3. How does propoxyphene cause death? Is it primarily by depressing respiration, or is there a previously unrecognized toxic effect on the heart?

4. Is there scientific evidence that propoxyphene adds significantly to the effectiveness of aspirin or other pain relievers in combination products?

The public hearing and FDA study will seek the best answers we can develop to these questions. Meanwhile, as the result of the actions I have announced today, the doctors and people of this country will be warned that propoxyphene should be taken only with care.

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

In re Petition to Suspend New Drug Applications for Propoxyphene

OFFICE OF THE SECRETARY

I. Issue

The issue presented to me is whether, as currently labeled and distributed, propoxyphene, a drug for use in the relief of pain, should be declared an "imminent hazard" under section 505(e) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 355(e), and approval of the new drug applications for the drug summarily suspended prior to the initiation of the ordinary procedures for withdrawal of approval of those applications. Thus, I must decide whether there is now sufficient evidence available showing that the continued use of propoxyphene constitutes so serious a threat to public health as to warrant an interim suspension of general distribution of the drug pending initiation and completion of the procedures to determine whether propoxyphene should be removed permanently from the general market.

This proceeding was initiated by a petition filed by the Health Research Group (HRG), a consumer advocacy group concerned with health matters. HRG also petitioned the Department of Justice to impose new restrictions on the production and dispensing of propoxyphene under the Controlled Substances Act, 21 U.S.C. 801. In its petition to me, HRG requests that, in the event I do not suspend marketing of the drug, I support the HRG petition at the Department of Justice.

II. Background

Propoxyphene hydrochloride, alone or in combination with aspirin, phenacetin, and caffeine, was first approved and marketed in 1957. The most widely sold brand names of propoxyphene products are Darvon, Darvon Compound, and Darvon Compound-65, all manufactured by Eli Lilly and Company.

The original approval of propoxyphene was on the basis of safety only. After the enactment of the Drug Amendments of 1962, the efficacy of propoxyphene products was reviewed by the National Academy of Sciences/National Research Council, which concluded that the products are effective for the relief of pain. In the early 1970's, the Food and Drug Administration approved as safe and effective additional products manufactured by Eli Lilly and Company containing propoxyphene: the napsylate salt of propoxyphene either alone (Darvon-N) or in combination with acetaminophen (Darvocet-N) or aspirin (Darvon-N with ASA). All propoxyphene products are "new drugs" and are subject to new drug application (NDA) requirements.

In 1977, through joint activity by the Department of Health, Education, and Welfare and the Department of Justice, all products containing propoxyphene were controlled under Schedule IV of the Controlled Substances Act for the first time, because of their potential for abuse. This action limited refills on propoxyphene prescriptions, and imposed certain labeling and recordkeeping requirements on manufacturers. In 1978, FDA revised the labeling of these products to contain additional warnings on adverse reactions, particularly adverse interactions of propoxyphene with alcohol, tranquilizers, sedative-hypnotics, and other central nervous system depressants; and to advise on management of propoxyphene overdoses.

III. History of this Petition

On November 21, 1978, Sidney M. Wolfe, M.D., Director of HRG, petitioned me to take one of two actions:

(*a*) "Ban immediately the marketing of propoxyphene as an imminent hazard under the Food, Drug, and Cosmetic Act, 21 U.S.C. § 355(e), and make it avail-