Dr. MINCHEW. Yes; I will go into the types of changes. On the documents that I have submitted, you will notice the types of changes required as paste-ons.

Senator NELSON. These weren't proposed changes, then, that were called to the attention of the company by the Division of Anti-Infective Drugs?

Dr. MINCHEW. Not at that point; no, sir. The Division of Anti-Infective Drugs does not have the responsibility for the comment on the promotional material per se. It is only reviewed there because this is where the medical expertise reviewed the New Drug Application and the package insert. The promotional implications of the material itself, however, is the primary responsibility of the Division of Medical Advertising.

Senator NELSON. So at this stage the Division of Anti-Infective Drugs apparently discovered——

Dr. MINCHEW. They did not raise any——

Senator NELSON. Did not discover any claims—medical claims—over and beyond what they thought there ought to be? Is that assumption correct?

Dr. MINCHEW. I think the types of problems that we asked for correction will be seen better as we go on.

Senator NELSON. All right.

Dr. MINCHEW. We explained that the visual aid was not acceptable as submitted and that it would need revision. We pointed out that our comments regarding this promotional piece were parallel, and in principle similar, to those previously made by us to the firm in connection with Pfizer's advertising activities for a similar product, Rondomycin. We proceeded to discuss with Pfizer representatives specific objections to the visual aid copy, page by page.

Among the important changes we requested were, that it be clearly specified that the once-a-day dosage was only a maintenance dose and that this dosage must be doubled in initiating therapy and for serious infections; that Vibramycin should be properly identified as another new member of the tetracycline family; that it be clearly stated that the antimicrobial spectrum of Vibramycin is comparable to other tetracyclines; that the need for culture and sensitivity of infecting organisms be pointed out; that use of data from clinical studies be limited to those cases in which sufficient cultures and sensitivity studies were carried out to demonstrate the effectiveness of the drug; and that a claim be dropped that suggested that less Vibramycin would be bound to bones or teeth than is the case with older tetracyclines since there was insufficient data to show this.

However, Pfizer informed us that they had already arranged for its detail men to gather for training sessions in preparation for the later marketing of the antibiotic. Many were en route to these sessions as we were meeting on September 5. They requested that they be permitted to use the uncorrected visual aid for these sessions. We agreed to this, provided Pfizer made clear to its staff the important revisions that were to be made before the aid could be used in detailing.

Mr. GORDON. Is there any evidence that Pfizer did actually make this clear to its staff?

Dr. MCCLEERY. Dr. Minchew is reluctant to comment on this because I was involved directly in these negotiations, and as a general answer