of the drug has been assimilated in the body to combat the infection being treated.

As can be seen from chart 4, the urinary excretion rate data corresponds very closely to the blood-level data. Thus the product A chloramphenicol was excreted at a much lower rate than Chloromycetin, Parke, Davis.

Particular note should be made of the fact that after 24 hours only 46 percent of the total chloramphenicol administered as product A could be accounted for by the urinary excretion rate test. This is in sharp contrast to Chloromycetin, Parke, Davis, where 76.4 percent of the drug was excreted in the same period of time. This point is especially significant because the Food and Drug Administration approved labeling for both products contains the statement that:

> Seventy to 90 percent of a single oral dose of 50 mg. of chloramphenicol is excreted in 24 hours in the urine of human subjects, with 5 to 10 percent as free chloramphenicol and the remainder as microbiologically inactive metabolites, principally the conjugate with glucuronic acid.

Thus, in this test, product A was not excreted in the urine in the 70- to 90-percent range mentioned in the official labeling, see chart 4.

The analytical procedures used in performing the blood-plasma level tests and the urinary excretion rate test for chloramphenicol were developed by Parke, Davis. These procedures were published by Parke, Davis scientists and, of course, are available to anyone who wishes to use them. The plasma and urine samples were analyzed by the colorimetric procedure—Glazko, et al., Arch. Biochem. 23:411, 1949, modified as described in Antibiotics Agents and Chemotherapy—1966, page 655.

A second study, designated in the charts as Study II, was conducted in precisely the same manner as described in Study I. Study II was done to verify the results obtained in Study I. The results of the blood plasma level test conducted in Study II can be seen in charts 5 and 6. The results of the urinary excretion rate test in Study II can be seen in chart 8. It can be observed from the charts that the blood plasma level tests and the urinary excretion rate tests of Study I and Study II are consistent.

In addition to colorimetric or chemical test for chloramphenicol in the blood, a microbioligical assay was also carried out in Study II.

Senator NELSON. May I interrupt, Doctor?

There has been a scheduled rollcall, so we will recess for 10 minutes.

(Short recess.)

Senator NELSON. The hearing will come to order.

Dr. Lueck, you were where when we interrupted you?

Dr. LUECK. Mr. Chairman, I was on page 7 of the supplemental statement, the second full paragraph, starting on the second sentence of that paragraph.

Senator NELSON. Fine, Doctor, proceed.

Dr. LUECK. The microbiological assay is important because it is a direct measurement of only the microbiologically active chloramphenicol, and does not pick up any of the inactive metabolites which are measured by the chemical determination. This test, which was performed on the same blood samples previously used for the chemical test, is an actual measurement of the ability of the drug to inhibit