Senator HATFIELD. Should all the drugs be subjected to this kind of test before they are put on the market?

Dr. LAWRASON. Yes, to the extent that they can. But in studying a diuretic, for example, the double-blind is really not necessary to determine whether or not there has been a diuresis within a patient, increase in urine volume.

Senator HATFIELD. What criteria do you use in determining when to use this double-blind study, on which drug, and when not to?

Dr. LAWRASON. In those diseases where there are truly objective measurements—for the most part laboratory measurements, or objective signs within the patient of changes that take place, whether it be with the electrocardiogram or other techniques—the double-blind is of only ancillary and confirmatory value. It is where observations are being made by the physician and patient, where possible bias is interjected, that the double-blind serves the greatest purpose.

Senator HATFIELD. Thank you, Mr. Chairman.

Mr. CUTLER. Mr. Chairman, could I supplement that for a moment? When Dr. O'Brien was testifying, he construed the 1962 Drug Amendments as requiring double-blind studies to prove effectiveness in all future drugs. We have prepared a memorandum on the legislative history of the 1962 amendments, including both the term, "adequate and well-controlled," and the term, "substantial evidence." We would like to submit this memorandum for the record, if we could. It shows that Congress does not believe double-blind tests are essential for "substantial evidence"—that the Congress was well aware that for some diseases and drugs there were at that time no satisfactory double-blind tests.

With respect to "substantial evidence," one of the very illustrations given at the time was the case of rheumatoid arthritis, where doctors continued to disagree as to which drug was the preferred drug, if any, for treating the disease.

Senator NELSON. That memorandum will be accepted for the record.

(The document referred to follows:)

LEGISLATIVE HISTORY

OF THE

DRUG AMENDMENTS OF 1962

MEANING OF "SUBSTANTIAL EVIDENCE" AND "ADEQUATE AND WELL-CONTROLLED INVESTIGATIONS" AS USED IN SECTION 505(d)(5) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT.

Under the Drug Amendments of 1962, Section 505(d) of the Federal Food, Drug, and Cosmetic Act was amended to include a new "effectiveness" test with those which a new drug application must pass before it is approved.

This test is set forth in Section 505(d)(5), which provides that the Secretary shall issue an order refusing to approve a new drug application if he finds that:

"[E]valuated on the basis of information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof. . . ." Sec. 505(d), Federal Food, Drug, and Cosmetic Act, as amended, 21 U.S.C. 355(d).