Senator NELSON. Go ahead, Doctor.

Dr. LEY. Combination therapy with antibiotics began almost as soon as two such agents became available.

As new antibiotic entities were developed, their use in combination preparations was quick to follow. Shortly after streptomycin was developed, it was mixed with penicillin and recommended for use in situations in which the cause of the infection was not readily apparent. This was followed in 1950 by the use of penicillin-sulfonamide combinations for the enhancement of the antibacterial action.

In the same year, penicillin was combined with dihydrostreptomycin for use, in the words of some of the promotional material for the product:

> * * * in the treatment of peritonitis, mediastinitis, brain abscess or conditions in which the causative organisms cannot be identified * * * mixed infections, common in the respiratory or urogenital tract * * * [and] for prophylaxis in surgery * * *

I would add parenthetically that this combination has been off the market for several years.

In 1952 penicillin was marketed in combination with APC and antihistamines. For those who have not had close contact with the medical profession, APC is aspirin, phenacetin and caffeine—a sort of glorified aspirin. This combination was recommended for the relief of symptoms and the prevention of complications of the common cold and other acute upper respiratory infections.

In 1955, tetracycline was combined with vitamins.

Senator NELSON. What was the rationale of that combination?

Dr. LEY. I have no information which would lead to any statement of rationale for this combination, Mr. Chairman.

Senator NELSON. Is that still in the marketplace?

Dr. LEY. That or a similar product is currently in the marketplace, but we have recently initiated action to remove it.

Senator NELSON. In the sentence before you mentioned that in 1952 penicillin was marketed in combination with APC and antihistamines and, recommended for relief of symptoms and the prevention of complications of the common cold and other acute upper respiratory infections. By whom was it recommended for that?

Dr. LEY. By the manufacturer.

Senator NELSON. Were there any scientifically controlled studies that indicated that it had any efficacy at all for this purpose?

Dr. LEY. To the best of my knowledge, the scientific studies in support of this claim were extremely limited if present at all. I have no personal knowledge of this file, but I would point out that this was 1952, 10 years before the enactment of the Kefauver-Harris amendment.

Senator NELSON. At which time proof of efficacy was not necessary?

Dr. LEY. That is correct.

Senator NELSON. Is that still marketed?

Dr. LEY. Dr. Jennings informs me that he believes this product is still marketed today.

Senator NELSON. So 18 years have gone by, or almost 18 since it was marketed in 1952. Are you aware of any well-controlled studies as of this date that indicate that this drug has efficacy?

Dr. LEY. Absolutely none, Senator.