Guardian of Safety: Dr. Frances Kelsey's Stand Against Thalidomide

Caroline Drenth
Tulane University, New Orleans, Louisiana, USA

Abstract: This case study explores the thalidomide tragedy of the late 1950s and early 1960s in the United States, which had far-reaching consequences for public health and perinatal care. The case examines the role of Dr. Frances Oldham Kelsey, a feminist leader and newly appointed medical officer at the US Food and Drug Administration (FDA), in the tragedy and her unwavering commitment as a public health officer. Kelsey's entrance into this government agency led her to an immediate and dramatic crossroads: would she approve a promising treatment based on foreign safety data alone, or demand more evidence despite delaying potential relief? Through historical and public health-based research, including first-hand testimony, this case explores the importance of feminist leadership, diligence, and trust in scientific judgment when establishing and safeguarding effective public health practices.

From 'Mr. Oldham' to Medical Pioneer: Kelsey's Remarkable Rise

On August 7, 1962, in a White House ceremony that made front-page news across America, President John F. Kennedy presented Dr. Frances Oldham Kelsey with the President's Award for Distinguished Federal Civilian Service. What was Kelsey's achievement that earned her one of the highest civilian honors established for government work? She simply did her job with exceptional diligence. As a medical officer at the Food and Drug Administration (FDA), Kelsey refused to approve the "wonder drug" thalidomide despite enormous pressure from its manufacturer, potentially saving thousands of lives in the process (Warsh 2024).

Kelsey's unwavering scientific judgment and moral courage in the face of corporate pressure created a defining moment in American pharmaceutical regulation. When Kelsey, at the time the freshest employee of the FDA, received the thalidomide application in 1960, she faced a profound dilemma: Would she fast-track a treatment that promised significant relief to thousands of pregnant women, relying on promises of safety from outside the United States government entities, or demand more evidence of its absence of risk, potentially delaying access to a seemingly transformative medication?

Kelsey's journey to this pivotal moment began years ago, in 1936, when she began her pursuit of a PhD in pharmacology at the University of Chicago under Dr. Eugene Geiling. When welcoming Kelsey to the program, Geiling penned an acceptance letter to "Mr. Oldham." This infuriated Kelsey. She felt it reflected the common belief that women in the workforce were depriving men of their ability to fulfill their role as primary providers for their families. Kelsey's anger at this response almost stopped her from accepting the position until a professor at McGill told her: "Don't be stupid. Accept the job, sign your name, and put "Miss" in brackets afterward" (Bernstein and Sullivan 2023 n.p.). She accepted the advice and, in 1936, began her journey toward a doctorate in pharmacology (Bernstein and Sullivan 2023; Ricard 2021).

While studying under Geiling, Kelsey noticed that her scientific mentor was "very conservative and old fashioned," and "he did not hold too much with women as scientists" (Kelsey 1991, 13). She later reflected on how her androgynous name influenced her graduate experiences, wondering whether she would have been able to take this critical step in her career had her name been more traditionally feminine (Magazine and McNeill 2017). Regardless of how Kelsey got her first step up, however, the two worked together for almost three years. When Geiling was recruited to investigate Elixir Sulfanilamide in 1937, the FDA temporarily recruited Kelsey alongside him for her first experience with the federal department (Warsh 2024).

During her doctoral program, Kelsey also conducted animal studies with rabbits when attempting to find a synthesis for quinine, a natural cure for malaria. During these studies, which Kelsey worked on during the mid-1930s, Kelsey noticed that some of the drugs administered to pregnant rabbits were bypassing the placental barrier. She also discovered that pregnant rabbits had a lower ability to metabolize the trial drugs than non-pregnant specimens and that the embryonic rabbits exposed to the drug could not metabolize the medication at all (Geraghty 2001b). The realization that a fetus was not only exposed to the medication despite the placental barrier but also that its reaction to the chemicals was different than that of a mature specimen was a revelation at the time and emphasized the vulnerability of a developing fetus, particularly within the context of clinical trials (Kotta-Loizou et al. 2024).

Kelsey's pioneering work with rabbits was an example of early recognition of physiological variation across different populations. While pharmaceutical companies typically tested medications on a narrow, homogenous sample of subjects—primarily non-pregnant male adults—Kelsey's work as a doctoral candidate would lead to her later understanding that drugs needed to be tested on representative samples of populations in order to gauge potentially drastically different physiological responses (Rudolph et al. 2023; Warsh 2024).

In 1938, Kelsey became the first woman to graduate with a PhD in pharmacology. She then joined the University of Chicago faculty (Bernstein and Sullivan 2023). She later attained medical education from the University of Chicago's medical school, joining the 6% of women physicians in the United States in 1950 (Kelsey 1991; Lester 2021).With almost a decade of experience in pharmaceutical research, she pivoted to primary care practice in 1950. This decision reflected her knowledge of what it would take for a woman to make a change in her field of choice—according to a reflection written by Kelsey after she retired, "[as] a woman, I needed the extra credentials. Let us face it, I needed all the help I could get" (Kelsey 1991, 29-30). This comment about her decision to pursue medical school demonstrated her understanding of the effort needed to gain credibility in the medical sciences. Her clinical experience would also allow her to approach her work with a patient-centered perspective, equipping her with the knowledge to evaluate the real-world implications of medical treatments (Kelsey 1991).

It was around this time that she began teaching pharmacology at the University of South Dakota Medical School (Bernstein and Sullivan 2023). This position allowed Kelsey to develop groundbreaking studies on the role of the placental barrier with medicine and how drugs could affect a fetus's development, a niche field of study that would serve her well in her future work with the FDA (Geraghty 2001b).

Kelsey officially rejoined the FDA in 1960 as a medical officer within the Bureau of Medicine. This position required her to review pharmaceutical applications and oversee any research or inspections that needed to be done following the submission of a potential new drug. Kelsey's position began in August of 1960, reviewing New Drug Applications (NDAs). Within a month of her tenure, the thalidomide application reached her desk. What followed would test

Kelsey's scientific judgment, professional courage, and determination to protect public health in ways no one could have anticipated (Geraghty 2001b).

Protecting America's Medicine Cabinet: The FDA's Evolution

The Food and Drug Administration (FDA) was established in 1906 under the Pure Food and Drug Act, which prohibited selling misbranded or contaminated goods. The FDA underwent notable change during the first half-century of its existence, from restricting narcotics to developing the Federal Food, Drug, and Cosmetic Act of 1938. The FDA used the Federal Food, Drug, and Cosmetic Act of 1938 to extend its ability to prosecute drug manufacturers and ensure consumer protection through pre-market approval and mandatory inspections of factory conditions done by FDA agents (Young 1964). The United States Congress developed this new safety law in response to the 1937 crisis over the medical administration of sulfanilamide, a raspberry-flavored elixir.[1] Designed to make medicine more palatable, the seemingly magical liquid dubbed Elixir Sulfanilamide caused 107 deaths—primarily of children—across the United States (Ballentine 1981).

Trials under the advisement and supervision of Geiling revealed the candy-sweet flavoring to be a mixture containing ethylene glycol, a toxic compound used in anti-freeze and hydraulic brake fluid (NIOSH 2023). At the time, there was no legal requirement for pre-distribution approval from the FDA; ethylene glycol was blindly presumed safe for consumption (Ballentine 1981). When the FDA received notice of the potentially fatal release of toxins, they worked to recover and study the drug with Dr. Geiling at the head of the project. Kelsey, then a PhD candidate in pharmacology, supported this FDA investigation by conducting post-collection tests of sulfanilamide (Ricard 2021).

While this tragic case prompted the implementation of stronger federal regulations and increased intervention in public health and safety through the 1938 Food, Drug, and Cosmetics Act, these new measures were still insufficient in fully ensuring consumer protection. In two short decades, another medical discovery would sweep the nation with grand promises, only to act as yet another marker of the progress still needed from the FDA regarding preventative measures to ensure public health and safety. By 1959, thalidomide had reached the United States and consumers used it to relieve pregnancy symptoms like morning sickness and insomnia. The medication promised wonderful results and had been in circulation in other European countries, most prominently Germany, for half a decade (White 2001).

