

Cultural Issues in Informed Consent

The idea behind informed consent in clinical research is a simple one. Ensure ethical clinical trials by fully informing patients of potential risks and benefits, and establishing whether the patient consents to treatment. Yet, it is clear in observing clinical trials from around the world, that supporting informed consent requires a strong commitment to patients as well as a deep understanding of the challenges involved in pursuing true and meaningful informed consent from patients.

Genesis of Informed Consent

Though the original wording of the Hippocratic Oath suggests that doctors are obligated to shield their patients from information about their care and prognosis, events in the early 20th century gave rise to the ethical standard known as informed consent. Human experimentation during World War II's Nazi era galvanized the world and appropriately called into question long-standing provider-centric "doctor-knows-best" approaches and shifted thinking to a more patient-centric approach. With the world watching, new principles were developed that created protections and rights for patients subject to medical treatment. These principles were incorporated into the Nuremburg Code and subsequently the Declaration of Helsinki in 1964, which has been updated and amended six times since its creation.¹

"In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The physician should then obtain the subject's freely-given informed consent, preferably in writing. "

-World Medical Association Declaration of Helsinki

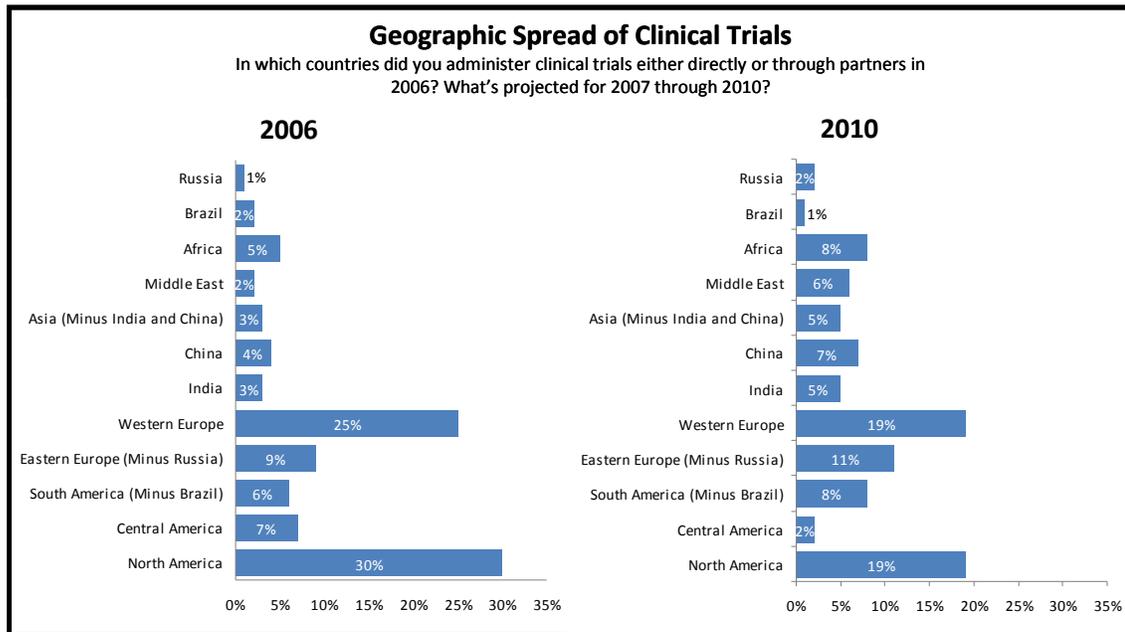
Current guiding principles are embodied in various international guidelines and standards including Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects and the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Good Care Practice (GCP).

¹ <http://www.wma.net/e/ethicsunit/helsinki.htm>

Global Trials, Global Cultures

As clinical trials continue to become more global, it is imperative for study sponsors to understand cultural differences that may impact care.

Clinical Trials Becoming More Global²



While regulations and ethical standards exist in Western countries, and internationally as embedded in the Declaration of Helsinki, the local practice of medicine is determined as much by standards as it is by customs. For example, there is a stigma against drawing blood in Burkina Faso. If a blood sample is part of the clinical trial, it could be difficult to obtain informed consent from patients. The Declaration of Helsinki recommends physicians obtain consent in writing, but the very concept of signing an informed consent document can be culturally troublesome:

“Although the signing of informed consent documents is frequently mandated by U.S. regulations, many individuals in Middle Eastern countries are opposed to signing such documents, because they strongly believe that giving their verbal agreement should be sufficient.”³

² Kumar, R., “Evolving Clinical Trials,” *Pharm Exec*, October 1, 2008.

³ Silverman, H. “Enhancing research ethics capacity: implications for protection of research subjects, avoiding exploitation and achieving global health,” *Middle East Fertility Society Journal*, Vol 10, No 2 2005.

Obtaining Informed Consent: Examples from across the world

Pfizer is a multinational research and development organization with facilities and experts around the world. Interviews with professionals in three different international geographies highlighted some of the challenges in obtaining informed consent. Below are three illustrative examples.

India

In India, the physician is held in very high esteem, and patients typically proceed with treatment regimens as recommended by their practitioner. This creates two distinct types of issues, one from the point of view of the patient and one from the perspective of the physician. A health care professional who practiced in India for more than a decade explained, "in many years of interacting with patients, I never once had someone ask me, 'what are the side effects?' or other such questions about their treatment." Generally, there is an acceptance of disease and its course which may prevent patients from pursuing treatment, or participating in clinical research.

