U.S. FOOD & DRUG ADMINISTRATION

Improving Informed Consent

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Office of Commissioner | US FDA

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CDER | US FDA

REdI Annual Conference: Innovation in Medical Product Development – May 30, 2024

Disclaimers

- Presenters' views are their own and do not necessarily represent FDA policies
- No disclosures

Learning Objectives

1. Describe the purpose of informed consent
2. Describe how two provisions in FDA's proposed rule can improve consent materials
3. Explain what a key information section is
4. Describe tools that can improve organization and understanding of consent

Note

- This is a high-level overview
- Please see the FDA regulations (21 CFR Part 50) and guidances for specifics

That's a lot to learn…

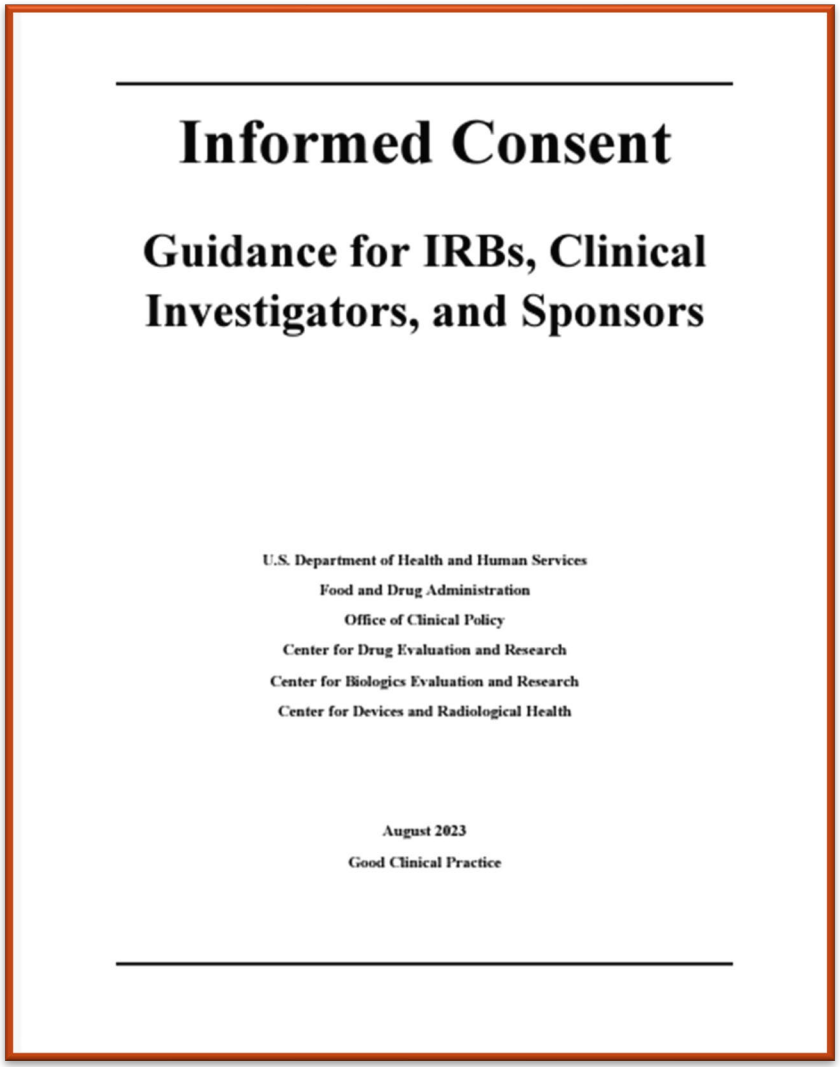
Good thing we have

ANSWERS

Question 1

What is Informed Consent?

Informed Consent Guidance



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

- Informed Consent
- Published August 2023

Informed Consent Is…

- Providing information to allow a person to make an *informed decision* about whether to participate in a study
- Helping a person understand the study
- Providing opportunity for questions
- Obtaining/documenting voluntary agreement to participate
- Providing information during the study

Informed Consent Process Is…

- An ongoing exchange of information with each prospective participant
- Does *NOT* end after consent form is signed
- Example: If a protocol changes:
  - additional information can be provided to participants

  and
  - participants may need more time to ask questions and obtain answers

Challenge Question A

CHALLENGE

Who is responsible for informed consent?

