

It should be noted that the drug chloramphenicol and all its product forms are subject to a batch-by-batch certification pursuant to the antibiotic regulations of the Food and Drug Administration. Therefore, the capsules studied in this report, which were all in commercial distribution, should have passed all the requirements contained in the antibiotic regulations, and the Food and Drug Administration should have certified that all those requirements were met.

On each of the samples mentioned above, certain laboratory tests contained in the U.S. Pharmacopeia and the antibiotic regulations were performed by Parke, Davis. None of the materials was found to be deficient in meeting the standards of those tests. However, as was mentioned in our earlier statement to the subcommittee, a reputable manufacturer frequently does more testing and has more expertise than is required to meet the minimum standards. This is certainly true for Chloromycetin, Parke, Davis.

It should be emphasized that Parke, Davis has defined the quality level of its Chloromycetin product in terms of clinically demonstrated efficacy. In fact, in 1964, before the Food and Drug Administration would certify batches of Chloromycetin manufactured by a new synthetic process, they required Parke, Davis to produce not only animal data supporting safety, but also blood level and clinical efficacy data in human subjects. Studies were performed to obtain this information and it was supplied to the Food and Drug Administration.

Laboratory tests and standards in addition to those required by FDA and the USP were developed by Parke, Davis to maintain this built-in quality in each batch of Chloromycetin that is produced. To mention just one of the additional tests, Parke, Davis explored a dissolution rate test on batches of chloramphenicol capsules. This test was performed on each sample of the chloramphenicol capsules obtained from the pharmacies.

Dissolution rate is a test performed in the laboratory to measure the length of time required for the dosage form, such as a capsule, to release the drug. The test was carried out using an official U.S. Pharmacopeia test solution, simulated gastric juice. The dissolution rate test is believed by experts to be a valuable tool to ascertain whether the manufacturing process produces a product which is readily absorbed into the bloodstream from the gastrointestinal tract of the patient. Indeed, this is one of the tests required in the procurement of chloramphenicol capsules by the Defense Supply Agency (DSA).

This point we think is very important in oral antibiotic therapy because without early and rapid absorption, the drug cannot be expected to reach the disease site sufficiently rapidly and in high enough concentrations to carry out its therapeutic action.

The results of the dissolution rate test are summarized in chart 1, which is attached, Mr. Chairman, to the supplemental statement.¹

It is seen from the chart that none of the competitive chloramphenicol capsules dissolved in simulated gastric juice as quickly or at the same rate as Chloromycetin, Parke, Davis. The Parke, Davis standards for dissolution rate, which have been adopted by the Defense Supply Agency, are as follows: The capsules shall release not less

¹ Charts 1 to 13 attached to Dr. Lueck's supplemental statement begin at p. 2151, *infra*.