ticular patient can determine by titrating the dose whether that individual patient is one of the minority who will respond adequately to the 32-milligram dose, or is one of the majority who will require at least 65 milligrams to achieve adequate analgesia."

Because of the abuse potential of DPX-containing products, they were placed in Schedule IV of the Controlled Substances Act in 1977. In an April 7, 1978 Federal Register notice (43 FR 14739), FDA revised labeling requirements to add warnings on adverse reactions; warnings on interaction with alcohol, tranquilizers, sedative/hypnotics, and other central nervous system depressants; and information on management of overdosage.

In the early 1970's after approval of new drug applications (NDA's) based on bioavailability studies, Lilly marketed new products containing the napsylate salt of DPX, either alone (Darvon-N) or in combination with acetaminophen (Darvocet-N) or aspirin (Darvon-N with ASA).

Since then, more than 50 abbreviated new drug applications (ANDA's) have been submitted and approved for over 30 "me-too" manufacturers of DPX products marketed under a variety of trade names.

Through the years, DPX-contining products have become among the most frequently prescribed prescription drugs in the United States. They peaked in popularity from 1973 to 1975, when retail prescriptions totalled over 39 million annually. While the total number of prescriptions has declined in recent years (total for 1978 is 31 million), DPX products are still very popular. among the 200 most prescribed drugs for the years 1972 through 1977 is shown in Table 1.

TABLE 1.—RANK AMONG THE TOP 200 MOST PRESCRIBED DRUGS [1]

	1972	1973	1974	1975	1976	1977
Darvocet-N (propoxyphene napsylate with acetaminophen)		87	24	20	18	[2] 12
Darvon 32 mg and 65 mg (propoxyphene hydrochloride)	35	47	68	71	78	93
Darvon Compound-65 APC	2	3	3	6	15	20

[1] Source: National Prescription Audit, IMS America.

[2] Darvocet-N was divided into two groups (50 and 100) for the year 1977 only. The 1977 rank for Darvocet-N 100 was 18; for Darvocet-N 50 it was 169. The 1977 ranking of 12 for Darvocet-N was derived by aggregating data for Darvocet-N 50 and 100, in order to simplify the comparison with previous years.

RECENT DEVELOPMENTS

During the 1970's clinical experience with DPX and publication of additional studies on the drug have given rise to some questions about its safety and efficacy. The reservations that FDA expressed in requiring certain labeling changes, described above, exemplify one result of such developments; another is the Drug Enforcement Administration's placement of DPX products in Schedule IV of the Controlled Substances Act.

On November 21, 1978, the Secretary of Health, Education, and Welfare was petitioned by the Health Research Group (HRG), Washington, D.C., to suspend approval of the NDA's for DPX-containing products under section 505(e) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 355(e), on the ground that the continued marketing of these drugs represents an imminent hazard to the public health. Alternatively, HRG requested that if the Secretary did not suspend approval of the NDA's, he would support HRG's petition to DEA that DPX be rescheduled as a Schedule II narcotic under the Controlled Substances Act (Ref. 1).

In response to the request of the Secretary for recommendations concerning these issues, FDA reviewed the following: Data cited by HRG; other available reports of studies on DPX in the scientific literature; information available from the Drug Enforcement Administration's Drug Abuse Warning Network (DAWN); data submitted by Lilly on fatalities resulting from DPX products; information presented before the Monopoly and Anticompetitive Activities Subcommittee of the Select Committee on Small Business, U.S. Senate, on January 31, February 1 and 5, 1979; and information considered at FDA's Drug Abuse Advisory Committee meeting on February 13, 1979.

On February 15, the Secretary announced his decision that evidence currently available does not warrant his invoking the imminent hazard provision of the Act. However, he directed FDA to take several specific actions to warn the public