A. The sponsor

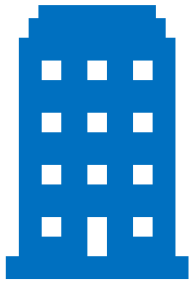
B. The clinical investigator

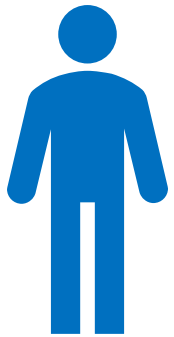
C. The IRB

D. The participant

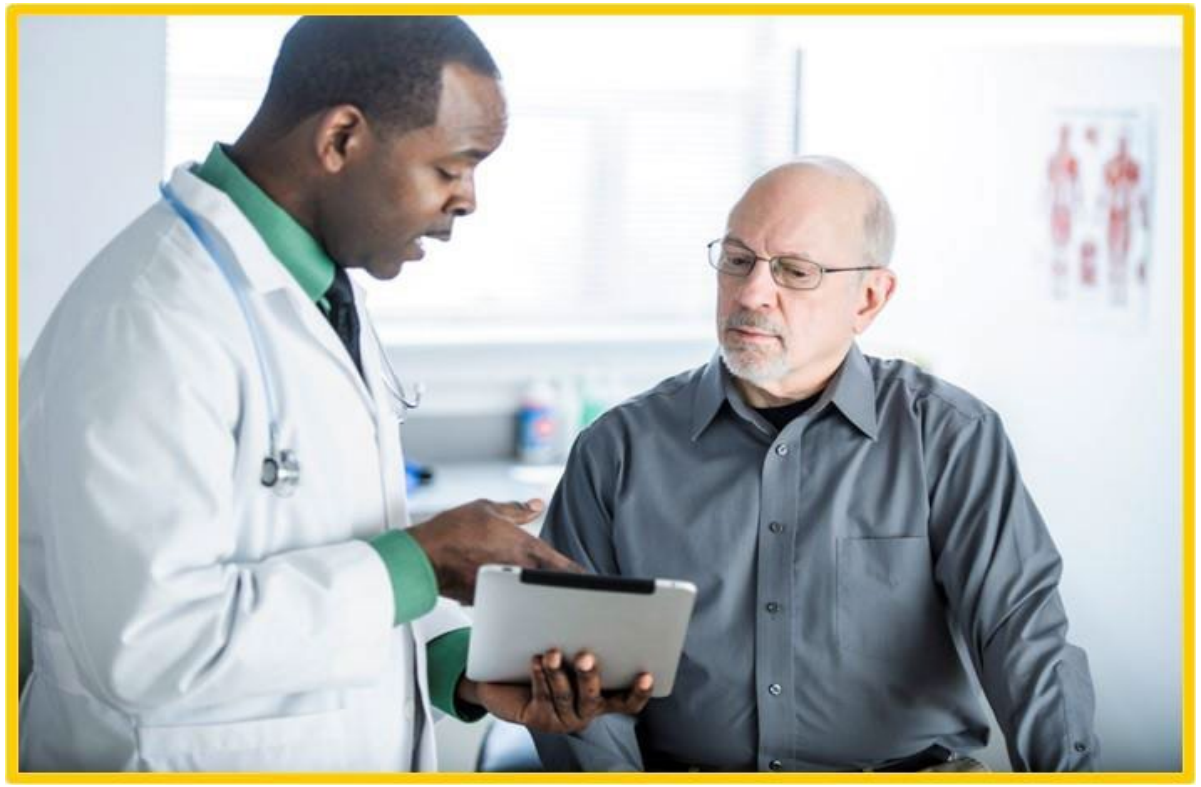
E. All of the above

F. A – C





Question 2



What are the elements of informed consent?

Informed Consent Elements

a) Required “Basic Elements”

b) “Additional Elements”

c) Required statement about ClinicalTrials.gov

d) Any other information that the study sponsor or investigator wants to include

21 CFR 50.25

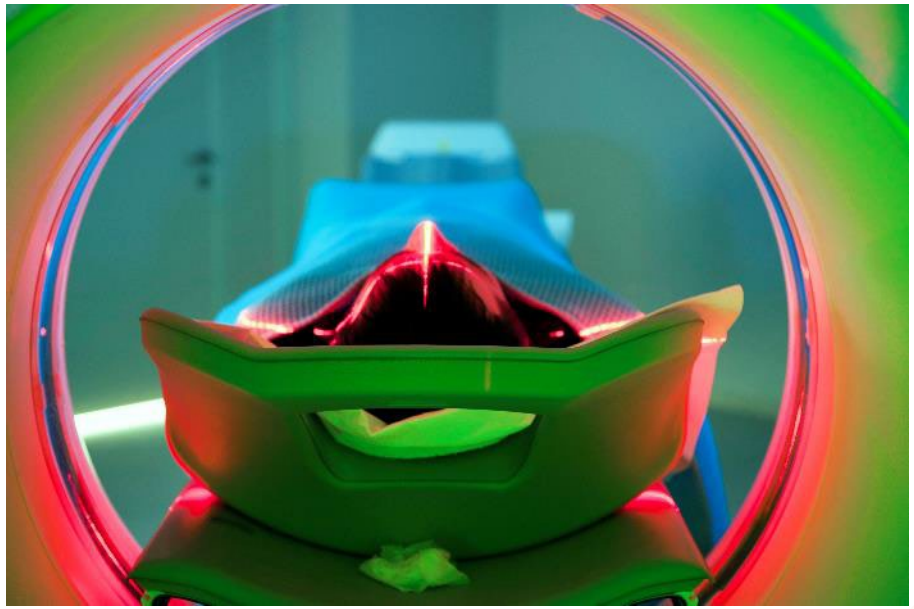
Basic Elements

Basic Elements

1) The study involves research
   - Purpose, duration
   - Procedures or interventions

Basic Elements

1) The study involves research
   - Purpose, duration
   - Procedures or interventions
2) Risks or discomforts



Basic Elements

1) The study involves research
   - Purpose, duration
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2) Risks or discomforts
3) Benefits

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1) The study involves research
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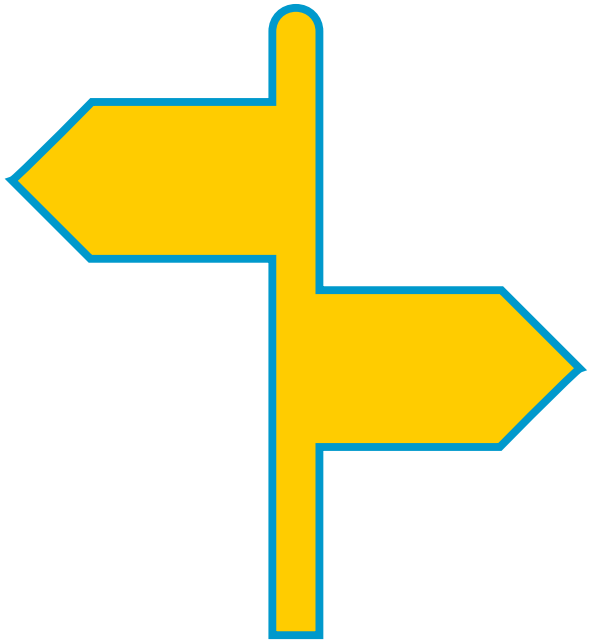
   - Procedures or interventions
2) Risks or discomforts
3) Benefits
4) Appropriate alternatives



Basic Elements

1) The study involves research
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3) Benefits
4) Appropriate alternatives
5) Confidentiality; FDA may inspect

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3) Benefits
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5) Confidentiality; FDA may inspect
6) Compensation for injuries

Basic Elements

1) The study involves research
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3) Benefits
4) Appropriate alternatives
5) Confidentiality; FDA may inspect
6) Compensation for injuries
7) Study contact