Miracle Drug or Hidden Menace? Thalidomide's False Promise

The German company Grünenthal developed Thalidomide in the early 1950s as a cough and cold remedy and cure for several cancers, leprosy complications, and illnesses associated with tuberculosis (Vargesson 2015; Woolf 2022). Commonly marketed in the United States under the names Thalomid, Contergan, or Kevadon, the medication was classified as an immunomodulator, or a medication intended to improve efficiency of the immune system through the modulation of white blood cell development (NCI 2011). After its 1957 release in Europe, thalidomide garnered a reputation as a "miracle drug" because it was an over-the-counter, non-barbiturate alternative to Valium, a commonly prescribed barbiturate used as a sedative. Non-barbiturates, usually benzodiazepines, pose a lower risk of overdose, as benzodiazepines do not slow down brain activity but instead induce the production of inhibitory chemicals that already exist in the brain

[1] Sulfanilamide is a generic antibacterial and antimicrobial substance used in medical and veterinary settings (PubChem n.d.)

and central nervous system (Olsen 1988). Thalidomide also served as a prescription sleeping pill intended for extended use, today commonly prescribed to treat leprosy with a month's supply at a time, presenting little risk of overdose and no addictive properties (Mayo Clinic 2025). The medication had already been legalized in 46 countries across Europe, North America, and Oceania, adding to the pressure to get thalidomide established in the American market (U.S. Thalidomide Survivors 2019).

Further, pharmaceutical companies emphasized the medication's anti-anxiety, nausea relief, and tension-relieving properties in thalidomide marketing, implying the medication's efficacy as a cure-all for people with pregnancy symptoms in their first trimester (Kelsey 1988). Despite this common use, Grünenthal was and still is adamant that the drug was never officially marketed toward pregnant individuals by their team explicitly (Grünenthal n.d.).

The relief from thalidomide was short-lived, as pregnant consumers birthed infants who presented with phocomelia, a birth defect in which limbs are extremely shortened and arise close to the torso (Dunn, Fisher, and Kohler 1962). Researchers found that thalidomide inhibited blood vessel formation, a crucial process during fetal development that produces a spatial framework guiding development and growth of limbs and organs in utero (Seidman and Warren 2002). Panicked parents of children with these congenital limb deficiencies were further distressed when their newborns had heart and eye defects and an absence of skeletal features. Besides their infants' physical ailments, the birthing parent ran the risk of developing peripheral neuropathy, a condition that occurs when the nerves outside the brain and spinal cord are damaged, resulting in limb pain, numbness, and weakness a result of this purported miracle cure (Kim and Scialli 2011).

More than 10,000 babies worldwide were born with birth defects caused by thalidomide between 1950 and 1960, and between 40% and 50% of these children died within the first month of life (NCI 2006). Additionally, pregnant individuals who consumed even a single dose, 100mg, were at risk of miscarriage (Medscape 2024; Kim and Scialli 2011). By the time the drug was labeled a teratogen, a substance that may cause harm or malformation to a fetus or embryo during pregnancy, thalidomide had affected the lives of thousands of families worldwide—both physically and emotionally—and would forever influence pharmacological regulation (Alliance and Health 2008).

Despite the catastrophe that thalidomide inflicted across the world, medical professionals did not immediately recognize the medication as the cause of these numerous health conditions in patients and, potentially, their fetuses. Consequently, pharmaceutical companies did not take the drug out of circulation until these malformations were linked to the medication. Instead, fueled by promises that the drug would shortly be in legal circulation in the United States, doctors across the country received medicine samples from Grünenthal and their American partner, Richardson-Merrell (Merrell), to pass quietly on to patients exhibiting the symptoms the drug claimed to relieve. These makeshift trial runs induced by pharmaceutical companies and participating physicians were completely legal, as most FDA legislation worked to respond to issues rather than prevent them (Yale Law School 2023; Burrows n.d.). This distribution of thalidomide began in 1959 under the guise of clinical trials and resulted in hundreds of American patients affected by the tragic aftereffects of the teratogen. The marketing scheme brought unnecessary pain and loss to the United States, and it would continue for another two years before Dr. Frances Kelsey and her team at the FDA discovered the truth about thalidomide.

Profit Over Precaution: The Companies Behind Thalidomide

Chemie Grünenthal, a German pharmaceutical company, developed in 1946 as a subsidiary of the soap and cosmetics manufacturer Dali Werke, Mauer, and Wirtz, and started producing medications for the post-war market. The company began developing thalidomide in 1954 as a synthetic alternative to natural barbiturates. The development of synthetic drugs, such as thalidomide, was a relatively new process. Before World War II, most drugs were developed using pre-existing, natural remedies and adjusting them for mass marketing and consumption (White 2001). This novel area of pharmaceutical expansion also proved to be highly lucrative, making the production and distribution of a sleeping pill like thalidomide an extremely attractive proposal to those within the pharmaceutical industry (Ridings 2013).

In developing thalidomide, Grünenthal used standard safety trials such as wheel running and the evaluation of the righting reflex in animal models, specifically mice. Wheel running measured activity on a wheel, which most rodents engage in readily in captivity (Novak, Burghardt, and Levine 2012). The righting reflex test tested the effects of the sedative on the reflex that helps rodents and humans recognize and correct postural imbalances (Wasilczuk, Maier, and Kelz 2018). Thalidomide successfully passed both (Ridings 2013).

After passing these safety trials, the drug underwent an efficacy test known as the "jiggle cage test," designed to evaluate its potency as a sleeping pill (Silverman 2002, 405). In this test, thalidomide-treated mice were placed in a cage configured to trigger a chemical reaction that produced hydrogen gas. The amount of hydrogen generated corresponded to the mice's movement levels; less movement indicated sedative effects. Although Grünenthal concealed the exact results of the study, the company used the data to promote thalidomide as an effective non-barbiturate sleeping medication (White 2001).

Grünenthal argued that the drug caused no significant adverse effects in animal models due to its poor solubility in water and limited absorption into the bloodstream. Based on this, they concluded that the medication had exceptionally low toxicity, providing their primary reasoning for why thalidomide should be released for human clinical trials. However, these observations alone were insufficient evidence to confidently assess the drug's safety, as they failed to account for other potential toxic effects or long-term risks. The company conducted only observational animal studies without performing blood or tissue concentration tests to verify their safety claims. Despite this limited testing, regulatory standards at the time allowed Grünenthal to proceed directly to human clinical trials (Botting 2015).

Grünenthal conducted a clinical trial on humans across four weeks in 1956. Three hundred patients received dosages between 25 and 200mg of thalidomide three times a day. At the end of the four weeks, comparative blood tests allegedly showed no change from the before-tests, but there is no empirical evidence available to support these claims, as most of the original test documentation and results were either destroyed or deliberately withheld by Grünenthal (Botting 2015). Additionally, despite the medication's intended long-term use, the trial only observed effects over four weeks. Grünenthal marketed thalidomide as a sedative that could be safely used indefinitely and emphasized its harmlessness as compared to barbiturate sedatives that were currently on the market. Starting October 1, 1957, the medicine quickly began to circulate in Europe, namely through Germany and the United Kingdom, being praised as a miracle cure as potential patients, both pregnant and not, marveled at Grünenthal's safety claims. The corporation began to collect these glowing reviews and, in 1958, reached out to the first of two American companies, Smith, French, and Kline (SKF), to promote and distribute thalidomide in the United States. The company declined, and Grünenthal turned to Richardson-Merrell instead (White 2001).

When Merrell's representatives first heard about thalidomide, the company was recovering from a major lawsuit brought against them regarding Triparanol, a drug intended to lower cholesterol that they had developed and sold between 1956 and 1959. The medication, which had not shown any signs of efficacy or safety in its 22 months on the American market, caused some patients to develop cataracts of the eyes, and was pulled off shelves after over 1,000 personal injury lawsuits were filed against Merrell and the company paid almost 200 million dollars in legal fees and fines during the aftermath. The corporation had put fiscal prosperity over public safety and ethical considerations, and were desperate to remedy their reputation in the eyes of the American public (Keeton 1968; Ridings 2013; White 2001).

