# FDA'S HOMEOPATHIC RISK-BASED ENFORCEMENT: COMPROMISED CONSUMER PROTECTION OR STEPPED-UP SCRUTINY?

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ABSTRACT

The U.S. Food and Drug Administration's (FDA) statutory authority under the Federal Food, Drug, and Cosmetic Act (FFDCA) includes foods, drugs, dietary supplements, and homeopathic products. How the FDA exercises this authority has life and death consequences for all Americans. For the last quarter of a century, the FDA has largely exempted homeopathic products from drug regulations even though the FFDCA classifies homeopathic products as drugs. Since 1988, Agency policy premised on enforcement discretion allowed the manufacturing and distribution of homeopathic drugs without the same pre-market FDA approval required for prescription and over-the-counter (OTC) drugs.

Today, the three billion-dollar homeopathic industry has created a deluge of new products never scrutinized for safety or efficacy. Consumers have experienced adverse events in recent years from homeopathic teething tablets, zinc intranasal products, and others containing toxic ingredients. In response, the FDA issued new draft guidance in December 2017 providing that any homeopathic product marketed without FDA approval would be subject to enforcement action like other drugs. Yet, given the abundance of homeopathic drugs already in the market and limited agency resources, the FDA announced that it would adopt a risk-based approach by prioritizing enforcement efforts on those products most likely to cause harm. In October 2019, the Agency updated its draft guidance again and extended the comment period through March 23, 2020.[1]

This article analyzes the FDA's revised draft guidance to assess the tradeoffs the Agency made and the potential shortcomings of its proposal. Critics claim the draft guidances could result in compromised consumer protection while proponents assert that the Agency has stepped up scrutiny. This article ultimately argues that, despite its shortcomings, the draft policy adopting a risk-based approach to enforcement of homeopathic

1. *See* Drug Products Labeled as Homeopathic; Draft Guidance for Food and Drug Administration Staff and Industry, 85 Fed. Reg. 918–919 (Oct. 25, 2019); *see also* FDA, DRUG PRODUCTS LABELED AS HOMEOPATHIC GUIDANCE FOR FDA STAFF AND INDUSTRY, Draft Guidance (Oct. 2019).

drugs in lieu of the prior enforcement discretion policy is a superior approach for safeguarding public health.

## INTRODUCTION

During the 1905 December holiday season in Baltimore, Maryland, three-month old George William Lancaster was fussing from what appeared to be indigestion. [2] To soothe him, George's mother administered medicine specifically designed for children.[3] She read the label and prepared the proper dose per the product's packaging.[4] Tragically, George never recovered.[5] A coroner later determined that George's death was directly attributable to the medicine his mother had provided, and warned the public not to use the medicine.[6] The same medicine caused the death of three other babies in Cleveland the following year.[7] Physicians were unable to revive or treat the infants after they had fallen into fatal stupors.[8] From 1904 to 1906, thirteen babies died due to opium and morphine poisoning resulting from this medication that could be purchased without a physician's advice or prescription.[9]

From 2010 to 2016, ten babies died whose parents had given them homeopathic teething tablets to soothe their pain.[10] An additional 400 adverse health events were reported to the United States Food and Drug Administration (FDA) associated with consuming the homeopathic teething medication.[11] These included fevers, lethargy, vomiting, tremors, and shortness of breath.[12] The products associated with the deaths and adverse events tested positive for inconsistent toxic levels of belladonna.[13] FDA

2. Edward Bok, *Babies Killed by "Patent Medicines,"* LADIES' HOME J., 39 (Apr. 1907), https://babel.hathitrust.org/cgi/pt?id=mdp.39015013140838;view=1up;seq=359;size=150 (describing the death of thirteen children whose caregivers had administered patent medicines "believed to be 'perfectly harmless.'"). Bok notes that the labels justified the parents' belief in the safety of the medicine, "But what a price they paid for accepting without question the statements on the labels!" *Id.*

3. Bok, *supra* note 2.

4. *Id.*

5. *Id.*

6. *Id.*

7. *Id.*

8. Bok, *supra* note 2.

9. *Id*.

