



OFFICE OF THE ASSISTANT SECRETARY FOR HEALTH

Informed Consent: From Theory to Practice

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November 6, 2019



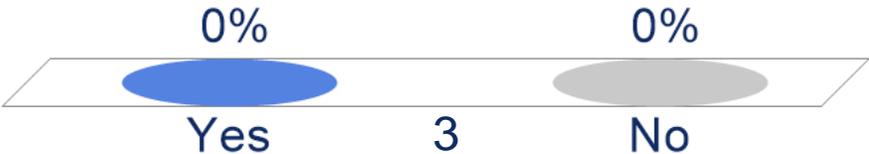
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Have you ever asked others to consent to participate in a biomedical research study with a treatment intervention?

- A. Yes
- B. No



Have you (or a close family member) ever been asked to provide consent to participate in a biomedical research study with a treatment intervention?

A. Yes

B. No



**WANT TO SHARE YOUR EXPERIENCE
OBTAINING OR PROVIDING INFORMED
CONSENT?**

The Significance of Informed Consent

- Belmont Report Principle *Respect for Persons*
 - Treat individuals as autonomous agents
- The Common Rule requirement
Informed consent must provide information:
 - Necessary for an **informed** decision about participation
 - In language **understandable** to the potential participant
 - Under circumstances that promote **voluntariness**

46.116(a)



**NEW INFORMED CONSENT GENERAL
REQUIREMENTS AT §46.116(a)(4)&(5)**

New General Requirements for Informed Consent (1)

The revised Common Rule explicitly establishes a standard for the kind of information to be given in informed consent document:

*The prospective subject or the LAR must be provided with the information that a **reasonable person** would want to have in order to make an informed decision about whether to participate*

§46.116(a)(4)



New General Requirements for Informed Consent (2)

Information presented in *sufficient detail*,
and *organized and presented* in a way that
**facilitates subject's understanding of why
one might or might not want to participate**

§46.116(a)(5)(ii)



Not merely a list of isolated facts



Focus: Facilitating subject's understanding of the reasons why they might or might not want to participate

If you were asked to participate in this study, **what information would you need and how would you like to receive this information** so that it would make sense to you and you could use it to make an informed decision about participating or not participating?



Example of Information About a Study Intervention

- *The purpose of this study is to determine whether receiving the intervention now **is better than** only receiving the intervention when your disease progresses. The trial will let us know which approach is more effective in treating your disease.*
- *Taking part in this study **may or may not make your health better**. While doctors hope that applying the intervention earlier **will be more useful** for your condition compared to applying the intervention only when your disease progresses, there is no proof of this yet.*

Is this sufficiently detailed?



What might sufficiently detailed information about an intervention look like? An Example

We want to find out if drug X is effective in treating inflammation of the pancreas in patients just diagnosed with acute pancreatitis.

X blocks inflammation...If it works, it could mean less damage to the pancreas, fewer medical complications (such as those that require admission to intensive care), and better treatment outcomes (such as a shorter hospital stay).



A Long List of Potential Side Effects About a Study Intervention

Neurological

- Chronic nerve damage
- Peripheral nerve damage
- Psychological intolerance (fear of loss of LAP monitoring function)
- Stroke/transient ischemic attack
- Subdural, epidural hematoma

Cardiac

- Acute coronary syndrome (sudden worsening of chest pain, heaviness or pressure)
- Arrhythmias (irregular heart rhythm)

**Providing a detailed list of isolated facts
≠
Facilitating understanding**

- Cardiac tamponade
- Damage to heart valves
- Emergency heart surgery
- Emergency vascular surgery
- Low cardiac output state
- Heart block
- Hypotension



List of isolated facts: *What about this?*

The risks of study drug are as follows

Common (>30%): Fatigue, Lymphocytopenia (low white blood cells, Low sodium, Shortness of breath,

Musculoskeletal pain, Decreased appetite, Cough

Less common (10-29%): Nausea, Anemia, Constipation, Increased serum creatinine, Colitis, Low potassium, Low magnesium, High calcium, Vomiting, Weakness, Diarrhea, High potassium, Low calcium, Swelling, Fever, Rash,

Abdominal pain, Increased serum AST, Thrombocytopenia, Increased serum alkaline phosphatase, Chest pain,

Weight loss, Joint pain, Increased serum ALT, Itching, Pneumonia, Pain

Rare (<10%): Immune-mediated Pneumonitis, Immune-mediated Colitis, Immune-mediated Hepatitis, Immune-mediated Nephritis and Renal Dysfunction, Immune-mediated Hypothyroidism and Hyperthyroidism



Is this description written in language generally understandable?

