the very nature of their disease, had low white blood counts. At no time in the early studies did these drops become of significant importance, so that we elected to terminate therapy.

Official recognition of the serious problems in terms of blood anomalies resulting from the drug was not made until about 1950 or 1951.

Senator NELSON. Do you mean to say that in the testing on animals, where the range of experimentation would be much more flexible, they did not try dosages of such a nature that demonstrated dramatic blood changes?

Dr. LEY. Yes, Senator Nelson.

In some of the animal studies which were conducted about 1950 or 1951, in dogs specifically, there were changes observed in the nature of temporary depression of bone marrow, anemias, which are quickly returned to normal after the drug was discontinued.

At no time, however, in dogs, as I understand the evidence, has an aplastic anemia been observed or described.

Now, our expert committee pointed out that any human being will respond with a temporary decrease in hemoglobin when given this drug. This normally disappears promptly after the therapy is terminated.

The estimate is that two grams a day will produce detectable temporary drops in hemoglobins in about 50 percent of the individuals receiving the drug.

Senator NELSON. You are saying, as I understood it, that these blood dyscrasias were noticed in 1950 and 1951. But I am saying what about the experimental data on animals submitted with the New Drug Application in 1949? Did the company indicate anything on blood dyscrasias at all?

Dr. GODDARD. No, sir.

Senator NELSON. They did not?

Dr. GODDARD. No, sir. In fact, it was not until 1953 that FDA itself carried out animal studies, dog studies, as a result of some of the problems being demonstrated in humans.

The early studies on this drug, of course, suffer all the problems that we have to live with in drug studies—as greater experience is gained in what we call phase 4, these adverse reactions then begin to become apparent.

But to my recollection and to Dr. Ley's recollection, there was nothing in the New Drug Application that indicated that the animal studies displayed any problems in the early stages.

Senator NELSON. Did I understand from the testimony that there were animal studies made prior to the application for marketing of the drug, and that those studies were submitted to the FDA at the time?

Dr. GODDARD. That is my recollection. We can dig that up again. But we have looked at it, and I recall that there were animal studies. I will have to look again.

Senator NELSON. Given a certain amount of this drug, a certain number of grams, the testimony has been that you get a blood dyscrasia, almost always, apparently. And I am just wondering why in the experimentation with animals, when they could use larger dosages