to ask the Bureau whether at that time in history that standard was being applied to all combinations.

Senator LEVIN. I would like to pursue that line of questioning, Mr. Chairman, if I could.

Was that in the regulation?

Commissioner KENNEDY. Now, having refreshed my knowledge of history or rather gotten for the first time the information I can tell you.

In 1972 what happened, Senator, was that a new salt of Darvon, the napsylate was marketed. The Bureau's policy at the time was that a new salt, but with the same active ingredient all they needed to show is bio-availability. That is the same amount gets into the bloodstream in the same period of time so that as much active ingredient is mobilized and available to do what it is going to do. So the napsylate salt was approved in 1972 but without any new clinical trials.

The combinations of the napsylate salt with aspirin and acetaminophen were not new combinations; they were combinations of a new salt but they did not have to meet those clinical trials. In fact, the efficiency studies that supported the introduction of that new salt in 1972 were the same ones that had actually supported the efficacy review that had permitted the continued marketing of those combination products in 1969.

Senator LEVIN. In 1977 I understand that the propoxyphene was placed on schedule IV.

Commissioner KENNEDY. That is correct.

Senator LEVIN. Did the manufacturers in general, or the specific manufacturer of Darvon agree to that or opposed to the schedule?

Commissioner KENNEDY. They did not oppose it.

Senator LEVIN. Do you have the power to require the manufacturer of Darvon to put on the label the same thing that he was required to do in 1972 and that is to state in a letter to physicians at that time that there was no evidence to demonstrate that 65 milligrams is more effective than 650 milligrams of aspirin?

Commissioner KENNEDY. We probably could.

Senator LEVIN. Do you think it is appropriate to have that on the label?

Commissioner KENNEDY. We would have to support it convincingly and quite possibly convince a judge.

Senator LEVIN. Is that your standard proof, "convincingly"?

Commissioner KENNEDY. It is not our standard but quite frequently or not infrequently when we propose labeling changes that a drug's sponsor does not agree with us, or finds it unreasonable, we find ourselves litigating the matter.

Senator LEVIN. Is that the standard used by the courts have you found?

Commissioner KENNEDY. Well, I would think, in general, I think it has been our experience if we can show a court that the scientific evidence with regard to efficacy or safety is on the side of the statement that we are asking the manufacturer to make, that we win.

Senator LEVIN. In your opinion is that statement true that you require the manufacturer of Darvon to make?

Commissioner KENNEDY. The "Dear Doctor" letter, yes.

Senator LEVIN. You think you could carry that burden of proof in court?