test, there was predictably less chance of human tooth staining with Vibramycin than with any of the other tetracyclines. This episode was followed up by the FDA and on December 8, 1967, an affidavit was obtained in which the physician stated, in addition to the above, that the detail man also stated that Vibramycin was more effective over a larger spectrum of bacteria, including certain staphylococcal and psuedomonal species, than were other tetracyclines.

A Bureau of Medicine physician, who is also a pediatrician, was in attendance at the American Academy of Pediatrics (AAP) meeting on October 25, 1967. He, too, was told by Pfizer representatives that there was predictably less chance of tooth staining with the Vibramycin and that Vibramycin was effective against certain organisms which were not susceptible to other tetracyclines. Staphylococcus and pseudomonas were specifically mentioned.

In addition, a letter was sent to the FDA from an assistant professor of pediatrics of a university medical school. He stated that at the American Academy of Pediatrics meeting in October it had been suggested to him by a Pfizer representative that Vibramycin would not cause tooth staining in children.

On December 22, 1967, the then Commissioner, James L. Goddard, called the president of Chas. Pfizer & Co., Inc., and informed him of these reports. This was followed by a letter from Dr. Goddard explaining FDA's objections in detail.

On December 22, 1967, a telegram was sent by the general manager of Pfizer Laboratories Division to all district managers, regional managers, and regional operations managers. The telegram, which was to be read to the company's field force, stated in part that:

> 1. "There is no evidence that Vibramycin does not cause tooth staining. To the contrary, as a tetracycline it must be assumed it does though no cases have been reported to date."

Senator NELSON. No cases of discoloration from Vibramycin?

Dr. MINCHEW. From Vibramycin.

> 2. "As a tetracycline, Vibramycin has essentially the same spectrum of antimicrobial activity as other tetracyclines. Claims of broader spectrum are not in accord with the evidence known to us at this time."

Vibramycin illustrates three problems which confront the FDA in approving a new drug for marketing. They are: first, the necessity for a most careful and critical evaluation of the data offered to establish the parameters of safe and effective use; second, the proper translation of the scientific data into labeling claims and warnings that will provide adequate prescribing information; and, third, the problem of improper promotion through oral detailing, despite extensive efforts in arriving at a complete understanding between FDA and the company as to the proper scope of the basic printed detailing piece.

Thank you for your attention. My associates and I will gladly attempt to answer any questions you may have.

Senator NELSON. We have had over the past year and a half at various times testimony about claims made by detail men that go beyond the approved claims authorized by the FDA in its package inserts and so forth. There have been studies that indicate that the detail man is a very influential force on the prescribing practices of the physician. This recognizes that some physicians don't have anything to do with detail men. I know some. It also recognizes that many