Dr. ADRIANI. I think it is 30 milligrams, I am not sure.

Senator BUMPERS. Thank you.

Senator NELSON. Thank you, Dr. Adriani.

Dr. ADRIANI. There is a typographical error in my statement. There are 32 milligrams of caffeine and in the Darvon compound I have 32 or something like that.

Senator NELSON. The printed record will be corrected to show 32 milligrams in your prepared text, which will be printed in full in the record at this point.

[The prepared statement of Dr. Adriani follows:]

STATEMENT OF JOHN ADRIANI, M.D., PROFESSOR PHARMACOLOGY AND ANESTHESIOLOGY, LOUISIANA STATE UNIVERSITY SCHOOL OF MEDICINE; CONSULTANT PHARMACOLOGY AND ANESTHESIOLOGY, DEPARTMENT OF HEALTH AND HUMAN RESOURCES OF LOUISIANA, NEW ORLEANS, LA.

DEXTROPROPOXYPHENE (DARVON)

Mr. Chairman: I appeared before this Committee on November 24, 1970, and testified on matters pertaining to the efficacy of certain internal analgesics, one of which was propoxyphene, the subject of today's hearings. Propoxyphene was introduced and marketed under the trademark name Darvon by the Lilly Laboratories in 1955. There has been doubt concerning the effectiveness of this drug as a "mild" analgesic since its introduction as a prescription item for oral use. Parenteral dosage forms are not available. Propoxyphene is chemically allied to methadone, a narcotic that is equipotent to morphine on milligram for milligram basis and with approximately the same degree of liability for causing physical dependence. Propoxyphene was described as a non-narcotic analgesic as far as therapeutic efficacy and addiction liability was concerned. It did not appear to have the propensity for causing physical dependence in nondrug dependent persons. It was known that it provided some degree of relief from withdrawal symptoms in persons manifesting physicial dependence to narcotics. The National Academy of Sciences—National Research Council Review Panel on effectiveness of drugs for the relief of pain, found propoxyphene to be less effective than is implied by claims of the manufacturer. On a milligram for milligram basis, propoxyphene was alleged to be equal to codeine in intensity and duration of analgesic action. The Panel found, however, that 65 mg of propoxyphene was equivalent to approximately 30–40 mg of codeine in analgesic potency. The Panel also concluded that 32 mg propoxyphene, in most instances, was no more effective than a placebo. Claims that propoxyphene has fewer side effects than codeine cannot be justified if effective doses of the two drugs are compared.

Beaver, in reviewing the literature on mild analgesics (Beaver, A.P.: American Journal of Medical Sciences 251, p. 576. 1966) noted that studies comparing dextropropoxyphene with aspirin or APC, propoxyphene 32.5 (65 mg) showed it to be consistently inferior to aspirin 325 mg or 650 mg or APC (Aspirin Phenacetin Caffeine) mixture. No convincing evidence has been introduced since this review that any way establishes the superiority of 65 mg doses of propoxyphene over 2 tablets of either aspirin or APC compound used alone.

Propoxyphene is generally combined with other analgesics. Apparently, it is not able to "stand alone" as an analgesic and must be fortified with other drugs to be effective. The original Darvon compound preparation contained 32 mg of propoxyphene, 327 mg of aspirin and 165 mg of phenacetin and 32 mg of caffeine. Darvon compound (65) contained the same amount of aspirin, phenacetin and caffeine and double the amount of propoxyphene. Darvon ASA contains 65 mg of propoxyphene and 325 mg of aspirin, the equivalent of 1 aspirin tablet. Other combinations are available also but none appear to have any superiority to the combination with aspirin. These added drugs were included in the form of pellets in the propoxyphene (Darvon) capsule.

Although there has been doubt about its effectiveness, little has been said about the safety of the drug. From time to time isolated case reports have appeared in the literature of fatalities from propoxyphene when doses in excess of 100 mg were ingested. Recently there has been a marked upswing of the number of adverse reports from the effects of the drug and reports of fatalities from