Making Informed Consent More Meaningful in the Era of the Revised Common Rule

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Disclaimer

The opinions expressed are those of the presenters and do not necessarily reflect the policy of the U.S. Department of Health and Human Services
Revisions to the Common Rule

- General compliance date: January 21, 2019
- One of the major goals for the revisions is to better protect research subjects through improved informed consent

“SACHRP would like to emphasize that we see these new consent requirements as providing an opportunity to fundamentally change and improve the consent process and the consent form”

SACHRP Recommendation on Key Information, October 17, 2018
What is the Purpose of Informed Consent for Research Participation?

Primary purpose is to help potential research participants make informed decisions about participation

- **Belmont Report Principle *Respect for Persons***
  - Individuals as autonomous agents who should not be treated merely as a means to someone else’s end

- **The Common Rule** requirement
  - Informed consent must provide information:
    - **Needed** for an informed decision about participation
    - In language **understandable** to the potential participant
    - Under circumstances that promote **voluntariness**

§46.116(a)
New Requirements for Informed Consent (1)

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

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)

(Text in blue represents what’s new in the revised Common Rule. Bolding added for emphasis only.)
New Requirements for Informed Consent (2)

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

§46.116(a)(5)(i)

(Text in blue represents what’s new in the revised Common Rule. Bolding added for emphasis only.)
SACHRP Recommendation on Key Information, 10/17/18

“...the key information summary as an opportunity to orient, guide, and assist potential subjects in the decision making process”
**New Requirements for Informed Consent (3)**

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)

(Text in blue represents what’s new in the revised Common Rule. Bolding added for emphasis only.)

Not merely a list of isolated facts
Is this “sufficiently detailed information”?

• The purpose of this study is to determine whether receiving the chemotherapy 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.

• We are doing this study because we want to find out if this approach is better or worse than the usual approach for your [cancer, precancerous condition, early detection, prevention of cancer, diagnosis, other].
Focus:
If you were asked to participate in a study, **what information would you need and how should this information be presented to you** so that it would make the most sense for you to use it to make an informed decision about participating or not participating?
What information would you need to make an informed decision about participation and how should this information be presented?
What a patient said about what was going through in his mind when an interventional treatment study was being explained:

“I didn't pay a lot of attention. I was mostly thinking up questions I would need answered regarding my own care, the treatment plan being proposed, how I might be affected, etc. After all, informed consent requires I be as informed as possible in order to make the best judgement for myself.”
What might sufficiently detailed information about a treatment intervention look like? An example

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

X blocks the body’s inflammatory process…If it works, it could reduce the damage to the pancreas caused by the inflammation and lead to fewer serious medical problems. This could mean that patients are less likely to need treatment in the intensive care, and may benefit from a faster recovery and a shorter hospital stay.
## A Long List of Potential Side Effects About a Study Intervention

<table>
<thead>
<tr>
<th>Category</th>
<th>Side Effects</th>
</tr>
</thead>
</table>
| 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)  
• Cardiac tamponade  
• Damage to heart valves  
• Emergency heart surgery  
• Emergency vascular surgery  
• Low cardiac output state  
• Heart block  
• Hypotension |

Providing a detailed list of isolated facts ≠ Facilitating understanding
Strategies for Organizing Information and Facilitating Understanding (1)

Put facts into context, e.g.,

- Provide the context for a piece of information. List of facts is generally not conducive in providing context.
- Consider providing people with some background of why the piece of information might be relevant to them, in other words, explaining to them why they would care.
- Explain the implications of a piece of information, how the information might matter for decision-making, instead of just providing the facts or the definition.
The Importance of Providing Context in Clinical Trials Involving a Treatment Intervention

- Therapeutic misconception is not uncommon
- Medical information is complex and often requires special knowledge to make sense
- Decisions are complex and impactful because they affect one’s health – something that is uniquely important to most people
- Additional complexities related to the nature of research:
  - Primary goal of research is to collect data to answer questions
  - Complex concepts such as randomization, normally not encountered much in daily life (or certainly not in clinical care)
  - Uncertainty about efficacy and risks of interventions
Example of Putting Information into Context: Framing the information

Provide information under headings framed into questions a prospective participant might ask would help them make sense of the information. For example,

- Who is this research recruiting? Why are you being asked to participate?
- What’s currently being done about your medical condition?
- Why are we (investigators) doing this research? How do we think we can improve on current practices?
- How might it matter for participants? What might participants gain out of it? What might be potential problems (risks) that participants need to pay attention to?
Example of Putting Information into Context:  
**What does it mean to be in a randomized study?**

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

This describes *how* the assignment is made. It does not explain the implications of *what it means* to be randomized.

What are the implications of randomization?

- You cannot choose which group you are in. The researchers, your doctors, and your loved ones cannot choose which group you are in.
- You must be okay with being assigned to either of the study groups.
- If you have a strong preference for one of the groups, you might not want to participate in the study.
Strategies for Organizing Information and Facilitating Understanding (2)

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

• Add pictures and icons to highlight or draw attention
• Display information in tables
• Include a schematic diagram of the study
Example of Sectioning Using Colors & Icons

Who is this research study recruiting?
We are recruiting people like you who have been diagnosed with sudden onset inflammation of the pancreas, also called acute pancreatitis, to participate in a research study.

What’s the current treatment for acute pancreatitis?
There is no known treatment to block or reduce inflammation in the pancreas. Current treatment for acute pancreatitis is mainly supportive, to reduce symptoms. This includes providing IV fluids to rest the bowel, controlling pain, and monitoring the disease for the development of complications.

