

# INFORMED CONSENT: AN IMPORTANT OBLIGATION INVOLVING HIDDEN ISSUES

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**Abstract:** *This article provides an overview of hidden issues in informed consent: the application of quality ethical standards to protect human research subjects, the lack of understanding of information in the informed consent form, and reoccurring legal aspects of informed consent. Clinical research professionals are expected to protect human research subjects by applying quality ethical standards. Ethics is squarely based on trust in the research process and confidence in health care providers. Some of the problematic issues in understanding informed consent include low literacy. Failure to follow ethical principles in the informed consent process can result in serious legal action through tort law (civil wrongdoing) and even criminal law (the lack of informed consent constitutes assault and battery).*

## Introduction

The application of quality ethical standards to protect human research subjects, the lack of understanding of information in the informed consent form, and legal aspects of informed consent are all issues in clinical research today. The greatest obligation in research is the protection of human research subjects. Adhering to ethical standards is the first step in meeting this obligation. This is an obligation that must be shared not only by the clinical investigator, but by the pharmaceutical sponsor as well.

In designing a consent form, the clinical research professional must make every attempt to make it as comprehensive and transparent to the human research participant as possible. Attempting to satisfy the various legal

and quality standards of each of the principle players, the institution's legal counsel reviews the informed consent form adding poly-syllabic words better defining boundaries of liability. The sponsor next scrutinizes the informed consent document addressing issues of GCP compliance and other quality standards of performance.

Over the past several years, another player has entered the clinical trials landscape: the lawyer. The legal community is now helping to referee the process of human research subject protection through tort law. Tort law is a civil wrongdoing that, in many cases, has a direct criminal implication: assault and battery. If clinical research professionals do not properly consent someone and something happens, serious legal

problems can arise. Table 1 lists two useful Web sites related to the legal aspects of informed consent. These sites contain comprehensive information on bioethics and clinical trial litigation as well as key regulatory documents (e.g., the Food and Drug Administration, the National Institutes of Health, the Office for Human Research Protection, and the International Conference on Harmonisation).

### TABLE 1 Useful Web sites on Legal Aspects of Informed Consent

- Alan Milstein's Web site: [sskrplaw.com](http://sskrplaw.com)
- [Regsource.doc](#)

## Ethical Standards

In September 2000, Donna Shalal, then Secretary of the Department of Health and Human Services, published an article in the *New England Journal of Medicine* about protecting research subjects. She said: "The vast majority of government supported (and regulated product development) studies adhere to strict protocols and the highest ethical standards. But even one lapse is one too many. The American people expect that clinical researchers will never compromise or neglect the safety of human subjects." The hidden message in this quote is that ethics is squarely based on trust in the research process and confidence in healthcare providers. Most people who read the newspaper read the headline, the byline, and the first paragraph, and then come to a quick conclusion. This tendency by people often has the effect of severely tarnishing the reputation of research professionals and reputation is vitally important.

Finding study participants is the biggest issue in clinical trials today. Eighty-five percent of clinical trials fail to meet their enrollment expectations. In addition, specific minority groups are not adequately represented. Clinical research professionals are adding to that problem. These individuals should be focusing attention on such things as protecting research subjects. Confidence, privacy, respect, and dignity are all crucial to engendering confidence in the clinical research process. Researchers sometimes get lost in the science and lose track of their constituency - patients. A perfect example of that is what happened in Philadelphia in 1999 when a young man lost his life because of his exuberance to do something to help other folks, and the person conducting the trial lost track of the true objective.

Privacy implies controlling the access by other individuals to data and information. Most academic medical centers become nervous and anxious when the Health Insurance Portability and Accountability Act is mentioned. This act (HIPAA) is very complex and difficult to understand.

