Capsule Dissolution

I take exception to Dr. Moore's implicit criticism and conclusions in his letter "Nondisintegration of a Capsule's Contents" in the February 1979 Open Forum[1].

First, it does not strike me as unexpected to find *in vitro* differences, using discriminating methods, in dosage forms as fundamentally different as tablets, capsules, and timed-release tablets. It seems grossly unjustified to impute "top manufacturers" on such a finding because it fails to take into account special patient needs, the clinical effects resulting from such differences, and the label claims of the manufacturer.

Second, I do not believe that the slower dissolution observed with the capsule was failure to disintegrate but more likely a failure of the capsule contents to wet readily. Incidentally, wetting problems are easily identified by sprinkling the contents onto water and noting whether they float. Under any conditions, I would not presume that a disintegration failure could be extrapolated to a general industry need and opportunity to make a fortune based only on dissolution test values.

Finally, for a more detailed discussion on capsule wetting problems and how to overcome them, readers are invited to read my paper[2] "Dissolution of Lithium and Magnesium from Lithium Carbonate Capsules Containing Magnesium Stearate."

Henry C. Caldwell
Research and Development
Smith Kline & French Laboratories
Philadelphia, PA 19101

Received March 15, 1979.

[1] W. E. Moore, *J. Pharm. Sci.*, 68 (2), IV (1979).
[2] H. C. Caldwell, *ibid.*, 63, 770 (1974).

Antibiotic Certification

I would like to comment on the editorial, "Antibiotic Certification—Obsolete and Archaic," in the February issue[1] of *J. Pharm. Sci.* I read it the day after retiring from FDA after 31 years plus of service in the subject field.

I agree with Dr. Feldmann and Dr. George Schneller that, when antibiotics were first marketed, they were extremely crude and that conventional methods were not applicable to assure their potency. I also agree that advances in manufacture have allowed the making of these pharmaceuticals with a degree of purity comparable to other chemicals.

I also agree that antibiotics should not be treated differently from other potent medicinal agents on the market.

I do, however, feel that to assure compliance through regular enforcement activities is not sufficient nor optimal.

Test results from postdistribution testing in the National Center of Drug Analysis have shown that some drug categories have 10–25% defective lots. None of these products was tested for sterility or absence of pyrogenicity, which could make the rate even higher.

I also know that the experience gained in the certification program has been beneficial in overall drug evaluations. Let me cite a few of many examples:

1. Expiration dates, required for antibiotics since the program began, were deemed necessary for *all* drug products in the most recent GMP regulations.
2. Metal particles were first observed in antibiotic ointments (ophthalmic), and limits for their presence are now prescribed for all drug products.
3. Full knowledge of manufacturers and their products was essential for the certification program, and Drug Registration lagged far behind in other areas.

Finally, having shown that such thorough hands-on experience does contribute to public safety and health, let me put the claim of increased cost of medicines in a proper perspective.

The certification service, which covers more positions than those used for the testing only (new antibiotic drug evaluation, inspection, *etc.*), has a budget near $6 million. This amount is about 0.3% in an industry where the total sales are estimated to be about $2 billion.

Peter J. Weiss
(Former Director, National
Center for Antibiotic Analysis, FDA)
1309 Caddington Avenue
Silver Spring, MD 20901

Received March 6, 1979.

[1] E. G. Feldmann, *J. Pharm. Sci.*, 68 (2), I (1979).