labeling of propoxyphene products which occurred in 1972. In 1976, I assisted the FDA in revising the propoxyphene labeling to reflect increased medical awareness (Finkel et al., 1976; McBay and Hudson, 1975) of the incidence of fatal overdose with propoxyphene alone and in combination with other central nervous system depressants.

I subsequently served as a FDA consultant to their Controlled Substances Advisory Committee in the matter of the advisability of scheduling Darvon under the Controlled Substances Act. The committee recommended placing propoxyphene products in schedule IV. The Department of Health, Education, and Welfare concurred in this recommendation, and, in February 1977, the Drug Enforcement Administration issued an order to that effect. Since 1976, I have continued to follow the literature on propoxyphene, in part because I am chairman, Advisory Panel on Analgesics, Sedatives and Anti-inflammatory Agents for the 1975–80 revision of the United States Pharmacopeia.

Now, concerning the general pharmacologic properties of propoxyphene, propoxyphene or dextropropoxyphene (Darvon) is structurally related to the potent narcotic methadone and is itself a narcotic in all pharmacologic and toxicologic respects.

It produces the full spectrum of pharmacologic effects in animals and man characteristic of the narcotics, and these effects are selectively reversed by the specific narcotic antagonist naloxone. Quantitatively, however, propoxyphene is substantially less potent on a milligram basis than narcotics such as morphine, hydromorphine (Dilaudid) and methadone.

In addition, high doses of propoxyphene have certain excitatory properties not noted with most other narcotics which, while they tend to discourage deliberate abuse of propoxyphene, make convulsions a common feature of propoxyphene overdose in addition to the usual narcotic overdose manifestations of respiratory depression and coma.

In relation to propoxyphene's analgesic efficacy, which seems to be one of the major subjects that has been talked about thus far in these hearings, on reviewing those studies which have appeared in the interim, I find little necessity to modify my evaluation of the efficacy of dextropropoxyphene which appeared in 1966 which I presented in my testimony on November 24, 1970.

Propoxyphene compared to placebo: In addition to the studies cited in my 1966 review, eight additional controlled analgesic studies have confirmed that a 65 milligram dose of propoxyphene hydrochloride or the equivalent 100 milligram dose of propoxyphene napsylate is statistically significantly superior to placebo in relieving postoperative and trauma pain, postpartum uterine cramping, postpartum episiotomy pain, pain subsequent to oral surgery in outpatients and chronic pain of mixed etiology.

A couple of studies have also succeeded in demonstrating a statistically significant difference between placebo and either 32 milligrams of propoxyphene hydrocholoride or the equivalent 50 milligram dose of propoxyphene napsylate; but these obviously represent threshhold or marginally effective doses of propoxyphene, the analgesic effect of which doses can only very rarely be measured in even the most sensitive analgesic assays.