Basic Elements

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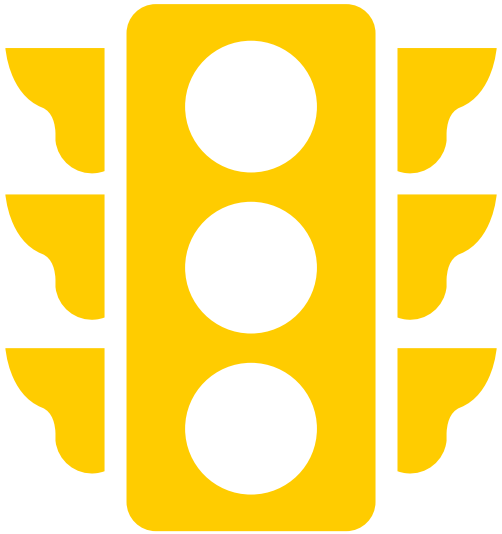
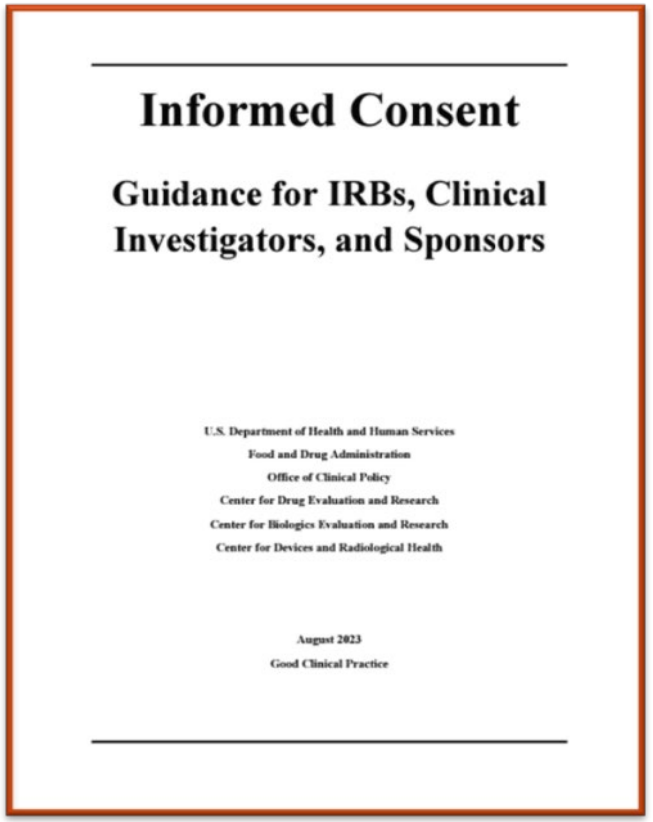
3) Benefits
4) Appropriate alternatives
5) Confidentiality; FDA may inspect
6) Compensation for injuries
7) Study contact
8) Voluntary participation



Additional Elements

1) Unforeseeable risks
2) Involuntary termination
3) Costs to participant
4) Withdrawal
5) New findings will be shared
6) Approximate number of study participants



That's a lot to put in a consent form…

- Don't write a book!
  - Longer consent forms limit understanding
- Avoid complex, legalistic forms

- Avoid high reading levels

Question 3

How does informed consent relate to the conference title:

“Innovation in Medical Product Development?”

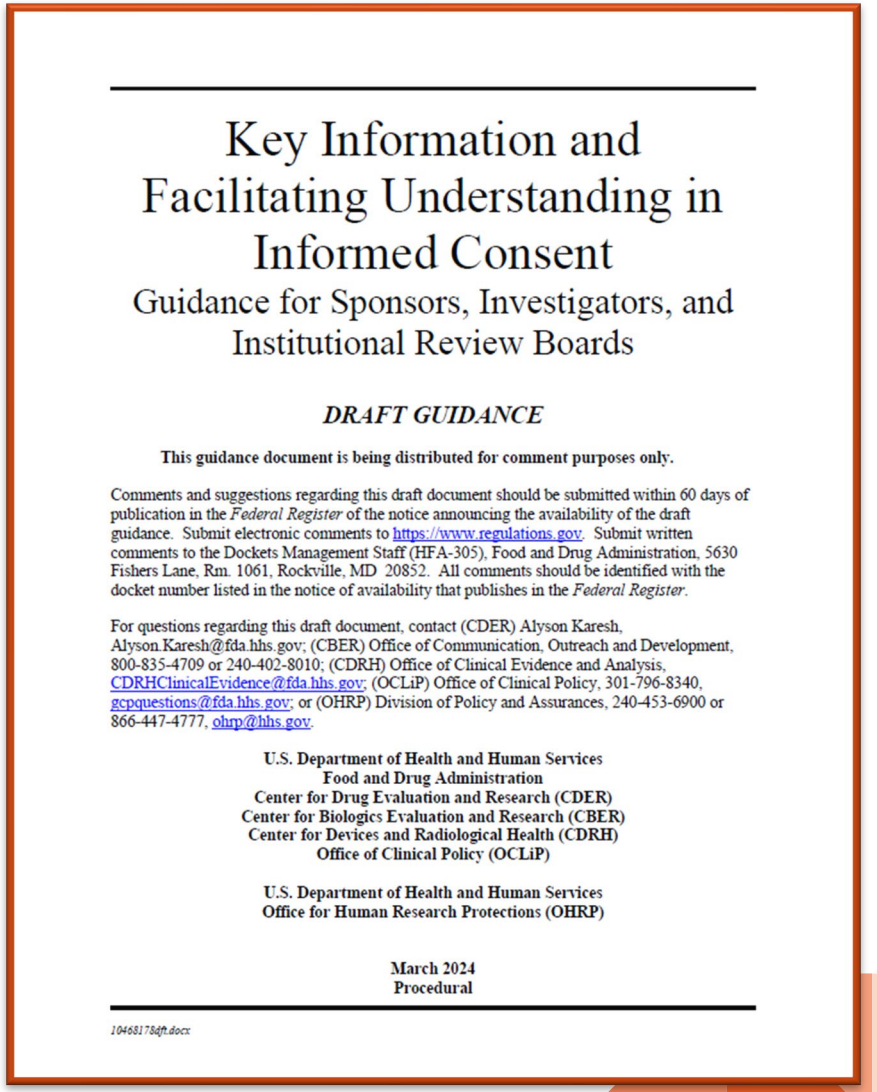
FDA Informed Consent Changes

- FDA Proposed Rule: “Protection of Human Subjects and Institutional Review Boards” (21 CFR Parts 50 and 56)
- Office for Human Research Protections (OHRP): “revised Common Rule” (45 CFR Part 46)

FDA proposed rule – 87 FR 58733, Sept. 28, 2022

New Informed Consent Joint Draft Guidance

- 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)
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Office of Clinical Policy (OCLiP)

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

March 2024
Procedural

10468178dft.docx

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)

Question 4

What is key information?