One of the main obligations of clinical researchers is to understand what ethical standards are. An article in *JAMA* in 2000 entitled "What Makes Clinical Research Ethical?" outlined seven ethical standards:

1. "The risks of the research should be minimized and benefits to the patient enhanced (through careful patient selection and quality monitoring and surveillance)." In academic medical centers, drug companies and contract research organizations monitor their studies, but this accounts for only a portion of research. For example, at Temple University about one third of all research conducted is monitored by drug companies and contract research organizations. National Institutes of Health studies and investigator-sponsored Investigational New Drug studies are not monitored. Most institutions, including Temple University, are starting to develop a research quality improvement office to audit studies.
2. "The research must be reviewed, approved, amended or terminated (the institutional review board [IRB])." The biggest issue for Temple University's IRB is the consent form. Simplification is not the issue, making the consent form friendly to the eye is. Ways to do this include using a tabloid format, diagrams, and pictures. Putting a quiz at the end, which Temple University calls discussion points, stimulates a conversation about the informed consent form (e.g., How often do you have to come back? Who do you have to call?). Informed consent is not merely a form, it is an everlasting process from the time the person says s/he will think about the trial until long after the study is over.
3. "The research subject should be adequately informed (through the use of a consent form that is understood to ensure the process of voluntary participation)." To really establish a firm foothold on autonomy, potential subjects must understand and comprehend the informed consent form, which leads to their voluntary participation in the study. When asking patients to do something that puts them at risk, they must clearly be in a position to both understand the procedures and comprehend the nuances of the study. People who participate in clinical trials are vulnerable due to the innate purpose of a clinical trial - to profile the pharmacology and indication of a new drug. Research participants agree to enroll based upon a voluntary decision and clinical research professionals must ensure that subjects are adequately protected.
4. "Respect for persons (The Belmont Report)." The Belmont Report outlines three basic principles: respect for persons, beneficence, and justice. Beneficence says 'do no harm', strongly implied in the Hippocratic Oath. If a study is not appropriately statistically designed, the incidence of harm greatly increases.
5. "The value of the research should enhance health and knowledge (not just constitute a commercial venture)."

6. "The research should be scientifically rigorous to ensure quality and validity (which includes monitoring and strict compliance to Good Clinical Practice)." Good clinical practice standards should be adhered to; they are an accepted way of thinking, a way of behaving.
7. "The selection of research subjects should be fair (Department of Health and Human Services, Office of Inspector General report, June 2000)."

**Subject Understanding of Informed Consent**

A 1993 survey of more than 90 million Americans found that 48% of adults had low literacy skills (Table 2). These people are functionally illiterate; they often lack the necessary life-skills to adequately function as a member of society and likewise lack an understanding of contemporary health care services. Approximately 33% of the people who apply for a job and take a basic arithmetic and reading test lack the skills to successfully pass these employment tests. How then can we expect these people to read and understand an informed consent?

Clinical research professionals should realistically sit with the potential

<p><b>TABLE 2</b> <b>Subject Understanding of Informed Consent</b></p> <ul style="list-style-type: none"> <li>• 48% of American adults have low literacy skills               <ul style="list-style-type: none"> <li>○ 67% never tell their spouse</li> <li>○ 53% never tell their children</li> <li>○ 19% never tell anybody</li> </ul> </li> <li>• About 33% of job applicants lack math and reading test skills</li> </ul>
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participant and thoroughly explain the consent form using words that are readily understood and comprehended but, due to time constraints placed upon the health care providers, they only have a fraction of the time necessary to adequately obtain truly informed consent. Clinical researchers (including the sponsoring pharmaceutical company) should ideally view these people not as patients or subjects, but as vulnerable research participants.

Among patients with low literacy skills, 67% never tell their spouse, 53% never tell their children, and 19% never tell anybody. As a result, it is very difficult to know what a patient brings to the table in terms of his/her ability to understand.

Clinical research professionals must always remember the purpose

<p><b>TABLE 3</b> <b>Standards for Determining Capacity</b></p> <ol style="list-style-type: none"> <li>1. Understand information relative to the decision that must be made</li> <li>2. Communicate with caregivers about the decision</li> <li>3. Cognitive and affective capability</li> <li>4. Resolution</li> </ol>
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of informed consent, that is - to impart information. According to the Code of Federal Regulations (which is legally binding) "The information that is given to the subject or his/her representative shall be in language understandable . . ." (21 CFR 50.20). The ethical and legal conduct of research requires informed consent whenever risk is to be borne by a human research

participant. Informed consent should be sufficiently understandable for the research participant to determine: the potential risks and benefits, his/her obligations, the health care provider's obligations, and the voluntary nature of the study. This total understanding results in the subject being part of the decision-making process.

