market. Congress decreed that claims of drug effectiveness must be supported by "substantial evidence"—meaning evidence derived from adequate and well-controlled clinical investigations on the basis of which it can fairly and responsibly be concluded by experts that the particular drug will have the effectiveness it is represented and purported to possess.

The task set forth before the Food and Drug Administration was a monumental one, to say the least.

In 1966 the Agency turned to the National Academy of Sciences/National Research Council for help. NAS–NRC agreed to undertake the evaluation of the more than 3,000 marketed preparations approved by the Food and Drug Administration between 1938 and 1962, that were still on the market, and to determine whether they were effective for the indications claimed in their labeling. The Drug Efficacy Study was established by NAS–NRC in June 1966 and some 30 panels were set up to evaluate various categories of drugs.

The results are summarized in *Drug Efficacy Study, A Report to the Commissioner of Food and Drugs from the National Academy of Sciences*, which was given to us in 1969. As the report notes, this review made "an audit of the state of the art of drug usage that has been uniquely extensive in scope and uniquely intensive in time" and is applicable to more than 80 percent of the currently marketed drugs.

Senator NELSON. You mean 80 percent of the different compounds? Is that what that means?

Dr. EDWARDS. 80 percent of all dosage forms that are available in the pharmacy.

Senator NELSON. Of all kinds of compounds.

Dr. EDWARDS. Right.

The report noted that the quality of the evidence of efficacy, as well as the quality of the labeling, was poor. Many of the presentations submitted by manufacturers in support of the claims made for the use of their drugs consisted of reports of uncontrolled observations and testimonial-type endorsements. There was a conspicuous lack of substantial evidence based on well-controlled investigations by experienced investigators. The panels specifically criticized the labeling of about two-thirds of the drugs that they evaluated. They have found too many of the package inserts to be poorly organized, repetitive, out-of-date, evasive, and promotionally oriented. The majority of the inserts were found to fail in their primary purpose of providing the physician and the pharmacist with authoritative and objective guides to prescribing or dispensing the drugs in question.

Senator NELSON. May I interrupt again, Doctor? Under the law the Food and Drug Administration has the authority to require that the package insert be accurate and make only justifiable claims and be in sufficient detail. In other words, you have the authority to control what goes into that package insert?

Dr. EDWARDS. That is correct.

Senator NELSON. What is the practice? The company makes up the insert—then when does the FDA get around to looking at it?

Dr. EDWARDS. Prior to approval of any new drug the company, the manufacturer, and the FDA sit down frequently in numerous