Senator NELSON. Pardon me, Doctor. Are all of the fixed combinations, save one, orally administered?

Dr. KIRBY. No, they are not oral. Some are injectable, such as combinations of penicillin and streptomycin.

Senator NELSON. Fixed combinations?

Dr. KIRBY. Yes. Some of the fixed combinations are injectable.

Senator NELSON. Do you know the number involved?

Dr. KIRBY. I do not know that number right off.

Mr. GORDON. Dr. Kirby, may I interrupt just a moment? Are you acquainted with the notice that was put into the Federal Register last week by the Food and Drug Administration on novobiocin? [1]

Dr. KIRBY. Yes, I am.

Mr. GORDON. Do you recall that there is a warning box in which it says novobiocin should be used only for those serious infections where other less toxic drugs are ineffective or contraindicated because of the following:

"1. The high frequency of adverse reactions, including hepatic dysfunction, blood dyscrasias and rashes.

"2. The rapid and frequent emergence of the resistant strains, especially staphylococci.

"3. Its spectrum of antibacterial activity is covered by several other safer and more effective drugs."

Would you comment on the hazards of novobiocin a little further?

Dr. KIRBY. Yes, sir. The hazards, I think, are considerable. I just referred to them here but did not spell them out in the detail that that statement has. And it is these hazards that persuaded Merck to stop marketing this drug after they had done so for a few years. The hazards at that time were well enough known that the drug had quite a restricted usage and was considered undesirable and that is why Merck stopped marketing it voluntarily.

Mr. GORDON. So, Upjohn then picked it up and combined it with tetracycline to——

Dr. KIRBY. Yes. I do not know whether they picked it up then or whether they had it all the time, but they had access to both it and tetracycline, and they thought that this would make a good combination which they then made and have in effect, called it a new product other than just tetracycline.

Mr. GORDON. Would it be reasonable to assume that Upjohn had access to the information on the hazards of this drug?

Dr. KIRBY. Oh, yes, they certainly did, just as much access as anybody.

In the test tube a synergistic action was demonstrated with some bacteria although studies by other investigators showed that the action was more often indifferent and sometimes was antagonistic. Novobiocin was active against staphylococci, a major problem at that time, and these organisms frequently were resistant to tetracycline. Thus, Panalba was promoted as a synergistic combination active against a wide spectrum of bacteria including staphylococci that were resistant to tetracycline and penicillin.

Senator NELSON. May I interrupt? You say thus, Panalba was promoted as a synergistic combination active against a wide spectrum of

[1] See pp. 5168–5171, infra.