50 Years: The Kefauver-Harris Amendments

50 Years Ago: How an FDA reviewer saved lives and spurred legislation

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This year the Food and Drug Administration celebrates the anniversary of the passage of the Kefauver-Harris drug amendments, which have ensured prescription drug effectiveness and safety for 50 years. But the legislation may not have been proposed if not for the persistence and grit of a recently-hired FDA medical officer, and two U.S. congressmen.

One of Frances O. Kelsey’s first assignments at FDA was to review an application for the drug Kevadon, a sedative more commonly known as thalidomide. Already approved in Canada and 20 European and African countries, thalidomide was widely prescribed for morning sickness during pregnancy.

But Kelsey was not satisfied with data provided by the pharmaceutical company. Based on her review Kelsey insisted that the data were incomplete and did not support the drug’s safety claims. She refused to approve thalidomide for sale in the United States.

Not bowing to pressure

Despite increasing pressure from the company, Kelsey’s opinion and FDA’s support did not waiver. Kelsey’s stand was tragically shown to be correct. In 1961, reports started to surface connecting thalidomide to severe birth defects. Thousands of children in Europe were born with shortened, missing or flipper-like arms and legs.

When The Washington Post reported on Kelsey and FDA’s role in averting the thalidomide tragedy in the United States, it stirred legislators in the Capitol.
The Dogged Congressmen

Two years earlier, Senator Estes Kefauver of Tennessee was decrying the lack of clear federal regulation in the area of drug approval. He called for revisions of the drug statues; few people listened, especially in Congress. The thalidomide tragedy gave rise to broader calls for drug controls and unearthed Kefauver’s bill to enhance drug regulation.

Representative Oren Harris was chairman of the Committee on Interstate and Foreign Commerce. During his final term in the House, he would introduce and sponsor the Drug Abuse Control Act, which required certain “stimulant, depressant, or hallucinogenic” drugs to require licensing before sale and distribution. He was the lead House sponsor of the Kefauver-Harris Amendment.

The Kefauver-Harris Amendment to the 1938 Food, Drug and Cosmetic Act represented a revolution in FDA regulatory authority. The legislation gave FDA weight to demand that drug makers prove their products were safe and effective before receiving approval to market them in the United States.

Prior to the legislation, drugs could be sold 60 days after companies filed with FDA, if the Agency did not object. Drug makers routinely sent new medications to doctors asking them to “try them out” on their patients.

Kefauver considered the amendment his "finest achievement" in consumer protection. It’s easy to see why. After the law was passed:

- Manufacturers had to provide evidence that proposed drugs were both safe and effective, demonstrated by adequate and well-controlled clinical investigations conducted by qualified experts.
- FDA was given 180 days to evaluate a new drug application, and the application would no longer become automatically effective.
- New drugs required an affirmative decision by the agency before marketing.
- Manufacturers had to maintain records of adverse events associated with drugs and report these promptly to FDA.

The Kefauver-Harris Amendment laid the groundwork for modern drug approvals. Ultimately, FDA established an evidence-based model for drug evaluation decisions that stands as the global standard. While thousands have been involved in those efforts, a rookie employee and two veteran lawmakers exemplified how dedicated professionals can make a difference.