2. The representation that dicloxacillin is "—useful in a *broad range* of skin and soft tissue infections". may be interpreted to mean "broad range" in terms of types of lesions, or "broad range" in terms of etiologic organisms. The latter would be inconsistent with the package labeling.

3. The featuring in the letter of statements such as "low incidence of side effects," "side effects—are exceptionally rare," "lower dosage does mean a lower incidence of side effects," "no direct toxicity," and "a notable lack of side effects" are misleading, especially in the absence of balancing information regarding the facts that, (a) the incidence and severity of adverse reactions are not shown or expected to be less than with other penicillins, (b) super-infection with resistant organisms may occur, (c) safety for pregnancy has not been established, (d) nausea, vomiting, flatulence, loose stools, pruritis, urticaria, skin rashes, allergic symptoms, changes in liver function tests, and eosinophilia have been associated with Dynapen therapy.

4. At no point in the letter, is the need for cultures and sensitivity, and the need to switch therapy if a Pen-G sensitive organism is isolated, expressed.

5. In the 1st paragraph, the indication is given "—in infections of the skin and underlying tissue where resistant staph are *so often* known or suspected." The words "so often" distort the meaning in such a way as to subvert the need to know by cultures or reasonably suspect resistant staph in any specific case.

6. Throughout the letter, in several places where "resistant staph" are mentioned, they are not specified as *Pen G*-resistant staph.

7. In the 2nd paragraph the question of resistance is brought up in a very clever way—"Resistance has not developed *during therapy.*" This is misleading in the absence of the information that, however, strains of pathogenic staph resistant to Penase resistant penicillins, including Dynapen do exist and are increasing in numbers and may cause clinical disease and even death.

8. The comparison of blood levels with Pen G and Pen V are objectionable, since Dynapen should not ordinarily be used exchangeably with Pen G or V. It might be appropriate to compare blood levels with oxacillin or cloxacillin.

9. The letter cites clinical data on "a variety of pathogenic staphylococcal infections" including Pen G sensitive staph. Also, overall percent improvement figures are given, I suspect based on clinical impressions and not on follow-up culture data, at least in some cases.

SUMMARY

The ad:

(1) Invites use of the drug in broader indications than those approved.

(2) Does not properly carry out the responsibility to emphasize the need to restrict the use of this drug to infections due to Pen G resistant staph infections.

(3) Does not present a fair and balanced view of the adverse reactions associated with use of this drug.

R. KAUFFMAN.

CORCORAN, FOLEY, YOUNGMAN & ROWE,
Washington, D.C., May 24, 1968.

Dr. JAMES L. GODDARD,
Commissioner, Food and Drug Administration,
Arlington, Va.

DEAR DR. GODDARD: On behalf of our client Bristol Laboratories, this is to express our appreciation to the Commissioner's office for the expeditious handling of the procedures required for the release of Dynapen, the Company's brand of dicloxacillin. While the ambiguities and confusion resulting from the initial handling of the labeling, release, regulation publication and certification of the three brands of dicloxacillin have placed the Company at a competitive disadvantage, the Administration's remedial efforts should permit the Company to make up some of the lost ground.

Unfortunately, new confusion has arisen in connection with certain language contained in the regulation for dicloxacillin which appeared in the Federal Register of May 17, 1968. As you know, antibiotic regulations with respect to labeling normally provide simply that the labeling for a specific antibiotic shall be in accordance with Section 148.3 of the regulations. Section 148.3 in turn is in large measure based on the requirements of Section 1.106 issued under Section 502(f)