FIXED COMBINATION PRESCRIPTION DRUGS

The Drug Efficacy Study focused attention on questions of efficacy peculiar to combination drug products. In its 1969 *Final Report to the FDA Commissioner,* the National Academy of Science stated:

> "It is a basic principle of medical practice that more than one drug should be administered for the treatment of a given condition only if the physician is persuaded that there is substantial reason to believe that each drug will make a positive contribution to the effect he seeks. Risks of adverse drug reasons should not be multiplied unless there be overriding benefit. Moreover, each drug should be given at the dose level that may be expected to make its optimal contribution to the total effect, taking into account the status of the individual patient and any synergistic or antagonistic effects that one drug may be known to have on the safety or efficacy of the other.
>
> "On these grounds, multiple therapy using fixed dose ratios determined by the manufacturer and not by the physician is, in general, poor practice."

This general opinion of combination drugs is shared by other expert bodies. The Council on Drugs of the American Medical Association in a letter accompanying the recent first edition of *AMA Drug Evaluations* says:

> "The effects of drugs are intrinsically so complex that it is generally advisable to administer multiple agents separately in order that the dosage and frequency of administration of the individual drugs may be varied in accordance with a patient's requirements. Therefore, most fixed-ratio combinations listed are not recommended. This reflects a long-standing policy of the Council."

FDA COMBINATION POLICY

The FDA is not opposed to combination drug products; it recognizes that many are safe and effective and provide important advantages to patient and physician.

For a combination to be approved under the law there must be substantial evidence that each active component contributes to the claimed effect of the product, a requirement since 1962. If this requirement is satisfied, two or more drugs may be combined in a single dosage form when, in good medical practice, they would be given concurrently and when putting them together in the same product in no way detracts from their safety and efficacy. Such a combination product should provide appropriate dosage for a significant patient population that can be defined in the labeling. A special case of this general rule is the addition of an ingredient that enhances the safety or effectiveness of the principal active component or minimizes its abuse potential.

ORAL HYPOGLYCEMIC AGENTS

SULFONYLUREAS

Following review of the findings of the University Group Diabetes Program (UGDP) on tolbutamide by FDA and several professional groups, FDA published last year* recommendations on the use of oral agents in the treatment of diabetes mellitus. The INDICATIONS AND WARNINGS section of the labeling of all sulfonylureas is now changed to read as follows:

INDICATIONS:

"Diet and reduction of excess weight are the

* FDA Current Drug Information, October 1970.