

Senator NELSON. Yes. The question raised was that the other chloramphenicols in the marketplace did not achieve the same blood level at the same time as Parke, Davis' chloramphenicol, is that correct?

Dr. LEY. That is correct, sir.

Senator NELSON. Is there any clinical evidence at all that demonstrates that one blood level has a better therapeutic aspect than the others?

Dr. LEY. There is no evidence of this sort currently in our files. I would like, if I may, to trace the history of that particular incident because it might be valuable in further discussion here this morning.

Senator NELSON. Fine.

Dr. LEY. In October of 1966, the date the chloramphenicol patent protection expired, several other firms petitioned us to approve certification for competing brands of chloramphenicol. In retrospect, the decision that was made at that time was in error. The staff of scientists at FDA considered that with a drug which could be synthesized, such as chloramphenicol can, which can be analyzed carefully and accurately, that permitting marketing on the basis of purely chemical standards of purity, identity, et cetera, would provide a product which was comparable in every respect to the original product in the marketplace. This assumption was subsequently found to be false.

At this point, when we recognized the blood levels from the later competing manufacturers of the product were at variance, in that they appeared more slowly than the blood levels from the Parke, Davis product, we faced the question of whether we could clearly define a blood level as being effective for this condition or that condition.

The decision which we finally made in December of 1967, Mr. Chairman, was a decision that each one of the competing firms could have one or the other of two choices. Either they could demonstrate by testing in human substance that the blood level which their product produced was equivalent to the same blood level of the Parke, Davis product which was supported by adequate clinical data in the past, or as their second choice, they could collect and submit to us clinical data demonstrating the efficacy of their product even though it had a lower blood level. None of the manufacturers elected to take the second course; all chose the first course of action. So that at this point in time, the three manufacturers of chloramphenicol who are currently marketing their product all have blood levels which are essentially identical when tested in human substance.

Senator NELSON. So there is no positive clinical evidence that one blood-level achievement in a period of time is more effective than another.

Dr. LEY. The information of this sort is extremely rare, and there are several studies in progress at the moment that might eventually prove that a lower dosage of chloramphenicol would be effective in treating, let's say, typhoid fever than the dosage which was first given in the literature, but these data are not yet in. This is the extent to my knowledge—and I'll have to ask Dr. Minchew to be absolutely certain—of the type of data that are available linking blood levels with clinical efficacy for this product. Is this correct?

Dr. MINCHEW. Yes.

Senator NELSON. Because the claims made by the PMA at that time, you know, were that this just proves the case that generics or that