a. Does not represent a true statement of effectiveness of the advertised product, "Indocin:"

(1) The approved package insert for the product does not contain the promissory concepts represented by "most cases" and "predictable."
represented by the words "the first." That the firm had previous knowledge of

(2) The approved package insert provides no basis for the comparative claim represented by the words "the first." That the firm had previous knowledeg of the impropriety of the claim is evidenced by that in an earlier, similarly-appearing ad the company more cautiously excluded this phrase from the quoted clause and substituted "a" for "the first."

b. Misleads by its use out of the article's context in such a way as to present an unfair and distorted view of the drug's identity, safety and effectiveness:

(1) The authors had not used the marketed "Indocin" capsules, but instead employed an experimental tableted formulation.

(2) The authors had only 15 pertinent patients from which the represented conclusion was drawn. The reader would have been forewarned, and not overly impressed, if he had known the generalization "in most cases" rested not on a large experience from which a generalization might not be misleading, but on only a favorable result in 8 out of 15 patients.

(3) An unknown and unspecified proportion of the above results were obtained by dosages well over the 200 mg. upper limit of approved dosage, e.g., 300 mg. per day. The physician reader could not know from the ad that he could not necessarily expect similar results by employing dosages approved as safe in the drug's package insert.

c. Misleads in that it is obsolete and fails to take into account more recent, more scientific, and less salubrious opinions of the same authors available to the firm in medical literature published about one year prior to the ad. The company was aware of the more recent literature and the facts are that:

(1) In 1965, the same authors published the results of a much better controlled and double-blind study on a larger population (26 patients crossed-over on both indomethacin and the competitive product, phenylbutazone).

(2) This was a study of the response to the marketed capsules within the limits of approved dosage, the authors ended the paper with a note of thanks to company personnel "for generous supplies of indomethacin," it was published in the same journal as the first article (*British Medical Journal*, 2: 1281, November 27, 1965), and was available well before the ad was created and published.

(3) The overall patient response greatly favored the competitive product to an extent that was statistically highly significant, e.g., when the two months blind trial was over ". . . 15 patients preferred phenylbutazone, 10 found them to be equally effective, and one preferred indomethacin."

(4) The authors' conclusions re Indocin were strikingly different (the key words "predictable" and "in most cases" no longer were included) after this study, i.e., ". . . the first non-steroid to produce a measurable reduction in joint size in selected cases of active rheumatoid arthritis."

(5) It should be noted that the authors' retention and the company's use of the phrase "the first" is highly questionable.

(a) Within the authors' results in the later article they included the observation that reduction in joint size occurred not only in patients on indomethacin, but on phenylbutazone as well, and that, taking into account both the number of patients improved and the measured extent of reduction, differences were not statistically significant.

Mr. Chairman, since your Committee may wish to consider the Hart and Boardman papers in some detail, I would like to make copies of both papers available for the record. I have gone into some detail on this point because it typifies several advertising practices which we regard as seriously misleading.

Congress already has recognized that it is dangerous to promote a new drug with inadequately-based claims for greater safety and comparatively greater effectiveness than established products. Safe promotion can be based only on adequate clinical data—and then only with a complete awareness that the limited experience with the new drug, accumulated during its investigational state, may change rapidly and significantly when the drug is released for general use by physicians. Also, experience will dictate changes from time-to-time as long as the drug is marketed.

Indomethacin was recognized from the first as a drug with a significant capacity for adverse effects. We believe its promotion over the first year of its approved marketing improperly presented the drug to the medical profession—both as to the range of its effectiveness and as to the margin of its safety.