

changes have been reported in some cases of propoxyphene overdosage in humans, it has been suggested that the local anesthetic effect of norpropoxyphene (and propoxyphene) might contribute to the toxicity or lethality of propoxyphene overdose by a deleterious effect on cardiac conducting tissue.

The effects of propoxyphene and of norpropoxyphene on cardiac conduction have been studied in vivo and in vitro in laboratory animals, and these studies are reviewed in the Blue Book that you received earlier. Therefore, I will not review the animal data at this time. Much of the knowledge concerning propoxyphene and norpropoxyphene pharmacology has come, understandably, from Lilly research. Lilly researchers have published their results regularly in refereed scientific journals, and this work has been confirmed and extended from time to time by other investigators, notably by Amsterdam and by Lund-Jacobson. References to the latter are cited in your Blue Book.

During the recent Senate hearings on propoxyphene, Dr. Lewman, the medical examiner from Oregon, stated that in patients taking propoxyphene every few hours, "The propoxyphene is being rapidly metabolized while the toxic [italics added] nor-propoxyphene metabolite is constantly building up because of its long half life." What Dr. Lewman fails to