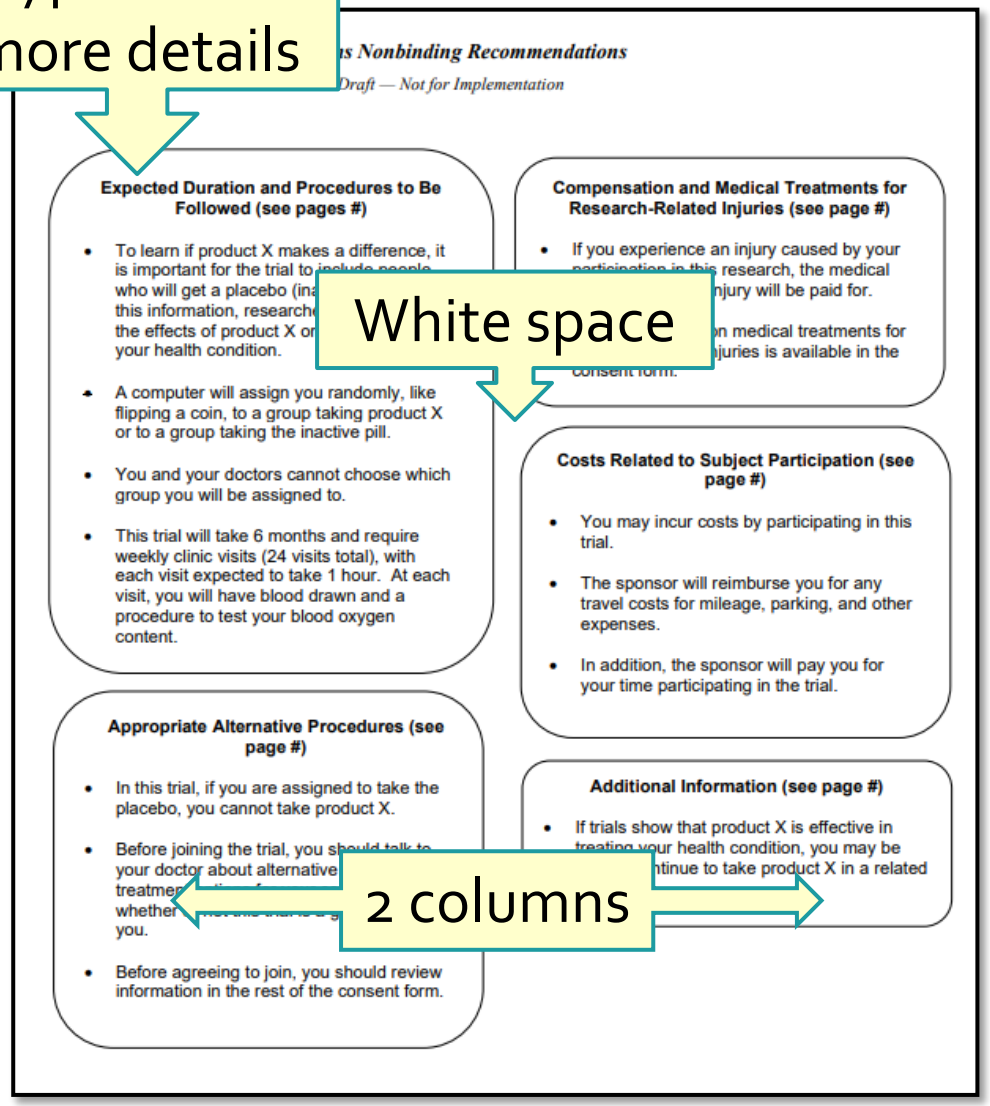

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Additional Information (see page #)

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A few pages

Bullet points

Simple text

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

Improving More Than Consent

- Essential to have better informed participants
- May help presenter convey information more clearly
- Improving the whole consent and adding key information can be a useful resource for participants
- May improve enrollment, help retain participants, and increase representativeness in trials

Ongoing Activities

- Developing Final Rule on HSP
- Developing joint draft guidance
  - Considering 70+ public comments
  - Communicating with interested parties on implementation

Main Takeaways Messages

- Informed consent is not just a signature or a document.
- Begin with key information (if rule is finalized as proposed)
- Be innovative, use images, videos and thoughtful design elements
- Engage participants and communities for participant-centered informed consent.
- **Look for opportunities to improve consent approaches now.**

Thank You!

GCPquestions@fda.hhs.gov


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