On why the research is being done:

The comprehensive treatment of cognitive impairment and other medical conditions may best be treated lifestyle modifications (e.g., cognitive and exercise training)....Studies that implement both targeted neurocognitive and exercise training interventions (rather than each alone) are showing greater promise on improving cognitive function in older adults. Combining these two intervention modalities simultaneously may be more effective than either intervention alone. ...

DISCUSSION: How can we convey this information more simply?



Strategies for Organizing Information and Facilitating Understanding (1)

Communicate clearly using plain language, e.g.,

- Avoid information overinclusion
- Avoid medical jargon and acronyms; or make sure to define them
- Use short sentences
- Avoid including too many ideas in a sentence
- Avoid using big complex words if possible; Use common everyday words
- Write in active direct voice, e.g., “we will call you” vs “you will be called”
- Check for errors; limit copying and pasting from other documents
- Ask a non-scientist to review



Strategies for Organizing Information and Facilitating Understanding (2)

Put facts into context, e.g.,

- Explain how a piece of information might matter for deciding to participate or not
- Consider explaining risks and benefits together in a connected manner
- Explain the implications of a piece of information, instead of just providing a definition



Is this description written in language generally understandable?

On what the study drug is:

XXX is a human monoclonal antibody that blocks the interaction between PD-1, PD-L1 and PD-L2. Binding of these ligands to the PD-1 receptor found on T cells, inhibits T cell proliferation and cytokine production. Upregulation of the PD-1 ligands occurs in some tumors and signaling through this pathway can contribute to inhibition of active T-cell immune surveillance of tumors. XXX is a human immunoglobulin (IgG4) monoclonal antibody that binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response, resulting in decreased tumor growth.

DISCUSSION: How can we convey this information more simply?



An Example of Putting Information into Context: *What does it mean to be in a randomized study?*

“Randomization means that you will be assigned to a group randomly, like the flip of a coin”

You gave an idea of *how* the assignment is done.
You did not explain **the implications of**
what it means to be randomized.

- You cannot choose which group you are in. Neither your doctors nor the researchers choose which group you are in.
- You must be okay with your assignment to either of the study groups



Some Reasons for Special Considerations for Clinical Trials Involving Patient Participants

- Therapeutic misconception is common
- Medical information is complex and often requires special knowledge to make sense
- Decisions are complex and impactful because they affect one's health
- Additional complexities related to the nature of research:
 - Primary goal of research is to collect data to answer questions
 - Complex concepts such as randomization
 - Uncertainty about efficacy and risks of interventions



