The bottle that contained a fatal remedy and inspired the new Federal Drug and Cosmetic (FDA) Act of 1938 - and more...

By Cecil Munsey PhD

Introduction

In the fall of **1937**, S. E. Massengill Company of Bristol, Tennessee developed **Elixir Sulfanilamide** that was an effective treatment for sore throats in people with streptococcal infections; so effective was it that a demand for a liquid formulation was created that could be given to children.

The company developed a sweet-tasting raspberry-flavored version that used **diethylene glycol** as a dissolving agent. Patients who used the liquid found their sore throats disappeared – *along with their pulses!* **Diethylene glycol** is better known today as antifreeze or brake fluid and ingesting it carries lethal consequences.

**** Now ****

In the fall of **2006**, Panama's social-security system issued a sweet-tasting raspberry-flavored cough syrup with **diethylene glycol** that killed 21 people. Here is how REUTERS News Service wrote up the current disaster:

Friday, October 13, 2006

Panama Probes Tainted Cough Syrup

PANAMA CITY, Panama – Police plan to investigate workers at a government laboratory in Panama after 21 people died from taking cough and allergy syrups tainted with a chemical used in brake fluid, a senior official said recently.

The deaths of mostly elderly men, who suffered kidney failure, puzzled medical authorities over the past month until U.S. experts traced the cause to generic cough syrups made by Panama's social-security system.

The medicines, some containing antihistamine, were adulterated with **diethylene glycol**, [boldface added] an alcohol used as a coolant in brake fluids and hydraulic systems, officials said.

The Health Ministry said it was likely that the medicines had been tampered with.

The sugar-free syrups, popular with diabetics, have been removed from clinics, and the government has told people not to use them.

Most of the victims have been men over age 60 who were being treated for high blood pressure, kidney disorders and diabetes, and 13 people remain sick from taking the medicines.

Health Minister Camilo Alleyne said the adulteration was discovered with the help of the U.S. Centers for Disease Control and prevention, and that the U.S Food and Drug Administration (FDA) also were helping.

In the spring of **2007**, after nine months of investigation, more information became available about the original source of the **diethyllene glycol** that poisoned 51 people to death and hospitalized 68 others in Panama in 2006 (see reprinted article above). Here is how the New York Time News Service reported the results of the 2007 investigation:

Wednesday, May 9, 2007

Company lacked license to sell pharmaceuticals, China says

BEIJING, China – A Chinese company that sold a batch of **diethylene glycol**, a chemical cousin of antifreeze that killed at least 51 people in Panama, had no license to sell pharmaceuticals, the government said…

The New York Times reported that China's 'Taixing Glycerine Factory' made the **diethylene glycol** and fraudulently passed it off as 99.5 percent pure glycerin to a Spanish company, 'Rasfer International,' which then sold it to Panama's 'Medicom SA.' Medicom then sold it to a governmental laboratory…

Saturday, May 19, 2007

Poisoned toothpaste possibly from China

NEW YORK – **diethylene glycol…** has been found in 6,000 tubes of toothpaste in Panama, and customs officials there said the product appeared to have originated in China.

Some of the toothpaste was re-exported to the Dominican Republic, customs officials said. A newspaper in Australia reported that one brand was found on supermarket shelves there and was recalled…

At about the same time, U.S. concern about the safety of imports from China rose after pet food containing a Chinese ingredient was tainted with another industrial chemical, **melamine.** The poison has killed or sickened an unknown number of dogs and cats across the country.

The U.S. authorities said farmed fish also had been fed meal spiked with **melamine**. Similarly tainted food also has been fed to pigs and chickens in the United States.

**** Then ****

Here is how *TIME Magazine* wrote up the first disaster of 40 years ago:

Monday, Nov. 1, 1937

Fatal Remedy

The newest and most spectacular specific [medicine] to come to the aid of ailing man last week caused the deaths of at least 41 people, the disability of countless more, the probable ruin of a Southern drug manufacturer and a nation-wide scare, the like of which had not popped out of medicine cabinets since the Jamaica ginger paralyzed Southwestern swiggers in 1930 [See *"Paralysis In a Bottle"* in the Selected References].