There are seven ethical requirements for a valid informed consent: capacity, disclosure, understanding, recommendation, decision, voluntariness (autonomy), and authorization. Capacity is the ability to understand, listen, and relate what is being said to past experiences. Disclosure means not using technical words that the patient does not understand. Recommendation does not have a place in informed consent when the healthcare provider is also the researcher. Decision is the resolve to make the determination to participate in the study. Voluntariness strikes at the heart of autonomy underscoring self-determination. Authorization is the subject's consent. Legal Aspects of Informed Consent

Failure to follow these ethical requirements and principles can result in serious legal action, as affirmed by tort law. Based on English common law, the legal opinions in tort law have gradually become part of the legislative process. Tort law is now having a greater impact on the doctor-patient relationship than any other branch of law and has helped to shape bioethics, especially in promoting patient autonomy. This is the law that gives ethics teeth. These teeth sink deeply and can potentially pull clinical research professionals apart for lack of compliance, thus tarnishing reputations. Tort law concerns civil wrongs and many civil wrongs are violations of criminal law. The lack of informed consent, using the reasonable person standard focusing on the information a reasonable person needs to know about their participation in a clinical

trial, actually constitutes, in many instances, assault and battery. There is a pathway toward autonomy that addresses the issue of tort law: capacity. Capacity is a person's functional ability as a decision maker. Table 3 describes standards for determining capacity.

Ensuring understanding of the information on a consent form, relative to the decision that must be made, includes adequate presentation of information, an awareness of the potential participant's attention span, an insight into the issues/problems and therapies presented, and an ability to remember the information in order to make a decision (See *Salgo v. Leland Stanford, Jr. University Board of Trustees – 1975*). To ensure adequate consenting of the research participant and foster self-determination, health care providers obtaining consent should begin to rethink their presentation style and the impact the research has on the patient.

An adequate understanding of the attention span of patients is critical to ensure comprehension. For example, a United States Navy study of submariners, who are considered to be among the Navy's most intelligent personnel, found them to have an attention span of approximately 18 minutes, complete with peaks and valleys. It should be recognized that clinical research professionals are speaking to patients who could be culturally, educationally, or financially disadvantaged in 'physician' language. Therefore, patients often fail to get the message.

Additionally, it is important when communicating with caregivers about a potential participant's decision to enter a clinical trial that the following questions are satisfactorily answered:

- Is the potential subject responsive?
- Can the person discuss his/her decision?

- Does the person have any disorder that would interfere with the capacity for making a decision?

Cognitive and affective capability means answering these questions:

- Can the person relate to the situation based on his/her life experiences?
- Can the person understand the importance of the decision?
- Can the person effectively understand the risk/benefit relationship?
- Does the person display any clinical disease processes associated with altered mental status that would indicate incapacity?

Resolution includes:

- Selecting of an option based on information
- Reaching a conclusion by setting aside uncertainties and participating in decision-making
- Ensuring that the person understands the concept of autonomy.

Obtaining informed consent is obviously a complex process, which clinical research professionals should take significant measures to do correctly, least lawyers, who know relatively little about clinical research, enter the research landscape and start telling the researchers how to do their jobs. Clinical research professionals know what absolutely needs to be done and, to ensure their survival, they must start doing it.

## Self Study Quiz - Answer Key

(See Pg. 10)

### Answers:

1. c. prisoners (Section 46.301 a)
2. a. true (Section 46.303 c)
3. a. minimal risk (Section 46.303 d)
4. c. a and b (Section 46.304 a and b)
5. b. Assent (Section 46.402 b)
6. a. true (Section 46.402 d)
7. b. false (Section 46.409 b)
8. a. guardian (Section 46.402 e)
9. a. the risks are not commensurate to those of non-prisoner volunteers (Section 46.305 [3])
10. c. Children (Section 46.402 a)