By the early 1900s, the pharmaceutical industry had become a dynamic business. In addition to the historical herbal remedies that had been passed down through generations, advances in organic chemistry were making a broad range of synthetic drugs available. Furthermore, the formulation of the drug, including the materials of drug tablets and intravenous solutions, could be altered and tailored to enhance the active ingredient of a drug. The existing drug regulatory agencies were poorly equipped for the growing pharmaceutical industry. In this environment of innovation with little oversight, the drug industry was ripe for mistakes to occur.

The first major drug tragedy in the United States involved sulfanilamide (1). Sulfanilamide was first discovered as an antibiotic in 1935. In September 1937 S.E. Massengill of Bristol, TN produced and shipped a new formulation of sulfanilamide in a syrup base of diethylene glycol. Diethylene glycol (2) was used to impart a sweet flavor to the mixture to make children more willing to take the medicine. Diethylene glycol is toxic, but the mixture was never tested for safety because testing was not required by the existing drug laws. The new formulation was called Elixir Sulfanilamide.

![Structures of sulfanilamide and diethylene glycol](image)

Reports of patient deaths arrived quickly. Massengill, with some reluctance, recalled all shipments. Government drug agents were called in and every shipment and prescription was carefully tracked. Of the 240 gallons of Elixir Sulfanilamide that were produced, just over 234 gallons were recovered. The unrecovered 5+ gallons of drug, however, had a terrible impact. Over 100 deaths were blamed on Elixir Sulfanilamide, and most were children in the southeastern United States. Almost all patients who received the drug suffered horribly. Diethylene glycol causes kidney failure with symptoms of abdominal pain, vomiting, and convulsions.

As a result of the Elixir Sulfanilamide tragedy, the US government created the Food, Drug, and Cosmetic Act of 1938. This act empowered the Food and Drug Administration (FDA) to oversee fully the safety and effectiveness of drugs in the United States.

Laws alone cannot guarantee drug safety. Several factors complicate the job of the job of the FDA.

1. Medical knowledge is expanding and growing more complex. What is known to be safe today may be found to be unsafe tomorrow.
2. Drug development and production is an international venture. While drug regulatory agencies have protocols in place to monitor all phases of a drug’s synthesis and manufacture, the complexity of the process is a major obstacle for ensuring safety. [The tone in the video is too strong on this point. Regulatory agencies have excellent procedures, but the procedures must be observed and overseen.]
3. Fraud and unethical behavior, while uncommon, are difficult to prevent.
4. The risks of a research endeavor like drug discovery can never be completely eliminated.

In spite of the flaws of an intended government oversight, the Food, Drug, and Cosmetic Act of 1938 was the start of a system of laws for protection of public interests while still allowing corporations to innovate and bring new therapies to the marketplace.