about the great profusion of new drugs, such as 101, of which only 14 were new entities?

What is the value of the other 90 or so drugs coming into the mar-

ketplace?

Dr. Moser. That's rather difficult to answer, sir. The problem is that when a new drug emerges it is extremely difficult to figure out what its ultimate place is going to be, and it does take time to sort them out. It takes considerable clinical study before one can be sure that this drug is indeed going to be a valuable contribution. It is a bit more than the average physician can do without the help of some fine investigators. I hadn't thought about 14 specific drugs, but I would assume that is a fairly good average of what we would get each year. The effective new agents do represent a handful.

Senator Nelson. What about those 87 new drugs which are simply the same chemical entities that are already in the marketplace now introduced as new drugs in some other combination? What is the pattern historically of the value of these new combinations?

Dr. Moser. Well, again, I think it is hard to generalize. I would suspect that many such drugs come out as a result of competitive drug manufacture. I don't know if combinations ever represent any significant contribution. Chlorothiazide when it first came out was superceded by hydrochlorothiazide. This was offered as a better drug, but ultimately it turned out to be quite similar.

I can't cite specific instances, but I think there are many cases where these combination drugs add very much to our ability to take care

of patients.

Senator Nelson. Thank you.

Dr. Moser. To continue, once the physician does manage to figure out which of the new drugs are indeed valuable agents—and this is not easy—the pressure may come from patients and often from one's own peers, this pressure to try a new, unfamiliar compound—that has been effectively merchandised—is an additional force to be considered in the therapeutic capability of the individual physician.

Yet I have observed an expanding spirit of skepticism and discontent with empiricism in therapeutics. I find more and more that modern practitioners demand drugs that have proper credentials. And this has precipitated a virtual renaissance in drug investigation.

The demands of the clinician to know more about drugs are being met by increasing capability in the laboratory. New insight and appreciation of the complexities of drug effects have come from several diverse avenues of investigation. Percutaneous biopsy, which is a technique using a needle where one can get a piece of tissue from the lung, liver, and so forth, and examine it on a microscope, electron microscopy, and immunofluorescent techniques have—which are techniques that can be used to identify specific substances within tissues that have been taken with biopsy, have resulted in dramatic revelations; the mysteries of intracellular morphology and physiology in the living organism has begun to yield.

Often, we are able to observe the specific site of drug action within the cell and subcellular structures. In other areas techniques continue to be perfected for assay of blood any tissue levels of drugs, intermediate products, enzymes, and hormones and thus we have come to learn more of the wonders and hazards of contemporary therapeutic

agents.