

Senator NELSON. I assume the changes were significant or you would not have bothered to make them.

Commissioner KENNEDY. Correct, sir. Thank you. Darvon, generically propoxyphene hydrochloride and combinations with aspirin, phenacetin, and caffeine, known as Darvon Compound, Darvon Compound 65, were first marketed in 1957 by the Eli Lilly & Co. after approval on the basis of safety alone.

After passage of the Drug Amendments of 1962, a panel of experts established by the National Academy of Sciences National Research Council reviewed propoxyphene products and concluded they were effective for the relief of pain. This group of drugs was then approved for effectiveness by FDA in 1969.

Senator NELSON. May I ask a question? You say "reviewed propoxyphene products." You are referring in that case to the combinations with acetaminophen and APC, as well as propoxyphene alone?

Commissioner KENNEDY. Only Darvon at that time and Darvon Compound and Darvon Compound 65. The new propoxyphene products containing the hapsylate salt of propoxyphene rather than the hydrochloride either alone or in combination with acetaminophen (Darvocet-N), (Darvon-N) or aspirin (Darvon-N with ASA) were approved and marketed in 1972. The term propoxyphene products, plural, refers to just propoxyphene in various dosages and terms.

Senator NELSON. Were these conclusions of the NRC based upon double-blind studies or review of the literature?

Commissioner KENNEDY. They were based entirely on review of the literature at the time. The NRC committees did no new studies of their own.

Senator NELSON. But they did review a good many of the drugs required to produce controlled studies to prove efficacy. You are saying they did not in this case?

Commissioner KENNEDY. That is right, they did not.

Senator NELSON. But in many drugs you have required that.

Commissioner KENNEDY. Yes; that is correct. For many years, propoxyphene-containing products have been among the most frequently prescribed prescription drugs in the United States.

I am putting up a chart for people who cannot see the chart in my statement so they can look at appendix A. Both the chart and the appendix show the number of outpatient prescriptions totaling over 39 million annually in those years, since 1964.

Products containing propoxyphene peaked in popularity from 1973 to 1975 with retail prescriptions totaling over 39 million annually in those years. While the total number of prescriptions has dropped to some 31 million for 1978, based on the projection of 9 months data, propoxyphene products are still very popular.

You will see that Darvocet-N, the napsylate compound ranked 12 and Darvon itself 93 and there is a point to be made about that just in passing. Something like 80 percent of the propoxyphene used out there is used in its various combination forms with aspirin, acetaminophen and whatever and when we are talking about use in the real world, we are talking primarily about combination use.

Senator NELSON. This is what I wanted to clarify for the record. Your chart shows the ranking of these four; three of them in combi-