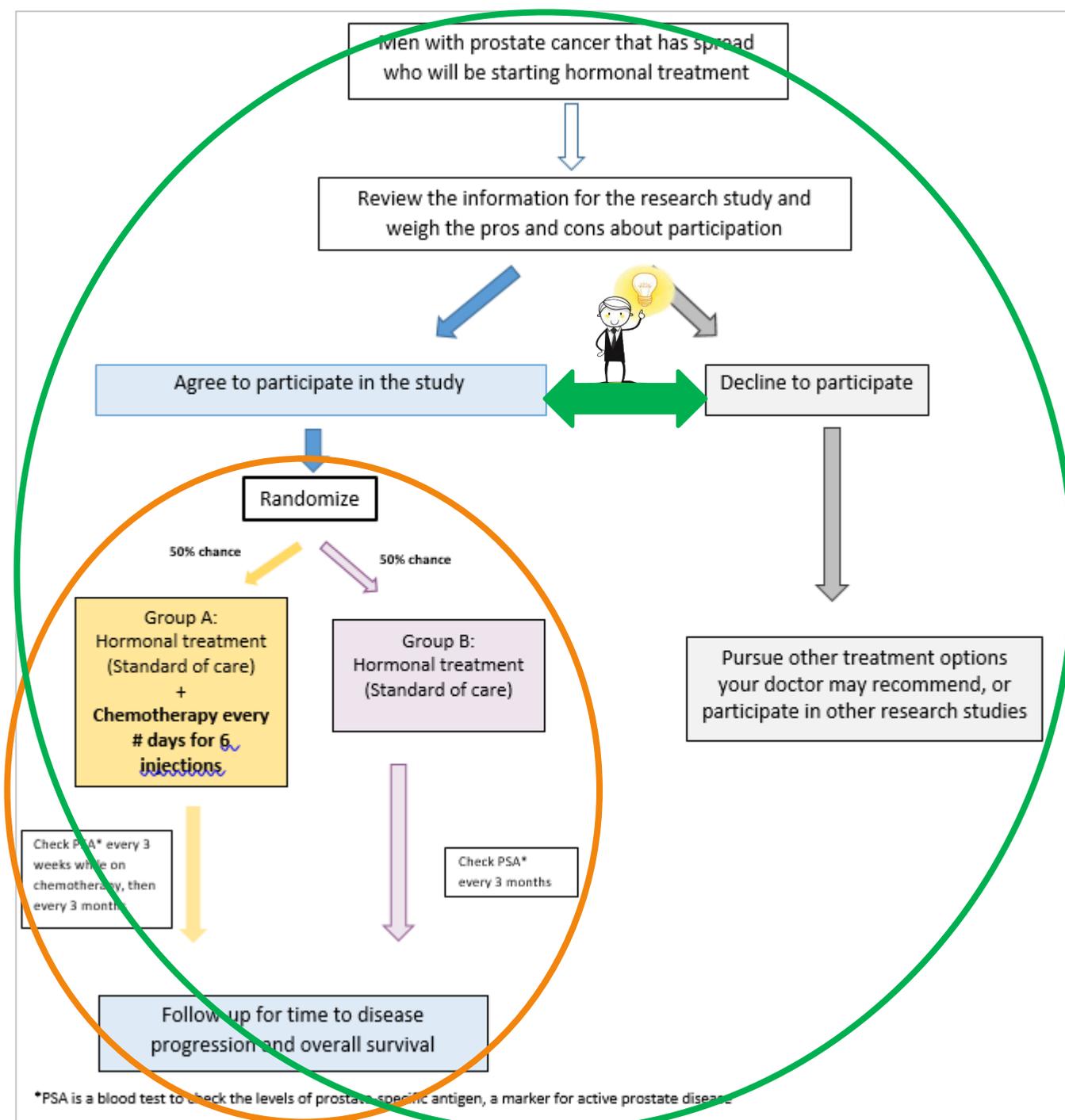
Strategies for Organizing Information and Facilitating Understanding (3)

Display information in formats that facilitate understanding, e.g.,

- Include a diagram of the study
- Display information in tables
- Provide information under headings framed into questions a prospective participant might ask to help them make sense of the information. For example,
 - *Why are we (researchers) doing this research?*
 - *What do we hope to learn from this research and why should it matter to you?*
 - *What might it mean to you to participate in this research?*



- Provide a Study Diagram to Help Frame the Decision Points
- Don't just focus on the information about the study intervention
- Focus: Facilitating subject's understanding of the reasons why they might or might not want to participate



Display Information Side by Side for Comparison

(Example of a study to treat acute pancreatitis)

If you receive the studied drug (50% chance)

You will receive the standard treatment for acute pancreatitis AND you will receive a pill to take by mouth three times a day for up to 9 times. **You will not know that this pill contains the studied drug and that you are in the intervention group.**

The studied drug has been known to cause bleeding more easily, but this is rare. See page X of the full consent form for more details.

You will have blood tests once a day while in the hospital to check for signs of inflammation.

If the studied drug is effective, other than symptom relief from the standard treatment, you may have less inflammation, less damage to your pancreas, fewer medical complications, and a shorter hospital stay.

If the studied drug is not effective, it will not help reduce the inflammation of the pancreas. You will only get the symptom relief from the standard treatment for acute pancreatitis.