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 Content

- Assess what elements of consent may be appropriate to include for a particular study
  - Required “Basic Elements”
  - “Additional Elements”
  - Information beyond elements
    - Note: Key information may comprise the entire consent, if it includes all basic elements (e.g., simple studies)

Key Information Example

Key Information

Voluntary Participation

Purpose

Key Information Example

Risks and Discomforts

Potential Benefits

Key Information Example

Duration and Procedures

Compensation and Treatments for Injuries

Other Alternatives

Question 5

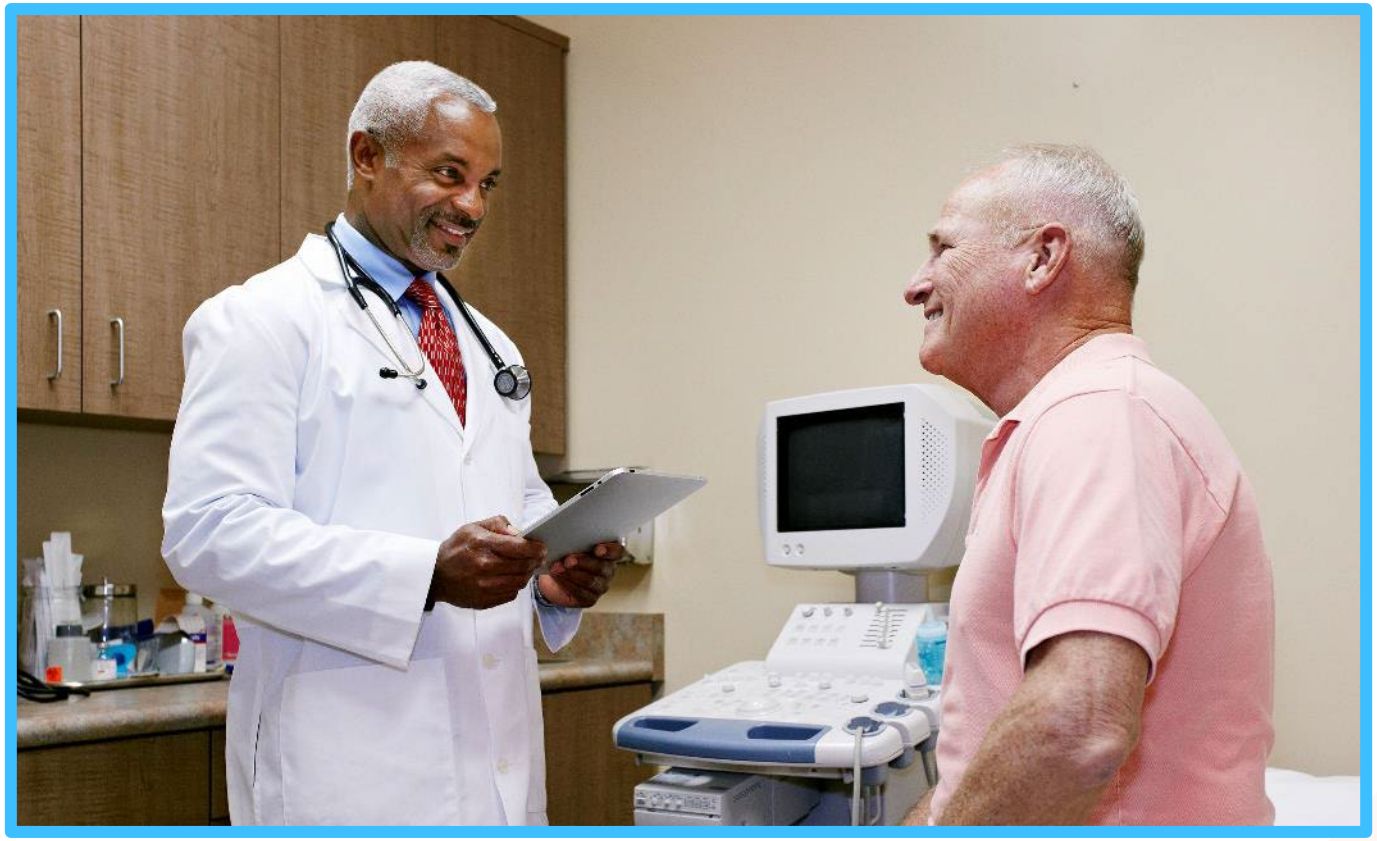
What is NOT key information?

Key Information is NOT…

- In place of consent process
- A change in responsibilities
- A “one-size-fits-all” approach for all studies

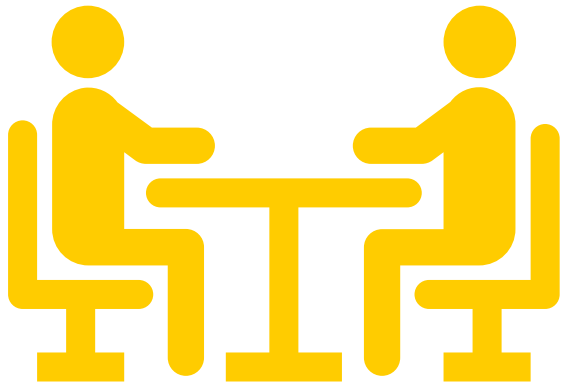
Question 6

How can consent materials be prepared to help people better understand a study?

