Commissioner KENNEDY. Oh, yes, we could require studies.

Senator NELSON. I mean are you required or not?

Some combinations of this drug were on the market before 1962 and I have forgotten the grandfather clause provisions if, in fact, there are some as to efficacy. There were some as to safety.

As I recall it, when we had hearings maybe 3 years ago reviewing the progress of the FDA and the NRC under the requirements of the 1962 act, drugs were classified as effective, probably effective, and ineffective. Is that correct?

Commissioner KENNEDY. That is correct.

Senator NELSON. And if they were not identified as effective, the FDA was requiring evidence of effectiveness under the provisions of the statute. Is that correct?

Commissioner KENNEDY. Yes. Maybe I can help, Senator. I was not trying to put up any challenge to the requirement for adequate and well-controlled policy demonstrating effectiveness. It applies retroactively under the terms you describe under the efficacy statute and it applies to products afterward.

The only difference I was trying to call attention to was a technical difference—effective, probably effective, and not effective apply to those pre-1962 drugs that are treated under the transitional provisions of the law and drugs introduced post-1962, all have to meet that standard.

Some of the Darvon combination products are present and some are post-1962 but the central point is that they have to meet that standard on a continuing basis and if we approve a drug on a limited set of trials that appear to demonstrate effectiveness and then a much larger body of research comes in that challenges that initial conclusion and appears to put the weight of the evidence on the other side, we are obliged to take up the matter again and reevaluate that new drug application and begin withdrawal proceedings if the burden of the evidence shows they are not effective.

Senator NELSON. I guess that is what is confusing me and I apologize for not having relooked at the statute. It has been 2 or 3 years since we have had hearings on this.

What I am really saying is the literature that I have looked at, and it may not be all of it, of course, but, in Dr. Moertel's studies and others I can recall none that found propoxyphene in combination with aspirin was more effective than aspirin alone—that is, no adequate controlled studies to refute Moertel's studies or, more positively to demonstrate adequately that in combination they are more effective.

If that is the case, then is it not under the law the requirement of the FDA—based upon the simple evidence there is to the contrary—to say: It is not clear from adequately controlled studies that they are more effective in combination and therefore, we now request the company to produce the study to prove it and if they cannot, the combination should not be in the marketplace.

Am I stating that correctly?

Commissioner KENNEDY. You are absolutely correct.

Senator NELSON. And that is a procedure we will be following?

Commissioner KENNEDY. That is why we are doing the review. This review is being done to evaluate safety questions because that kind of