

1. A team of researchers proposes to conduct a study in which participants will be randomized to one of two versions of an informed consent form in order to compare their usefulness. Many argue that consent forms for research studies are often seriously flawed. They are growing in length and complexity, becoming ever more intimidating, and perhaps inhibiting rather than enhancing participants' understanding. Participants may not even read them, much less understand them.

The study is part of a larger project aimed at developing a new treatment for avian influenza. The goal of the protocol is to find ways of generating and collecting viral antibodies from the blood of healthy subjects after injecting them with an avian flu vaccine. The vaccine—already approved by the Food and Drug Administration at a lower dose—has been studied in about 450 people. The approximately 150 people participating in the new study will receive the highest dose used in previous studies, which about fifty people have received without serious side effects. They will be randomized to have the vaccine injected into either their buttocks or an arm to see which location is better for producing viral antibodies. Blood will later be drawn on three or more occasions so that researchers can extract antibodies.

The primary risks of participating are side effects from the vaccine. Most subjects will have mild pain and tenderness at the injection site. Based on what happened in earlier studies, some subjects will develop severe pain and tenderness and flu-like symptoms. More serious risks, including allergic reactions, are possible, though none occurred in previous studies. Participants will also be exposed to the risks and discomforts of having their blood drawn. The initial consent form developed by the avian flu vaccine researchers is ten pages of single-spaced text. In the substudy comparing consent forms, participants would be randomized to receive either the regular consent form or a concise form that is about three and a half pages but covers all of the categories of information required by applicable federal regulations.

The investigators propose that the usual informed consent requirements be waived for the substudy. Prospective subjects will be told that a consent substudy is taking place, but they will not be presented with an additional form or have a separate consent interview. They will simply be asked if they are willing to be randomized to one of two consent documents. If they agree, they will receive one of the forms, but will not be told which one. If they decline, they will be sent the longer form.

Should the institutional review board agree and let full informed consent be waived?

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2. Mr. P is a 62-year-old man with an extensive history of heart disease and severe heart failure. He underwent coronary bypass surgery ten years ago and has had two heart attacks in the past five years. His quality of life has been deteriorating due to his increasing inability to independently perform many daily activities. He currently lives with his wife and daughter.

Eight months ago, as a result of severely debilitating stage IV heart failure, doctors implanted a Left Ventricular Assist Device into Mr. P's chest as so-called destination therapy. The LVAD helps the heart to maximize the volume of blood it pumps into the body. However, many of the device's controls, as well as its power source (a rechargeable

battery), are outside the patient and connected to the pump by tubes and wires that pass through the patient's abdominal wall. Originally used only as a "bridge" to support hospital-bound patients for whom a heart transplant was both urgent and imminent, LVADs are now also used as destination therapy for patients who are ineligible for a transplant. In such cases, patients are sent home with LVADs, which are considered the final stage of treatment for their heart failure.

Mr. P's doctors had told him that the LVAD would improve his capacity for self-care and allow him to lead a more active life. However, his health after its implantation was compromised by chronic wound infections, sepsis, and renal failure. He spent the first five months following the implantation in the hospital; during much of this time, he was in the intensive care unit. He eventually returned to his home but has continued to grow weaker. He now sleeps a great deal, eats poorly, walks little, and needs help to go to the bathroom. He also complains of significant pain.

After three months at home, Mr. P has asked to be readmitted to the hospital so that doctors can disable his LVAD. He understands that he will likely die within hours after the device is turned off, but he no longer wishes to live in his current state. In particular, he cites the indignity of being helped to the toilet and his continuing debilitating fatigue as reasons for his request.

Should Mr. P's physicians accede to his request and disable his LVAD?

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3. The May 1, 2007, Wall Street Journal reported the case of Penelope London, a four-year-old suffering from a rare cancer. Penelope was diagnosed when she was just sixteen months old as having an aggressive form of neuroblastoma. Doctors gave her only a 25 percent chance of being cured. Three years later, she has undergone not just multiple bouts of the standard cancer treatments—chemotherapy, radiation, bone-marrow transplants, and surgery—but also experimental therapies that have been in progressively earlier stages of human testing. These therapies have yielded varying results for her, but have managed to keep her alive.

In November 2006, Penelope's cancer had recurred and no treatment was working. That was when her father heard of Neotropix Inc., a company in Malvern, Pennsylvania, that is developing an experimental cancer drug. The drug contains a live virus that normally strikes pigs. Experiments show that, when introduced into the human body, it may attack certain kinds of cancer cells. However, the drug is still in the earliest phase of safety testing and has only been given to six humans. The first patient died—from the cancer, not the drug—but the Federal Drug Administration put the trial on hold to definitively determine this. Neotropix expects the resumed first-stage testing to last another eighteen months.

Yet Penelope is running out of time. The Wall Street Journal described her as dying and in great discomfort—she was admitted to New York University Medical Center because her pain medication wasn't working. The Londons, desperate to try anything that would help their daughter, asked Neotropix to make the experimental drug available to her. On April 18, after many board meetings and a consultation with an ethicist, Neotropix refused.

