of any drug is inadequate to judge its value. It is apparent that more reliable information on effectiveness of indomethacin can be obtained from the third group, the controlled studies."

Four independent, well-controlled studies have shown that indomethacin is not more effective in rheumatoid arthritis than is aspirin, which is still the drug of choice according to the AMA.

The third problem is the use of euphemistic language in warnings and contraindications when strong language is required. The reviewing medical officer recommended that the following wording be included as a contraindication: "Indocin should not be administered to children."

This is clear and strong, but this essential warning ended up as follows:

"Since the experience with Indocin in children is limited, it is recommended that this drug should not be administered to pediatric age groups until the indications for use and dosage have been established."

There is quite a difference in clarity and conciseness between the version recommended by FDA's medical officer and the one adopted by the firm and finally approved by the FDA. The result was that the message did not get through. In a poll by Modern Medicine which was reported in its August 1, 1966 issue, almost 10% of the pediatricians who reported treatment of rheumatoid arthritis prescribed indomethacin during a thirty day period in the first year of its marketing life. During this time (first year of its marketing life by July 1966), five deaths in children being given this drug were reported. Up to the beginning of 1968, 9 deaths in children were reported. A stronger warning was adopted later at the insistence of the FDA.

Why didn't the FDA insist on a strong warning in the first place? The reason given by Dr. Hodges was that there wasn't enough data to show that it was dangerous or safe for children. Yet, even though the statute insists that substantial evidence of safety and efficacy should be presented for uses of a drug, it appears that the FDA modified the requirements and used soft warnings for children because the drug was tested in only 55 children and there was not enough evidence to show lack of safety and efficacy.

The fourth problem is that of the overpromotion of Indocin. Here is a drug with very limited uses and yet, it is reported that it has a wholesale sales volume of over $40 million per year and is one of the 200 most frequently prescribed drugs.

The New Drug Application for Indocin was originally approved for use in only the following 4 conditions:

(*a*) Rheumatoid arthritis.
(*b*) Rheumatoid (ankylosing) spondylitis.
(*c*) Degenerative joint disease (osteoarthritis) of the hip.
(*d*) Gout.

The most frequently occurring illness is Rheumatoid Arthritis, for which, according to AMA's NEW DRUGS, aspirin is the drug of choice, and Indocin should be used only when aspirin fails or cannot be used.

The FDA testified that Indocin is being used beyond its approved indications and that some physicians regard the drug as a general purpose analgesic, antipyretic, anti-inflammatory agent and the 1966 promotion of the drug featured this effect.

The fifth problem is that of false and misleading claims which, the FDA testified, have been made for this drug and which necessitated a remedial "Dear Doctor" letter and a Bureau of Medicine recommendation of prosecution under the Food and Drug Act.

I am also inserting at this point a staff memorandum dealing with Merck's advertisement of Indocin in the British Medical Journal of 1967–68.

(The memorandum follows:)

MEMORANDUM

To: Senator Gaylord Nelson, chairman, Monopoly Subcommittee
From: Benjamin Gordon, staff economist
Subject: Comparison of ads for Indocin in the British Medical Journal and the Journal of the American Medical Association, 1967–68

None of the advertisements for Indocin in the British Medical Journal (BMJ) in the years 1967–68 included any prescribing information. Some of these ads say, "Detailed information is available to physicians on request." Others do not even make this reference to indicate the desirability of obtaining information on the drug prior to prescription and administration.