10. Jen Christensen & Jamie Gumbrecht, *Teething Tablets May be Linked to 10 Children's Deaths, FDA Says*, CNN (Oct. 13, 2016, 12:46 PM), https://www.cnn.com/2016/10/12/health/hylands-teething-tablets-discontinued-fda-warning/.

11. *Id*.

12. *Id*.

13. *Id*.

warned parents to cease using the medicine that could be purchased over-the-counter and to instead consult a doctor.[14]

Despite the passage of 100 years and numerous regulatory advances between these two incidents, the tension between profits for industry and protection for consumers continues. As history professors are often fond of saying, the names, the dates, and the people may change, but the ideas remain the same.[15] This same tension between industry profit and consumer protection plays out across multiple venues every day. This tension exists in environmental regulations, the automotive industry, the energy world, textile and manufacturing processes, and of course, in the food and drug realm. Commerce and consumer health often collide in a free market economy. Regulation is the seesaw ever attempting to balance economic security and consumer safety. The most salient question in the history of food and drug regulation—possibly in all government regulation—is whether public policy should err on the side of public health or on the side of businesses' freedom to engage in commerce until certain conduct is proven dangerous.[16] How much science should inform that debate, the type and quality of the science, who provides it, and how much danger is an acceptable level of risk are questions regulators have struggled to answer through the ages. In a time of rising health care costs, revitalized understandings of how food can be medicine alongside intense food and drug innovation, this debate carries on to new frontiers like the growth of the homeopathic industry. Yet, this growing industry feels eerily similar to the patent medicines of the past. An examination of today's homeopathic industry can leave one familiar with the history of food and drug regulation in the U.S. with an unsettling sense of déjà vu.

The FDA's statutory authority under the federal Food, Drug, and Cosmetic Act (FFDCA) includes, among other things, foods, drugs, dietary supplements, and homeopathic products.[17] How FDA exercises this authority has life and death consequences for all Americans. For the last quarter of a century, FDA has largely exempted homeopathic products from drug regulations even though the FFDCA classifies homeopathic products as drugs.[18] Since 1988, Agency policy premised on "enforcement discretion" allowed the manufacturing and distribution of

14. *Id.*

15. At least my history professor, Mr. McCarthy, always said this.

16. PHILIP J. HILTS, PROTECTING AMERICA'S HEALTH: THE FDA, BUSINESS, AND ONE HUNDRED YEARS OF REGULATION 67 (2003).

17. *See, e.g.*, Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–392 (2018).

18. 21 U.S.C. § 312 (2018).

homeopathic drugs without the same pre-market FDA approval required for prescription and over-the-counter drugs.[19]

Now the three billion-dollar homeopathic industry has created a deluge of new products never scrutinized for safety or efficacy. Consumers have experienced adverse events in recent years from homeopathic teething tablets, zinc intranasal products, and others containing toxic ingredients.[20] In response, the FDA issued new draft guidance in December 2017 providing that any homeopathic product marketed without FDA approval would be subject to regulatory and enforcement action just like other drugs.[21] However, the FDA's ability to immediately exercise its enforcement authority over all homeopathic products already in the market is limited considering the broad range of food, dietary supplement, drug, medical device, tobacco, and cosmetic products the Agency is already responsible for regulating. Thus, given the abundance of homeopathic drugs already in the market and limited agency resources, FDA announced that it would adopt a risk-based approach by prioritizing enforcement efforts on those homeopathic products most likely to cause harm.[22]

This article analyzes FDA's draft guidance to assess the tradeoffs the Agency made and the potential shortcomings of its proposal. Critics claim the draft guidance could result in compromised consumer protection while proponents assert that the Agency has laudably stepped up scrutiny. Part I provides a historical overview drug regulation in the United States within the framework of the FFDCA. Part II examines where homeopathic products fit within the FFDCA and explains how FDA has regulated these products in the past. Part III explains why changes in the contemporary homeopathic marketplace necessitate enhanced enforcement and a different regulatory approach today. Part IV analyzes FDA's response to the problems presented by the growing homeopathic industry and explains the Agency's December 2017 Draft Guidance and revised October 2019 Draft Guidance proposing a risk-based enforcement scheme in lieu of the prior enforcement discretion policy. Part V critiques the draft guidances and ultimately argues that a risk-based approach to enforcement of homeopathic drugs is a superior approach to safeguarding public health.