Even in light of Merrell's damaged public image, Grünenthal reached out to Merrell to negotiate their role in marketing and selling the drug in the United States and the corporation eagerly accepted the opportunity to introduce the first "completely safe" sedative, according to Grünenthal, to be sold over the counter (Silverman 2002, 405). Three months later, Merrell began distributing 2.5 million pills to 1200 physicians as a privately run clinical trial. The company delivered the medications with a promise that both American and international companies had fully tested the dosage, safety, and usefulness of thalidomide and that the doctors had no obligation to report the results of their patients using the medication if they were disinclined to, nor did they have any legal obligation to inform their patients that the medication was still in the testing stage. This pseudo-experiment began nearly a year and a half before thalidomide was submitted to the FDA for official government approval (Junod 2008; Silverman 2002).

The American Gambit: Thalidomide's Stealth Entry into America

According to a report that Kelsey released in 1988, "new drugs were cleared for marketing on the basis of safety *claims* [emphasis added] alone" (Kelsey 1988 n.p.). This meant that without observed deficiencies in the application, the Bureau of Medicine within the FDA could not prevent a medication or treatment from being legal for public consumption (Kelsey 1961; Seidman and Warren 2002). The FDA's New Drug Branch within the Bureau of Medicine allowed FDA agents only 60 days to identify issues with the drug evaluations before automatically approving nationwide circulation. Additionally, despite the FDA's increase of legislation in 1938, which required drug sponsors to submit safety data to the FDA before the company could begin marketing a drug, there were no explicit restrictions on what kind of data or information needed to be provided (Burrows 2018). If the FDA could not provide sufficient evidence that a drug was explicitly unsafe for public use, the pharmaceutical company submitting the New Drug Application (NDA) would be free to market and sell the medication. Furthermore, even without FDA approval, it was legal at the time to distribute the drug to medical facilities, and thalidomide had already reached doctors and patients by the time the FDA began its review (Silverman 2002). On September 12, 1960, Kelsey received the thalidomide case as her first assignment within the Bureau of Medicine (Kelsey 1988). Kelsey would be working alongside two others who had also been assigned to the case. The three-person team consisted of chemist Lee Geismar, pharmacologist Jiro Oyama, and Kelsey, the medical officer. Organization members expected this approval to be an open-and-shut case because, according to Kelsey's supervisors, "there [would] be no problems with sleeping pills" (Kelsey 1991, 49).

Each team member conducted their work as a separate entity, as each was part of a distinct bureau within the FDA. Kelsey and Geismar even worked in the same building but had never exchanged words until the two began to work together on the thalidomide case. The three officers would conduct their research and trials independently, exchanging data primarily through written

memos and official documentation. This fragmented arrangement created significant challenges for information sharing and collaborative problem solving, making the 60-day review period dangerously inadequate for thorough pharmaceutical evaluation. Such structural inefficiency created a serious risk: medications could potentially receive default approval and reach public consumption before the Bureau of Medicine completed comprehensive safety studies (Kelsey 1991).

More detailed and explicit instructions for drug approval, such as requiring results of animal studies, how the drug behaves in the human body, an analysis of the risk-to-benefit ratios, and even how its manufactured, processed, and packaged, are now required. Prior to the thalidomide case, however, the FDA had few specific requirements for NDAs. Richardson-Merrell's only legally required task was to provide proof, in whatever form they saw fit, that thalidomide was safe and effective (Henriquez Abramuk 2023). Despite this, Kelsey and her team still had certain questions to work through when investigating an NDA for a medication like thalidomide. Primarily, their tasks involved reviewing any preclinical or human trials done by the company that submitted the NDA or developed the medication, comparing reviews of other medicines on the market, and assessing methodology in order to spot inconsistencies during the approval process (Seidman and Warren 2002). The FDA's main goal, specifically within the Bureau of Medicine, was to ensure the drug was safe—NDA review was not necessarily an evaluation of drug functionality (Greene and Podolsky 2012). For Kelsey's team, the goal was to determine whether thalidomide would pose a public health threat based on empirical evidence and testimony collected by Grünenthal and delivered to the FDA through Merrell (White 2001).

The team faced significant challenges in conducting a thorough evaluation of thalidomide, as the scientists were stationed in separate buildings, complicating the exchange of critical information. However, despite these obstacles, their timeline and separation worked to their advantage in some ways: only one member of the team needed to identify a safety issue to halt the drug's approval, and ultimately, all three officers independently flagged concerns with thalidomide during their pilot tests. Kelsey claims that, though they each had their hesitations with the drug, it was Geismar's doubts that allowed the initial pause in the approval process. Geismar's training as a chemist in Germany, where thalidomide was developed, was advantageous, as most of the existing literature was in German. While Geismar did not conduct chemical tests herself, her analysis revealed that all the studies conducted by Grünenthal were superficial. Grünenthal's investigation into thalidomide was remarkably limited: key areas such as long-term toxicity, organ-specific effects, and the drug's metabolism in the body were either overlooked or entirely absent. These omissions highlighted a glaring lack of rigor in Grünenthal's research, raising significant concerns about the drug's safety and the company's commitment to thorough scientific investigation (Botting 2015; Kelsey 1991; White 2001).

Oyama, the team pharmacologist, conducted animal studies on strains of rabbits, mice, rats, dogs, hamsters, cats, and even armadillos, pigs, guinea pigs, and ferrets that focused on the discovery of any potential toxic effects of the drug concerning its potential use (Williams 2024; FDA 2018). After trials on non-pregnant animals, the study expanded to include pregnant animals that received varying levels of the medication at different points in their pregnancies. Notably, Oyama administered dosages as high as 5000mg/kg to pregnant rats, mice, and rabbits with no malformations in their offspring (Botting 2015; Williams 2024). However, he noted concerns about drug absorption in animal model trials, as thalidomide did not absorb well into the body when digested, an effect that Grünenthal's reports suggested meant the medication would not have significant negative side effects. This low absorption level also resulted in the suggested dosage

for thalidomide being extremely high—up to 1000 mg a day (Rehman, Arfons, and Lazarus 2011). Despite this conclusion from the data received by the FDA, however, Oyama's main concerns, much like Geismar's, lay with the data that Merrell provided. The chronic toxicity reports were incomplete. Thalidomide had only existed for half a decade at this point, and all clinical trials had been conducted over a period under six months, meaning there could be no definitive promise regarding adverse long-term effects on a drug intended for long-term use (Abdel-Megid 2022).

Kelsey's role as chief medical officer was to review all clinical trials by evaluating and advising on protocol design, endpoints, and analysis for drug approval, as well as analyze any chemical or pharmacological studies conducted during the 60-day FDA investigation (FDA 2018). The NDA submitted by Merrell contained no negative information about thalidomide, making Kelsey suspicious that the information provided was not based on rigorous clinical trials or scientific data. Purely based on the evidence provided, thalidomide was safe. The issues instead arose from what was not included in the initial reports (Ruthenberg 2020) Most of the reports in support of thalidomide were closer to testimonials rather than scientific studies, and there was not enough clinical support in the literature provided (Kelsey 1991).

This collection of glowing support for thalidomide and lack of data regarding risk potential triggered Kelsey's scientific instincts. Despite being new to the FDA and knowing that delaying a medication like thalidomide, with all the grand promises attached, could harm both patients and her professional standing, she chose to prioritize scientific rigor over expedience, and request more information regarding thalidomide.

Kelsey and her team notified Merrell of these discrepancies, and the company attempted to provide more information. The team still found deficiencies, requiring the company to conduct a full resubmission of the product for review, a request made on November 20, 1961 by Kelsey to Dr. Joseph Murray, a bacteriologist and main contact at Richardson-Merrell. Upon request for resubmission, he persistently challenged the FDA team's request, repeatedly calling and visiting Washington. He had expected that, since the drug had been marketed and widely distributed across Europe for four years, the FDA could not have substantial reason to withhold drug approval (Abdel-Megid 2022).