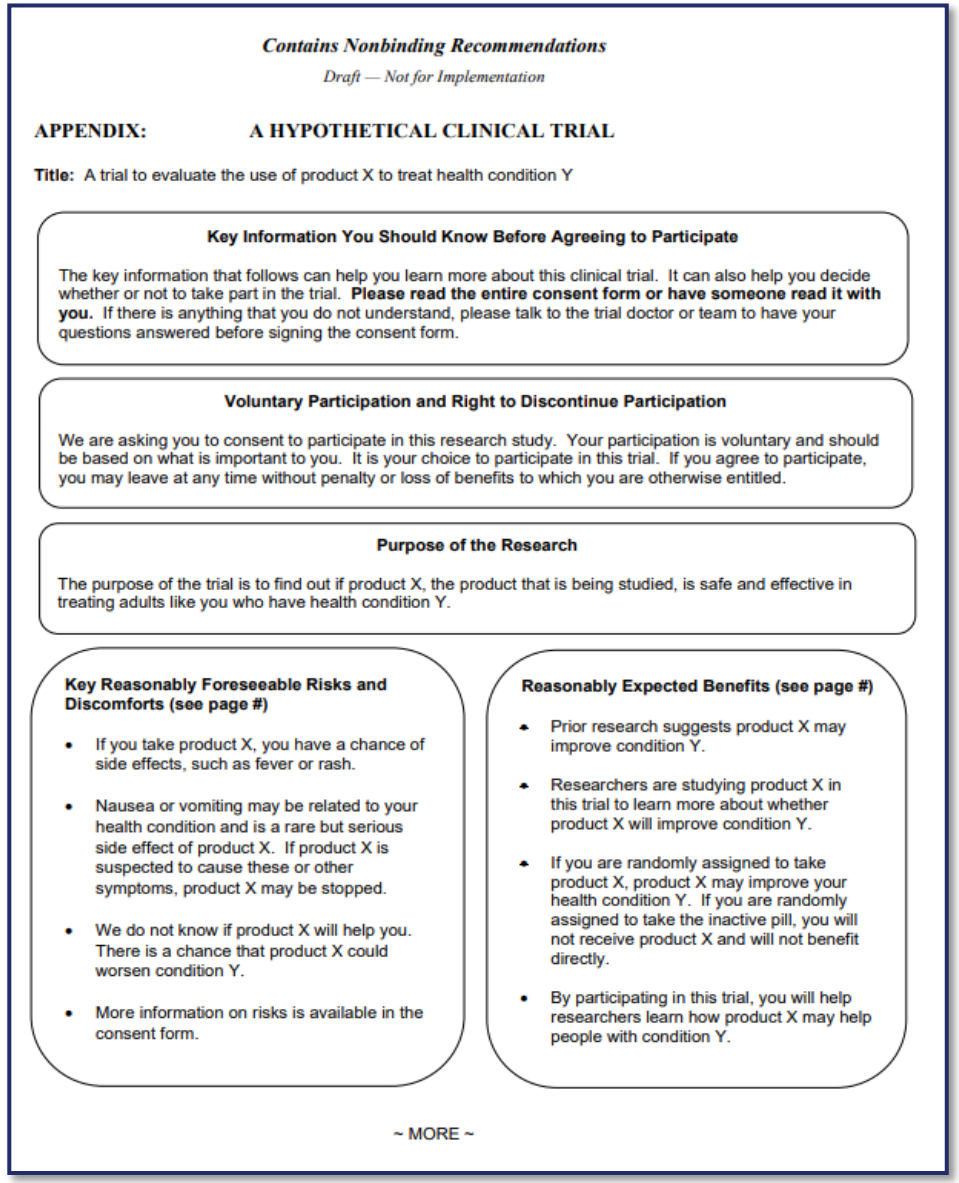


Facilitating Understanding

- The whole consent must
  - Present research information in sufficient detail
  - Be organized to help facilitate the participant's understanding of why someone may want to participate



Key Information Design



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.

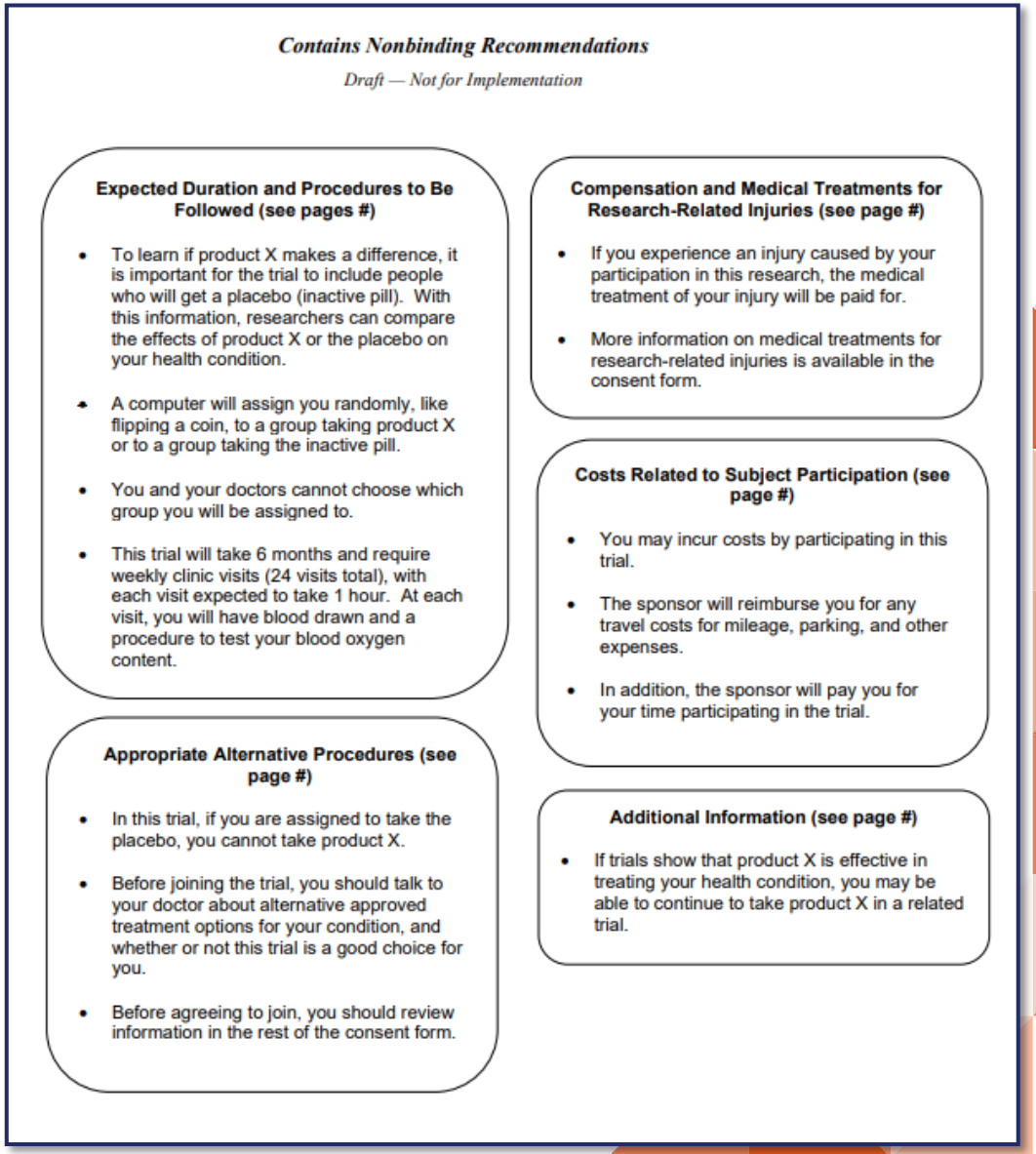
Key Reasonably Foreseeable Risks and Discomforts (see page #)

