Revised labeling submitted May 10 was still considered unsatisfactory. There were further meetings and telephone conversations about the labeling held on June 28, July 7, and July 10.

On July 7, 1967, a representative of Pfizer, called the Commissioner to urge prompt action on the application, stating that everything had been approved and that clearance had been too long delayed. Dr. Goddard had previously invited the industry to bring to his personal attention any instances of what is regarded as undue delay in new drug clearance.

The final clearance was in process during the week of July 24. A monograph establishing standards of identity, strength, quality, purity, and safety, and the final labeling describing safe and effective conditions of use were the last parts of the clearance.

This final review developed the fact that we did not have a firm understanding with Pfizer as to the conditions under which the drug would be introduced and promoted to the profession. While the file indicated that all questions had been resolved, the labeling submitted by the firm did not support this.

Three defects were identified:

1. The first page of the insert stated that Vibramycin had several useful properties not observed with previously available tetracyclines.

2. The medical review had noted the importance of adhering to the recommended dosage because of greater absorption and longer persistence, yet the insert said that the drug had been given to volunteers for long periods at high doses without evidence of toxicity, a statement which deemphasized the importance of following the recommended dosage.

3. The insert claimed the drug was useful in acne, whereas the medical review had noted that the studies in acne included only a few cases and lacked objective criteria for evaluating improvement.

Dr. Ley, the then Director of the Bureau of Medicine, called the company, discussed these points, and told them the product would not be approved until these issues were resolved. At a meeting on Monday, July 31, Pfizer representatives continued to protest these changes, contending they had been made after the company had been given informal approval of the package insert. They confirmed their objections in writing. However, the matter was resolved by the company agreeing to make the necessary changes, and on August 10, 1967, the certification monograph was published.

Mr. GORDON. Doctor, may I interrupt at this point?

Dr. MINCHEW. Yes.

Mr. GORDON. The application for Vibramycin, I notice, was submitted on June 22, 1966. The certification monograph was published on August 10, 1967. Now, if the claims for the product had not been so broad, is it reasonable to assume that it could have been put on the market much earlier?

Dr. MINCHEW. I think that is a fair statement, Mr. Gordon. I would not be able to pinpoint exactly at what point the approvability would have been implemented, but I believe the testimony indicates that a significant part of this last few months was dealt in discussing and negotiating over labeling.

Mr. GORDON. It does take a long time to negotiate, is that correct? Could that be the answer to the problem that Senator Hatfield was discussing a short while ago, that the firms make claims which you