Battle of Wills: When Corporate Pressure Met Scientific Integrity

Kelsey stood her ground, however, and while reviewing the newly submitted thalidomide application in February 1961, the team found evidence that she had made the right call. A study by Dr. Leslie Florence, published on December 31, 1960, reported cases of peripheral neuropathy after long-term use of thalidomide, providing what Kelsey's team believed was the first sign of a serious side effect linked to thalidomide (Florence 1960). The effects were extremely severe for some patients who developed intense pain and atrophy in axial musculature, and Florence's study suggested these symptoms may be irreversible damage caused by the medication. Florence's discovery validated Kelsey's initial concerns. If thalidomide could cause severe nerve damage in adults taking it as prescribed, more proof of safety would surely be needed before the FDA could ethically approve its circulation. Yet, delaying approval meant potentially denying relief to thousands of patients. No matter the final choice, Kelsey's work had already impacted countless Americans, many suffering ailments from anxiety to insomnia, who were awaiting access to what European doctors had proclaimed a breakthrough treatment. (Seidman and Warren 2002).

Florence's study reached the FDA late—in early February—because of an ongoing mail strike and prompted the request for even more literature discussing the safety and validity of thalidomide from Merrell, delaying any potential release on American soil even further (Kelsey

1991). The team later learned that Dr. Heinrich Mückter, one of the founders of Grünenthal, had identified over 150 cases of this symptom since its release to the public but claimed it was merely a result of occasional allergies (Evans 2014).[2] Despite Mückter's downplaying this severe side effect, the Federal Institute for Drugs and Medical Devices in Germany began to regulate thalidomide distribution by requiring a prescription for its dispersal in May 1961 (Silverman 2002).

Concerns about Merrell's intentions deepened when Kelsey questioned Murray about Florence's study nearly three weeks after the FDA had received the information. Kelsey suspected that Murray knew about the report beforehand but had not disclosed it, only addressing it after she and her team addressed their concerns about this new data. This withholding of critical data prompted an FDA investigation into Merrell's negligence regarding consumer safety, though no definitive evidence of delinquency was found (Kelsey 1991).

Escalating Tactics: Gender Expectations and Marketing Maneuvers

After this incident, Kelsey's wariness increased. Rightfully, she found it troubling that there was so much dereliction of duty, both on the side of the pharmaceutical company and the investigative department of the FDA. She felt as though this oversight of negative side effects in patients using thalidomide presented concerning implications for the gaps in public health safety even with FDA intervention (McLeod 1995). Additionally, Kelsey was concerned about Merrell's lack of pre-existing knowledge on the effects of a medication the company was trying to market as one of the safest sedatives available, which raised serious questions about their scientific credibility and commitment to consumer safety (Kelsey 1991; Warsh 2024).

In light of the Florence paper, Murray traveled to Germany to investigate the claims of peripheral neuritis, and Mückter informed him, just like he had informed German pharmaceutical companies and regulatory forces, that the correlation was actually due to a poor diet and occasional issues resulting from allergies to thalidomide. This was the same information Mückter had given British distribution companies as well when they notified thalidomide's parent company—that the symptoms should go away as soon as the patient stopped taking the medication, and that the pharmaceutical companies should "sit back and enjoy the revenues" (Evans 2014, 8).

Even with the information provided by Murray through Mückter, Kelsey continued to pursue her suspicions. She and her team requested information on any clinical trials Merrell had conducted across the United States, as the original NDA had listed around 60 physicians who were in possession of and legally distributing the medication for this purpose, and found several cases of permanent nerve damage cataloged in reports completed by Merrell. The team's request for clinical trial information revealed that a large number of physicians had been distributing thalidomide to patients without keeping proper records of treatment outcomes. Merrell had told the doctors that FDA approval was imminent, leading to lax documentation procedures in American clinics (Kelsey 1991).

The spring and summer of 1961 brought a new intensity from Richardson-Merrell against the FDA. Kelsey recalled that "they came to Washington, it seemed, in droves. They wrote letters as often as they telephoned—as often as three times a week. They telephoned my superiors and they came to see them too … most of the things they called me, you wouldn't print." (Seidman and Warren 2002, 498). Kelsey continued to request more information, but she was experiencing

[2] Mückter was a scientist in Nazi camps and used individuals in concentration camps in Poland as subjects in trials for an anti-typhus vaccine. He narrowly avoided Polish prosecution, and started Grünenthal with other Nazis and Nazi sympathizers (Evans 2014).

significant pressure, and tensions between her team in the FDA and Merrell's agents were escalating (Seidman and Warren 2002).

Faced with Merrell's attempts to shift the narrative away from their inability to provide significant safety data, Kelsey remained steadfast in her commitment to evidence-based evaluation, refusing to allow marketing tactics to overshadow the potential dangers posed by the drug despite knowing her decision might deny relief to thousands of Americans. Rather than provide sufficient evidence that the drug was safe for the medical market, they began to compare the safety of thalidomide to barbiturates, a drug class that dominated the tranquilizer market in 1961. Marilyn Monroe's publicized death, for example, was caused by barbiturate overdose (Hertel and Neff 1962). The company attempted to capitalize on this anti-barbiturate momentum, claiming that "if Marilyn Monroe had taken thalidomide she would still be alive" (Kelsey 1991, 59). In response, Kelsey admitted that while this was technically a true statement, it did not outweigh the risks, both known and unknown, associated with thalidomide (Kelsey 1991).

Protecting Public Safety: Corporate Deception Exposed

The initial, drawn-out concern with thalidomide surrounding the risk of peripheral neuritis prompted Kelsey, Oyama, and Geismar toward the question that would change the course of FDA history: if the medication had this effect on a fully-developed patient, how would thalidomide affect a fetus? This question was new to the field of clinical testing and held a significant amount of attention after the discovery that embryos and fetuses could not metabolize drugs in the same way an adult body could be due to undeveloped kidneys, an observation Kelsey worked and expanded on in her post-doctoral years. These new concerns and studies, in conjunction with Kelsey's research on the placental barrier and thalidomide's unique inability to be absorbed and quickly disposed of in the human body, pushed the question of how thalidomide may affect fetal development to the primary research focus.

There were few other known occurrences of adverse effects on fetal development from drugs taken by pregnant individuals, and understanding of this concept was extremely limited (Oong and Tadi 2024). At this point, there were no FDA regulations requiring testing of reproductive or fetal effects, and teratology was a nonexistent field. The novel realization made by Kelsey's team was: "When you give a drug to a pregnant woman, you are exposing, in fact, two people to the drug, the mother and the child." (Kelsey 1991, 61). This realization that a fetus would potentially experience side effects from a medication taken by the pregnant individual was critical in the thalidomide case, and would shape the beginnings of teratology, or the study of adverse effects of medication on fetal development (Kelsey 1988).

While revolutionary for public safety, concerns over fetal effects added a layer of difficulty for Merrell in getting thalidomide approved. The only recorded information on the effects of thalidomide on pregnancy included a small sample of expectant individuals in late pregnancy to determine if the medication would increase their overall comfort in their third trimester, which did not satisfy Kelsey's need for confirmation that the drug was safe for use when pregnant (Kelsey 1991). When asked if there was any evidence supported by patients who took thalidomide consistently throughout their pregnancies, Merrell declined to answer. The corporation had no evidence of this kind, and there was no legal obligation to present it (Warsh 2024). Murray offered to put safety labels regarding potential risks for both the pregnant individual and the fetus on the packaging, but refused to fully indulge Kelsey's attempts to ensure the public's safety (Kelsey 1991).