19. Amy Gaither, *Over the Counter, Under the Radar: How the Zicam Incident Came About Under FDA's Historic Homeopathic Exception*, 62 ADMIN. L. REV. 488, 489, 504 (2010).

20. *Id*. at 517; Christensen & Gumbrecht, *supra* note 10.

21. FDA, DRUG PRODUCTS LABELED AS HOMEOPATHIC GUIDANCE FOR FDA STAFF AND INDUSTRY, Draft Guidance (Dec. 2017).

22. *Id*.

## I. HISTORICAL OVERVIEW OF DRUG REGULATION IN THE UNITED STATES

> In the early stages of federal law, the focus seemed to be more on foods. As far as the public was concerned, food safety was indeed more important than drug regulation. When medication regulation was imminent, lawmakers most often referred to more dangerous medications, such as narcotics. Nonprescription medications were relegated to the backwaters of federal regulation, much like a poor relative no one wants to invite to a family reunion.[23]

Before 1800, the regulation of food and drugs barely existed in the United States, and laws pertaining to those products appeared only on the local books.[24] For example, Massachusetts regulated the weight of bread in 1646, prohibited the adulteration of bread in 1720, and imposed criminal penalties for the same in 1785.[25] As rare as local food laws were, drug laws were even rarer. The only instance of drug regulation at this time occurred in 1630 when a man named Nicholas Knopp was fined in Massachusetts for fraudulently selling an alleged cure for scurvy; the product contained mostly water.[26]

Global trade and increasing drug imports served as the catalyst for spawning federal regulation with the Import Drugs Act of 1848.[27] The country "had become the world's dumping ground for counterfeit, contaminated, diluted, and decomposed drug materials—a dangerous situation."[28] The Act created new United States customs laboratories to test imported drugs for compliance with the purity and potency standards set forth in the United States Pharmacopeia (USP)—an annually published compendium of drug information created in 1820.[29] However, support for the program eventually waned until it was discontinued.[30]

After the Civil War, increased trade between the states again underscored the need for federal regulation of the food and drug space.[31] Interstate commerce was a driving force for a federal scheme as new producers competed with products containing lesser quality ingredients (such as lard created from cottonseed oil and oleomargarine posing as butter) and

23. W. STEVEN PRAY, A HISTORY OF NONPRESCRIPTION PRODUCT REGULATION 2 (2003).
24. *See id.* at 5.
25. *Id*.
26. *See id.*
27. *See* Ch. 70, 9 Stat. 237 (1848).
28. Wallace F. Janssen, *The Story of the Laws Behind the Labels*, FDA CONSUMER MAG. (1981),https://www.fda.gov/downloads/AboutFDA/WhatWeDo/History/FOrgsHistory/EvolvingPowers/UCM593437.pdf.
29. *See id.*
30. *See id.*
31. *See id.*

as patchwork regulations at the state level burdened producers trying to manufacture products differently for various states.[32]

### *A. Undiluted Fraud*

> Gullible America will spend this year some seventy-five millions of dollars in the purchase of patent medicines. In consideration of this sum it will swallow huge quantities of alcohol, an appalling amount of opiates and narcotics, a wide assortment of varied drugs ranging from powerful and dangerous heart depressants to insidious liver stimulants; and far in excess of all other ingredients, undiluted fraud.[33]

At the end of the nineteenth century, medical practice was still far from a science and was fractured among various practitioners—including allopathy, osteopathy, homeopathy, eclecticism, and vitalism.[34] It was difficult for patients to discern the credible from the cunning. Many patients also lived in remote, rural areas, making house calls impractical or travel to a doctor's office difficult.[35] Thus, isolated social circumstances coupled with the inability to readily distinguish quality care from

