the drug is at the pharmacy and in the patient's medicine cabinet. Responsible producers will generally accept for credit out-of-date goods returned by a pharmacist.

B. Therapeutic consequences of product differences

Clinicians, pharmacists and others have reported the significance—in some cases, the hazard—of changing to different brands or formulations of so-called generically identical drugs. No complete scientific study of the entire problem has been made, but published findings are persuasive indications of the risks involved in generic prescribing.

The dissolution rate of a compound may be influenced by the finished formulation, as with dicumarol tablets reported by Levy-Nelson (*Journal of the American Medical Association*, September 9, 1961) and others. Levy has also cited differences in absorption rate of spironolactone, leading to a fourfold overestimation of proper oral dosage. Similar experiences with formulations of, cortisone, prednisone, and other steroids have been reported, as well as with the antidiabetic tolbutamide in certain tablet preparations.

Probably the most telling review of this issue was that recently published by Sadove, Rosenberg and Shulman of the University of Illinois Hospital and Hines VA Hospital (*American Professional Pharmacist*, February 1965). Their experience is presented from the viewpoint of hospital staff members who are not always informed of changes made in the hospital's inventory of drugs, and who have found therapeutic variations later traced to switches among so-called "generic equivalents". They cite the marked irritancy resulting from switching to an erythromycin preparation containing a different salt; the decreased shelf life of a soluble barbiturate preparation using a different vehicle; the effect of buffering agents on local anesthetics, with marked differences in irritation, onset, and duration; the irritating consequences of a new container which used a closure high in heavy metal content; a case of idiosyncratic reaction to a test drug that unexpectedly caused a thrombophlebitis because of a different vehicle used in its preparation; and so on.

In commenting on the proposal to obtain drugs from different sources at lower cost through "generic" prescribing, they say:

"The specifications of . . . two products were identical. The clinical results were entirely different . . . in many instances it is physically impossible to compare two similar products without extensive, carefully-controlled laboratory and clinical trials. Though it is admirable to keep the cost of drugs to a minimum and it is admirable to know and prescribe drugs generically, the generically-similar product exerts, in many instances, a very different reaction from the one anticipated.

"It is practically impossible for one not skilled in the area of clinical pharmacology to know what is—and what is not—a real 'equivalent'.

"Above all, the lack of available data would preclude substitution without prior equation of the many factors which could materially alter apparent equivalency."

Their conclusion was "that generic equivalency is frequently a fable without basis in fact; chemical equivalency of the primary agent or agents is *not* necessarily clinical nor pharmacologic equivalency".

IV. RELIABILITY OF PRODUCT

The Basic principle presented here is a physician should be in a position to judge and select products on the basis of his knowledge of the reliability of the product and experience with the past performance of the producer. This method gives added protection to the patient—who should be assured that high standards of reliability are being used in prescribing and dispensing pharmaceutical products for his use—and promotes high standards of production and control that go beyond minimal enforceable levels.

Except in large and exceptionally well-equipped institutions and consulting laboratories, facilities for providing independent and reliable assays of drug quality do not exist. The resources of the average physician, pharmacist or hospital are not adequate for comparing physical qualities of competing products. Under these circumstances, the system of *responsible identification* by trademark or brand name plays an important role. It enables the physician to judge quality of product on the basis of its producer's established reputation. And since respon-