- 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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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.

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.

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)

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

Study on Design Features

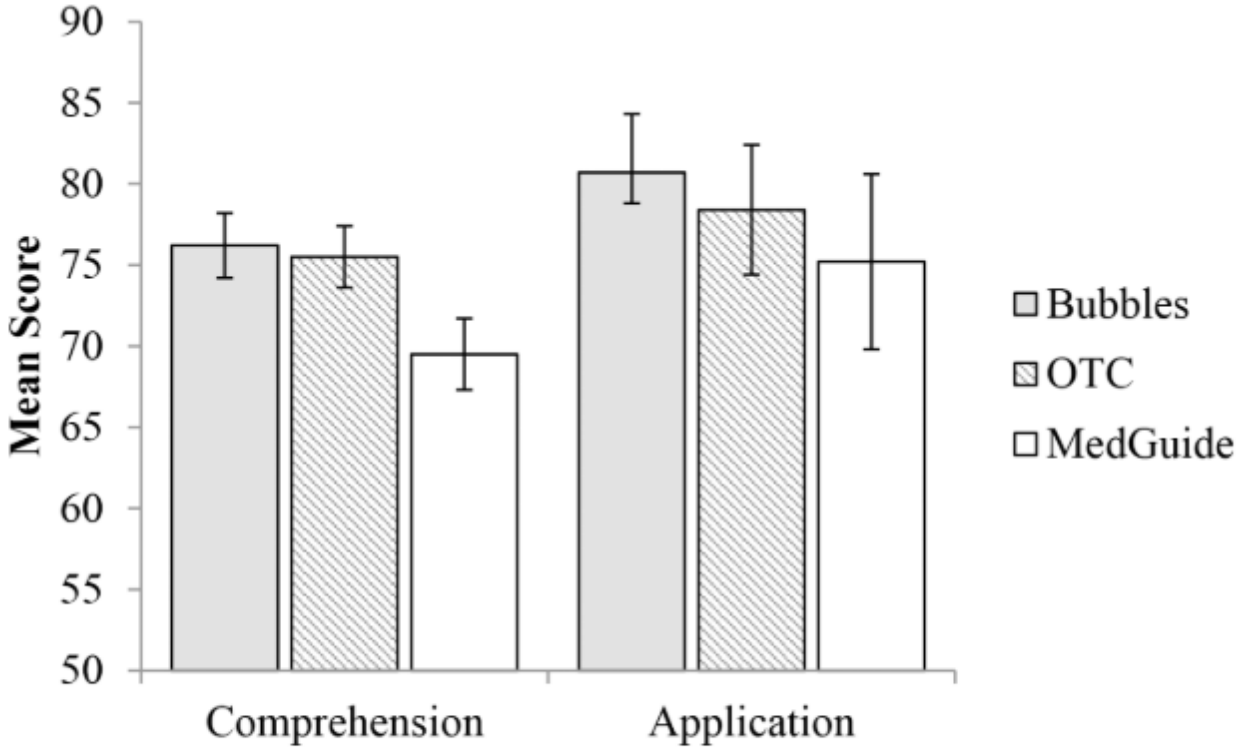

Figure 3.
Effect of Patient Medication Information Handout Format on Comprehension and Application Scores.
Bar graph shows the mean comprehension and application scores for participants in each of the three experimental conditions. Error bars are 95% confidence limits.

Results: Bubble format improves comprehension

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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X may improve your
If you are randomly
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X and will not benefit
- By participating in his trial, you
researchers lea
people with co

~ MORE ~

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Additional Information (see page #)

- If trials show that product X is effective in treating your health condition, you may be
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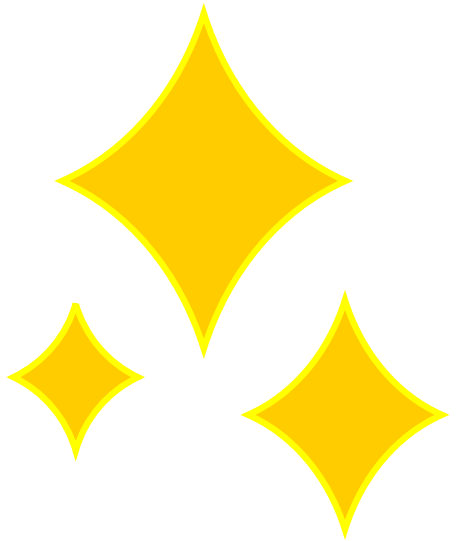
Question 7

Is there only one way to prepare a key information section?