Most victims of last week's medical catastrophe suffered from gonorrhea, some had septic sore throats. Latest remedy for those grave conditions—and a good remedy in case of scarlet fever, erysipelas, and cerebrospinal meningitis—is **sulfanilamide**. Noting a great demand for sulfanilamide, 61-year-old Dr. Samuel Evans Massengill, who compounds veterinary medicines

in a good-sized factory at Bristol, Tenn., this summer decided to add that drug to his line. Knowing that his Southern customers prefer their medicines in bottles, he sought something in which to dissolve sulfanilamide, that had hitherto been taken in tablets and intravenous injections only. He decided to use **diethylene glycol**, a close relative of the alcohol used to keep motorcar radiators from freezing, never before put to this purpose. Whether **diethylene glycol** is poisonous by itself or in this solution was not made clear last week. The one indisputable fact was that S. E. Massengill Co. made up **several 80-gallon batches of sulfanilamide solution. This was labeled an elixir, a technical pharmacological term for a drug sweetened and dissolved in alcohol, and shipped to 375 retailers.** The retailers, one as far away as Puerto Rico, dispensed this "elixir" with and without prescriptions, in reddish brown flasks **[Figure 1]** whose yellow labels read:

Elixir SULFANILAMIDE, suggested for the treatment of all conditions in which the hemolytic streptococci appear. Dose — begin with 2 to 3 teaspoonsful in water every four hours. Decrease in 24 hours to 1 or 2 teaspoonsful and continue at this dose until recovery. S. E. MASSENGILL CO., manufacturing pharmacists.

First warnings of trouble sounded when people who took this medicine for sore throats developed nausea, cramps and inability to urinate. First known deaths occurred in Tulsa, Okla.; next in East St. Louis, Ill.; next at Mount Olive, Miss.; then in Madisonville, Tex.; Carey, Miss.; Copley, Ohio; Clayton, Ala.; and St Louis, Mo. Autopsies revealed destroyed kidneys and livers.

Chief of the Federal Food & Drug Administration, a pugnacious Kentucky lawyer named Walter Gilbert Campbell, has agents posted throughout the country, watching for just such pharmaceutical accidents. Those men last week confiscated every last flask of the Massengill "elixir" upon which they could lay their hands. A Federal agent at Bristol said to Chief Campbell: *The most amazing thing about the company was the total lack of testing facilities. Apparently they just throw drugs together, and if they don't explode they are placed on sale.*

Dr. Massengill cooperated with the Food & Drug men by sending warning telegrams to all his sulfanilamide customers.

The Pure Food & Drug Bill up before Congress last session would have made Dr. Massengill liable to Federal prosecution. But the bill failed and there is no law which makes a pharmacist responsible to the Federal Government for selling untested drugs. However, Dr. Massengill is liable to civil damage suits from relatives of the 41 dead.

**** In-between ****

As it came out in the aftermath of the 1937 incident, the chief chemist at Massengill, Harold C. Watkins, tried one solvent after another before settling on **diethylene glycol** as the "appropriate" dissolving agent. The concoction was checked for flavor and fragrance, and then manufactured in batches totaling *hundreds of gallons*. The liquid, Elixir Sulfanilamide, was put into **bottles of 4 ounces each** (none known to have survived) and shipping began on **Sept. 4, 1937**. To the largest wholesalers, the fatal remedy was shipped in one-gallon bottles **[Figure 1]**, only one of which has survived to this day and is in a private collection.

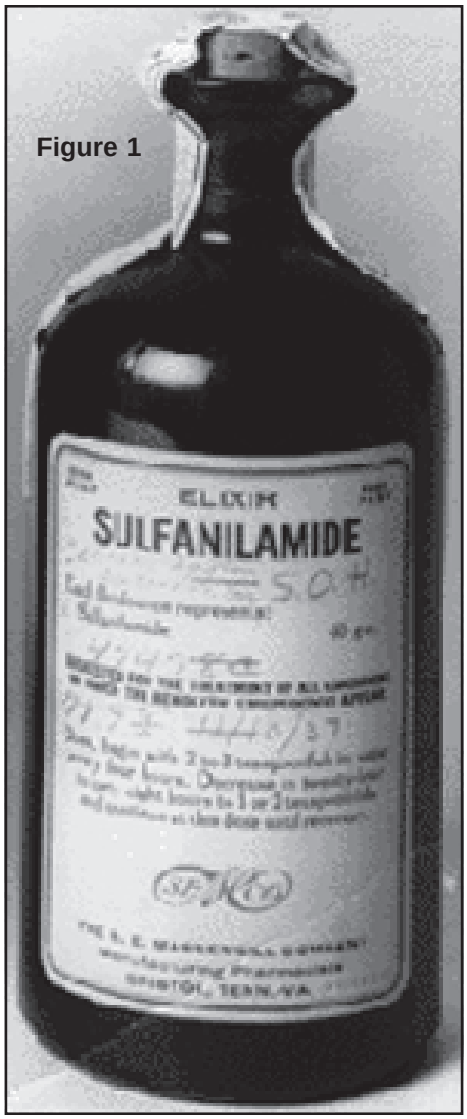

Figure 1

Tulsa, Okla., was the first city in which reactions were reported. By early October 1937, 10 patients in the practice of James Stephenson, M.D., had died immediately after taking the bright red liquid.

