the manufacturer of the drug taking all necessary steps to assure the safest possible use of the drug?

Before discussing these questions and alternatives, however, it may be useful to outline what has been done in the past. Chloramphenicol was first isolated in 1947 from a soil sample collected in Venezuela. It was found that liquid cultures of the organism, Streptomyces venezuelae, possessed marked effectiveness against several Gram negative bacteria and also exhibited antirickettsial and antiviral activity. Shortly thereafter the chemical structural formula was determined and the antibiotic was prepared synthetically. And, as you know, it was later patented by Parke, Davis & Co.

In 1948, chloramphenicol was produced in amounts sufficient for clinical trials and general clinical use. It was found to be of value in the therapy of a variety of infections, including epidemic typhus in Bolivia and scrub typhus and typhoid fever in the Malay Peninsula.

Mr. GORDON. How about the United States?

Dr. GODDARD. I am talking now about the early uses of it, where it was used against epidemics particularly.

On January 12, 1949, the Parke, Davis New Drug Application for Chloromycetin, that company's brand of chloramphenicol, was allowed by FDA to become effective.

This followed clinical trials in the United States on appropriate types of infections, Mr. Gordon.

In the summer of 1949, as the result of new legislation, chloromycetin was classified as a "certifiable antibiotic," subject to the batch certification provisions of the Food, Drug, and Cosmetic Act.

Senator NELSON. In the New Drug Application, did any of the experimental data submitted to FDA indicate the development of blood dyscrasias or other adverse side effects?

Dr. LEY. None, sir.

Senator NELSON. How long did they experiment with it?

Dr. GODDARD. Clinical trials, Dr. Ley, went forth over about 18 months?

Dr. LEY. From early 1948 until 1949, as I recollect, was the period that the clinical trials were in progress, both overseas and in this country.

Senator NELSON. These were first on animals, I take it?

Dr. GODDARD. It would have been animal work on toxicity, "LD 50's" and things of this nature would have been carried out. But the clinical trials were directed toward the patients with specific infectious diseases.

Senator NELSON. I notice in reading the literature, and some of the testimony, that the experts always strongly urged or state that it is necessary that continuous blood tests be made, and that as soon as any changes are indicated in the blood, therapy be stopped immediately.

You mean that in all these trials they saw no blood changes at all?

Dr. LEY. Senator Nelson, in some of the early work in the Malay Peninsula, I was involved myself personally. We studied at that time the early report in 1948, covering about 50 patients with scrub typhus, and two patients with typhus fever. We occasionally noted drops in white blood cell count in these patients, who frequently, by