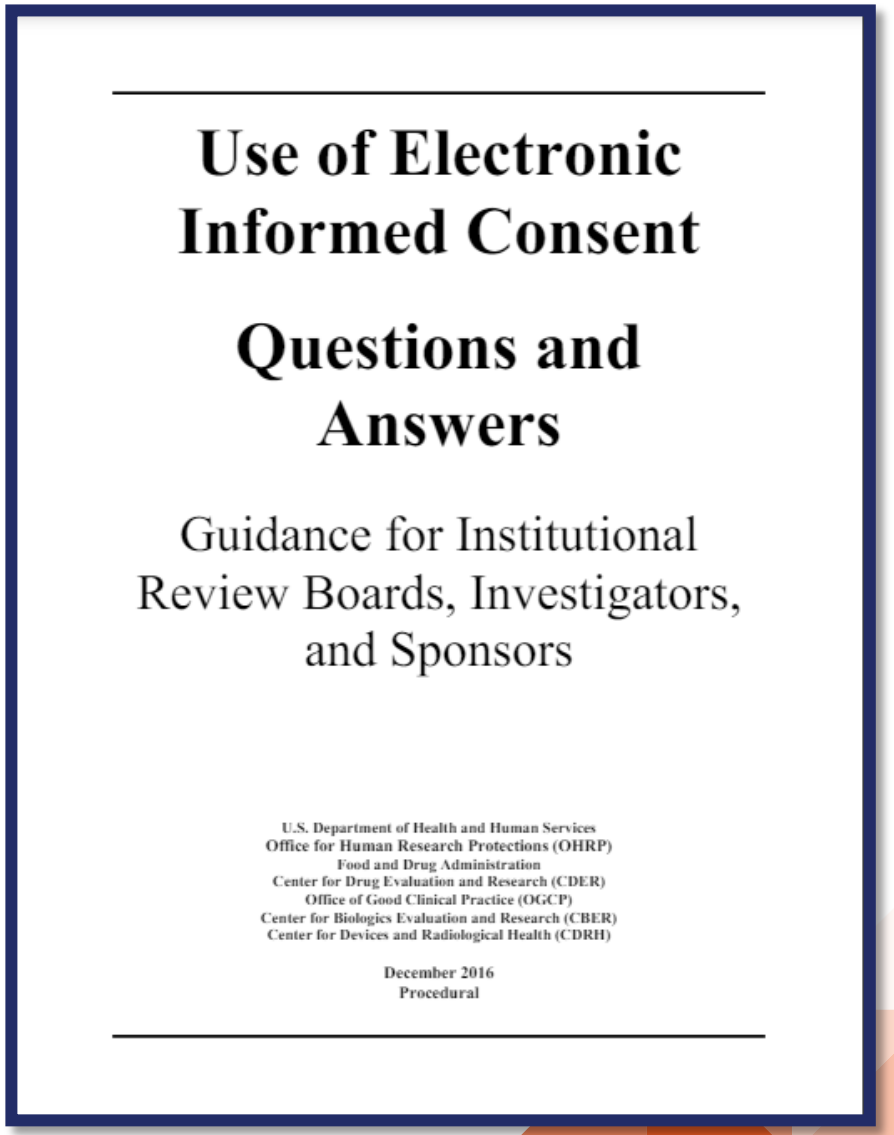
Consider Multiple Approaches

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



Electronic Consent Joint Guidance

- Electronic Consent
- Published December 2016



Use of Electronic Informed Consent

Questions and Answers

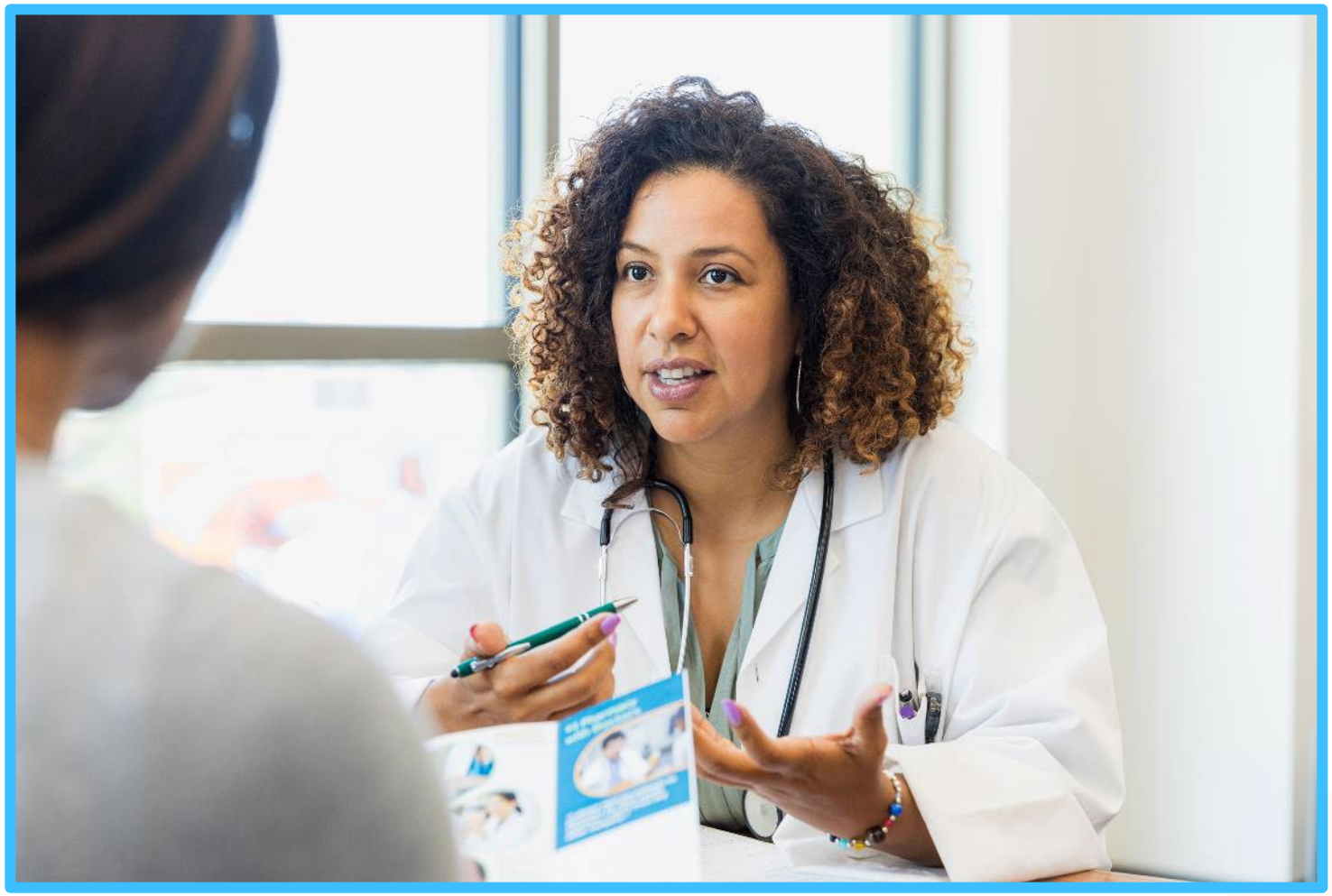
Guidance for Institutional Review Boards, Investigators, and Sponsors

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

Question 8

Why are the new consent provisions important?