Additionally, it creates a sort of quandary for the physician between choosing to guide the patient through the uncertainties new treatments can bring, and maintaining their position as a clinical expert. Because the patient often considers the physician in such high regard, explaining the different options available, or the possible negative effects of a treatment could make it appear as though the physician is not knowledgeable.

Japan

Similar to physicians in India, health practitioners in Japan are held in high-esteem by patients and patients are less likely to ask questions about their treatment or treatment options than might be typical in the U.S. Physicians are employed by health institutions that often combine a hospital, a clinic, medical school and research center. Culturally, there is a social obligation from the physician to the institution. As such, if anything happens to a patient being treated that is outside the expectations of the course of their disease or condition, the physician is held personally responsible and would be expected to resign from his or her post.

The effect of this high level of trust between a patient and physician can mean explaining to a patient the potential benefits and hazards of research, as recommended by the Declaration of Helsinki might be informative, but perhaps not obtaining "consent." Part of the spirit of informed consent is the weighing of pros and cons by the patient, but if they don't believe there could be any cons, are they giving adequate consent?

Mali

As in many countries in Africa, the informed consent process in Mali is multi-layered. The first step for any proposed research effort is to approach the elders of the community in which the study is being considered. If the sponsor is from outside the community, the visit to the community elders would be facilitated by a local host. The second step is for the elders of the tribe or village to assess whether the proposed research effort would be of benefit to the community. If the assessment is positive, the leaders discuss the program with the people living in the village and ask for their assent to participate.

After these steps have been taken, perhaps over a series of weeks or months, the local study investigator would then begin to ask patients to participate in the study and engage them in the informed consent process that takes place between a physician and patient.

Pfizer's Commitment to Patients and Medical Advances

As a leading sponsor of international clinical trials, Pfizer is dedicated to supporting the safeguards and protections that exist for the patients who consider participating in clinical trials and to the greatest extent possible, working within the cultural expectations of the locales where we operate. Two overarching themes serve as guides:

1. The first time in any country, or new region, the Quality Assurance group of Pfizer does an assessment of both medical standards and cultural expectations before any protocol is written or informed consent documents are prepared.
2. Pfizer does not conduct clinical trials for "Western diseases" like heart disease or high cholesterol in developing nations, if the disease is not prevalent locally. Trials mirror the disease burden of the hosting country, for example, HIV/AIDs trials in Africa, to ensure that the research findings translate into a benefit for the local population.

Pfizer's work complies with international standards, including ICH-GCP and CIOMS guidelines. Our organization strives to ensure each participant fully understands the potential risks and benefits of treatment, receives accessible information, and is treated with the care and respect that international guidelines mandate and that our organizational culture dictates.

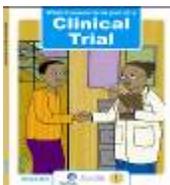
Pfizer also works to build the ethics knowledge base of the complete range of healthcare stakeholders from governments, to physicians to patients with innovative programs around the world.

Pfizer's Ethics Programs Related to Informed Consent



Afro-Guide

This project aims to provide "points to consider" in conducting clinical research in African countries to incorporate different cultural and religious sensitivities of African society with internationally recognized ethics principles in clinical trials. Pfizer will provide initial seed money for Afro-Guide and work with committee members to set up formal committee and move forward with a three-year plan to produce an internationally recognized document.



See Speaking Book case study for more details.

Clinical Trial Speaking Book Working with the World Medical Association, the Steve Biko Centre of Bioethics, the South African Medical Association and Books of Hope, Pfizer created a "speaking book" for illiterate people to explain the fundamentals related to participating in a clinical trial.

The speaking book is a book that uses cartoons in addition to text, which is spoken when the corresponding button is pushed for that page. It helps to teach or inform illiterate patients and their families to better understand issues (in this case clinical trial rights, roles and responsibilities). 4,000 books will be distributed in South Africa and three other Sub-Saharan countries before the end of 2008.



Debating Matters UK and India

This is a debating competition for high school students in the United Kingdom which will be extended to India in 2009. Pfizer has proposed topics as well as served as judges for the 2007 and 2008 competitions. This venue provides exposure to a wide range of young people and encourages thoughtful discussion of the ethical issues in clinical research.

As these examples show, effective implementation of informed consent takes commitment because there are several practical challenges that persist even in the face of good-faith efforts and expert understanding. It is important to grasp these challenges so the clinical research community can continue to work to make informed consent meaningful, practicable and accessible to patients, and provide them with the protection that true informed consent conveys.

Discussion Questions

1. How should discrepancies between local cultural expectations be reconciled with international standards for informed consent?
2. Would it be possible to have a single worldwide standard for obtaining informed consent in clinical research studies? Why or why not?
3. What steps should be taken to assure potential research subjects are adequately informed taking into account cultural expectations and international standards?
4. In some cultures, women aren't allowed to make decisions about participating in a study, without consulting their husband. Is it ethical for a Western sponsor to enroll them in a study based on the consent of their husband, knowing that their rights are diminished in the local culture? Should the sponsor exclude women from such cultures, where women's rights are poorly recognized? Would it be unethical to exclude them?
5. Should patients who are illiterate be asked to sign a written informed consent, assuming the information is discussed with them verbally? If not, how should an investigator document the patient's consent?