# INFORMED CONSENT: IMPORTANT FOR TREATMENT DECISIONS AND ADVANCING RESEARCH

RARE TOOLKITS

Global Genes
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## Introduction

Prior to undergoing certain medical procedures or participating in a research study or patient registry, patients will go through a process of providing their informed consent. The process includes the signing of a consent form that spells out a number of issues surrounding a treatment the patient will be undergoing. It is an important process that recognizes the patient's fundamental right to understand treatments, options, their associated risks, and their right to take an active role in deciding whether to participate in research or pursue a particular treatment.

Informed consent is both a legal and ethical requirement. It is based on the concept that patients have the right to know their medical options, understand the potential consequences of those choices, and make informed decisions about their own healthcare.

The legal requirements for informed consent vary from state to state, and federal regulations provide minimum requirements for informed consent that providers and researchers must meet. In some instances, state laws require specific information be provided to patients as part of an informed consent process. These laws may also dictate the types of procedures that require informed consent from patients. In other cases, states provide general requirements and may call for the disclosure of "reasonable" information or call for "full and complete disclosure," according to the American Cancer Society.

## Introduction (cont'd)

### Understanding Complex Medical Issues

Fundamental to the process of informed consent is that patients understand what their medical provider is telling them about their condition, the treatment options, and the risks associated with these options. The ability of patients to understand the information their physician provides during the informed consent process will vary greatly. As many as nine out of 10 Americans have limited health literacy skills, according to the U.S. Department of Health and Human Services (HHS).

Health literacy is defined by HHS as "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions." Healthcare literacy can be affected by the patient's language skills, education, cognitive impairment, learning disabilities, hearing or vision impairment, as well as such things as stress and feelings of intimidation.

Informed consent is more than a document. It is a process. As part of this process, patients should be able to gain access to the information they need to make an informed decision about their own care. This includes being able to ask questions of their doctor, access to supplemental information that explains a particular medical condition or procedure, and adequate time to review the information and reach a decision. It is critical that patients feel as if they have the information they need to make a decisions about treatment and that they get answers to any questions or concerns they have prior to providing their consent to treatment.

Even when patients provide written consent for a procedure, researchers have found that they often do not understand the information in the consent form, according to the National Quality Forum, a Washington, D.C.-based nonprofit working to improve healthcare. After signing a consent form, the organization reports that as many as 45 percent of patients can't identify a major risk of surgery and many cannot answer basic questions about the procedures they have agreed to receive. In fact, 60 to 69 percent did not read or understand the information in the informed consent form even though they signed it. This suggests that despite ongoing efforts to improve the informed consent process, it remains flawed, and that both providers and patients need to do a better job of ensuring a comprehensive understanding of all elements of a procedure.

# SECTION 1: PATIENTS' RESPONSIBILITY TO THEMSELVES

Patients may feel an impulse to sign a consent form and move on, but the informed consent process is an opportunity to play an active role in the direction of the care for their disease. They should take this process seriously and insist on understanding the information being presented to them.

The American Cancer Society lists a number of questions that patients may want to ask during the informed consent process. The list is not intended to be complete, but serves as a starting point for questions patients should consider. They include:

- What is my diagnosis (the medical name for the illness I have) and what does it mean?
- How serious is my diagnosis?
- What treatments are recommended?
- Are there other treatment options? What are they?
- What benefits can I expect from the recommended treatments and the other options?
- What are the risks or complications of the recommended treatment and the other treatment options?
- Are there problems or side effects that may be caused by the treatments?
- What will be done to help prevent or relieve these problems or side effects?
- What are the side effects of the treatment – immediate, temporary, and long-lasting?
- How will having treatment affect my normal functions and everyday activities?
- How would not having treatment affect my normal functions and everyday activities?
- How long will treatment last?
- How long will it be before I can go back to my normal activities?
- How much does the treatment cost?
- Will my insurance cover it? How much will I have to pay?

Patients should consider bringing a list of written questions to appointments with doctors and take notes during the conversation. They may also consider recording their meetings and bringing a friend or family member along to help take notes and ask questions. As new questions arise, patients should not hesitate to ask. If the doctor says something they do not understand or uses medical terminology with which they are not familiar, patients should ask for an explanation. It will not be possible for a patient to provide informed consent if they do not understand what they are consenting to or why.

### Four Steps to Informed Consent

Joanna Smith, CEO of Healthcare Liaison, which advocates for individual patients with complex medical conditions, says she walks her clients through a four-step process to see if they understand the issues before them to ensure they are providing their informed consent. This includes having them in their own words (without medical jargon) explain their medical problem; describe the possible treatment choices and their risks and benefits; the treatment choice on the table and why the doctor decided to pursue that (as well as the other choices and why they were not pursued); and what happens if the patient does nothing.

> "If my client can tell me those four steps, I know they understand the body of knowledge they need to know in order to make an informed decision," says Joanna. "Without those four steps, they are shooting blind. They may or may not really understand what is happening to them."