Murray's frustrations grew as the trial continued, because he believed "Christmas [was] the season for sedatives and hypnotics," and was hoping to get thalidomide officially on the market in time for the holidays (Kelsey 1991, 63). This argument had lasted a full year rather than the expected 60 days, and it seemed as though a second Christmas would come and go without thalidomide on the shelves. In September 1961, Merrell held a conference, putting its clinical investigators under intense scrutiny. The company criticized the FDA, calling the organization, and Dr. Frances Kelsey herself, "obstructionist" in their attempts to get thalidomide on the market. However, a question from the crowd quieted the conjecture against Kelsey from Merrell: "is thalidomide safe in pregnancy?" (Kelsey 1991, 63). The hush alerted the audience to the fact that the data that would allow for thalidomide to be accepted by the FDA simply did not exist (Kelsey 1991).

This conference marked a pivotal moment for Kelsey in the thalidomide case. When Merrell publicly accused her of thwarting thalidomide's arrival to the American public, she had the opportunity to soften her stance and let thalidomide into the U.S. pharmaceutical market. The professional and personal costs of her year-long resistance were now evident—pharmaceutical representatives had maligned her character, and her superiors had suggested she simply could not stand the pressures of working in public health. Yet, when the conference room fell silent following the pregnancy safety question, Kelsey felt as though her scientific judgement had been vindicated. This was no longer a procedural delay, but a deliberate decision to prevent what she now suspected to be an extremely harmful medication from reaching the American public (Kelsey 1991).

Richardson-Merrell's persistence continued despite mounting evidence of thalidomide's dangers. Just a few weeks after the conference, Murray informed Kelsey that Merrell's representatives received news from German medical practitioners of increased pregnancy complications correlated with patients who had taken thalidomide. Despite this new evidence, Murray claimed no explicit connection between the two events could be found. FDA records show that Murray's claims were blatant lies. Merrell indeed held evidence of thalidomide causing limb, organ, and nervous system deformation during fetal development: one of its clinical investigators had delivered multiple deformed babies as a result of the parent taking thalidomide (Geng 1973).

On November 30, 1961, Murray informed the FDA that thalidomide was being temporarily withdrawn from the German market after scientists there discovered a potential link between the medication and increased rates of phocomelia across Europe. Even with the yearlong debate, Kelsey's team was shocked by this possibility. Most of the objections previously made by the FDA against the public consumption of thalidomide were based on theoretical possibilities— the fact that there was no proof the drug was safe—rather than proof it was unsafe. The FDA immediately dispatched bureau agents stationed in Germany to investigate and Merrell claimed they would suspend American clinical trials pending further information (Kelsey 1991).

Despite this claim, Merrell's following actions revealed a pattern of deception. The company sent a warning letter on February 21, 1962 notifying 60 physicians, the number listed on the original NDA, of this link between fetal abnormalities and thalidomide. This left approximately 20,000 patients across the country exposed to 2.5 million thalidomide tablets with no knowledge of their dangers (Seidman and Warren 2002). When Merrell officially withdrew their NDA on March 8, 1962, they simultaneously requested approval for three new clinical trials of thalidomide for non-pregnancy use. The withdrawal letter claimed that all investigations had been halted in December, contradicting what the FDA now understood about ongoing distribution. This discovery prompted Kelsey's team to demand a comprehensive list of all physicians supplied with the drug on April 11, revealing the full extent of Merrell's misrepresentation (Kelsey 1991).

On April 6, Dr. Helen Taussig, a pediatric cardiologist at Johns Hopkins University, confirmed the FDA's fears: thalidomide caused the uptick in birth defects, and more providers had received samples of the drug than Merrell initially disclosed. Taussig had received requests from German investigators to analyze evidence of heart defects seen in newborns affected by the medication. She traveled to Germany in early 1962 to investigate the congenital heart disease that was spreading across the European continent. Taussig acted as a first-hand contact to show Kelsey the evidence of thalidomide's effects: photographic evidence, case histories, and testimonies from physicians that solidified the FDA's theory that thalidomide was the root cause of the increase in birth defects being seen in the United States (McFadyen 1976). In particular, Taussig noted that over the course of her career prior to thalidomide, she had seen only one or two cases of congenital limb malformation or missing limbs, but many of the physicians she had visited across Europe had seen upwards of 50 cases in the last three years (Warsh 2024).

Even with the insufficient restrictions established by the FDA at the time of the thalidomide investigation, it became clearer with each conclusive piece of evidence that Richardson-Merrell had been using questionable strategies to promote and distribute thalidomide, and the consequences were more disastrous than anyone could have predicted. These tactics went as far as the undisclosed authorship of false research studies and scientific articles that were subsidized by the pharmaceutical company and hiring influential doctors to present intentionally misleading information to investigators during America-based clinical trials, including information that "the drug was virtually ready to be approved" (Kelsey 1991, 72). Taussig's contacts in Germany had informed her that studies conducted by non-Grünenthal affiliates had shown teratogenic effects in embryonic rabbits in the years after the medication was initially announced market-safe in Europe, a fact that was well-known by European physicians but had conveniently slipped through the cracks when Merrell relayed information to the FDA (Warsh 2024).

Though tensions continued to rise as evidence against thalidomide was accrued, Merrell still had the law on its side. Not only did the NDAs Merrell had submitted for the medication strongly suggest that Merrell had plausible deniability regarding its negative effects on both adult and fetal patients, but the sheer lack of record regarding any communication Merrell may have had with contacts in Europe and the effectiveness of the recall in the United States made it nearly impossible to develop a concrete argument that the corporation had exhibited exorbitant amounts of negligence regarding thalidomide's safety before public consumption (McFadyen 1976; Seidman and Warren 2002). However, Vick Chemical Company, a subdivision of Merrell, stated that they never obtained evidence regarding how much thalidomide was received or properly disposed of after the recall (McFadyen 1976).

Richardson-Merrell's executive vice president, Robert Woodward, told the FDA commissioner that the thalidomide recall had been completed as of July 20, 1962. However, an FDA inspector visiting the Merrell headquarters in New York on July 23 found employees engaged in phone calls to physicians with access to thalidomide and an extensive list of providers who had made no effort to contact patients who had been given the drug, nor kept records of their thalidomide prescriptions (Seidman and Warren 2002).

As the thalidomide research team gathered more evidence of the drug's teratogenic effects, Merrell, in light of these mounting discoveries, finally revealed the truth regarding its list of physicians. The scope of the issue was much larger than Kelsey and her team at the FDA initially anticipated. Merrell had distributed the drug to over 1,000 physicians across the United States, spanning every medical area of expertise. The FDA's next task was to meet with each physician, collect any drug samples that they had on hand, request any records regarding prescription or

circulation of thalidomide, and if the doctors had noticed any complications with pregnancy or birth while on thalidomide. Only three reports emerged via this strategy, and out of those, there were 10 identified cases of phocomelia (Kelsey 1991). One of the identified cases was from a nurse who gave birth to a baby lacking any limbs who "may have had access to the item" (Thomas 2020 n.p.) during her pregnancy because of her proximity to medical practice. Doctors who received the medicine from Merrell also reported side effects in those who took the medication while pregnant, such as loss of vision and peripheral neuritis (Thomas 2020).

After Merrell revealed they had been withholding evidence from the FDA commissioner, Kelsey held a meeting with Merrell representatives in July 1962 to discuss their knowledge of thalidomide's toxic side effects. Rather than focusing on the issues surrounding Merrell's distribution of the drug and lack of action once asked to notify physicians in possession of the medication, they continued to emphasize the importance of the holiday season for selling tranquilizer-type prescriptions, asking Kelsey to reconsider the thalidomide application Merrell had withdrawn. Kelsey stood her ground, knowing her choice to fight had been solidified, and Merrell's thalidomide application remained in the "withdrawn" pile. (Kelsey 1991).

Beyond the Bottle: Kelsey's Triumph on Capitol Hill

On April 11, 1962, Taussig and Kelsey presented her findings to the American College of Physicians (ACP), where she showed photos and recounted the clinical evidence presented to her in Europe of heart defects and phocomelia. This speech was covered by the *New York Times* but media outlets considered this a one-time event rather than a developing story. Despite this, the article caught the attention of Tennessee Senator Estes Kefauver, who had been building a case against the American drug industry since 1959. Kefauver was primarily focused on reducing the prices of medications, and had introduced a bill in early 1962 attempting to do so, but was largely ignored by the rest of the United States Senate (McFadyen 1976).

