of which is most fully established and best understood." U.S.P. is now revised every five years by a committee representing the nation's schools of medicine and pharmacy, certain government agencies, medical and pharmaceutical societies, and other professional organizations.

National Formulary.—Because the U.S.P. was selective in its inclusion of drugs, restricting its coverage of those drugs the utility of which the committee considered the "most fully established," many other valuable and widely-used drugs were not included. To cover these, the American Pharmaceutical Association, a professional association of pharmacists, began publishing in 1888 the *National Formulary* (N.F.). The N.F. also has served as a guide to drugs sometimes before they appear in U.S.P., and frequently after they are removed from U.S.P.

The monographs of the U.S.P. and N.F. have been recognized in every federal law pertaining to drugs, starting with the Food and Drug Act of 1906, as legal standards. Drug products containing ingredients conforming to the criteria in these compendia have permission to carry the designation "U.S.P." or "N.F." on their labels and packages.

It is important then to understand just what these standards guarantee as well as what they do not guarantee:

1. In general, the information in these compendia is descriptive only of the chemical properties of active ingredients and adjuvants and the laboratory procedures required to demonstrate substance identity and allowable limits of purity. Significant as this information is, the chemical tests and specifications do not by themselves give full information on the pharmacologic or microbiological activity of the substances listed. Additional studies of a given drug product are still necessary to reveal the presence of certain physical characteristics such as particle size, crystal form, surface properties and other attributes which influence the biological availability of the pharmacologically active compound in question. Only an extensive and integrated physical-chemical-biological research program can determine the ultimate pharmacological action of the compound along with the characteristics which must be controlled to guarantee safety and efficacy.

Moreover, it is rare to find an active drug compound used *by itself* in therapeutic treatment of a patient. Frequently, the finished product will contain other materials to facilitate or augment the action of the principal ingredient. Often the complete preparation contains more than one active ingredient. The selection of these active ingredients and ancillary materials—in terms of their purity, function, concentration and appropriateness—is of central importance to achieve maximum efficacy and safety.

In short, the complete formulation of a finished product for use by a patient involves much more than is covered by the information in these compendia.

2. U.S.P. and N.F., stemming from an era in which the pharmaceutical formulation of active ingredients was largely performed by the local pharmacist, contain some occasional information on simple compounding. But they do not cover the complex processes of modern mass production, and they give relatively little guidance to standards in this area. Neither do they cover other considerations of great importance to modern production and distribution, such as long-term stability.

Many of these things are not covered, because in fact they cannot be reduced to precise standardization that would be meaningful with respect to all manufacturers alike. Production of quality pharmaceutical products is not entirely a science; it is also an art and craft involving experience and know-how and professional pride. The experienced industrial pharmacist calls upon skills and a background of knowledge unique to him.

3. Because of the prodigious effort required of so many authorities working on U.S.P. and N.F. revisions, these compendia are revised only at five year intervals with supplemental addenda published occasionally in the interim. However, numerous new drug products may be introduced without being included in either compilation for several years. The regulatory agencies, of course, do not depend solely on the compendia for establishing standards, and new products are monitored from the start on a product-by-product, company-by-company basis (see below). But, until a consensus is worked out within the U.S.P. and N.F. mechanism, there is no set of standards for these new items.

AMA New Drugs.—In view of these limitations, it is understandable that regulating bodies and large purchasing groups have set up other reference standards.