# SECTION 2:
# THE INFORMED CONSENT FORM

The informed consent form will vary from institution to institution and be tailored to a specific treatment at issue in the form. Nevertheless, many elements in an informed consent form will be typically found in other informed consent forms. In its **"A Practical Guide to Informed Consent,"** (http://www.templehealth.org/ICTOOLKIT/html/ictoolkitpage8.html) Temple University spells out the basic elements based on American Medical Association guidelines. These include:

- The diagnosis, if known;
- The nature and purpose of a proposed treatment or procedure;
- The risks and benefits of proposed treatment or procedures;
- Alternatives (regardless of costs or extent covered by insurance);
- The risks and benefits of alternatives; and
- The risks and benefits of not receiving treatments or undergoing procedures.

Each institution determines for which procedures and treatments informed consent is required. But in addition to these general elements, informed consent forms should make clear that the patient's decision is voluntary and that they have the right to delay or choose not to have a procedure.

For patients deemed unable to make a decision to consent either because of age or condition, a legally appropriate representative will need to act in their place and sign the consent form.

# SECTION 3: INFORMED CONSENT FOR RESEARCH PARTICIPANTS

For a variety of reasons, patients may consider participating in a research study. This may be because of their interest in furthering an understanding of a disease that they have, or to get access to get access. Though the process of informed consent for research participants will be similar to what patients go through for conventional treatments, it is generally more complicated because of additional issues that need to be weighed by the potential participant.

During the informed consent process for a research study, there will be a discussion of a range of issues, such as the goals of the study, costs, risks, and compensation. Under federal regulations, according to the U.S Department of Health and Human Services, researchers are required to provide the following information to potential research participants:

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
- A description of any reasonably foreseeable risks or discomforts to the subject;
- A description of any benefits to the subject or to others which may reasonably be expected from the research;
- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;
- For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
- An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Each institution conducting clinical research will have that work overseen by an Institutional Review Board (IRB) to see that it complies with ethical requirements. The IRB will determine what information is included in the informed consent form for a particular study and what else should be included.

Among the other information that should be considered during the informed consent process is whether there are any potential conflicts of interest that the researchers may have. This includes whether the researchers have equity in the company that owns a drug being tested, holds patent rights, is being paid by the study sponsor, or has other financial interest that could affect their interaction with participants with the study.

# SECTION 3: INFORMED CONSENT FOR RESEARCH PARTICIPANTS

### Registries and Privacy

**Patient registries**, online databases used for research purposes with information about patients with a specific disease, may provide fewer risks than most clinical studies, but may be a cause for concern for patients because of privacy issues.

These databases gather such things as medical information about individual patients including family history and ongoing medical events. Patients are asked to update the information regularly. Though the information is detailed, the registries are de-identified, so the patient's name, address, and other information that may identify the patient is coded and unavailable to researchers.

Nevertheless, because rare diseases affect small populations, it is possible that a patient may be identifiable through the medical history. It is also possible that the database could be breached. If a researcher is conducting a study that a patient in the registry may be an appropriate participant, the registry will reach out to the patient on behalf of the researcher. For more information about registries, see the upcoming Global Genes Toolkit "Rare Disease Registries: Advancing Disease Understanding, Treatments and Cures."

### Children and Consent

Because rare diseases often involve children who are too young to legally provide their own informed consent, their parent or legal guardian must provide it. Nevertheless, an IRB may determine that children who are able to do so, should be involved in the informed consent process and provide their approval in addition to the consent from the parent or legal guardian. Though most states consider 18 as the age of adulthood, it does vary. There are also circumstances that may permit someone younger than the legal age of adulthood to provide their own consent to medical procedures.

Even in cases where a child is too young to provide consent, an IRB may deem it necessary for the child to provide informed consent if a child participating in a study reaches the age of adulthood while it is ongoing. Parental permission and child assent are not equivalent to legally effective informed consent for the now-adult subject, according to HHS.

One parent of a child with a rare disease noted that the issue of informed consent for a clinical trial can be complicated in cases of divorce, which is prevalent among parents of children with special needs. In such cases, unless clear legal authority is given to one parent, researchers may feel it is necessary to get informed consent from both parents, particularly if it is for an experimental treatment that carries significant risks. These parents may find that they are in disagreement on the correct path to pursue and must find a way to reach a decision that is in the best interest of the child.

# SECTION 4:
# INFORMED CONSENT IN THE REAL WORLD

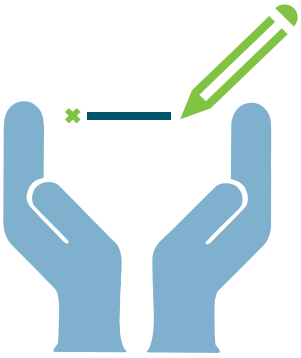
Patients' experience of informed consent can vary widely. Sometimes, it can fall far short of what the process is supposed to be. Susan Krug has the ultra rare disease hypophosphatasia, also known as soft bones. The genetic disease results in an enzyme deficiency that prevents bones from hardening as they should, which leads to deformities, fractures, the loss of teeth, and other health problems. Susan recently went through the informed consent process as part of a clinical trial in which she is participating. She found the forms were more legalistic than medical in tone, and that her doctor was unable to provide clear answers to her questions.

