

Dr. WOLFE. That is right.

In doing that, for Darvon, because it was a pre-1962 drug, the National Academy of Sciences, particularly for the 32-milligrams, the smaller size Darvon which was then widely used, found that it really was not much better than a placebo.

Mr. TWARDY. But the FDA did allow Darvon to stay on the market, and gave a blanket approval to the effectiveness of the 65-milligram dose, did it not?

Dr. WOLFE. That is correct, because, as I stated, as long as it could be shown that that form, the 65-milligrams, was better than a placebo, that would meet the test of effectiveness.

Mr. TWARDY. So in short, the FDA did deem the 65-milligram dosage of Darvon to be effective?

Dr. WOLFE. Right, more effective than a placebo, and therefore meeting the law.

Mr. TWARDY. I might have missed this, but to whom is the advertisement that Lilly has here for Darvon circulated? Is it to the public as a whole or just to doctors?

Dr. WOLFE. There is an ad that appears—I have seen that same ad in five or six medical journals in the last month or so.

Mr. TWARDY. But it is circulated then to the medical profession?

Dr. WOLFE. That is right. I think that if physicians saw this kind of ad, if patients saw that kind of ad, they would be much more inclined to use Darvon.

Mr. TWARDY. That is all; thank you.

Senator NELSON. Thank you, Dr. Wolfe.

Dr. WOLFE. Thank you.

[The prepared statement of Dr. Wolfe follows:]

TESTIMONY OF SIDNEY M. WOLFE, M.D., PUBLIC CITIZEN'S HEALTH RESEARCH GROUP

Senator Nelson and members of the subcommittee: Thank you for the invitation to discuss our petitions to ban or severely restrict the use of propoxyphene, most commonly known as Darvon.

In the November petitions, we pointed out that Darvon led all other prescription drugs in the annual number of drug deaths and, as was pointed out by N. Kozel of the National Institute for Drug Abuse, Darvon is probably related to even more deaths per year than heroin and morphine combined.

Since the original petitions we have obtained more information—particularly about the toxicity in animals and humans of propoxyphene and especially its main metabolite, norpropoxyphene. We have also learned that a substantial portion of Darvon deaths are not due to suicide but are accidental and often occur in people chronically using the drug for pain or, in some cases, for its euphoric effects.

PROPOXYPHENE AND NOR-PROPOXYPHENE BLOOD LEVELS IN CHRONIC DARVON USERS

When people use propoxyphene (PX), the drug is metabolized by the liver to nor-propoxyphene (NPX). Whereas the $\frac{1}{2}$ life of PX in the blood is only 12 hours (meaning the time it takes for the drug to fall to half of its highest level), the main metabolite, NPX, stays around much longer, having a half-life of 38 hours. Because of this long half-life, people using Darvon on a chronic basis accumulate large amounts of the metabolite NPX in their blood.

Much of the early human toxicology on PX looked just at blood levels of the drug itself and unless the blood level was 1 or 2 micrograms per milliliter (ml.) of blood, or more, the death was often not attributed to PX. In cases of