32. *See id.*

33. SAMUEL HOPKINS ADAMS, THE GREAT AMERICAN FRAUD 3 (4th ed. 1905).

34. *See* PRAY, *supra* note 22, at 9. Allopathic medicine refers to conventional practices, products, and therapies used to treat illness. *See* U.S. FOOD & DRUG ADMIN., COMPLEMENTARY AND ALTERNATIVE MEDICINE PRODUCTS AND THEIR REGULATION BY THE FOOD AND DRUG ADMINISTRATION, GUIDANCE FOR INDUSTRY (2006), https://www.fda.gov/RegulatoryInformation/Guidances/ucm144657.htm; *see also, e.g.*, N.Y. EDUC. LAW § 6521 (McKinney 2019) (defining the practice of medicine as "diagnosing, treating, operating or prescribing for any human disease, pain, injury, deformity or physical condition"). Osteopathy refers to "the diagnosis of disease and the treatment thereof by a system of manipulation of the limbs and body of the patent with the hands by kneading, rubbing or pressing upon the different parts of the body." Yale Law Journal, *The Requirement of a License to Practice Osteopathy*, 12 YALE L.J. 446, 447 (1903). In 1813, a New Hampshire farmer named Samuel Thompson patented a system of medicine known as eclecticism that relied "exclusively on botanical remedies, steam baths, and rest." Ronald Hamowy, *The Early Development of Medical Licensing Laws in the United States, 1875-1900*, J. LIBERTARIAN STUD., 73 (1978), https://mises.org/library/early-development-medical-licensing-laws-united-states-1875-1900. Vitalism is the belief that illness results from impairments to the vital energy supporting all body systems. *See* S.J. Melzer, *Vitalism and Mechanism in Biology and Medicine*, 19 SCI. 470, 18 (Jan. 1 1904), https://www.jstor.org/stable/pdf/1631043.pdf?refreqid=excelsior%3Ab89b7a946a706789609848368d89332d; *see also* Alain Pottage, *Unitas Personae: On Legal and Biological Self-Narration*, 14 L. & LITERATURE 275, 282 (2002) (explaining "the classical understanding of vitalism as the belief in a creative or nutritive force commanding the development of living beings"). Self-proclaimed vitalist practitioners believe in treating any illness by focusing on the entire human system and the vital energy underlying all bodily functions, while acknowledging the lack of scientific evidence supporting the practice. *See, e.g.*, Mary S. Wallis, *My Approach to Medicine: Vitalism*, IMPROVED HEALING (Mar. 9, 2017), https://improvedhealing.com/blogs/improved-healing-natural-healing-products/my-approach-to-medicine-vitalism.

35. *See* PRAY, *supra* note 23, at 9.

quackery led many Americans to seek self-treatment measures. In this environment, "a peculiar breed of salesman arose . . . [and] [t]the products they sold were known as patent medicines," bottles of hope claiming to cure every health calamity imaginable.[36]

The phrase "patent medicine" is misleading because the United States Patent Office did not regulate these products (such regulation would have required manufacturers to disclose their formulas, which they were loath to do).[37] Manufacturers merely registered their trade names with the United States Patent Office, thereby preventing other snake oil salesmen from appropriating them.[38] Thus, patent medicines bore labels promising incredulous cures while not listing the ingredients.[39] They were further accompanied by multiple pieces of advertising listing all the reasons why the consumer should purchase the product and the benefits to be gained from doing so, yet the ads "were devoid of valid scientific or medical content."[40] Even more disturbing, patent medicines often contained addictive drugs such as heroin, morphine, cocaine, opium, and alcohol without any warning to the consumer; such products were commonly marketed for use in children.[41]

Experts studying the history of patent medicines convey that their story is one "of the special brand of quackery" involving "an age-old tale of consumer gullibility and . . . a saga of manufacturer irresponsibility in the face of obscene profits."[42] Edward Bok, the editor of *Ladies' Home Journal* for thirty years, initially confronted patent medicines with the radical decision in 1892 to rid the journal of all advertisements for such products.[43] His next move involved writing an editorial titled "Why 'Patent Medicines' Are Dangerous," wherein he exposed the lack of governmental control over the formulas and ingredients, the absence of regulation over the medicine makers who shipped their nostrums by mail without ever seeing a patient in person to render a diagnosis, and the medicine makers' opposition to state legislative efforts to compel labeling requirements (such as publishing an ingredient list).[44]