Susan is currently participating in a late-stage clinical trial. She says she was presented with informed consent documents when she showed up for the first day of her clinical trial, but was told that she could not take them home to review. She said she was essentially presented with the choice of signing the documents on the spot and getting access to the experimental drug in the trial, or not participating. "I felt a little pressure to sign quickly on the trial form," she says.
She doesn't think the informed consent process works well. She said four mothers of children in the trial told her they don't know whether they will have access to the drug once it is FDA approved. They don't know if they will be compensated for their travel costs. And they don't know what the potential side effects from the drug are. Even though they wonder about these things, they don't know who they can to talk for answers.

"'We don't know what we were signing. We just signed it,'" Susan says they told her. "For most of them, it was life or death. Either get your kid on this drug or they are going to have respiratory failure."

### An Agreement, Not a Contract

The National Institutes of Health notes that after learning about the risks, benefits, rights, and responsibilities involved in a clinical trial, a patient agrees to participate and signs an informed consent document, it does not signify a legal obligation on the part of the patient. As the document should make clear, patients have the right to leave a trial at any time for any reason and without penalty.



# SECTION 5: SHAPING INFORMED CONSENT

By the time a potential research participant is presented with an informed consent form, it has gone through an extensive legal and institutional review board process. It is not the starting point for a negotiation with researchers over the study. They will not be able to alter the conditions spelled out in the document. The individual's only choice is to sign the consent form and participate in the study, or not.

This does, however, represent an important opportunity for rare disease advocacy groups to get involved early in studies, before the consent forms are created, to ensure that data from a study is leveraged as best as possible. This includes questions about what information they will have access to from a given study, whether data will be shared with patients, available to other researchers, and how widely that data will be shared.

Patient advocacy groups working with researchers as sponsors or helping with enrollment of patients have an opportunity to shape how data is used and other ways to enhance the benefits of a study to its participants. Though there is an ongoing dialogue between researchers and patient groups over such issues, it is becoming more common for patient groups to seek a more active role in helping design clinical trials. These groups should make clear from the start that they want to have an active role in shaping the consent form if these are issues of concern.

John Wilbanks, chief commons officer of Sage BioNetworks, a Seattle-based nonprofit organization that promotes open science and patient engagement in the research process, says that patient groups may want to think about a set of issues to consider regarding research studies and says if they hope to play an active role in shaping these issues and the consent form, they must play an active role early in the process of designing a study. Among the questions to consider are:

- Will patients get a copy of their own data and if so, in what form and what timeframe?
- Will researchers be required to share their data with other researchers?
- Will the patient organization have access to the study data and under what terms?
- What happens to the insights that are created from the study?
- If drugs are devices created as a result of the study, will patients get anything in return, such as discounts on the drug or device?

Though patient advocacy groups can expect it to be difficult to get researchers to agree to some of these issues, John Wilbanks says they do have leverage because of the important role they can play in recruiting patients to participate in studies and keeping them committed to them. Raising these issues after the informed consent form is created will be too late.

> "Recruitment is unbelievably hard. It's really expensive and trying to engage patients enough so they stay in the study is really hard," says John. "If you can access a source of patients through an organization that has permission—social permission, cultural permission—to contact those people regularly to say, 'Hey, you should enroll in this,' or 'Have you done your tasks this week for the study.' That's going to work faster than almost any acquirable resource can."

# SUGGESTED RESOURCES

- One of the challenges patients may face during the informed consent process is understanding the language around clinical trials. The **National Institutes of Health's Senior Health** page provides a glossary of key terminology relating to clinical trials. http://nihseniorhealth.gov/participatinginclinicaltrials/termstoknow/01.html
- CenterWatch is an information service for research professional and patients about clinical trials. A PDF of its pamphlet **"Understanding the Informed Consent Process"** can be downloaded from its website http://www.centerwatch.com/pdfs/informed-consent-brochure.pdf
- The **U.S. Department of Health and Human Services** offers answers to frequently asked questions about informed consent. This can be found at http://www.hhs.gov/ohrp/policy/consentfaqsmar2011.pdf
- The federal regulations regarding the basic requirements of informed consent are spelled out in the U.S. Department of Health and Human Services regulations **Title 45 Code of Federal Regulations, Section 46.116** http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.116
- Organizations seeking to create informed consent forms and improve the informed consent process can consult Temple Health's **"A Practical Guide to Informed Consent"** http://www.templehealth.org/ICTOOLKIT/html/ictoolkitpage1.html

**Global Genes Would Like to Thank All of This Toolkit's Contributors and Participants**

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