Mr. GORDON. Does that letter violate the law or any FDA regulations?

Dr. EDWARDS. Mr. Hutt, do you wish to answer that?

Mr. HUTT. I think it is clear that the letter does constitute labeling as defined in our regulations and specifically 21 CFR 1.105(e)(2). As to whether it violates our requirements for a supplemental drug application, I would simply tell you two of our regulations, 21 CFR 130.9 (a)(3) and 21 CFR 1.106(b)(4)(i) require a supplemental NDA unless the labeling involved is the same in language and emphasis as labeling already approved, and consistent with and not contrary to such approved labeling. As already indicated, we do regard this as lacking fair balance and not properly putting forth all the facts. Accordingly, it would be in violation of those two sections.

Mr. GORDON. Wouldn't it be a good idea to inform the medical community of the labeling, and the relative value of Darvon as an analgesic?

Dr. EDWARDS. This, of course, gets into the whole subject of relative effectiveness. As Dr. Simmons and I pointed out, it is extremely difficult, using the current methodology to fully evaluate the analgesics. Within broad parameters, we think we can very definitely say that Darvon is no better than aspirin. To get much more accurate than that with the information that we have at this particular point, it would be rather difficult.

Senator NELSON. In this study codeine appears to be less effective than aspirin.

Dr. EDWARDS. Again, I think that Dr. Simmons pointed out that that is very indicative of the problem generally. Codeine is recognized as one of the better analgesics. It is a very potent analgesic.

Senator NELSON. You stated that Darvon is less effective than codeine—but this study said that codeine was less effective than aspirin, and Darvon is less effective than aspirin.

Dr. EDWARDS. From this particular study, that statement would be accurate. As Dr. Simmons pointed out, we do have other studies showing it is the equivalent, and less effective in general, to aspirin.

Dr. SIMMONS. There is a lot of literature in this area, Mr. Chairman. You have to put them all together and come up with the soundest judgment you can. I think it would be a mistake to rely on only one study, and that is one of the difficulties.

Senator NELSON. Do any of the studies say that they are equivalent?

Dr. SIMMONS. Aspirin and Darvon?

Senator NELSON. Do any of the studies assert that they are equivalent?

Dr. SIMMONS. One of the problems is that there aren't too many studies that directly compare the two drugs in the same patient. Considering all the available evidence, we simply come out with the assessment that says they are about equal. Some good studies suggest Darvon is a little less effective than aspirin.

Senator NELSON. In this well-controlled study, aspirin is stated to be superior.

Dr. EDWARDS. Right.

Senator NELSON. And 65 mg. of Darvon is a little better than placebo.

Dr. EDWARDS. Right.