drug is recommended for development by the corporation's scientific advisory board and submitted as a New Drug Application (NDA) to the FDA for review and approval for marketing". This period may be extended several additional years before a drug product is finally approved. The orderly progression in the development from a chemical compound to a drug product, that is, from the early toxicity tests in a mouse to a safe and effective drug product in man is an extremely time consuming and costly procedure. It is estimated that for each drug produce that receives an effective NDA, in excess of 6,000 chemical agents are investigated for their potential usefulness in the treatment or prevention of disease.

The enactment of the Kefauver-Harris Amendments to the Food, Drug and Cosmetic Act in 1962 added a second basic statutory requirement, proof of therapeutic effectiveness, to the 1938 amendments. Prior to 1962 the statute was primarily concerned with a need to demonstrate safety of a drug product.

The current regulations have placed under much closer scrutiny the evaluation of chemical substances employed in the treatment of human disease. The development of a new chemical entity for use as a therapeutic agent has also become a much more complicated and laborious process. The regulations have thus added materially to the cost and the time required to develop a new drug product.

The first phase of a drug's evaluation is confined to study in appropriate species of animals. As much as a year may be required to establish the systemic absorption, tissue distribution, metabolism and elimination as well as the pharmacologic action and toxic potentials in laboratory animals. The biochemist, the pharmacologist, and the toxicologist must establish the basic data that warrants the first administration of the drug to man. It is unfortunate that in the present state of the art that this information gained from animal experimentation can only be considered an indicator of its potential action in man. The orderly progression of drug development from "mouse to man" is fraught with both difficulties and disappointments.

When the information that has been accumulated from the extensive animal research warrants the trial of the potential drug in man, a special form (FDA Form 1571) is completed for submission to the Food and Drug Administration. (A sample copy of a blank form is attached for your information). The assembly of the information required to complete this form may require as much as two months and constitutes a "Notice of Claimed Investigational Exemption for New Drug" (IND). The filing of this IND informs the FDA that the pharmaceutical company is prepared to initiate limited studies in man to determine whether or not the information gained from the animal studies can be confirmed.

The IND filed with the FDA represents a body of information gathered on a chemical entity or its combination products through animal experimentation. The cost involved in preparation and submission, however, reflects but a fraction of the total research expenditure to this point in the development of a marketable product. The manhours of laboratory personnel, cost of animals, laboratory space, and equipment utilized in the screening of perhaps hundreds of compounds to discover a potentially "safe and effective" new drug product, represent the "hidden costs" of drug research.

Prior to the 1962 amendments to the Food, Drug and Cosmetic Act, it was the sole responsibility of the manufacturer to exercise his judgment in establishing the reasonableness and safety of first administering an entirely new drug product to man. Today, however, he shares that decision with the FDA which has the added responsibility of reviewing the information set forth on Form 1571 and concurring in the decision to enter into Phase I in the process of drug development. The IND is a total profile, containing all information that is known with respect to the chemical structure of active ingredients, biologic activity, pharmacologic action, dosage form, i.e., tablet, capsule or liquid, detailed process of manufacture and means of identifying ingredients both qualitively and quantitively, facilities for production, and a data sheet that provides all pertinent information for a prospective investigator.

The development of a drug product must necessarily be tailored to the chemical and physical nature of the active ingredients, anticipated therapeutic effects, the route of administration, the duration of action, and the ratio of pharmacologic and physiologic action to toxic potential. These developmental steps require an average of twelve months and are not instituted without the cautious control of