Combining active ingredients – What you should know.

The combining of drugs without the specific approval of the FDA is subject to regulatory enforcement. The use of existing approved drugs in combination, new dosing, or a new application other than what is currently indicated by the FDA requires a New Drug Application (NDA). In order for the new combination of approved drugs to be approved, an NDA requires that clinical studies be completed and submitted to provide evidence of the safety and effectiveness of the new combination of drugs. The use of Rx drugs in an OTC is strictly prohibited. The official new drug definition is as follows:

Code of Federal Regulations
Title 21: Food and Drugs
PART 310—NEW DRUGS § 310.3 Definitions and interpretations - excerpt
As used in this part:

(g) *New drug substance* means any substance that when used in the manufacture, processing, or packing of a drug, causes that drug to be a new drug.

(h) The newness of a drug may arise by reason (among other reasons) of:

(1) The newness for drug use of any substance which composes such drug, in whole or in part, whether it be an active substance or a menstruum, excipient, carrier, coating, or other component.

(2) The newness for a drug use of a combination of two or more substances, none of which is a new drug.

(3) The newness for drug use of the proportion of a substance in a combination, even though such combination containing such substance in other proportion is not a new drug.

(4) The newness of use of such drug in diagnosing, curing, mitigating, treating, or preventing a disease, or to affect a structure or function of the body, even though such drug is not a new drug when used in another disease or to affect another structure or function of the body.

(5) The newness of a dosage, or method or duration of administration or application, or other condition of use prescribed, recommended, or suggested in the labeling of such drug, even though such drug when used in other dosage, or other method or duration of administration or application, or different condition, is not a new drug.

How are products that combine two or more drugs regulated?

A product that combines two or more drugs is regulated by **The Center for Drug Evaluation and Research (CDER). CDER** regulates combination drug products, including those that involve drugs provided in a single dosage form ("fixed combination" drug products) or as separate co-packaged drug products. 21 CFR 300.50 provides specific requirements for fixed combination prescription drug products.

You should refer any specific questions about combination drug products to the responsible reviewing Division in CDER's Office of New Drugs. If you are unsure which CDER Division would be responsible for the review of your product, or if you have a general inquiry, please contact the Regulatory Affairs Team in CDER's Office of New Drugs at (301) 796-0700.