If you receive the placebo (50% chance)

You will receive the standard treatment for acute pancreatitis AND you will receive a pill to take by mouth three times a day for up to 9 times. **You will not know that this pill is a placebo and that you are in the placebo group.**

A placebo does not contain any drug. It is an inactive compound that does not have any treatment effects or side effects.

You will have blood tests once a day while in the hospital to check for signs of inflammation.

You do not stand to receive any benefits that might result from the studied drug because you are not receiving it.

The placebo does not add anything to the symptom relief that you will receive from the standard treatment for acute pancreatitis.

If the studied drug is not effective, it would not have mattered that you do not receive it. Your treatment is essentially the same as the current standard of care treatment for people with acute pancreatitis.

If you decide not to participate

You will receive the standard treatment for acute pancreatitis OR any other treatment options your doctor may recommend

Example: What are the side effects and other relevant facts about the standard treatment, so that potential participant can compare them to the study and:



understand the reasons why they might or might not want to participate

New General Requirements for Informed Consent (3)

- New requirement that certain **key information** must be provided **first**
- **Key information:**
 - About **why one might or might not want to participate**
[Often include, though not limited to, information about purposes, risks, benefits and alternatives]
 - Must be presented in **concise and focused** manner



§46.116(a)(5)(i)



Reasons for Why One Might or Might Not Want to Participate:

Some Examples

Why might one want to participate?

- *I want to help researchers find a better treatment for future patients like me. I have little or no preference for receiving the treatment in either study group. I am willing to accept a 50% chance of receiving the study drug and a 50% chance of not receiving it.*
- *Participating in the research gives me a chance to get the study drug at no financial cost to me.*

Why might one NOT want to participate?

- I do not want any chance of receiving the study drug because doctors do not really know if it will make me live longer.
- I do not want any chance of receiving the study drug because I don't want to get the side effects.
- I'm going to talk to my doctor to see if there is another way which gives me a better chance to get the study drug.

What Might the Key Information Section for a Clinical Trial Include?

General background information to put things into context for prospective participants in the subjects' population

- Who is the research recruiting? Why are you being asked to participate?
- What's currently done about your medical condition?
- Why are we (investigators) doing this research? How do we think we can improve on current practices?

Overview summary of the study with meaningful details for someone in the subjects' population

- How will the study be done? What does it mean to you to be randomized?
- How will the treatment groups differ in risks, benefits, and other important aspects?
 - How might being in the study or not affect your health?
 - Why might you want or not want to participate?

What Might the Key Information Section for a Clinical Trial Include? ... *Cont.*

Summary of additional non-health related key concerns common to this subject population

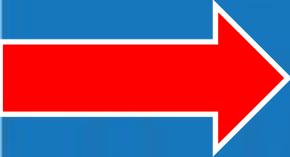
- Who will pay for the treatments and procedures in the research?
- What kind of burden (time, effort) may be involved?
- Will we tell you the findings of the research?

More on Key Information

- Key information should provide concise & focused information for why one might or might not want to participate
 - Idea is that reading this section will give prospective subjects a meaningful sense of the study and if they are inclined to participate, then it will provide a framework to help them better understand the more detailed information provided in the rest of the consent document
- It is part of the consent document for which §46.116(a)(5)(ii) requirements for sufficient detail and organization/ presentation apply
- There is no need to repeat the information already provided in the key information section in the rest of the consent form
- What is key information may differ significantly from study to study



OHRP PUBLIC OUTREACH WEBSITE

 www.hhs.gov/About-Research-Participation

Resources for the public to learn about participating in research and making informed decisions



