Commissioner KENNEDY. Yes; that is approximately correct with one reservation. Recall that we are talking here about patient prescriptions. The index we are reporting here is an index based on retail pharmacy sales. There obviously is an additional amount of use in hospitals. That use might tilt the statistics a little bit but I think not very much.

Now, as I mentioned NAS–NRC reviewed propoxyphene products for efficacy in the late 1960's. The chairman of the NAS–NRC Drug Efficacy Study Group Panel on Drugs for Relief of Pain was Louis Lasagna, an expert in the field of clinical pharmacology and analgesia.

A 1966 article review by William T. Beaver, another expert in the field of analgesia, concluded the following:

> In summary dextropropoxyphene is a mild oral analgesic which has proven superior to placebo in doses of 65 milligrams but which is of questionable efficacy in doses less than 65 milligrams. The drug is definitely less potent than codeine, the best availalbe estimates of the relative potency of the two drugs indicating that dextropropoxyphene is approximately one-half to two-thirds as potent as the latter drug. Likewise, dextropropoxyphene in 32-milligram to 65-milligram doses is certainly no more, and possibly less effective than the usually used doses of aspirin or APC.

FDA announced the results of the DESI review in 1969. The announcement described the indications for which the drugs were deemed effective—for the relief of mild to moderate pain.

Reservations about the efficacy of propoxyphene continued to be expressed during the 1970's. For example, R. R. Miller and associates in 1970 reviewed all available double-blind studies of propoxyphene and concluded that "* * * It is no more effective than aspirin or codeine and may even be inferior to these analgesics."

C. G. Moertel and associates in a 1972 double-blind study of single doses of propoxyphene, aspirin, and other oral analgesics in patients with cancer, were unable to show that even 65 milligrams of propoxyphene was significantly superior to placebo. In this study, aspirin was the most effective analgesic tested.

R. R. Miller in a second review in 1977 concluded that propoxyphene was no more effective than placebo in three studies, whereas in five others propoxyphene was not more effective than other analgesics.

On the other hand, Sunshine and others, in a 1978 study, found propoxyphene napsylate at 200 milligrams, twice the recommended dose, to be significantly better than placebo. The lowest dose used—50 milligrams—was only slightly better than placebo but the usual dose of 100 milligrams was not tested.

Mr. Chairman, in your letter of invitation you asked me to comment on the reasons for the sustained popularity of propoxyphene as an analgesic in view of its limited effectiveness. The answer to this question is complex and involves a number of factors.

First, I think it is important to point out a significant number of people—typically 30 to 35 percent—in clinical trials on analgesics obtain pain relief from placebo.

Recent research suggests that this placebo response is due to activation within the brain of the same neural receptors that are affected by narcotics. The pain relief obtained is just as real, and may be just as great in many instances, as that provided by drugs. The placebo response may be enhanced by encouragement from the prescribing physician. Thus, any prescription analgesic is likely to offer pain