July 25, 1967.—Interoffice memorandum (FDA) concerning test results with the new formulation of dicloxacillin for oral suspension. No difficulties are cited.

July 6, 1967.—Submission by Bristol. In the conference of 6/19/67, it had been agreed by Bristol and FDA to cooperate in preparing a poll of experts on the labeling of dicloxacillin. This submission states that since FDA had subsequently, through Dr. Minchew, declined to cooperate in a personal presentation of this poll, Bristol had gone ahead with it. The written responses of 16 physicians tend to support Bristol's position as outlined above.

July 17, 1967.—Interoffice memorandum (FDA) points out that Bristol's poll did not raise question of whether therapy should be switched from dicloxacillin to penicillin G., if warranted by bacteriological results.

July 18, 1967.—Submission by Bristol giving tabulated summary of results of their poll on dicloxacillin. The important questions and responses are as follows:

(1) Is there data to indicate a trend to an increasing number of strains of staphylococci becoming resistant to the semi-synthetic penicillinase-resistant penicillins?

Yes—4, No—10.

(2) In your opinion should a penicillinase-resistant penicillin be reserved for the treatment of infections due to penicillinase-producing staphylococci when the penicillin has been shown to be highly effective both bacteriologically and clinically in infections due to streptococci and pneumococci?

Yes—2, No—12.

(3) In your opinion would reserving a penicillinase-resistant penicillin for infections due to penicillinase-producing staphylococci prevent or materally delay the appearance of resistant strains of the organism?

Yes—0, No—13.

September 1, 1967.—Telephone conversation between Dr. Peltier (Bristol) and Dr. McQueen (FDA) concerning labeling for dicloxacillin. Dr. McQueen stated that the recommendation of the Medical Advisory Board on this question would be ready within a week.

September 7, 1967.—Telephone conversation between Dr. Peltier (Bristol) and Dr. McQueen (FDA). Dr. Peltier was informed of the wording for the indications section of the package insert recommended by the Medical Advisory Board.

September 12, 1967.—Conference convened to discuss Britsol's latest proposed labeling for dicloxacillin in the light of the Medical Advisory Board recommendation. The only point remaining at issue was the statement advising use of penicillin G or phenethicillin in the event that the infecting organism prove not to be a pencillinase producing staphylococcus. Bristol wanted to substitute the phrase "other appropriate antibiotic therapy" for mention of specific drugs. Dr. Hodges (FDA) stated that this substitution seemed to obscure the intent of the advisory board and would not be acceptable. After discussion this statement was agreed to by both parties: "When the infecting organism is susceptible to penicillin G the physician is advised to use penicillin G, phenoxymethyl penicillin, phenethicillin or other appropriate antibiotic therapy, because of the possible appearance in the environment of organisms resistant to the penicillinase-resistant semi-synthetic penicillins."

* * * * * * *

September 21, 1967.—Telephone conversation to Bristol by Dr. Smith (FDA) to request minor revisions in the labeling.

September 25, 1967.—Conference between FDA and Bristol on moisture limits, pH and chlorine content of dry powder for oral suspension. Resolution of these matters was agreed upon.

September 26, 1967.—Submission by Bristol of additional stability data to substantiate their claim of a 12 month expiration date.

September 26, 1967.—Submission by Bristol of confirmation of matters discussed in telephone conversation of 9/21/67.

October 5, 1967.—Pharmacology review of coated form of dicloxacillin oral suspension. There is no expectation of increased toxicity associated with this formulation but it is suggested that data on toxicity of the flavoring agents be requested "as a final precautionary check."

October 9, 1967.—Telephone conversation to clarify questions about flavoring agents in dicloxacillin oral suspension. Bristol is to submit toxicity studies of this formulation in the near future.

October 16, 1967.—Submission from Polak's Frutal Works, Inc. Middletown, New York, supplying information on the composition of Imitation Antibiotic Flav-O Lok 3X 610049.