36. *See id*.
37. *See id.*
38. *See id.* at 9–10.
39. PRAY, *supra* note 23, at 10.
40. *See id.*
41. *See id.* at 11.
42. *See id.* at 9.
43. *See id.* at 21.
44. *See generally* Edward Bok, *Why "Patent Medicines" are Dangerous,* LADIES' HOME J., 18 (1905). Bok wrote a series of other articles, including "A Diabolical 'Patent-Medicine Story" and "Pictures that Tell Their Own Stories." Edward Bok, *A Diabolical 'Patent Medical Story,* LADIES' HOME J., 20 (1905); Edward Bok, *Pictures that Tell Their Own Stories,*

### *B. State Attempts While Quacks Abound*

*"Quacks abound like locusts in Egypt"*[45]

States could have passed pure drug laws at this time under the authority conferred by the Tenth Amendment. Under the Tenth Amendment, those powers not expressly delegated to the federal government in the Constitution are reserved to the states, including "police power," namely, "the power to protect the health, safety and welfare of citizens."[46] However, states faced insurmountable burdens if they tried to pass any drug laws. Samuel Hopkins Adams exposed the president of the Proprietary Association and producer of Hall's Catarrh Cure F.J. Cheney's method for thwarting state attempts to regulate drugs: whenever a newspaper received payment to run the patent medicine advertisements, Cheney executed a contract containing a clause in red text that explained the contract would be void if the state passed legislation regulating patent products.[47]

Despite such a strong disincentive for regulation, states recognized the need for a change to the status quo. The 1905 annual report of the Massachusetts State Board of Health included a review a several patent medicines and found that some of those medicines advertised as not containing alcohol actually contained up to 41.6%.[48] Shortly thereafter, the New York State General Committee for Safeguarding the Sale of Narcotics was formed and set to work drafting a bill that would require clear labels on patent medicines disclosing the presence of such ingredients.[49] However, state attempts were often unsuccessful, causing some states to support federal efforts to impose a floor for the regulation drugs. During federal hearings on proposed regulation for both food and drugs, L.J.

LADIES' HOME J. (1905). Bok's investigative journalism in subsequent years exposed thirteen deaths of children aged two weeks to two years old directly attributable to the ingestion of patent medicines containing morphine or opium. *See* PRAY, *supra* note 23, at 24.

45. T. Romeyn Beck, *A Sketch of the Legislative Provision of the Colony and State of New York, Respecting the Practice of Physics and Surgery*, N.Y.J. MED. 139 (1822) (quoting WILLIAM SMITH, THE HISTORY OF THE PROVINCE OF NEW-YORK FROM THE FIRST DISCOVERY TO THE YEAR M.DCCC.XXXII 212 (1814)).

46. Michael H. Cohen, *Holistic Health Care: Including Alternative and Complementary Medicine in Insurance and Regulatory Schemes*, 38 ARIZ L. REV. 83, 87 (1996); *see* U.S. CONST. amend. X.

47. See PRAY, *supra* note 23, at 25. Multiple patent medicine manufacturers adopted what later became known as this "red clause" practice because it was so successful at ensuring their products maintained unencumbered access to the marketplace. *See id*.

48. *Want Proper labels on Patent Medicines, Committee to Safeguard the Sale of Narcotics is at Work, Many to Support its Bill, Statement in Plain English Demanded of the Presence of Alcohol or Narcotic Drugs*, N.Y. TIMES (Mar. 12, 1906).

