same molar dose under similar conditions in an appropriately designed study. Two drug products are considered therapeutically equivalent if they are pharmaceutical equivalents and if they can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling. The FDA believes that products classified as therapeutically equivalent can be substituted for each other, with the full expectation that the substituted product will produce equivalent clinical effects and safety profile as the original product.

HISTORY OF BIOEQUIVALENCE EVALUATION IN THE UNITED STATES

In 1938, the U.S. Congress enacted the Federal Food, Drug, and Cosmetic Act. The new law required, among other things, that a "new drug" product would need to provide proof of safety before it could be marketed. The New Drug Application (NDA) was established to provide a mechanism for proof of safety of drugs to be submitted to the FDA. Regulations were promulgated as to the form and content of the data to be submitted for an NDA. Originally, only toxicity studies were required along with informative labeling and adequate manufacturing data.

Drug Efficacy Study Implementation (DESI)

In 1962, The Kefauver–Harris Amendment to the Food, Drug, and Cosmetic Act required that all new drug products subsequently approved for marketing must have adequate evidence of effectiveness as well as safety.[1] The FDA was assigned the responsibility for receiving, reviewing, and evaluating required data submissions and enforcing compliance with the law. An applicant submitting an NDA was now required to submit "substantial evidence" in the form of "adequate and well-controlled studies" to demonstrate the effectiveness of the drug product under the conditions of use described in its labeling. The new drug effectiveness provision of the law also applied retrospectively to all drugs approved between 1938 and 1962 based on safety only. The FDA contracted with the National Academy of Sciences/National Research Council (NAS/NRC) to review this group of drugs for effectiveness. The NAS/NRC appointed 30 panels of experts and initiated the Drug Efficacy Study. The panels reviewed approximately 3400 drug formulations and classified them either effective or less than effective.[2] The FDA reviewed the reports and any supporting data and published its conclusions in the Federal Register as DESI notices. The DESI notices contained the acceptable marketing conditions for the class of drug products covered by this notice.

Many drug products had active ingredients and indications that were identical or very similar to those of drug products found to be effective in the DESI review but lacked NDAs themselves. Initially, in implementing the DESI program, the FDA required that each of these duplicate drug products should have its own approved NDA before it could be legally marketed. Later, the FDA concluded that a simpler and shorter drug application was adequate for approving duplicate DESI drugs for marketing and, in 1970, created the Abbreviated New Drug Application (ANDA) procedure for approving duplicate DESI drug products.[3–5] The FDA believed that it was not necessary for firms seeking approval of duplicate DESI drug products