Dr. LAWRASON. At this point, several of the investigators employed a controlled-study method known technically as placebo substitution. This is a highly useful method of confirming drug action. It is a single-blind study. Here the patient is placed on various medications including placebo at different stages, but does not know when the different drugs, which are identical in appearance, are being added or removed. These studies confirmed that the therapeutic response obtained on indomethacin was due to the drug, since the symptoms rapidly returned when the patient was given the placebo medication.

In the 1961–65 period we are discussing, this method was not only sound but respected. Even though criticized earlier in these hearings, it still remains valid today. The skilled physician, deeply concerned over the patient's comfort and progress, soon learns the characteristic pattern of the fluctuations in the activity of the individual's disease. By his experience he easily recognizes an exacerbation of symptoms of the disease, and he is able to regain control with reinstitution of the effective therapy. To imply that these clinical investigators purposely choose to institute placebo at the point in the patient's disease when the patient is about to experience an exacerbation of his illness is sheer nonsense and is a reflection on the scientific integrity of the observer and also on his moral character.

Mr. GORDON. May I interrupt here just a moment?

Dr. LAWRASON. Yes, sir.

Mr. GORDON. I do not like to be in a position of defending any previous witness, but it seems to me that if a writer points out a flaw in an investigative method, I do not think he is thereby imputing dishonesty, is he?

Dr. LAWRASON. I do not believe this was said, Mr. Gordon. I believe the implication was that one could give a placebo or an active compound, and then at the time one expected an exacerbation to occur or a remission, a change in the cyclic character of the disease, the investigator would change medication. This is what this refers to.

Mr. GORDON. Yes, but it does not necessarily impute dishonesty, does it?

Mr. GADSDEN. Even though I am not a doctor, I think the implied criticism of the single-blind study is that it is open to this kind of variation. If this criticism is implied, then I think Dr. Lawrason's comments are appropriate.

Dr. LAWRASON. I would like to refer to Dr. O'Brien's testimony, in which he said that a study of this type—namely, the single-blind placebo—was designed in such a way that the bias is in favor of the drug.

Mr. GORDON. That is a statistical bias, I would think. At least, that is the way I understood it.

Dr. LAWRASON. He did not say "statistical."

Mr. GORDON. Well, we are talking about statistics. As I said, I do not want to defend anybody, but my understanding is that the bias was a statistical bias rather than a personal bias. But I do not want to read meaning into his words.

Let me ask you this: In referring to the 1961–65 period, are you implying that clinical trials using control groups were not used before 1961?