

20. This report dated February 17, 1969 gives the results of a blood serum level study after single doses of—

- a. One "Albamycin" capsule (novobiocin sodium) 250 mg
- b. Two "Albamycin-T" capsules (novobiocin sodium, 125 mg and tetracycline HCl, 125 mg)
- c. Two "Panalba" capsules (novobiocin sodium 125 mg and tetracycline phosphate complex, 250 mg)
- d. Two "Panalba" capsules Revised (novobiocin sodium micropellets, 125 mg and tetracycline HCl, 250 mg)

Note: This report has been submitted by Upjohn as a part of IND 5517.

Discussion: This study shows again the low novobiocin serum levels (approximately 35%) obtained with the present marketed combinations "b." and "c." when compared to the standard "a." (100%) containing novobiocin alone in the same 250 mg dose. The "Panalba" capsules Revised with novobiocin sodium micropellets give serum levels which approach (85%) the 100% of the "Albamycin" capsule.

Conclusion

For approximately ten years it has been observed from blood serum level studies that the "Panalba" (novobiocin and tetracycline) combination results in markedly lowered and occasionally zero blood serum levels of novobiocin and the tetracycline serum level is slightly lowered. This would serve to defeat any purposeful effectiveness the two drugs may have had in combination and certainly leaves a great doubt whether this combination has ever been more or even as effective as tetracycline alone in the spectrum in which tetracycline is expected to be effective.

MAX B. McQUEEN, M.D.

Senator NELSON. Also I would ask if you could supply us with the study they made. Is it a very bulky one?

Dr. LEY. The actual volume of the comments on this—this is a summary memorandum of the review of the individual records, and may represent a mere summary of the total information available. The information, Dr. Jennings tells me, runs to two volumes, which would be about 4 inches of paper.

Senator NELSON. I would just like to read into the record an excerpt from Dr. McQueen's report and then ask a question or two. These reports, as I understand it, were obtained by your inspector from the files of the Upjohn Company, is that correct?

Dr. LEY. That is correct.

Senator NELSON. And they had not been supplied voluntarily by the Upjohn Company to the FDA?

Dr. LEY. That is correct.

Senator NELSON. And these were reports of studies made by the Upjohn Company itself, or whomever they selected to make the study, is that not correct?

Dr. LEY. They utilized, I think, exclusively physicians outside of Upjohn to perform the clinical investigations.

Senator NELSON. So these are Upjohn's own reports, studies on its own drug Panalba. Here is an excerpt from Dr. McQueen's report:

Reports of four crossover studies comparing various Panalba dosage forms with novobiocin alone, and tetracycline alone. These studies clearly indicate the marked depression of novobiocin serum levels to subtherapeutic levels when given in combination with tetracycline. These reports are dated May 18 and 23, July 21 and August 17, 1960.

Would you like to comment on the meaning of that statement?

Dr. LEY. The meaning of that statement, Senator, is that when you compare blood levels of patients given tetracycline and novobiocin alone, against those receiving the combination of tetracycline plus