

Kefauver-Harris Amendments Revolutionized Drug Development



President John F. Kennedy hands Sen. Estes Kefauver the pen he used to sign the 1962 Amendments to the Federal Food, Drug and Cosmetic (FD&C) Act. Those looking on include Frances Kelsey, second from left, the FDA medical officer who refused to approve the new drug application for Kevadon, the brand name for thalidomide in the United States.

Fifty years ago, landmark legislation was signed into law by President John F. Kennedy that established the scientific safeguards used today by the Food and Drug Administration (FDA) to ensure that consumers will not be the victims of unsafe and ineffective medications.

The year 1962 was one filled with drama on the national and international stages. The world came to the brink of nuclear war over the presence of Soviet missiles in Cuba. Astronaut John Glenn became the first American to orbit the Earth. The first James Bond film ("Dr. No") was released. Actress Marilyn Monroe died.

Set against this turbulent backdrop was the devastation of thalidomide, a sedative used to treat morning sickness in pregnant women that was causing birth defects in Europe,

Canada and other countries.

Fast federal action to prevent that kind of devastation from happening in the United States came in the form of the 1962 Amendments to the Federal Food, Drug and Cosmetic (FD&C) Act.

Commonly called the Kefauver-Harris Amendments, they were sponsored in Congress by Sen. Estes Kefauver (D-Tenn.) and Rep. Oren Harris (D-Ark.). Once signed into law by President Kennedy on Oct. 10, 1962, the amendments established a frame-

work that required drug manufacturers to prove scientifically that a medication was not only safe, but effective.

FDA Commissioner Margaret Hamburg, M.D., notes that the 1938 FD&C Act had serious shortcomings at that time. For example, manufacturers could sell a drug if the FDA didn't act within 60 days to prevent its marketing. And FDA had no authority to enforce good manufacturing processes.

"With the passage of the amendments, FDA was no longer a helpless bystander while unproven medicines were streaming into pharmacies and onto patients' bedside tables," says Hamburg.

From Hearings to History

In 1959, the Senate began hearings on ways to strengthen the drug provisions of the FD&C Act. They were led by Kefauver, who chaired the Senate Subcommittee on Antitrust and Monopoly.

FDA historian John Swann, Ph.D., explains that Kefauver's interest at the time was in drug pricing and marketing, believing that patients were paying too much and being misled by extravagant advertising claims. Kefauver introduced legislation to enforce truth in labeling and marketing.

Enter Kevadon, a brand of thalidomide that the William S. Merrill Company hoped to market as a sedative in the United States. The company was stopped in its tracks by FDA medical officer Frances Kelsey, Ph.D., M.D., who refused to approve the drug application because of insufficient safety data, with the submitted evidence being more anecdotal than clinical.

And by 1962, the devastation caused by this drug in other countries had become big news in the United States. Thousands of children had been born with shortened, missing or flipper-like arms and legs.

The public furor was immediate. Unknown to FDA, the company had

already distributed the thalidomide to 1,200 physicians in the United States—including those treating pregnant women. The agency launched a nationwide campaign to recover all supplies of the drug. At a press conference, President Kennedy warned Americans that they might have a dangerous drug in their medicine cabinets. There were 17 births of deformed infants tied to thalidomide in the U.S.

Kefauver reintroduced his legislation to include provisions drafted by FDA specifically designed to prevent a disaster like thalidomide. Harris was Kefauver's co-sponsor in the House of Representatives.

The legislation was passed unanimously by both houses of Congress on Oct. 2, 1962, and signed into law by President Kennedy eight days later.

The Major Changes

The new authorities given to FDA by the Kefauver-Harris Amendments:

- required that manufacturers prove the effectiveness of drug products before they go on the market, and afterwards report any serious side effects.
- required that evidence of effectiveness be based on adequate and well-controlled clinical studies conducted by qualified experts. Study subjects would be required to give their informed consent.
- gave FDA 180 days to approve a new drug application, and required FDA approval before the drug could be marketed in the United States.
- mandated that FDA conduct a retrospective evaluation of the effectiveness of drugs approved for safety—but not for effectiveness—between 1938 and 1962.
- allowed FDA to set good manufacturing practices for industry and mandated regular inspections of production facilities.
- transferred to FDA control of

prescription drug advertising, which would have to include accurate information about side effects.


- controlled the marketing of generic drugs to keep them from being sold as expensive medications under new trade names.

"The history of drug development in the United States is one of continued progress punctuated by transformative events, and passage of the Kefauver-Harris Amendments is one of those transformative events," says Douglas Throckmorton, M.D., deputy director of FDA's Center for Drug Evaluation and Research. "As a result, FDA's drug development process is considered the gold standard to which other countries aspire."


Then and Now

In 1962, Andy Warhol's soup cans arrived in the art world. Anti-apartheid activist Nelson Mandela was jailed in South Africa. Conservationist Rachel Carson's "A Silent Spring" was published, energizing the environmental movement.

And a law took effect that, in Swann's words, "changed the way the public looks at the federal government."

He explains, "FDA was not an unknown entity but after 1962, members of the public really started taking notice and having expectations that the government will protect them. And FDA rose to that challenge 50 years ago." 

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