Senator DOLE. Dr. Meier, could you summarize the letter to Dr. Ortiz which is attached to your testimony.

Dr. MEIER. Yes, I will be glad to try to do that.

The critical issue is the limitations of inferences that one can draw from a retrospective study. The burden of this letter is to try to bring into sharp relief the reasons for some of the limitations.

Perhaps the most significant comment in the Sartwell report that led me to feel it was important to meet with the FDA people was the suggestion which I hope I can find that the retrospective study is really an ideal method for carrying out investigations of this kind. I do not find that statement. If you do, I would appreciate it.

In any event, the kind of limitation that arises comes from the two sources in my direct statement, primarily from those two sources. One is that you have no opportunity to see anything about the population which did not wind up in the hospital, which did not wind up with the relative designation on the death certificate if you are doing a mortality study. Information was not gathered on these subjects with a view to evaluating the pill. It may be true as in the hospital studies that you are interviewing the patients and thus gathering information directly related, but that information is gathered after the event of thromboembolism and in the presence of a large body of information that pills may be implicated.

In consequence, as I indicated in the direct testimony, it may very well be the case that a doctor having a patient whose symptoms might suggest thromboembolic disease might be more likely to press ahead and make that diagnosis if he knew the patient were on the pill than he might otherwise be. If he is not dealing with that patient in the context of a study in which he has a regular protocol to follow in evaluating the patient, this could introduce a very serious bias.

The other major limitation which comes in in considering retrospective studies is that there may well be associations which were not allowed for in the plan for the studies, and one such of small magnitude shows clearly in the Sartwell report. There were a number of student nurses who had thromboembolic disease and they had a very high rate of pill use. Well, it is not in the least surprising that student nurses, (a) might be more liable to thromboembolic disease, being on their feet more than most of us are; it is not in the least surprising that they should be on the pill, because they are in the place that the pill might be more accessible. If we have any reliability at all for a causal mechanism for showing the relationship, it might be difficult to disentangle these. It is much more likely one will be able to see anything that is going on in any sort of prospective study. As I have indicated, the only kind of satisfactory study is one in which you have concurrent control. It is the point closest to my heart that despite repeated assurances from one expert to another that it is not possible to carry out such studies in the United States, I strongly believe that it is possible to carry out such studies and that it is very important that we should do so.

Senator DOLE. On page 15 of your statement, you state the pill has not been shown to be associated with unacceptable risks as far as thromboembolism and cancer is concerned. That is contrary, of course, at least in part, to some of the testimony we have had from