7. "The History and Development of Oral Penicillins in Japan," Ryochi Fujii, Tokyo University Hospital, a paper given at the 5th International Congress of Chemotherapy (pages 275–278 of proceedings, C 3/2).

8. "Sensitivity of staphylococcus aureus to lysostaphin, cephalotin, benzyl penicillin and semi-synthetic penicillins," Hawiger, J. and Jeljaazewicz, J., Poland, a presentation (p 35 *et seq.* of proceedings, B 1/8) at 5th International Congress of Chemotherapy.

9. "Studies on enterotoxin-B production in methicillin-resistant aureus-staphylococci, "Dornbusch K., Hallander, H. O., Laurell, O., and Lindbom, G., Sweden, an article reporting on cases during 1964–1966 in the University of Uppsala (27 deaths), presented at the 5th International Congress of Chemotherapy (proceedings p 39 *et seq.*, G 1/11).

10. "Changing Patterns of Bacterial Resistance to Antimicrobial Drugs," Gill, F. A. and Hook, E. W., Cornell University Medical College, a paper published in *American Journal of Medicine*, p. 780–795, 39: November 1965.

Other references were mentioned as being available. Later in the meeting Dr. Minchew gave the reference to an article in *Arch. Int. Med.* 111, No. 6, June 1963, titled, "Persistance of Staphylococcus to Methicillin and Oxacillin." He mentioned also that at the annual meeting of 1968 the Epidemic Intelligence Service, National Communicable Disease Center, 22 resistant organisms from 18 patients in one hospital were reported.

In sum, there is ample and continuing evidence that there is cause for concern by the Government and antibiotic producers in relation to the problem.

Dr. McCleery called attention to the Bristol submission in February regarding the resistance problem. He said the information had been discussed within FDA and with outside authorities and found to be invalid for the claims Bristol is making. Dr. Ley concurred and agreed that the Bristol submission was unresponsive to the question of resistance. He reiterated that he felt the FDA-prepared guideline to proper indications should be incorporated into the remedial letter.

The visitors again indicated that the guideline was not in accord with the package insert. The expansion of the contraindications was cited as an example. However, Dr. McCleery pointed out that the same information was in another part of the insert and that it should be emphasized. He said he had hoped that Bristol would be on the "side of the angels" and indicated that on further reflection the firm might come to agree with setting the place of Dynapen in proper perspective, notwithstanding the "legalistic" reliance on the package insert which it was entitled to take advantage of.

On the preceding point, Mr. Meers said in effect that his client is for public health protection assuming that it is reflected in the OPC (package insert).

The discussion turned to the proposed ad. Dr. Ley said the ad copy had been reviewed and found to require a small number of corrections. These were identified by Dr. Kauffman.

There was some discussion regarding the language to be used in identifying the ad as "corrective" (as distinguished from "correct"). This was left for Bristol to consider and to propose language at the next meeting.

Drs. Ley and Minchew emphasized that the Commissioner wanted a "corrective" ad and that it could take more than one form. It was left that Bristol would propose modifications in the submitted ad at the next meeting.

Dr. Ley turned the discussion to considerations of the status of shipment of goods beyond the firm's control. He said the FDA was concerned about the large amount of material so shipped.

Dr. McCleery commented that on May 24 a Bristol detail man had visited an Arlington physician and had left behind the so-called "keeper" promotional material. Dr. Ley indicated that preliminary reports from our inspectors reflected that 90,000 "keepers" had been procured, of which 25,000 were intended for hospitals and 65,000 for physicians.

Mr. Simonton admitted it was intended that the "keepers" be left behind and attempted to reconcile Bristol's (Gulick's) May 27 letter, which said that "3 copies were given to salesmen to use as 'keepers'."

Dr. Minchew said that about 30,000 were shipped on May 23 to some 300 salesmen—(see area covered in first of this memo).

Dr. Minchew asked if the firm had record of what the detailmen are saying now to physicians about Dynapen. (See comment by Bristol later on this question).

The discussion continued to the question of shipments of Dynapen. Dr. Ley said that the figures given in Bristol's letter were not in accord with the inspec-