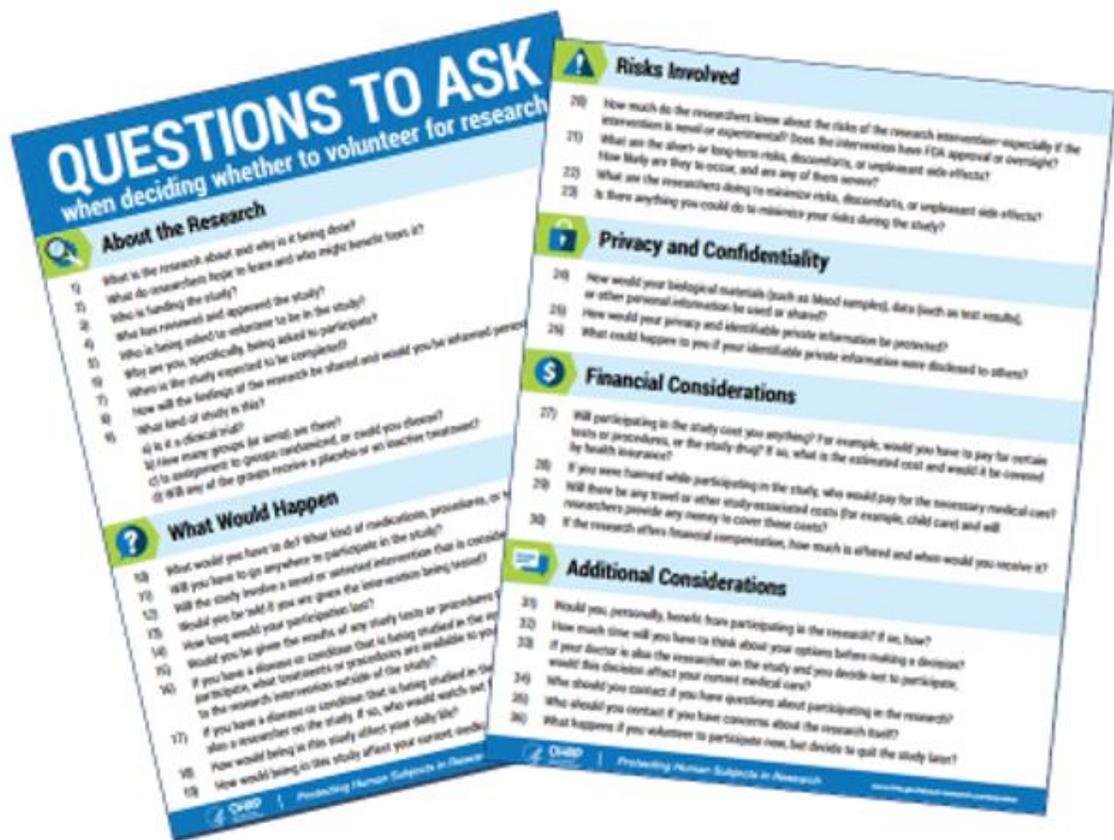
Videos



Information



Tools



About Research Participation

What you need to know before you decide.

Informational Videos

View in [English](#) or [Spanish](#)

OHRP has created a series of short videos with basic information about research. These videos are intended to help potential participants understand how research works, what questions they should consider asking, and things to think about when deciding whether to participate in a study.

These videos are intended for public use and distribution, and we invite you to use and share them freely. We welcome you to link to them from your website.



[Part 1: What is Research?](#)

This video provides basic information about scientific research, the goals of research, and discusses how clinical research differs from medical care. (3:00)



[Part 2: Clinical Trials](#)

This video discusses types of human research with a focus on clinical trials, and explains common terms that potential participants should know. (4:20)



[Part 3: Questions to Ask](#)

This video emphasizes that participating in research is voluntary and encourages potential participants to ask questions and get the information they need to decide whether to participate. (4:44)



[Randomization](#)

This video explains the concept of randomization in research studies and what potential participants need to know when volunteering for a study with a randomized design. (7:25)



[Institutional Review Boards \(IRBs\)](#)

This video explains the concept of Institutional Review Boards (IRBs), which review certain research studies involving human volunteers to ensure that the studies meet ethical standards and regulatory requirements. (6:45)

Please refer to the text of the revised Common Rule available on OHRP's website for a complete and accurate description of the regulatory requirements



Contacts and Resources

- Contact us or submit your questions to OHRP@hhs.gov
- Visit OHRP website at www.hhs.gov/ohrp
- Bookmark this page for quick reference to OHRP resources on the revised Common Rule: www.hhs.gov/ohrp/education-and-outreach/revised-common-rule/index.html





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thank you 😊