Kefauver requested that Taussig give her testimony in May before Representative Emmanuel Celler's Antitrust Subcommittee in favor of his bill, which was stalled in the Senate. Taussig presented her findings once more, but this time the story was completely passed over by the American press, leaving this critical moment in public health history without a platform, and Kefauver with a bill that remained tabled (McFadyen 1976).

In mid-July 1962, Kefauver and his staff decided to help break the thalidomide story to the press once more as an effort to revive their bill. Morton Mintz, one of the top reporters at the *Washington Post*, received information from Kefauver that thalidomide would have almost certainly been released to the public had it not been for Kelsey's perseverance. Mintz interviewed Kelsey immediately, and on July 15, "'Heroine' of FDA Keeps Bad Drug Off Market" (Mintz 1962 n.p.) appeared as front-page news (McFadyen 1976; Mintz 1962). This article sparked a mass media movement, with editorials and follow-up stories on drugs and drug control, and with thalidomide at the forefront of the American public's minds, Congress had no choice but to act (McFadyen 1976). Kefauver continued to push his amendments to the 1938 Food, Drugs, and Cosmetics Act with Kelsey at the forefront of his argument. After a speech on July 18 in which Kefauver commended her for her dedication to the American public, Kelsey testified before the Senate on August 1 regarding the Bureau of Medicine's role in preventing the deadly sedative from reaching the American public. Her speech, which eviscerated the American Medical Association and Pharmaceutical Manufacturers Association, in addition to Richardson-Merrell, for their lobbying tactics against Kefauver's amendment proposal, swayed the public even farther toward the side of further FDA intervention and passing the amendment. Alongside Taussig, Kelsey was one of the

only women in the room, and these two doctors were the only people who testified who could ask "what if *we* had been prescribed thalidomide?" Their insight swayed both the Congress and the public in favor of Kefauver's bill (Elliott 2017; Warsh 2024).

In October 1962, Kelsey and Taussig, among the others who were in support of further FDA jurisdiction, finally felt victorious. Congress passed the Kefauver-Harris Amendments to the 1938 Food, Drug, and Cosmetics Act. These amendments mandated three main points to protect future consumers: the establishment of efficacy requirements, the strengthening of regulatory oversight, and the requirement for informed consent in clinical trials involving human subjects. These requirements established a need for companies to ensure medications were proven to provide the intended therapeutic effects. This also allowed the FDA to require more comprehensive testing and evaluation of drugs before they reached American markets, and ensured that individuals participating in drug trials would be fully informed about the risks and benefits of any experimental treatments they received (Goodrich 1963).

This set of amendments to the FDA's power established another level of testing that would force medical companies to test for every complication, including pregnancy. Kelsey's legacy left the FDA a safer, more inclusive place by elevating awareness of drug safety in pregnancy through the prevention of a massive public health crisis. She received the President's Medal for Distinguished Federal Civilian Service by President John F. Kennedy in 1962 for "refusing to compromise her exacting standards for patient safety" (Geraghty 2001a, 254). She became a model example of an FDA agent and was promoted to the head of the Investigational Drug Branch of the FDA, a reward for her steadfast commitment to public safety (Warsh 2024). Her diligence and strong moral compass served as an outline for the handling of cases going forward. Kelsey's role in the thalidomide crisis set the stage for the necessary development of representative population sampling in clinical trials and is a testament to the importance of regulatory vigilance and the pivotal role of individuals' work, particularly that of women, in safeguarding public health.

Representative population sampling, or selecting a more specific group of individuals that represent the portion of the population intended to be the target audience for a pharmaceutical during clinical trials, is a critical part of ensuring that medications do not present misleading information. This is because, by ensuring the participant base for the medication has the same or similar health measures (with thalidomide, accounting for pregnancy, for example), the data collected in pre-clinical or clinical trials accurately represents potential complications with a new medication. The Kefauver amendments establishment of efficacy and regulatory requirements strongly promoted representative population sampling, and this method of testing is still used today to minimize unknown adverse effects (Rudolph et al. 2023). Kelsey's steadfast commitment to thorough evaluation and skepticism toward pharmaceutical claims prevented widespread devastation in the United States. Her resilience, expertise, and advocacy for women's health and the inclusion of teratology in studies were undoubtedly an asset to the FDA's focus on protecting the consumer, and today's Americans share in the benefits of safety subsequently provided by Kelsey's tireless work in the 1960s and beyond (Warsh 2024).

The Aftermath: A Swinging Pendulum of Protection

Despite the FDA's extensive investigation into Richardson-Merrell and the physicians recruited by them, the company's and doctors' records were not substantial enough to acquire a full understanding of thalidomide's effects in the United States. The FDA's investigation identified 17 individuals with congenital limb deficiencies as a result of their parent taking thalidomide, with eight parents who claimed that they had obtained the medication overseas. Thalidomide survivors

in America and Europe have been, or are still working to, be compensated by the government for their struggles, but there are an estimated 10,000 people worldwide with cases of phocomelia or other noted effects of the drug, such as congenital heart defects and sensory impairment, that have no definitive link to thalidomide. Today, the US Thalidomide Survivors group has 76 members and suspects that there are more unaccounted for with birth defects because of Richardson-Merrell's abuse of the limited clinical restrictions (US Thalidomide Survivors 2019).

The tragic effects of Merrell's clinical trials and quiet distribution of the teratogen still hold a significant impact on individuals in the United States and worldwide, but no charges were pressed against the company. Due to sparse reports on the drug's effects and doctors known to have distributed thalidomide refusing to talk, there is little concrete evidence that thalidomide had definitively caused birth defects or peripheral neuropathy. Beyond this, regulatory bodies in the United States and Europe were still developing pharmaceutical regulation policies, leaving Grünenthal and Richardson Merrel's negligence hard to define (Thomas 2020). In 1963, FDA agents investigating the company's distribution of thalidomide reported 24 counts of ways in which Richardson-Merrell had violated the Food, Drug, and Cosmetic Act including false claims of thalidomide's safety when distributing the drug. Merrell had informed physicians that the medication was completely harmless without adequate clinical trials, and, according to doctors whose names were redacted for safety concerns, this resulted in known cases of phocomelia in infants born to healthcare workers that were documented as early as 1962.

The Department of Justice reviewed this submission from the FDA against Merrell, which claimed that "criminal prosecution is neither warranted nor desirable" as of September 1964, prompting the case against the corporation to close. (Thomas 2020, n.p.). The letter from Merrell that informed the FDA of this decision also contained a significant falsehood: "Only one malformed baby had been born in the United States as a result of its mother's use of Kevadon" (2020, n.p.). By the time the FDA noted and recorded this as a false statement, as 10 definitive phocomelia cases had been attributed to thalidomide, and six more were tentatively correlated with the medication, the Department of Justice had rendered its decision. Richardson-Merrell would not be prosecuted for its crimes against the public. This lack of prosecution, in combination with the series of events that unfolded after the FDA denied thalidomide approval, resulted in a dramatic shift regarding pregnant people's care in the United States. The physicians Richardson-Merrell had reached out to in 1959 with the first trial dosages had been aware that the company was conducting a clinical trial and were unsure of potentially adverse side effects but still chose to administer the medication to their patients, over the course of two years (Warsh 2024). A distrust of pharmaceuticals developed, and physicians and patients alike began to focus on avoiding drug exposure as the primary goal during pregnancy, even going as far as taking people with epilepsy off their seizure medications. In this example, doctors observed an exacerbated number of seizures, injuries, and deaths associated with epilepsy in pregnant people, as well as an increased risk of fetal subjection to maternal convulsive seizures (Huynh et al. 2024).