Besides being nervous about the substantial risks to Penelope, chief executive Peter Lanciano was concerned that the FDA would put the drug's trial on hold again if she died after receiving it, despite some indications from the FDA that it would not. If the trial were again delayed, the drug would take longer to reach others who need it—in effect sacrificing future patients to help Penelope now.

Neotropix is also concerned about itself. The small, start-up business is only a few years old and has limited funds. The bad press if the treatment did more harm than good for Penelope could sink the company, meaning that no future patients would ever benefit from this drug or any others it might develop. In the article, P. Sherrill Neff—managing partner in Quaker BioVentures, a venture-capital firm with a substantial investment in Neotropix—claimed that, in this situation, “There is no right answer.”

Nevertheless, the company had to reach a decision. Was it the right one? Or should Neotropix have given Penelope London their experimental drug?

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4. Dan is at the hospital bedside of his 13-year-old son, Rob, who was admitted the previous night with severe breathing difficulties. Rob is heavily sedated but conscious. Dan has been told that his son may have cancer; tests done during the night showed that he has very elevated white blood cell counts.

The next morning, Rob's oncologist RS talks with Dan. He confirms that Rob has cancer—acute lymphoblastic leukemia. He says the disease is curable, but that treatment needs to start immediately since the boy's white blood cell count is “50 times higher than it should be.” RS also explains that Rob is eligible for a Phase III clinical trial:

Dan: You do anything you need to do to fix him! I don't care.

RS: I know you don't care—

D: Whatever you gotta do to fix my son, do it!

RS: I know. I— D: (Interrupts) You don't have to tell me all the lingo. Just fix him! RS: I know. But I do need to tell you. (Laughs) And I know you're not gonna completely understand this because—

D: (Interrupts) Whatever you need to do, do it!

RS: Well, and that's what we will do.

D: Yeah, I'll sign anything you want. Just let me drive my son home.

RS persists despite frequent interruptions from Dan. He discusses the clinical trial and its four “arms,” how one of these is the standard therapy, how Rob would be randomized to one of the arms, that participation in the study is voluntary, that Rob can be withdrawn from the study if he has too many side effects. He explains that the research study is not strictly speaking experimental; it will provide Rob with the “best known” treatment for childhood leukemia.

Dan is frustrated and concerned that all this discussion is delaying his son's treatment. He says, “I just wish you could give the order and we could get this thing started.”

RS responds, “The bottom line is, if you feel uncomfortable with the study we can give him standard therapy.”

Dan: "That's your decision! I'm an electrician, I can wire your house, but I couldn't. . . . it's your call. You're the doctor."

Ultimately, Dan signs the consent form to authorize his son's participation in the research study. The gesture is perfunctory. "Whatever you think is best for my son, I'll do it. I'll sign anything!"

Is this informed consent?

Did RS respond appropriately to Dan's insistence that he didn't need "all the lingo" about the clinical trial? That he, the doctor, should make the right decision for his son? Should proxy decisionmakers like Dan be encouraged to regard themselves as qualified decision makers? Or should their stated preference for another potential proxy—the child's doctor—be honored? To what extent should the ethical appropriateness of these and other possible responses be evaluated against the clinical urgency to treat? Or the doctor's conviction that the best known treatment for the patient is the clinical trial?

Abstracted from Hastings Center Report, Jul/Aug 2004, Vol. 34 Issue 4, p12-13

5. Twenty-year-old Z saw an advertisement in her college newspaper offering money to young women willing to donate ova to infertile couples. Z needed the money to pay her tuition, and she liked the idea of helping someone have a family. After exchanging some basic information with the agency that placed the advertisement, she agreed to undergo pharmaceutical stimulation of her ovaries in order to provide gametes, and the agency matched her with an infertile couple she liked and wanted to help.

The agency had already informed the infertile couple that the assisted reproductive technology they wanted to use to have a child could cost them several tens of thousands of dollars. At a minimum, they expect to pay Z for the service she is providing them and to compensate her for her discomfort and inconvenience. They will also pay for Z's medical testing and care, for her psychological testing and consultations as needed, and for two lawyers, one for themselves and one for Z, who will negotiate and prepare a written contract that will set the parameters of Z's relationship with the infertile couple.

In the process of drafting and negotiating the contract, Z's attorney learns that the infertile couple wants Z to undergo genetic testing for certain abnormalities and disorders: cystic fibrosis, fragile X, thalassemia, and a karyotype. When Z's lawyer communicates their request, Z is agreeable and has no questions. Like many people her age, she has little appreciation for health risks and long-term burdens, and the only contract she has ever entered into on her own is a lease for her first apartment. She does not have her own physician, and she has barely begun to think in more than abstract terms about the family she wants one day to have.

What are the obligations of the professionals working with the infertile couple and with Z in this case?

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