JANUARY 1979
VOLUME 68 NUMBER 1

JOURNAL OF PHARMACEUTICAL SCIENCES

The *Journal of Pharmaceutical Sciences* is published monthly by the American Pharmaceutical Association (APhA) at 2215 Constitution Ave., N.W., Washington, DC 20037. Second-class postage paid at Washington, D.C., and at additional mailing office.

Offices—Editorial, Advertising, and Subscription: 2215 Constitution Ave., N.W., Washington, DC 20037. Printing: 20th & Northampton Streets, Easton, PA 18042.

Annual Subscriptions—United States and foreign, industrial and government institutions $50, educational institutions $50, individuals *for personal use only* $30; single copies $5. All foreign subscriptions add $5 for postage. Subscription rates are subject to change without notice. Members of APhA may elect to receive the *Journal of Pharmaceutical Sciences* as a part of their annual $70 (foreign $75) APhA membership dues.

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CONSISTENCY IN STABILITY TESTING

For various reasons, we don't watch much in the way of television programs at our house, but the other evening we took in a football game. During this battle of the gridiron, one of the commercials was an advertising spot for a long-life automobile battery. The emphasis of this advertising pitch was the confidence the motorist could place in the reliability of the product to start his or her automobile "month after month after month."

To a significant extent, pharmacists, physicians, and patients expect—and even assume—that this kind of long-term potency will be found to at least a comparable degree in the drug products that they dispense, prescribe, or consume. Unfortunately, however, such faith is sometimes misplaced. Drug products generally deteriorate with time; some do so faster than others, to the point that a significant possibility may exist that the product—just as the rundown auto battery on the coldest day of winter—won't work, or do the job expected of it, when it is really needed.

Solution of this problem is complex and involves at least three broad elements: (*a*) stability testing to determine if the product deteriorates, how it does so, and at what rate; (*b*) packaging and storage conditions that can be employed to minimize instability and enhance effective shelflife; and (*c*) expiration dating to inform users how long the product can be relied upon to perform satisfactorily given the proper conditions of packaging and storage.

Over the past decade, industry, regulatory agencies, the official compendia, and the pharmacy profession have all been deeply involved in the subjects of packaging, storage, and expiration dating of drugs. Specifications have been developed and implemented for "tight" and "well-closed" containers; sharper standards have been developed for light protection; numerical definitions have been established for storage temperatures, such as "cold," "cool," "room temperature," "warm," and "excessive heat"; guidelines for expiration date timetables, and requirements as to the drugs to be covered, have been established; and so on.

However, less apparent progress has been made in reaching agreement on criteria in the first and most fundamental area; namely, how stability testing is to be conducted. Specifically, agreement is needed on uniformity of approach with regard to systematic, consistent, and standardized testing and test procedures.

But it now appears that this gap is about to be filled. At several conferences for drug industry technical and scientific personnel this past October, Food and Drug Administration spokesmen devoted their presentations to the subject of stability testing. In one instance, the FDA official predicted that FDA would be issuing stability "guidelines" within a month or two. If his prediction is accurate as to timing, the promised guidelines may have appeared before this column is published.

At another conference, a second FDA speaker focused on some specifics in describing "what FDA expects from stability testing." He stated, for example, that accelerated study data to establish a tentative two-year expiration date on a drug product should contain at least three months of storage at 37 to 40° Celsius and 75% or higher relative humidity. He also touched on the test intervals to be employed in conducting stability tests; specifically, he recommended *"at the initial date of manufacture, three, six, nine, 12, 18, and 24 months, and each year thereafter. The tentative expiry date may in this manner be extended to whatever shelflife may be justified by data from these studies."*

Enough in the way of details was provided to suggest that what FDA has on the drawing board will offer clear and understandable directions, whether or not there is agreement outside the agency as to their scientific validity in fulfilling the intended purpose.

Hence, without in any way prejudging the anticipated guidelines in this latter regard, it is welcome news that some definitive proposals are well along in the regulatory pipeline. The existence of guidelines alone should go far in resolving the present hodge-podge approach to stability testing of drug products.