This practice of minimizing pregnant people's exposure to medication continued for almost two decades until 1979 when the American Academy of Pediatrics Committee of Drugs recognized antiseizure medication medications (ASMs) for improving the chance of fetal development to 90%, as opposed to the risk of fetal malformation while on ASMs, which is 4-5% (Committee on Drugs 1979). This new information regarding medication effects on pregnancy and fetal development settled the fear of taking medication while pregnant that had consistently penetrated the way pregnancy care was established in North America but drew attention to a new question:

why was there no established rule surrounding gestational study in clinical trials (Huynh et al. 2024)?

The recognition of ASMs as critical for improving fetal outcomes despite their associated risks highlighted the inadequacy of excluding pregnant people from clinical trials. For decades, this exclusion was based on concerns about fetal harm, but it perpetuated a lack of robust data on the safety and efficacy of medications during pregnancy. ASMs' demonstrated benefits forced a reconsideration of this cautious approach, emphasizing the need for a nuanced understanding of the risk-benefit profiles of medications in pregnant populations. This shift in perspective began to affect legislation in the late 1990s, nearly half a century after Kelsey's fight for a more comprehensive analysis and data collection ended (Huynh, Voinescu, and Bui 2024).

Leadership Beyond Safety: The Enduring Legacy of Dr. Frances Kelsey

Kelsey's leadership transformed pharmaceutical regulation far beyond thalidomide. Her actions directly influenced the 1962 Kefauver-Harris Amendments, which created fundamental changes in protocol regarding testing and approval of medications in the United States. By insisting on scientific rigor even as it seemed to delay a promising treatment, Kelsey's work established a precedent that prioritized the safety of consumers over commercial interests and began to investigate the pharmaceutical industry's one-size-fits-all approach to clinical trials. Her leadership underscored that biological variation and different physiological states, much like pregnancy, necessitated representative population sampling in clinical trials, leading to critical questions in contemporary medical research. As we reflect on Kelsey's legacy, we must consider: Who is still being systematically underrepresented in clinical trials? How did gender biases in medical research potentially contribute to the oversight of pregnancy-specific risk in pharmaceutical testing before thalidomide? What parallel biases may exist in contemporary medical research? What barriers prevent equitable population sampling, and how can they be overcome? Each of these questions stems from Kelsey's pioneering efforts, highlighting how her commitment to scientific integrity and inclusive research methodologies continue to shape our understanding of public health safety today. Her legacy is a reminder that medical progress requires not just innovation in treatment but also safety evaluations to ensure that medical advances protect and benefit everyone.

Epilogue: Thalidomide in the 21st Century

In 1998, the FDA approved thalidomide as a treatment for leprosy and blood cancer, specifically multiple myeloma, after nearly four decades of being banned worldwide (Kim and Scialli 2011; PMC n.d.). The drug is legal under prescribed use only in the United States and with strict restrictions on its use by patients who are or plan to be pregnant during their treatment (London Science Museum 2019). The FDA's thalidomide webpage also provides explicit warnings regarding the obtainment and consumption of the drug, stating that "you will bypass important safeguards designed to protect your health (and the health of others)" if the drug is acquired through non-medical channels (FDA 2018, n.p.).

References

Abdel-Megid, Maya. 2022. "The Thalidomide Disaster Part 1." *Medium*, April 29. medium.com/@mayaabdelmegid/the-thalidomide-disaster-part-1-1a42b1a97c35 (April 17, 2024).

Ballentine, Carol. 1981. "Taste of Raspberries, Taste of Death: The 1937 Elixir Sulfanilamide Incident." *FDA Consumer*, June.

Adam Bernstein and Patricia Sullivan. 2023. "Frances Oldham Kelsey, FDA Scientist Who Kept Thalidomide off U.S. Market, Dies at 101." *Washington Post*, August 7. washingtonpost.com/national/health-science/frances-oldham-kelsey-heroine-of-thalidomide-tragedy-dies-at-101/2015/08/07/ae57335e-c5da-11df-94e1-c5afa35a9e59_story.html (April 14, 2024).

Botting, Jack Howard. 2015. "The History of Thalidomide." In *Animals and Medicine: The Contribution of Animal Experiments to the Control of Disease*, ed. Regina Botting. Cambridge: Open Book Publishers, 183–98. books.openedition.org/obp/1991 (January 16, 2025).

Dunn, P. M., A. M. Fisher, and H. G. Kohler. 1962. "Phocomelia." *American Journal of Obstetrics & Gynecology* 84(3): 348–55. doi.org/10.1016/0002-9378(62)90131-X.

Elliott, Ellen. 2017. "Women in Science: Helen Taussig (1898-1986)." *The Jackson Laboratory*, October 18. jax.org/news-and-insights/jax-blog/2017/october/women-in-science-helen-taussig (May 6, 2024).

Harold Evans. 2014. "Thalidomide: How Men Who Blighted Lives of Thousands Evaded Justice." *The Guardian*, November 14. theguardian.com/society/2014/nov/14/thalidomide-drug-men-blighted-lives-evaded-justice (April 14, 2024).

FDA. 2018a. "Review Team Responsibilities." fda.gov/about-fda/center-drug-evaluation-and-research-cder/review-team-responsibilities (April 14, 2024).

———. 2018b. "Thalidomide (Marketed as Thalomid) Information." fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/thalidomide-marketed-thalomid-information (April 16, 2024).

Florence, A. Leslie. 1960. "Is Thalidomide to Blame?" *British Medical Journal* 2(5217): 1954. doi.org/10.1136/bmj.2.5217.1954.

Veronica Geng. 1973. "Thalidomide: The American Experience." *The New York Times*, April 29. nytimes.com/1973/04/29/archives/thalidomide-the-american-experience.html (April 14, 2024).

Geraghty, Karen. 2001a. "Commemorative Issue: Protecting the Public: Dr. Frances Oldham Kelsey." *AMA Journal of Ethics* 3(11): 418–20. doi.org/10.1001/virtualmentor.2001.3.11.prol2-0111.

———. 2001b. "Protecting the Public: Profile of Dr. Frances Oldham Kelsey." *AMA Journal of Ethics* 3(7): 252–54. doi.org/10.1001/virtualmentor.2001.3.7.prol1-0107.

Goodrich, William W. 1963. "FDA's Regulations Under the Kefauver–Harris Drug Amendments of 1962." *Food, Drug, Cosmetic Law Journal* 18(10): 561–69.

Greene, Jeremy A., and Scott H. Podolsky. 2012. "Reform, Regulation, and Pharmaceuticals — The Kefauver–Harris Amendments at 50." *The New England Journal of Medicine* 367(16): 1481–83. doi.org/10.1056/NEJMp1210007.

Henriquez Abramuk, Maria F. 2023. "Chapter 83 - New Drug Application." In *Translational Sports Medicine, Handbook for Designing and Conducting Clinical and Translational Research*, eds. Adam E. M. Eltorai, Jeffrey A. Bakal, Steven F. DeFroda, and Brett D. Owens. Cambridge, MA: Academic Press, 425–27. doi.org/10.1016/B978-0-323-91259-4.00102-8.

Huynh, Amanda Tieu-Mi, Paula Emanuela Voinescu, and Esther Bui. 2024. "When Pregnancy Becomes an Inclusion Criterion in Neuroscience Research." *JAMA Neurology* 81(1): 7–8. doi.org/10.1001/jamaneurol.2023.4506.

Junod, Suzanne White. 2008. "FDA and Clinical Drug Trials: A Short History." U.S. Food and Drug Administration. fda.gov/media/110437/download (April 14, 2024).

Keeton, Page. 1968. "Some Observations About the Strict Liability of the Maker of Prescription Drugs: The Aftermath of MER/29." *California Law Review* 56(1): 149–59. doi.org/10.2307/3479501.

Kelsey, Frances O. 1988. "Thalidomide Update: Regulatory Aspects." *Teratology* 38(3): 221–26. doi.org/10.1002/tera.1420380305.

———. 1991. "Autobiographical Reflections." Unpublished manuscript. profiles.nlm.nih.gov/spotlight/fk/catalog/nlm:nlmuid-101584643X1-doc (April 14, 2024).

