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June 7, 1988

To: Bart Gledhill, Chair, Institutional Review Board

From: Jack Shearer, Member, Institutional Review Board

Subject: Proposed Renewal of Experiment "Pulmonary Gas-Rates in Man", with P. I. Paul Meyer, IRB No. 80P-109

At our June 2, 1988, meeting of the Institutional Review Board (IRB) I voted against approval of Paul Meyer's proposed experiment. I am writing this to explain my vote.

In the past when the IRB had a problem with a proposed experiment we have been able to work with the experimenter and arrive at changes that were acceptable to everybody. In these cases the issue has been some aspect of the protocol, or what needed to be said in the consent form, or whether the participant's identity would be safeguarded, and so on. Why couldn't I do the same with this experiment? What's different? I have to admit that at first the difference I perceived was felt at the gut level rather than understood in a rational way. Unfortunately my understanding evolved slowly. I could not articulate what I felt. No doubt this contributed significantly to the seemingly endless and pointless discussions we had, and to the feeling by some that I was being unreasonable. My March 10, 1988, memo to the IRB was my first real attempt to say what is bothering me, but I now see it was incomplete. So I welcome this second chance to explain my position.

To begin with I'd like to distinguish between "probability", which I'll use to mean the likelihood that something will happen to a human subject as a result of participating in an experiment, and "threat", which refers to the seriousness of what can happen.

In almost all of the protocols the IRB reviews, the threat is trivial. Typically what's involved is collection of urine, or blood, or use of some other low-threat procedure. Nothing even remotely life threatening is involved. In Meyer's proposed experiment the threat is death by cancer. The probability of this is small, but the threat is as large as it can be; it's hard to conceive of a worse threat to a human subject. Hence I see this experiment as being different in kind from almost all the other experiments the IRB considers. It was this difference I felt at the gut level and to which I was reacting.

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I've come to believe that the greater the threat, the greater the obligation on both the experimenter and the IRB to make sure that as few humans are exposed to it as possible. In a situation like this, humans should not be asked to face such a threat, even if the probability is small, unless two criteria are met. First, it must be clear there is an essential need for the information the experiment will provide. Second, it must be clear the needed information cannot be obtained by some other method that reduces or eliminates the threat or the number of human subjects needed.

I view Meyer's experiment as defective in the second of these two. Initially, when I wrote my March 10 memo, I believed it might be defective in both. Since then he's obtained additional information from the Navy which convinced me that there is an essential need for the data. But I am not convinced that there are no alternatives to the exclusive use of human beings. In experiments with this level of threat the experimenter should make an extensive attempt to avoid or reduce the use of human subjects. This includes looking for and, if possible, developing animal models.

Let me put my dilemma this way. Suppose somebody showed me evidence suggesting that, with some reasonable amount of work, a suitable animal model could be developed. Would it be worth delaying the use of human subjects to find out? I certainly think so. In other words, human subjects should be used in this kind of experiment only as a last resort, after it's clear other approaches won't work. That being the case, how can I give my approval when it's not clear that anybody has seriously tried to look for alternatives?

At the meeting Paul Meyer said the information I want does exist, and that he will collect it for me. If he does, and if the evidence is convincing, I'll change my vote. As I said, I've become convinced there is a real need for the information this experiment will provide. The remaining question is how to get it with the least reliance on or threat to human beings.

Jack H. Pleam

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