Improving More Than Consent…

- Critical to have better informed participants
- May help presenter convey information more clearly
- Can provide a useful resource
- May improve enrollment, help retain participants, and increase diversity

Question 9

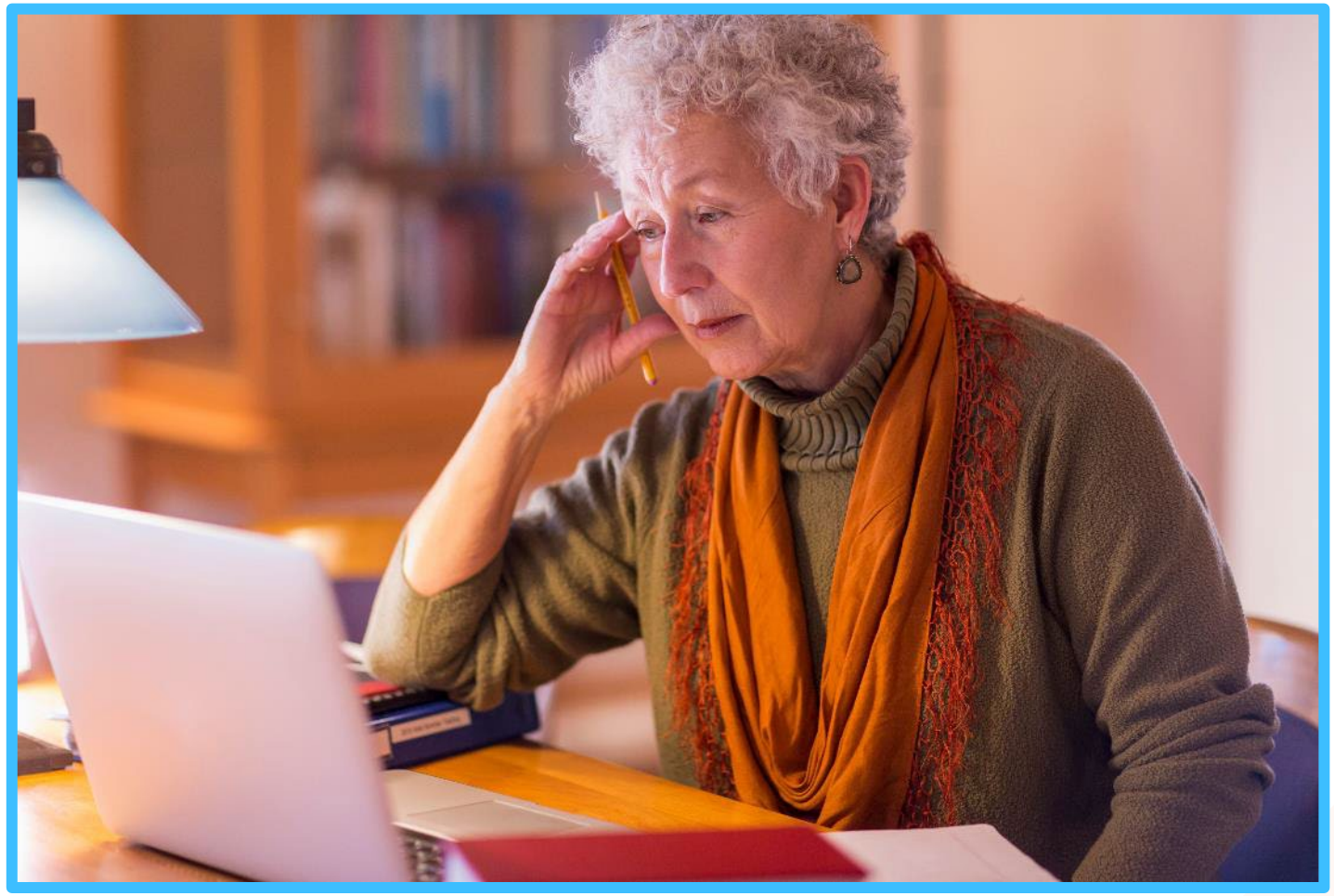
What's Next?

Next Steps

- FDA must publish final rule
- Work with OHRP to finalize guidance

Question 10

Want to know more about Informed Consent?



FDA Resources

- FDA guidance on Informed Consent (2023)
- FDA/OHRP *draft* guidance on Key Information and Facilitating Understanding in Informed Consent (2024)
- FDA/OHRP guidance on the Use of Electronic Informed Consent Q&A (2016)
- FDA Informed Consent Regulations – 21 CFR Part 50
- FDA Proposed Rule on Protection of Human Subjects (87 FR 58733, Sept. 28, 2022)

Challenge Question B

CHALLENGE

Which of the following statements about key information is true?

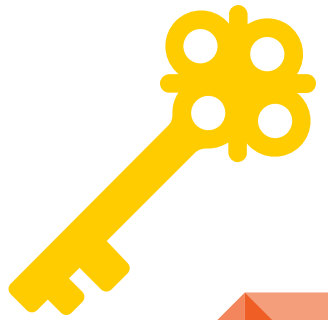
A. The consent form must begin with key information.

B. Key information must include all basic and additional consent elements.

C. Key information must use bubbles, two columns, and white space.

D. Key information must be limited to two pages.

E. Nothing specific is required



Bonus Question

Who is responsible for key information?

A. The sponsor

B. The clinical investigator

C. The IRB

D. The participant

E. All of the above

F. A – C

Main Takeaways

- ✓ Key information must be presented first*
- ✓ Be organized
- ✓ Be clear and concise
- ✓ Be innovative with content and approaches

*once FDA proposed rule is finalized

Main Takeaways

Suggest Acting Now

- ✓ Start adding a key information section
  AND
- ✓ Start improving approaches to the whole consent form and process now

Questions

THANK YOU!