

So Darvon standing alone was, at best, a weak analgesic with some advantage over sugar pills. Aspirin with a full dose of Darvon in his double-blind studies provided essentially no improvement in pain relief.

Now, if the argument of those who advocate the use of Darvon or prescribe it is that they are prescribing it because their patient is allergic to aspirin or acetaminophen, I suppose it might be a justifiable reason. But about 80 percent of what they are prescribing is propoxyphene with aspirin anyway, so for all of those prescriptions the argument about allergy or gastrointestinal bleeding certainly makes no sense.

Commissioner KENNEDY. That is correct.

Senator NELSON. Now, if these studies by Dr. Moertel are correct that Darvon added to aspirin has no additional significant effect why does not the FDA prohibit the combination?

Moertel's studies indicate that adding Darvon to aspirin does not increase effectiveness. Why then permit the patient to be exposed to an additional drug with the side effects it has if, in fact, it is not additive or synergistic in combination?

Commissioner KENNEDY. Let me say two things in response to that, Mr. Chairman.

First, the Moertel study was the only one available, or if all studies on this point agreed, we would not be in difficulty but as I tried to indicate in my testimony the results of controlled clinical trial on the effect of analgesics are plagued with inconsistency between trial and it is a very difficult matter to decide.

Senator NELSON. There may very well be studies I have never heard of, but in the testimony and in the literature and in the references I have looked at from the hearings we had 8 years ago, and in the testimony thus far, I do not see any double-blind studies that show that Darvon added to aspirin is more effective than aspirin alone.

Have I missed any?

Commissioner KENNEDY. Well, we will review those studies. I do not know of any specifically, Senator Nelson. The point I was trying to make rather is that studies on Darvon compound alone and on Darvon in various combinations it comes out differently in terms of its relative efficacy in different people's hands.

Moertel's studies only covered cancer patients. For example, one might expect differences between that type of study done on patients with other sorts of pain.

My point is not that there is evidence that this particular compound is more effective than either ingredient alone, but that there is a lot of ambiguity in clinical trials in this whole area and I was going to go on and say that FDA is going to review the evidence on these products over the next year.

It may very well be that we will find that some of the combinations are not effective, but it will be a difficult business to sort out.

Senator NELSON. But the FDA has taken a very correct and strong stand on the 1962 amendments, which require proof of efficacy based on well-controlled scientific studies. Everybody who has testified and who is an expert in this field, of course, has said there is a great deal of subjectivity in judging pain relief.