Why are we doing this research study?
We want to find out if a drug called Drug B can reduce the severity of pancreatic inflammation and related medical complications in patients just diagnosed with acute
### What are the two study groups & how do they compare?

| **If you receive Drug B**  
  **(50% chance)** | **If you receive the placebo**  
  **(50% chance)** |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>You will receive the standard treatment for acute pancreatitis AND you will receive a pill to take by mouth four times a day for up to a week. You will not know that this pill contains Drug B and that you are in the Drug B group.</td>
<td>You will receive the standard treatment for acute pancreatitis AND you will receive a pill to take by mouth four times a day for up to a week. You will not know that this pill contains Drug B and that you are in the placebo group.</td>
</tr>
<tr>
<td>Medically serious side effects from taking Drug B are rare. See page X of this form for more details.</td>
<td>A placebo does not contain any drug. It is an inactive compound that does not have any treatment effects or side effects.</td>
</tr>
<tr>
<td>You will have blood tests once a day while in the hospital to check for signs of inflammation.</td>
<td>You will have blood tests once a day while in the hospital to check for signs of inflammation.</td>
</tr>
<tr>
<td>We do not know if Drug B can help treat your disease. If it is effective, you may have less inflammation, less damage to your pancreas, fewer medical complications, and a shorter hospital stay.</td>
<td>You do not stand to receive any potential benefits (and will not experience any side effects) that might result from Drug B 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.</td>
</tr>
<tr>
<td>If Drug B is not effective in reducing the inflammation of the pancreas, you will only get the symptom relief from the standard treatment for acute pancreatitis.</td>
<td>If Drug B is not effective or harmful, 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.</td>
</tr>
<tr>
<td>There is a possibility that Drug B could make your condition worse.</td>
<td></td>
</tr>
</tbody>
</table>

Displaying Information Side by Side
A Study Schema Could Help Frame the Decision Points

Focusing on certain information only could cause unwanted misconception
How Might We Think About Key Information Section?

• Key information section should provide concise & focused discussion about why one might or might not want to participate
  ▪ Idea is that reading this section would give prospective subjects a meaningful sense of the study, enough for most people to determine whether they are inclined to participate or not.
  ▪ And for those who are so inclined after reading that section, it also provides a framework to help them better understand the more detailed information provided in the rest of the consent form.

• As part of the consent form: provide sufficient detail, and appropriately organize and present the information.
What a patient advisory panel* said

The first page of a consent document is critical “real estate” for communicating valuable information.

It would be opportunity lost if they are filled with information that patients generally could not care less about, such as:

• Headers with technical titles and information about funding agencies and investigators
• Generic introductions and descriptions about research participation

An example for conveying key information

Research to Study Biological Effects of Aspirin on Smokers

We do not expect participants in this study would receive any meaningful health benefits. By participating in this study, you will help us learn more about whether aspirin could be used to prevent lung cancer.

Why are we doing this research study?
Smokers have a higher risk of getting lung cancer. Some scientists suggest that aspirin might be able to help, but we need evidence to support this. In this study, we want to study how aspirin might affect certain cells and cell mechanisms that might indicate protections against cancerous changes for chronic smokers. This research would help us better understand if aspirin could be used to prevent smokers from developing lung cancer.

What do study volunteers have to do?
This study asks healthy smokers to take a pill once a day for 12 weeks. The study will assign volunteers randomly, like the flip of a coin, to one of two groups. One group of volunteers will get a pill that always contains aspirin. The other group will get a pill that contains aspirin only half of the time (the other half of the time, the pill will not contain any medicine). All the pills look the same. Volunteers and researchers will not know, and will not be able to choose which group volunteers will be in. Before and after the 12-week period, we will gently swab the inside of volunteers’ noses, and collect some urine from them to study certain mechanisms and changes in the cells.

What does participation in the study mean to you?
This is not a treatment study. This study is done to help us learn more about aspirin and its effects on certain cells and cell mechanisms. For the dosage and duration of aspirin that volunteers are getting, we do not expect any durable effects on the bodies to provide participants with any meaningful health benefits. Participating doesn’t mean that you will get lung cancer in the future. It also doesn’t mean that by participating, you will be protected.

While there is unlikely to be any health benefit, there may be risks and discomforts to you for participating in the study, but we don’t expect them to be serious. They include:

- Aspirin is a common over-the-counter medicine. The dose used in this research is [provide information about the dose of aspirin used in the research, how the doses compare in the two groups, what might be the commonest and the most serious side effects, and whether researchers expect any significant differences between the two groups]. Review the rest of this document for more details.
- The nasal swabs may cause minor discomfort including minor nose bleed that will not last.
- Urine tests will not include tests for illegal substances. We will protect your identity and the information associated with your participation in this research.

It will not cost you to participate. We will pay you $100 after each of the two study visits for the nasal swab and the urine collection.

Participation in this research is voluntary. You do not have to participate. While you are participating in this study, you should not also participate in another research 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
Human Research Volunteer Informational Videos

These short videos provide basic information about human research, including clinical trials, medical research, and other kinds of research. They help potential research volunteers understand how research works, what questions they should ask, and things to think about when deciding whether to participate in a study.

Videos on Clinical Research Basics

- Part 1: What is Medical Research?
- Part 2: Deciding to Participate in Clinical Trials
- Part 3: Questions to Ask Before Volunteering in Clinical Trials
- Explaining Randomization in Clinical Trials

Videos on Other Types of Human Research

- Research with Medical Records and Specimens from Medical Care
- Participating in Social and Behavioral Health Research

About Research Participation

What you need to know before you decide.
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
• Check out OHRP 2018 Exploratory Workshop Meeting new Challenges in Informed Consent in Clinical Research [September 7, 2018]
• Check out OHRP Luminaries Lecture Series Use of eConsent in Human Subjects Research [February 4, 2020]
Remember!

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.