

new drug. Experience has shown that a majority of so-called experts has often been wrong in initially condemning a new drug, just as new inventions in other fields are usually regarded with skepticism and often with hostility. The new ground for rejection of a new drug application is therefore expressed in terms of 'a lack of substantial evidence,' evaluated on the basis of all the information before him, that the drug will have the effect claimed for it. The term 'substantial evidence' is defined in terms of the kind and quality of the investigations that must support the claims." Statement by Senator Eastland, 108 Cong. Rec. 16304 (August 23, 1962).

"In the entire realm of medical science nothing is more difficult and more subject to honest differences of competent opinion than the determination of the therapeutic merits of drugs in human beings. Experts have sharply opposed views concerning the proper treatment of many common diseases, and each school of thought has strong champions. Many highly qualified physicians are convinced of the value of corticosteroid drugs in relieving rheumatoid arthritis; there are others who prefer aspirin; still others are proponents of a variety of other treatments." Testimony of Eugene N. Beesley before Senate Subcommittee on Antitrust and Monopoly, December 7, 1961, p. 1998.

"Mr. BEESLEY. . . . By 'substantial' evidence we mean less than preponderant, or conclusive, evidence.

"We mean that, where a reasonable number of clinicians have conducted tests which show that a drug has the claimed effects, FDA should permit the drug to be marketed even though other tests by other clinicians do not show the same effects. This is a case of difference of medical opinions, which, as Dr. Hussey had said, should not be resolved by the fiat of any authoritarian body but by each physician in his own practice.

"Senator KEFAUVER. All right.

"Then we seem to be pretty well agreed all the way around, sir." *Id.*, at p. 2012.

Only at a few points in the hearings was there focus upon "controlled" investigations. When Dr. Charles May, Professor of Pediatrics at New York University, testified, the concept of a controlled examination was used to distinguish the facilities available to the individual physician. See Hearings before the Subcommittee on Antitrust and Monopoly, July 18, 1961, p. 204.

The same distinction was emphasized by the testimony of Dr. Louis Goodman, Professor of Pharmacology at the University of Utah. See *Id.*, at pp. 217, 243.

The one witness before the Senate hearings who stated that he had "often testified to the importance of double-blind controlled trials in clinical research" insisted that his statements did not constitute a demand for such trials on all new drugs. The witness, Dr. Louis Lasagna, asserted that:

"The emphasis should be on scientifically acceptable evidence, of whatever quality and quantity required to give a reliable answer to the questions posed concerning the drug's effects." Hearings before the Senate Subcommittee on Antitrust and Monopoly, July 19, 1961, pp. 282-283.

In discussing the subject of phraseology, Dr. Lasagna concisely stated a view which permeated the hearings: "I would hope that if such a bill were passed, that there would be every opportunity for a flexibility of interpretation." *Id.*, at p. 288.

The legislative history also includes a statement by Dr. I. S. Ravdin introduced into the hearings before the House Committee on Interstate and Foreign Commerce. The statement was signed by a large number of doctors from all parts of the country, including Drs. Michael E. DeBakey and Paul Dudley White. The statement made the following points:

"(1) Medicine is in part an uncertain science. There is at the present time no precise method for determining absolute efficacy or effectiveness. Such a determination must frequently be based upon medical opinion, and medical opinion is not always unanimous.

"(2) Physicians very often have differing opinions about the usefulness of an agent in treating a particular disease. Many eminent physicians, for example, favor the use of the corticosteroids in the treatment of rheumatoid arthritis, but others believe that the corticosteroids are not the drug of choice for this purpose.

"Under such circumstances, it is difficult, if not impossible, to determine the exact effectiveness of the corticosteroids in treating rheumatoid arthritis. . . ." Hearings before House Committee on Interstate and Foreign Commerce, August 20, 1962, p. 207.

Perhaps the most complete discussion of the problems involved in the working of the substantial evidence standard and the methodology of investigating drugs