Dr. BEAVER. Would not?

Senator NELSON. Would not.

Dr. BEAVER. That is correct. What I am saying here is that there are a few situations where you would want to give either codeine or propoxyphene alone.

To my view, the major use of either of these drugs is in combination with drugs such as aspirin or acetaminophen and actually the drugs aspirin and acetaminophen are the first line drugs among the mild analgesics, and then one can add narcotics to them.

Now, getting back to my sixth point, controlled clinical trials of analgesics invariably compare the *average* responses of *groups* of patients to the various treatments.

While the average relative performance of various analgesics is the best predicator of how the generality of patients with pain will respond, individual patients may, for reasons which we simply do not currently understand, derive a better analgesic effect from a drug which on the average is less effective than another.

Controlled clinical trials of analgesics are not currently designed to explore this phenomenon, and the determination of the optimal analgesic regimen for any given patient must ultimately be based on the empirical observation of the effect of various analgesics in that patient.

It is, therefore, in the patient's interest to have as wide a variety of effective analgesics available as possible, even though some of these may on the average be less efficacious than others.

Item No. 7—virtually all controlled clinical trials of analgesics, including propoxyphene, have involved comparison of single administrations of various analgesics; however, in the practice of medicine, most patients receive not a single dose but repetitive doses of analgesic drugs for the control of their pain.

While up to this time the results of single administration studies have seemed to constitute reasonably accurate predicators of the relative performance of analgesics when administered repetitively—if one keeps in mind the impact of the development of tolerance to narcotics—it is conceivable that repeated administration of some analgesics results in a higher level of efficacy than would be predicted on the basis of single-dose administration.

Propoxyphene has a substantially longer half-life in the blood than other mild analgesics such as codeine, acetaminophen or aspirin. When administered every 4 to 6 hours, as mild analgesics usually are, there will be a significantly greater cumulation of propoxyphene levels than with alternative mild analgesics.

We do not currently understand the relationship between the blood level of an analgesic and the analgesic effect experienced by the patient, but a plausible argument can be made on the basis of blood level data that one might expect greater analgesia after a few repeated doses of propoxyphene relative to alternative mild analgesics than is, in fact, seen in single administration studies.

Unfortunately, few analgesic studies of repeated dosing have been done to examine this hypothesis, and those that have been done are difficult to interpret. It is, therefore, possible that practitioners empirically find that propoxyphene products are more effective in regular