October 17, 1967.—Submission from Fritzsche Brothers, Inc. New York, N.Y. containing the formula for Aromalok Pineapple Imitation # 31194.

October 19, 1967.—Letter from FDA to Bristol stating that approval of package circulars for dicloxacillin has not been made.

October 23, 1967.—Submission by Bristol containing formulas of flavoring agents used in spray-coated dicloxacillin for oral suspension and acute toxicity data in rats and dogs on this product.

October 30, 1967.—Pharmacology review stating that the material contained in the submission of 10/23/67 satisfies the requests raised in the previous review of 10/5/67.

November 16, 1967.—Interoffice telephone conversation in which it is stated that Dr. Wright (FDA) approves of minor change in the wording of the dicloxacillin monograph.

November 16, 1967.—Telephone conversation between Bristol and FDA in which FDA states a preference for retention of the analytical tests originally proposed in the monograph. This was accepted by Bristol.

November 17, 1967.—Drug control review notes stating that stability data are now adequate to support the sponsor's requests, that the flavoring agents are acceptable and that an inspection has indicated that good manufacturing practices are being followed.

December 1, 1967.—Medical Officer's review of additional clinical studies designed to compare the efficacy of two dosage schedules—250 mg qid and 125 mg. qid in the treatment of minor infections due to coagulase positive staphylococci. The following conclusion is offered: "Bristol's contention that dicloxacillin at a dose level of 125 mg qid provides adequate therapy for staphylococcal infections of the skin and soft tissues of moderate severity, is probably justified. I feel that higher doses should be recommended in those cases where there is significant expectation of complications arising from the infection.

January 5, 1967.—Telephone conversation between Dr. Smith (FDA) and Dr. Holvey (Bristol) in which the sponsor was informed of certain further suggested revisions in the labeling.

February 23, 1968.—Conference between Bristol and FDA in which Bristol again presented its position on methicillin resistant staphylococci (see notes of 5/31/67.) 11/25/66 and 7/20/66). Additional data was presented in which it was demonstrated that among Bristol's employees, exposure to semi-synthetic penicillins was not associated with any nasal carriage of methicillin resistant staphylococci, but that a high level of exposure caused carriage of *S. aureus* to be changed to carriage of *S. Epidermidis.* Dr. Minchew (FDA) stated that the other two producers of dicloxacillin had now submitted labeling conforming to all our requests and that these would be acted upon. Similar labeling has been prepared by Bristol but not yet submitted.

February 23, 1968.—Telephone conversation between Dr. Smith (FDA) and Dr. Peltier (Bristol). Dr. Peltier stated that revised labeling would be submitted but said also that Bristol might consider withdrawing its application.

February 26, 1968.—Submission by Bristol of revised labeling for dicloxacillin. The sponsor wishes "to state for the record that we are not in agreement with" the changes requested by FDA and now accepted. The statement noted in the above note of 9/19/67 is deleted.

February 19, 1968.—Submission by Bristol of preliminary results of an in-plant survey of nasal flora. These results are noted in the above note of 2/23/68.

March 5, 1968.—Telephone conversation between Dr. Smith (FDA) and Dr. Peltier (Bristol) confirming wording changes suggested by Dr. Smith for the labeling submitted on 2/26/68. Dr. Peltier agreed that previously submitted promotional material is no longer to be considered.

March 5, 1968.—Submission by Bristol of corrected package inserts for dicloxacillin.

March 5, 1968.—Submission by Bristol confirming the telephone conversation of the same date, and clarifying points raised by a letter of 1/13/67 (these points are clear in the above note for that date).

March 8, 1698.—Interoffice memorandum from Dr. Smith (FDA) to Dr. Ley (FDA) confirming the opinion of the Division of Anti-infective Drugs that the applications of all three companies for sodium dicloxacillin should be approved, and that the labeling submitted by all of them is acceptable.

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