When FDA inspectors reached Massengill's Tennessee plant, they found that Tulsa would not be the only site of the problems. Two hundred forty gallons of "elixir" had been shipped across the country, from California to Virginia.

A short time later, Walter Campbell, the FDA's chief chemist, held a press conference in Washington, D.C., during which he said that 14 people had died after taking the Massengill product. He said that the FDA could not legally investigate or prosecute the matter unless it could be shown that there was something wrong with the label on the bottles. He had, however, begun a national investigation, as his agency was the only one with any possible jurisdiction. Campbell would go on to become Commissioner of Food and Drugs in 1940.

The 1906 Pure Food and Drug law had no prohibition per se of dangerous drugs. Campbell was fortunate in that the medicine was labeled an "elixir," which technically is a liquid containing alcohol, so he went ahead with his investigation in hopes that the technicality would be sufficient cause to investigate.

The full field force of the FDA in the United States, 239 inspectors, began to search out the druggists and doctors who had received the shipments. Massengill proved to be trouble. At the beginning of the crisis, on Oct. 15, 1937, the FDA had asked the company to recall from doctors, druggists and distributors whatever was left of the shipments. The company sent out a notice that all who had received a shipment of "fatal remedy" should send back the preparation, but said nothing about the reason for the return or the emergency nature of the recall. The recall was largely ignored. It wasn't until four days later that the company was told it had to send out a second notice, indicating that the drug was

life-threatening.

By the end of November 1937, 107 deaths had been reported, many of them children. Not counted in the statistics was Watkins, the chemist who had caused it all, who died from a self-inflicted gun wound – suicide! It is unclear how many more victims there were beyond those reported, but the FDA investigators kept the number of deaths down by recovering, within four weeks, more than 90 percent of the original shipment. **About 6 gallons, apparently, accounted for all the deaths.**

Less than a month later, when it was clear the episode was over, the question of prosecution arose. Samuel Massengill himself wrote to the AMA, staking out the company's position. The deaths were regrettable, he said, *"but I have violated no law."*

Sam Massengill was charged on more than 170 counts of misbranding. The court fined him $26,000 - the highest amount possible at the time.

The Newly Revised Law

The AMA (American Medical Association), pushing for a new law, issued a statement noting that the death toll from ill people taking useless quack medications was far higher than the 107 who died as a result of using Elixir Sulfanilamide. A proposed law was already in Congress, and pressure to pass a stricter food and drug law had been on for four years. The mail poured into Congress and the bill, left for dead, was revived and readied for passage. The new **Food, Drug, and Cosmetic (FDA) Act was passed on June 15, 1938.** It enhanced safety requirements and has provided the framework for drug research and marketing that stands to the present – drug makers have to show their products are safe before they are put on the market. [After the Kefauver-Harris Drug Amendments were passed in October 1962 new drugs have to be "safe **and** effective."]

The 1938 law was a landmark in civil governance, not just for the United States, as it turned out, but for democratic governments around the world. In the years to come, each nation of the developed world would adopt its central principles. It was the first law to require the checking of drugs before they went to market. It put into law the notion that the scientific approach — not the commercial, not the anecdotal — would be the standard for modern society. It was, in fact, one key factor that created the modern pharmaceutical industry.

By the 1940s and the advent of penicillin from a British university laboratory, most pharmaceutical companies had not yet made that crucial transition, from being chemical factories to basing their business on medical research and development. When scientists offered commercial companies the right to penicillin, for free, one company after another turned the chance down. Taking penicillin from the lab to commercial quantities was carried out prominently in a government laboratory in Peoria, Ill. But by the 1950s, the companies had made a big transition. They dropped thousands of useless patent medicines and similar products from manufacture — as in the case of Smith, Kline, which dropped 14,940 of its 15,000 products and began concentrating on only 60 products for its success. Until 1940, none of the important medicines had been created in industry, and the Sharp and Dohme Catalog contained not a single exclusive prescription medicine.

POSTSCRIPT: The deaths in the first incident in 1937 and the most recent in 2006 / 2007, call to mind a similar outbreak in late 1995 and early 1996 in Haiti, where 31 children died after taking acetaminophen syrup that was contaminated with **diethylene glycol**. AND at least 98 people died in the early 1990s in separate outbreaks in Nigeria and Bangladesh because of **diethylene glycol**-contaminated acetaminophen, according to a Center for Disease Control report.

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