

The most important issue affecting other combinations will be the FDA's interpretation of effectiveness. The agency insists that in order to remain on the market the combinations must be proven more effective than the individual ingredients. "This obviously means that each active ingredient be effective and make a contribution to the product's therapeutic effect," says Dr. B. Harvey Minchew, acting director of the FDA's Bureau of Medicine.

The companies will argue this standard exceeds the language of the law. As long as a combination is useful at all, they maintain, it should be legally authorized for sale; physicians can then make a choice based on their scientific knowledge and professional judgment. Both sides expect the antibiotic battle to be protracted. "It could drag on for years in the courts," worries one FDA man.

Most of the drug mixtures were first marketed many years ago when the FDA required proof only of drug safety; very few passed carefully controlled clinical trials of efficacy. Although practicing physicians now rely on many of them, the FDA must decide which are worthwhile and which are not. Delicate considerations enter in: Should the agency apply exacting modern-day standards of medical effectiveness or can it rely on the informed opinion of experts and the medical profession's acceptance?

Dr. Ley's decisions will be watched not only by industry but by pro-consumer forces, particularly Democratic Rep. L. H. Fountain of North Carolina. Mr. Fountain heads a House investigating committee that is deeply dissatisfied with some of the FDA's recent regulatory decisions. The Congressman contends the FDA has been dilatory and uncertain on protecting the public, and he will probably goad the agency if he detects what he considers reference to the economic concerns of the companies.

Along with the possibility of abandoning some popular products, the pharmaceutical companies face the burden of expensive and extensive testing to prove the efficacy of other combinations. One firm estimates that it may cost \$250,000, require as many as 300 volunteer patients and consume over a year to test just one combination. The trials are difficult because the efficacy of the mixture must be compared with that of each active ingredient. Some experts insist the task is almost impossible. "This is the kind of research that it's hard to get talented people to do," says Dr. Louis Lasagna, a Johns Hopkins Hospital drug-testing expert.