Kim, James H., and Anthony R. Scialli. 2011. "Thalidomide: The Tragedy of Birth Defects and the Effective Treatment of Disease." *Toxicological Sciences* 122(1): 1–6. doi.org/10.1093/toxsci/kfr088.

Kotta-Loizou, Ioly, Agathi Pritsa, Georgios Antasouras, Spyridon N. Vasilopoulos, Gavriela Voulgaridou, Sousana K. Papadopoulou, Robert H. A. Coutts, Eleftherios Lechouritis, and Constantinos Giaginis. 2024. "Fetus Exposure to Drugs and Chemicals: A Holistic Overview on the Assessment of Their Transport and Metabolism across the Human Placental Barrier." *Diseases* 12(6): 114. doi.org/10.3390/diseases12060114.

Lester, Lucille A. 2021. "The 1950s: The Quota System." In *Women and the Practice of Medicine: A New History (1950-2020)*, ed. Lucille A. Lester. Cham: Springer International Publishing, 1–23. doi.org/10.1007/978-3-030-74139-6_1.

Los Angeles Times. 1962. "From the Archives: Marilyn Monroe Dies; Pills Blamed." *Los Angeles Times*, August 6. latimes.com/local/obituaries/archives/la-me-marilyn-monroe-19620806-story.html (April 14, 2024).

Mayo Clinic. 2023. "Thalidomide (Oral Route) - Description and Brand Names." mayoclinic.org/drugs-supplements/thalidomide-oral-route/description/drg-20066301 (May 9, 2025).

McFadyen, R. E. 1976. "Thalidomide in America: A Brush with Tragedy." *Clio Medica* 11(2): 79–93.

McLeod, J. G. 1995. "Investigation of Peripheral Neuropathy." *Journal of Neurology, Neurosurgery, and Psychiatry* 58(3): 274–83. doi.org/10.1136/jnnp.58.3.274.

McNeill, Leila. 2017. "The Woman Who Stood Between America and a Generation of 'Thalidomide Babies.'" *Smithsonian Magazine*, May 8. smithsonianmag.com/science-nature/woman-who-stood-between-america-and-epidemic-birth-defects-180963165/ (April 21, 2024).

Morton Mintz. 1962. "'Heroine' of FDA Keeps Bad Drug Off Market." *Washington Post*, July 15. washingtonpost.com/wp-srv/washtech/longterm/thalidomide/keystories/071598drug.htm (February 15, 2024).

National Cancer Institute. 2006. "Thalidomide." cancer.gov/about-cancer/treatment/drugs/thalidomide (April 16, 2024).

National Institute for Occupational Safety and Health. 2023. "Ethylene Glycol: Systemic Agent." Centers for Disease Control and Prevention. cdc.gov/niosh/ershdb/emergencyresponsecard_29750031.html (April 13, 2024).

Novak, Colleen M., Paul R. Burghardt, and James A. Levine. 2012. "The Use of a Running Wheel to Measure Activity in Rodents: Relationship to Energy Balance, General Activity, and Reward." *Neuroscience and Biobehavioral Reviews* 36(3): 1001–14. doi.org/10.1016/j.neubiorev.2011.12.012.

Olsen, Richard W. 1988. "Barbiturates." *International Anesthesiology Clinics* 26(4): 254–62. doi.org/10.1097/00004311-198802640-00003.

Oong, Ginny C., and Prasanna Tadi. 2024. "Chloramphenicol." In *StatPearls*. Treasure Island, FL: StatPearls Publishing. ncbi.nlm.nih.gov/books/NBK555966/ (April 14, 2024).

PubChem. 2023. "Sulfanilamide." National Library of Medicine. pubchem.ncbi.nlm.nih.gov/compound/5333 (April 21, 2024).

Rehman, Waqas, Lisa M. Arfons, and Hillard M. Lazarus. 2011. "The Rise, Fall and Subsequent Triumph of Thalidomide: Lessons Learned in Drug Development." *Therapeutic Advances in Hematology* 2(5): 291–308. doi.org/10.1177/2040620711413165.

Ricard, Alicen. 2021. "Dr. Frances Oldham Kelsey and Her Fight Against the FDA." West Coast Women in Engineering, Science, and Technology, March 19. sfu.ca/wwest/WWEST_blog/dr--frances-oldham-kelsey.html (April 13, 2024).

Ridings, James E. 2013. "The Thalidomide Disaster, Lessons from the Past." In *Teratogenicity Testing: Methods and Protocols*, ed. Paul C. Barrow. Totowa, NJ: Humana Press, 575–86. doi.org/10.1007/978-1-62703-131-8_36.

Rudolph, Jacqueline E., Yongqi Zhong, Priya Duggal, Shruti H. Mehta, and Bryan Lau. 2023. "Defining Representativeness of Study Samples in Medical and Population Health Research." *BMJ Medicine* 2(1): e000399. doi.org/10.1136/bmjmed-2022-000399.

Ruthenberg, Klaus. 2020. "About the Futile Dream of an Entirely Riskless and Fully Effective Remedy: Thalidomide." In *Ethics of Chemistry*. Singapore: World Scientific, 141–67. doi.org/10.1142/9789811233548_0006.

Science Museum. 2023. "Thalidomide." sciencemuseum.org.uk/objects-and-stories/medicine/thalidomide (April 13, 2024).

Seidman, Lisa A., and Noreen Warren. 2002. "Frances Kelsey & Thalidomide in the US: A Case Study Relating to Pharmaceutical Regulations." *The American Biology Teacher* 64(7): 495–500. doi.org/10.2307/4451354.

Silverman, William A. 2002. "The Schizophrenic Career of a 'Monster Drug.'" *Pediatrics* 110(2): 404–6. doi.org/10.1542/peds.110.2.404.

Katie Thomas. 2020. "The Story of Thalidomide in the U.S., Told Through Documents." *The New York Times*, March 23. nytimes.com/2020/03/23/health/thalidomide-fda-documents.html (April 15, 2024).

US Thalidomide Survivors. 2019. "True Story of Thalidomide in the US." usthalidomide.org/our-story-thalidomide-babies-us/ (March 13, 2024).

Vargesson, Neil. 2015. "Thalidomide-Induced Teratogenesis: History and Mechanisms." *Birth Defects Research Part C: Embryo Today: Reviews* 105(2): 140–56. doi.org/10.1002/bdrc.21096.

Warsh, Cheryl Krasnick. 2024. *Frances Oldham Kelsey, The FDA, and the Battle Against Thalidomide*. New York: Oxford University Press. doi.org/10.1093/oso/9780197632543.001.0001.

Wasilczuk, Andrzej Z., Kaitlyn L. Maier, and Max B. Kelz. 2018. "The Mouse as a Model Organism for Assessing Anesthetic Sensitivity." *Methods in Enzymology* 602: 211–28. doi.org/10.1016/bs.mie.2018.01.008.

White, Allen E. 2001. "Thalidomide and the FDA: Authority Overstepped or Legitimate Safety Measures?" *SSRN Electronic Journal*. doi.org/10.2139/ssrn.294563.

Williams, Julia. 2024. "FDA Modernization Act 2.0: The Beginning of the End for Animal Testing in Drug Development." *Animal Law* 30: 139–68.

Woolf, Alan D. 2022. "Chapter 2.4 - Thalidomide Tragedy, 1950s." In *History of Modern Clinical Toxicology, History of Toxicology and Environmental Health*, ed. Alan D. Woolf. Cambridge, MA: Academic Press, 165–75. doi.org/10.1016/B978-0-12-822218-8.00058-2.

Yale Law School. 2023. "Author of Thalidomide History Tells Drug's Hidden Story." YLS Today, September 19. law.yale.edu/yls-today/news/author-thalidomide-history-tells-drugs-hidden-story (April 13, 2024).

Young, James Harvey. 1964. "The Government and the Consumer: Evolution of Food and Drug Laws The 1938 Food, Drug, and Cosmetic Act." *Journal of Public Law* 13(1): 197–204.