C. "Adverse Reactions" section—The statement dealing with changes in liver function studies is still vague and non-specific. The other two package inserts specify that these consisted of elevations in SGOT and alterations in cephalin floculation.

D. "Dosage and Administration" section—The statement that dicloxacillin is best absorbed when taken on an empty stomch (1 to 2 hours before meals) is still absent, although it is present in the other two package inserts. In his memo of January 15, 1968 Dr. Hodges stated that this point had not yet been resolved, but would be the same in all three inserts. If this point does have some merit, we would suggest it be included in all three package inserts.

III. *Bristol's labeling for "Dynapen":*

A. In reference to page 2: The second and third sentences of paragraph 1 should be inserted as a separate paragraph following present paragraph 2.

B. The "Actions" section of the package insert for Dynapen capsules omits the word "most" in the sentence "Dynapen is active against [most] Gram-positive cocci . . ." while the package insert for Dynapen suspension includes the word "most." It is recommended these inserts for the same product be consistent.

IV. *Ayerst's labeling for "Veracillin":*

A. The first page marked January, 1968, job number 66–517, is in the form of an ill-concealed promotion and must be rejected. We suggest that the properties of the drug which follow the "dots" be rewritten in an appropriate discussion form comparable to the "Description" section of the Bristol package insert for Dynapen.

B. In reference to page 2: The present second paragraph of the "Indications" section should be moved below the present fourth paragraph.

C. It was suggested by Dr. Minchew and others during revision of the dicloxacillin labeling that the precautionary statement regarding intestinal overgrowth should read ". . . discontinuation of dicloxacillin therapy should be considered" since in some instances it might not be advisable to discontinue the drug. However, the "Veracillin" labeling states ". . . medication should be discontinued . . ." It is recommended that the "Veracillin" labeling be made consistent with the other two.

V. It was noted that the labeling for Bristol's and Wyeth's products contain within the "Indications" section the instruction regarding 10-day treatment of Group A Beta-hemolytic streptococcal infections, while Ayerst includes this information in the "Dosage" section. Since dicloxacillin is not ordinarily recommended for treatment of Group A Beta-hemolytic streptococcal infections, it might be considered contradictory to include instructions for treating such infections in the "Indications" section. Because of this consideration it would be appropriate to limit this statement to the "Dosage" section of all the dicloxacillin labels.

Also the words "Group A" should precede "beta-hemolytic" in the Wyeth "Pathocil" labeling.

R. S. McCLEERY, M.D.

MEMORANDUM OF TELEPHONE CONVERSATION

MARCH 27, 1968.

Between: Hubert C. Peltier, M.D., vice president and medical director, Bristol Meyers (AF 15–068); and Herbert L. Ley, Jr., M.D., Director, Bureau of Medicine.

Dr. Ley read to Dr. Peltier the three changes in the approvable letter for the Bristol dicloxacillin product. Dr. Peltier objected mildly but indicated that the changes were consistent with the general philosophical approach the agency was taking to this drug.

Dr. Peltier objected that in his opinion the FDA action on dicloxacillin was discriminatory against this particular product in view of the existing labeling for other products. Dr. Ley pointed out that it would be wise for Dr. Peltier to observe changes in product labeling over the next year. The two individuals engaged in a long discussion regarding the philosophical concept of restriction in usage of the semi-synthetic penicillins. At the conclusion of the discussion neither individual had changed his position and it appeared that Dr. Peltier recognized that from the Commissioner down to the working level the agency was taking the approach of restricting usage by appropriate labeling for the semi-synthetic penicillins.

HERBERT L. LEY, Jr., M.D.