The experimentalist is always asked, How do you get from your animals to man? It must be admitted that all or nearly all work with experimental animals has as its ultimate objective something that ap-

plies to man.

Experience has shown that if you work with an organism or species which is far removed from man on the phylogenetic scale, if you work with a mouse rather than, say, with a dog, the danger of extrapolation that you will ultimately make is increased. It is, therefore, as a general rule, considered a little safer to jump from, let us say, a subhuman primate to man. What kind of results are we talking about and what is this jump? One of the things that may be of interest to you is the qualitative nature of the responses you are seeing. If you do examine the effect of something on a series of animals moving up the phylogenetic tree and you see much the same kind of effect occurring in each one of them, you will feel fairly confident that if man were exposed to the same thing he would exhibit the same signs and symptoms. You can appreciate that if you had only done the work with mice and then jumped to man that there is a possibility that there might be a striking species difference which would vitiate your extrapolation.

So there are these questions of the qualitative similarities that may or may not be present when you do this kind of work. There is also a question of the quantitative nature of the responses and the same sort

of considerations apply.

Now, as to the next part of your question, suppose we had results in various species, including the primate, and we want to jump over to man, can we do this, or what other work is indicated? One of the things, of course, that one would like to think of as a theoretical possibility, perhaps, is: Could we do experiments on men? This question is not at all ridiculous and, in fact, we do do experiments on men.

One of the factors that will govern this is the nature of the kind of things we are working with and the nature of the effects they produce.

It is fortunate, in this sense, that the sort of pollutants that I have been talking about are not noted for their high toxicity. They are irritating materials and they do fall into a class where considering the possibility of doing human experiments is quite on the books. As a matter of fact, we have proposed to our sponsors in a tentative form a possible continuation of some of the work that we are doing in human subjects. However, there are difficulties. I mentioned at the beginning what we really want to know is the effect of very low concentrations of these pollutants over protracted periods of time. Well, you can put an animal in a chamber and conduct experiments on him for a quite high fraction of his total lifespan or, in fact, for his total lifespan, but you cannot do this with human subjects. So it is a little difficult at the moment to see how we can perform the necessary experiments on human beings. Short-term ones we can do, but short-term ones are not what we are really interested in.

I seem to have talked around this question, Mr. Chairman. I do not

know whether I have answered your question.

Mr. Daddario. Well, we can get into it more deeply later. I do think this is important to us, however, so that we might know what time scale we are talking about and how, in fact, we can have confidence in criteria to be established through such laboratory techniques, recognizing they are extremely important. I do not assume that this is not an