U.S. GOVERNMENT MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
FOOD AND DRUG ADMINISTRATION,
June 5, 1968.

To: John J. Jennings, M.D.
From: Edwin M. Ortiz, M.D.
Subject: Memo dated May 28, 1968 from Dr. Minchew regarding Vibramycin

I would like to know the names of the Pfizer representatives who met with Dr. McCleery, Mr. Chadduck and Dr. Minchew.

Pfizer submitted a supplement to their Vibramycin form 5 (NDA 50-006, 50-007) to state under "Actions" the results of a study which showed Vibramycin to be more active *in vitro* against certain strains of staphylococci than other tetracyclines. This submission had been reviewed by Dr. Dye and Dr. Borowsky. In our meeting of April 23, 1968 (with memo) we told Mr. Avergun, Dr. McDermott, and Dr. Sikowski that the supplement was not acceptable for the following reasons:

1. It was based on only one *in vitro* study.
2. Incorporation of these data into the labeling would give a false implication of clinical efficacy.
3. Tetracyclines are not drugs of choice in the treatment of staphylococcal infections.
4. As voluntarily stated by Dr. Sikowski, this represents a transient phenomenon. Staphylococci develop resistance to new tetracyclines in a short period of time.

Multiple attempts by the representatives to modify the statement were immediately rejected by us. It was decided that Pfizer will submit a rephrased statement for our review and evaluation. Several weeks later we received a communication from Pfizer withdrawing the original supplement.

FDA never encouraged the use of these data in promotional material. In fact, our main objection to the incorporation into the labeling was its potential use in promotional literature if it became part of the approved labeling.

APPENDIX V

DOCUMENTS ON DYNAPEN (DICLOXACILLIN) FROM FDA FILES

CHRONOLOGY OF DYNAPEN (DICLOXACILLIN) CASE

BRISTOL LABORATORIES, SODIUM DICLOXACILLIN MONOHYDRATE (DYNAPEN)

November 10, 1965.—Antibiotic Form 5 for sodium dicloxacillin monohydrate submitted by Bristol. This contains suggested regulation for certification of 125 and 250 mg. capsules and 62.5 and 125 mg/5 ml. oral suspension. Clinical data on 198 clinical cases treated with dicloxacillin are also included.

January 6, 1966.—Letter to Bristol from FDA recommending 1) performance of a reproduction study if the product is to be used in premenopausal women and 2) submission of methods, controls and acceptance limits for potency, moisture, pH, identity, crystallinity and microbial assay.

January 28, 1966.—Memorandum from A. Kirshbaum to Mr. Ogles concerning tests performed by FDA on samples of dicloxacillin. The following tests were performed: 1) Assay of 1 mcg. sensitivity discs, 2) Acute toxicity in mice, 3) Microbiological assay for dicloxacillin using the cylinder plate assay method and *Staphylococcus aureus* as the test organism. Using this method 7 of 9 batches showed no loss of potency in two weeks, 4) Bristol's recommended chemical analysis using the infrared spectrum of the beta-lactam moiety. Since this group is shared by all other penicillins, it is suggested that an oxygen flask combustion method for chlorine content be used in addition to assure the identity and purity of dicloxacillin. It is further recommended that Bristol be asked to supply stability data and a reference standard of the drug.

February 10, 1968.—Telephone conversation between J. Davitt and J. Lamar (FDA) and Dr. G. Woodard (Woodard Research Corporation). Concerning teratology studies to be performed by Dr. Woodward for Bristol, FDA recommended that rabbit pups to be delivered by cesarean section should be examined first