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[Docket No. 77N-0266; DESI 10996]

PROPOXYPHENE

PUBLIC HEARING

Agency: Food and Drug Administration (FDA).

Action: Notice of Public Hearing.

Summary: The Commissioner of Food and Drugs announces that FDA will hold a public hearing to receive information and opinions from interested persons on the issues of the safety and effectiveness of propoxyphene-containing drug product and whether additional regulatory action is needed in regard to these drugs. The hearing is part of an extensive review of propoxyhene undertaken at the direction of the Secretary.

Dates: The public hearing will be held on April 6, 1979, at 9 a.m. Written or oral notices of participation are due no later than March 23, 1979.

Address: The public hearing will be held at the Snow Room (Room 5051), HEW North Building, 330 Independence Avenue SW, Washington, D.C.

Written notices of participation should be sent to the Hearing Clerk (HFA-305), Food and Drug Administration, Department of Health, Education, and Welfare, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857. Oral notices of participation will be accepted from persons who find insufficient the time available for submitting a written notice.

For further information or to give a notice of appearance orally, contact: Robert Nelson, Bureau of Drugs (HFD-120), Food and Drug Administration, Department of Health Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301-443-3800.

Supplementary information:

TERMINOLOGY

In this notice, DPX, the abbreviation for the dextrorotatory insomer (dextropropoxyphene) to which is attributed the analgesic effect of propoxyphene, is used to denominate propoxyphene-containing products generally. In some instances, the notice clearly specifies individual drug products or groupings of drug products containing DPX (e.g., combination drugs, or the drugs in the hydrochloride or the napsylate salt forms).

BACKGROUND

Propoxyphene (NPX) hydrochloride alone and in combination with aspirin, phenacetin, and caffeine was first marketed in 1957 by Eli Lilly & Co. (hereinafter referred to as "Lilly"). Under the law applicable at that time, the drug products (Darvon, Darvon Compound, and Darvon Compound-65) were approved for marketing based solely on evidence of safety. When demonstration of efficacy became a requirement in 1962, DPX was among the drugs reviewed for FDA by the National Academy of Sciences/National Research Council (NAS/NRC). In the Federal Register of April 8, 1969 (34 FR 6264), FDA announced the conclusion that DPX products (with the exception of the 32-milligram (mg) dose of propoxyphene hydrochloride) were effective "for the relief of mild to moderate pain."

In 1972, because of misleading claims made by Lilly, FDA required the firm to issue the following statements to physicians in a "Dear Doctor" letter: "There is no substantial evidence to demonstrate that 65 milligrams of Darvon is more effective than 650 milligrams of aspirin (two 5-grain tablets), and the preponderance of evidence indicates that it may be somewhat less effective. The preponderance of evidence indicates that Darvon is somewhat less potent than codeine. The best available evidence is that Darvon is approximately two-thirds as potent as codeine. Furthermore, there is no substantial evidence that, when administered at equianalgesic doses, Darvon produces a lower incidence of side effects than codeine."

In the Federal Register of December 27, 1972, (37 FR 28526) FDA announced a change in the labeling requirements for these products and acknowledged the limited effectiveness of the 32-mg dose of DPX hydrochloride in that: "recent studies have shown that this dose does have an analgesic effect in a certain fraction of the population with mild to moderate pain. While 32 milligrams of proproxyphene is a weak analgesic dose, only the physician attending a par-