bination product. For this reason we are proposing a more vigorous type of action than we would in the case of a product where no safety question is involved. But the intention is the same, it is just a question of time.

The manufacturer of a drug falling into the "effective, but," category is told what labeling or formulation change is required to meet the recommendations of the NAS panel. Depending upon the action the firm elects to take, the drug will fall into one of the other four categories, that I have mentioned above and the appropriate time limit would apply.

If the companies do not provide the required evidence of efficacy, FDA then initiates action to withdraw approval of the New Drug Application or, in the case of antibiotics, to repeal the applicable regulations which permit the products to be marketed. Companies have the opportunity to request and show reasonable grounds for a public hearing, but whether the drug will be permitted to remain on the market during the course of a hearing depends upon the degree of hazard which its continued distribution may present to patients.

In the summer of 1968, we began to receive the NAS/NRC reports on the antibiotic combination drugs. The conclusions of the Academy panels were in line with what experts in the antibiotic field, and pharmacology textbooks, such as The Pharmacological Basis of Therapeutics by Goodman and Gilman, had been saying for years.

The Academy found the antibiotic combinations "ineffective as fixed dose combinations." Although individual active ingredients were concluded to be useful in treating specific disease entities, no greater effectiveness was shown for the combinations.

Mr. DUFFY. Doctor, if I may interrupt at this point, it is a statement such as the one you just made that gives me considerable trouble, "no greater effectiveness was shown for the combinations." Somehow I read some sort of a test of relativeness in there. And although you tell me this is not the case, perhaps you could explain to me how this is not a relative evaluation. I assume these are your words and that you are not still quoting the panel?

Dr. LEY. These are our words.

Mr. DUFFY. You are not quoting the panel?

Dr. LEY. I will be pleased to answer that. The judgment, in the case of a new drug entering the marketplace, is a question of whether a product should or should not be marketed, always involves the weighing of a benefit to be achieved from the drug versus the risks associated with the drug.

This is always true. And it is not a comparative evaluation. There are instances when we will accept drugs for marketing where the drug may have various serious side reactions in 25 to 40 percent of the patients receiving it, some of them even lethal. But if there is evidence that a drug may possibly cure cancer in 50 percent of the patients receiving it, then we feel that the benefit far outweighs the risk. In this particular case in our opinion, in the opinion of outside experts, and in the opinion of the Academy panel there is no benefit accruing to the patient from the combination of antibiotics as compared to the single preparation. The patients only effect is at least doubling of side effects. So that within this product, combination antibiotics,