our own review of investigational studies as they are submitted by the sponsor to us, we compare the results of one investigator with the results of another investigator. These observations should generally match. There may be a serious discrepancy between the two observations by two different people. Either there are problems with the material supplied to them or second, there are problems with the investigator and the investigation. One such instance happened. A firm, by error, mixed a combination drug product that was in the investigational stages of testing with a dose of scopolamine, an atrophine-like product, which was approximately 10 times that which the formula required. The dose was so high that there were obviously going to be side effects—dryness of the mouth, dryness of the skin, increased temperature, things of this sort. Indeed, these side effects were reported by one of the investigators directly to the firm, who then insisted on a recall of the investigational drug, which was quite appropriate, as it was improperly compounded. However, the investigator referred to in case No. 1 had reported not a single adverse effect when he had given the drug to the patient. This was one of our chief clues that there was a problem, with the investigator referred to in case No. 1.

Senator NELSON. But suppose you had two of them like the one who did not report?

Dr. LEY. Mr. Chairman, we never find a neat situation in which the files contain only two studies. There are always a half dozen or more studies in our file. Sometimes I wish that we had fewer better controlled studies, but the facts of life are that we do have this opportunity for internal checking.

Senator NELSON. What is your conclusion as to the investigators who found no toxicity at all?

Dr. LEY. My conclusion is that here is an investigator we should take a very careful look at. If everyone else in the file finds a very significant toxicity and one investigator out of the group does not, that man needs a careful visit from our staff.

Senator NELSON. Wouldn't it put a much greater degree of integrity in the system if the sponsor of the IND was not also the sponsor of the drug, that it was from an independent source, whether it is the FDA or anything else, and the investigator was responsible to an independent source, which had no financial interest or any other interest in promoting the drug—in fact, whose only interest was in ascertaining the scientific facts? Wouldn't that eliminate a lot of bias consciously or unconsciously on the part of an investigator?

Dr. LEY. I have read the testimony before earlier hearings, Mr. Chairman. I know this concept has been presented on several occasions to your committee. Theoretically, I grant that the introduction of an unbiased, dispassionate evaluator could possibly contribute to the drug testing system. On the other hand, I would also say that another answer that might be equally acceptable would be for the drug sponsor to conduct his monitoring operations more effectively and more objectively than some. This is the point, of course, that is in question.

Senator NELSON. That assumes that all sponsors are of great integrity and conscientiousness. Now, let's assume that most of them are or that 95 percent of them are, or 99 percent of them are. I have no notion. That still does not get at the famous case of thalidomide in which Dr. Kelsey played a very significant role. The drug company