What the instructions did not disclose here were many serious side effects listed in the package insert. One such was that—

Indocin may cause single or multiple ulceration of the stomach, duodenum, or small intestine. There have been reports of severe bleeding and of perforation with a few fatalities.

Some other side effects listed in the package insert are drowsiness, tinnitus, mental confusion, depression and other psychic disturbances, blurred vision, stomatitis, pruritis, urticaria, angioneurotic edema, skin rashes, and edema.

In Bulletin No. 88, issued July 21, 1965, it was suggested that the detail men use this sales approach:

So, doctor, let's examine the relative lack of side effects of "Indocin."

In six out of ten patients on "Indocin," you need anticipate no adverse effects whatsoever.

In two out of three of these ten patients, some bothersome effects might occur. Bothersome is probably as severe an adjective as we can use to describe these effects because in most patients they are tolerable, and transient.

Mr. Chairman, as you know from our testimony last May there were a series of events that occurred between 1965 and 1967 which involved our dealing with Merck regarding its advertising and promotion of Indocin. The Assistant General Counsel, Food and Drugs Division, of the Deparment of Health, Education, and Welfare spoke publicly in October 1966 regarding our opinion as to the misleading nature of an Indocin advertisement which appeared in the Journal of the American Medical Association and elsewhere. Conferences were held with Mr. Henry W. Gadsden and his associates in the Merck managament in November 1966.

Senator NELSON. So there is not any requirement on the part of the American Medical Association that the drug company make claims in their advertising in compliance with approved indications by the FDA?

Dr. MCCLEERY. I don't believe that their code of approval of advertising copy includes the requirement that it conform to the package insert. They do have their own code, which they follow. And they state in each journal that it is applied to all advertising submitted to the journal before an ad is approved.

Senator NELSON. Do you mean to say that the American Medical Association, the AMA Journal, knowing the claim made in an ad in their medical journal goes beyond approved claims by the FDA is still willing to accept that ad?

Dr. MCCLEERY. I would not want to say that the staff of the journal is aware of the information in the package inserts or that they are not, or why they make the judgments they do.

Senator NELSON. So far as you know, they do not require as a matter of advertising policy that the company inserting an ad comply with FDA-approved regulations as to that drug?

Dr. MCCLEERY. So far as I know they do not, but I do not know just what their standards precisely might be.

Senator NELSON. Are you aware of the fact that any number of times ads have been put in the AMA Journal which made claims beyond approved indications by the FDA?

Dr. MCCLEERY. I am aware, Mr. Chairman, that on quite a number of occasions we have felt the necessity to charge ads as false or mis-