Senator NELSON. Thank you, Dr. Ley.

I noticed on page 10, you state, "I need not tell you that clinical investigation of drugs is an inexact science and there are very few cases of clinical drug investigations where all conditions are perfect." That is not the standard, anyway; is it? Is not the standard well-controlled studies?

Dr. LEY. The standard, Mr. Chairman, is adequate, well-controlled studies. The practical detail by which adequate, well-controlled studies are achieved in real-life research situations is not quite as simple as the words would imply. There is a rare facility, and my staff has indicated only two that they have observed over a period of many years, in which in their opinion, every aspect of the operation was as perfect as it is humanly possible for it to be.

Senator NELSON. Only two; where is this?

Dr. LEY. Only two instances with two investigators. More commonly, we find that with the press of life in a busy medical center, there are minor deficiencies in the way records are kept or retained on the part of the investigators responsible for new drug testing. These investigators most commonly are very pleased, happy, and cooperative in correcting such problems. But it is a rare situation where you find everything present in the way the regulations call for it to be.

Senator NELSON. I notice in the statute that the language for the standard is that "the term 'substantial evidence' means evidence consisting of adequate and well-controlled investigations. including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."

That is the standard, is it not?

Dr. LEY. Yes, sir.

Senator NELSON. On page 9 in the second case that you mention, you say "The other case involves a general practitioner in a small New York State community who had been named as an investigator on 45 IND's and NDA's for 14 different drug companies. We doubted the availability of the patient population sufficient to participate in some of the studies submitted."

My question would be: What qualifications does this general practitioner have in the first instance by virtue of scientific training and experience to evaluate the effectiveness of the drug involved?

Dr. LEY. Mr. Chairman, the particular area in which a clinical investigator operates may be as simple as that of dose-range finding, in which case the qualifications necessary for this type of work are relatively simple.

Senator NELSON. What do you mean by dose-range finding?

Dr. LEY. This is a procedure in which the drug, after phase 1 testing or as a part of phase 1 testing, may be given in varying dosage schedules to either subjects or patient to find the minimal level at which the drug either produces adverse reactions or side effects, or the minimal level at which the drug produces an effect upon the disease process under study. This type of investigation requires a relatively standard type of experience that is well met in practically all physi-