than in human experimentation, that they did not discover anything that would warrant the attention of the FDA at that time concerning the side effects of this drug.

Dr. GODDARD. Senator, let us reexamine the original NDA and see what that discloses. But I will also point out that the studies required at that time were not to the degree and depth that they have been since the 1962 amendments. They were not as sophisticated—the animal studies, I am speaking of—as they now are. So therefore it is quite possible that this was missed at that time.

(The subsequent supplemental information follows:)

STATEMENT OF THE FOOD AND DRUG ADMINISTRATION CONCERNING ANIMAL STUDIES CONTAINED IN THE ORIGINAL CHLOROMYCETIN NDA

Clinical use of Chloromycetin was originally proposed in NDA 6655. Sometime after the NDA was made effective, the drug was made certifiable.

A reprint of an article by R. H. Smith *et al.* (Chloromycetin: biological studies, J. Bact. 55: 425, 1948) was filed as part of the NDA. Although the bulk of the article deals with microbiological studies, the following animal experiments are reported:

1. Acute toxicity studies in mice (I.V., S.C. and P.O.) and dogs (I.V. and I.M.).
2. Subacute toxicity studies in mice (S.C. and P.O.), rabbits (S.C.) and dogs (I.M. and P.O.).
3. Absorption and excretion studies in dogs.

Senator NELSON. Go ahead.

Dr. GODDARD. When chloramphenicol was first introduced in 1949, it was widely heralded as a broad-spectrum antibiotic, effective against an impressive range of micro-organisms. It was also considered to be largely nontoxic. There was no indication at that time that the drug had any serious side effects.

Early in 1950, however, a few published reports drew attention to the possibility that chloramphenicol might cause serious and fatal blood dyscrasias. The 1951 edition of New and Non-Official Remedies warned that "changes in the peripheral blood or blood forming organisms have been reported during the use of chloramphenicol." An editorial in the Journal of American Medical Association, June 28, 1952, referred to additional reports of blood disorders. It went on to say—

A second and more serious type of reaction that has been encountered is production of a true aplastic anemia. In the experience of one group this anemia has occurred in patients who have previously received one or more courses of chloramphenicol without untoward effect. When the drug was subsequently administered, even in small doses, a severe blood abnormality has appeared. Even deaths have been reported.

In response to these reports, FDA conducted a nationwide survey of case records in hospitals and clinics in an attempt to evaluate the magnitude of the problem and to determine whether a cause and effect relationship existed between the drug and the disease. This survey produced records of 410 cases of serious blood disorders, of which 177 were definitely known to have been associated with chloramphenicol. In 61 cases choramphenicol was the only drug administered. In half of these 177 cases the blood disorders were fatal. They include aplastic anemia, hypoplastic anemia, thrombocytopenia, and granulocytopenia. In June 1952, the FDA referred the case histories obtained in the survey to the National Research Council (NRC).