strate the safety and efficacy of new products in controlled clinical trials. Investigational new drug (IND) regulations developed in 1963 have been applied to investigational biologics, including experimental vaccines, as well as to drugs.

In 1972, the Food and Drug Administration (FDA) combined selected elements of the Public Health Service Act with certain provisions of the 1962 amendments of the Food, Drug, and Cosmetic Act to establish regulatory procedures and standaids for licensure of biological products. Under the 1972 regulations, FDA bolstered its authority to remove from commerce products not in compliance with certain regulations, for example, those establishing standards for vaccine and efficacy, As reported in the *Federal Register* on August 18, 1972: (37 FR 16679)

> Section 351 of the Public Health Service Act does not explicitly confer the authority to deny or revoke a license on the ground that the product is ineffective or misbranded. Because all biological products are drugs, and because the Federal Food, Drug, and Cosmetic Act does contain explicit authority to control the effectiveness of misbranding of all drugs, applicable provisions of the Federal Food, Drug, and Cosmetic Act were redelegate as published in the ***Federal Register*** on February ***25, 1972 (37*** FR *4004).*

In 1973, FDA promulgated a new set of regulations authorizing FDA to review and evaluate the safety and efficacy of biological products licensed prior to July 1, 1972. Based on the findings of its safety and efficacy reviews, FDA may leave intact, modify, suspend, or revoke manufacturers' licenses for particular products already on the market. '

'Procedures and standards authorized under these regulations, which also can be applied to the evaluation of products that have not yet been marketed, are discussed in detail in ch. *3. See* also app. 3.2, 3.3, and 3.4.

Appendix 3.2
STATUTORY AUTHORITY AND PROCEDURES FDA USES TO EVALUATE THE SAFETY AND EFFICACY OF PRESCRIPTION DRUGS

Ever since 1906, the Federal Government has required legitimate drug manufacturers to demonstrate that their products can be used by humans at a level of safety acceptable to Government scientists and officials. In 1906, Congress passed the Food and Drugs Act, which banned the manufacture and interstate commerce of adulterated or misbranded food and drugs.

Thirty-two years later, stimulated by a tragic event —over 100 people died from ingesting a sulfanilamide mixture made with the deadly toxin diethylene glycol —Congress passed the Food, Drug and Cosmetic Act of 1938 (USC, Title 21). This act strengthened the Federal Government's standard for safety and expanded the scope of the 1906 law to include cosmetics.

In 1962, Congress amended the Food, Drug and Cosmetic Act of 1938, again to strengthen safety requirements, and in addition, to establish efficacy as a criterion for licensure of prescription drugs to be marketed in this country. Congressional passage of this act was stimulated, at least in part, by the thalidomide tragedy in England and other European countries.

The effect of increasingly rigid Federal standards for the safety and efficacy of prescription drugs sold in this country has been a matter of controversy since the enactment of the 1906 Food and Drugs Act. On the one hand, prescription drug manufacturers complain about the costs associated with conducting premarketing clinical trials. Some contend that the rigorous safety and efficacy criteria established and enforced by the Food and Drug Administration (FDA) discourage innovation in the development of new drugs, and further, that the American public may be deprived of potentially useful new therapeutic entities as a result (Warden, 1978). On the other hand, FDA believes that tough Federal standards for safety and efficacy are necessary to help protect the American public from potentially dangerous and inefficacious prescription drugs (Kennedy, 1978). Neither viewpoint is substantiated by overwhelmingly supportive data. Judgments regarding the value of Government standards for drug safety and efficacy, therefore, are still based on one's sense of values. Thus far, Congress appears to have valued the public's protection more than it has industry's concerns about innovation and costs.

To evaluate the safety and efficacy of a new prescription drug product, FDA's Bureau of Drugs (BOD) first requires the sponsoring manufacturer to present data from preclinical testing of the product in animals. Before initiating clinical testing (in humans), a drug manufacturer must submit to FDA an acceptable investigation new drug application (IND). If FDA approves this application, the manufacturer may proceed with Phase I, II, and 111 clinical trials. Phase I clinical trials are used to assess the safety of