

that "certain strains of *Proteus* and *Pseudomonas* have responded to Vibramycin." A claim for acne was regarded as unacceptable. A cautionary statement against use in pregnancy was needed. Under "Adverse reactions," we recommended that the effects on the nails be added, that the observations in animals of liver and thyroid changes of undetermined significance be included, and that rare adverse effects on blood be reported.

We had discussed some of this tentatively in January, when Pfizer representatives called to inquire about progress on the application, and we met with them again on February 14, 1967, to go over the points I have noted.

The company disagreed strongly with our recommendations that the observations regarding animal thyroid effects should be in the labeling. They felt that this would place them at a competitive disadvantage in relation to other products whose labeling included no such discussion. They also did not want to delete the statement regarding efficacy in the treatment of *Staphylococcus aureus* infections.

Senator NELSON. May I interrupt a moment? The sentence above that, "They felt that this would place them at a competitive disadvantage in relation to other products whose labeling included no such discussion." Are you referring to other tetracyclines?

Dr. MINCHEW. Yes.

Senator NELSON. Did the other tetracycline products indicate the same animal thyroid effects?

Dr. MINCHEW. Yes, sir; in general they do show similar effects in the animals, and the inequity which is described here as having been emphasized by Pfizer is a result of evolutionary changes that are always going on in terms of package inserts.

Senator NELSON. Did you require the other types of tetracycline to refer to the animal thyroid effects?

Dr. MINCHEW. We have not to date, but we are currently actively revising the labeling of all tetracyclines. This was initiated in the spring of 1967.

Senator NELSON. So that all of them will be required to have the same reference to the animal thyroid toxicity?

Dr. MINCHEW. This is our intention; yes, sir.

Senator HATFIELD. What is your intention? How do you implement your intention? I think that the way you describe it, it sounds like there is a certain inequity here that you are imposing upon one company that you are not imposing upon other companies. Why haven't you taken steps already?

Dr. MINCHEW. We have taken steps to discuss with them revisions in the package insert.

Senator HATFIELD. Are they still marketing under the old methods?

Dr. MINCHEW. Yes, sir.

Senator HATFIELD. What is your time factor?

Dr. MINCHEW. The time factor in this one has now been drawn out to over a year now since we began negotiations and discussions with the companies about changing the package inserts of all of the tetracyclines.

Senator HATFIELD. I am not quite certain as to your procedure. It sounds like you are rather negligent in not taking faster action, if you think it is important enough to have it put on Pfizer. Why haven't you taken immediate steps to have it included in the others?