49. *See id.*

Vance, an inspector associated with the New York Food Commission, lamented how "the food law of New York State was a dead thing, and that the State had become on that account one of the best dumping grounds in the country for 'fake' and inferior products."[50]

Even if states could have successfully passed and implemented effective regulation, such regulation would only have reached food and drug products produced and sold wholly within state lines under the Commerce Clause.[51] Meanwhile, a doctor named Harvey Washington Wiley was conducting a series of experiments whose publicity began paving the way for federal food and drug intervention.[52]

### *C. The 1906 Pure Foods and Drugs Act*

Since 1862, Dr. Wiley had worked in the Division of Chemistry, the pre-cursor agency that would later become the United States Food and Drug Administration (FDA).[53] The Division of Chemistry was originally situated within the United States Department of Agriculture (USDA) and was later renamed the Bureau of Chemistry in 1901.[54] Firm in his belief that manufacturers were slowly sickening the American public by adding chemicals to food products without any government oversight, Wiley received federal funding to conduct a series of experiments in 1902 to test the safety of these chemicals.[55] After recruiting a dozen young, healthy men to eat meals prepared with the common additives of the time (for example, formaldehyde), observing the deleterious effects such chemicals had on the men's previously strong constitutions, and publicizing the results of the media-proclaimed "Poison Squad" experiments, the stage was finally set for federal regulatory action.[56] The subsequent release of Upton Sinclair's 1906 novel *The Jungle*, detailing Chicago's unsanitary

50. *Do Not Want to Make Alcohol Conspicuous, Drug Manufacturers Would Put It In Small Type on Labels. Fear the Effect on Sales, Proprietary Association's Man Says that the New Food Law Will Make Labels "Scare Crows,"* N.Y. TIMES (Sept. 21, 1906). Vance spoke on behalf of consumers, who were largely unrepresented at the hearing dominated by industry interests. *See id*.

51. U.S. CONST. art. I, § 8, cl. 3.

52. *See* John P. Swann*, FDA's Origin,* U.S. FOOD & DRUG ADMIN. (June 23, 2014).

53. *Id.*

54. *See* HISTORY OF FDA'S INTERNAL ORGANIZATION (Mar. 31, 2018).

55. *See* Deborah Blum, *Death in the Pot*, 4 LAPHAM'S Q. (2011).

56. *See id.*; *see also Poison Squad Escapes Federal Food Experts*, N.Y. TIMES (May 22, 1904). News of Wiley's experiments found their way into popular culture as well. *See* "Song of the Poison Squad" by Lew Dockstader's Minstrels, October 1903; *see also* Carol Lewis, *The 'Poison Squad' The beginnings of food & drug regulation in the U.S.*, FDA CONSUMER MAG. (2002); DEBORAH BLUM, THE POISON SQUAD: ONE CHEMIST'S SINGLE-MINDED CRUSADE FOR FOOD SAFETY AT THE TURN OF THE TWENTIETH CENTURY 80–97(2018).

and cruel meat manufacturing processes, also helped spur national action.[57]

Accordingly, the driving force behind the 1906 Pure Food and Drugs Act was the unsafe food production and preservation practices of the time—drug regulation was a minor addition to the Act, which may help explain why so many loopholes existed for drugs after the Act was passed.[58] In his autobiography, Wiley described the atmosphere during the period leading up to the passage of the 1906 Act:

> The committee rooms were jammed with attorneys for the canning industries using preservatives in food manufacturing, for drug and whisky interests and for proprietary medicine venders, pleading that exemptions under the act be extended to the products of their clients, that the law was too harsh and would ruin business, that other laws should be passed instead, and that the pure food and drugs law was an act of insanity anyhow.[59]

Wiley also detailed the cast of industry stakeholders opposing the law: manufacturers of materials used to adulterate foods and drugs, "so-called 'recitifiers,' . . . who made fraudulent whisky out of alcohol, colors, and flavors; the patent-medicine fraternity of fraud and hokum; [and] the dishonest misbranders and mislabelers of food and drug products."[60] Of the entire sordid scene, Whiley claimed the worst "evil the pure food and drug law sought to remedy was that of 'patent' medicines, with the various nostrums, salves, appliances, poisons, magic, and sheer fraud this group of ghouls foisted upon the suffering humanity of that period."[61]

In the face of heavy opposition, Congress passed the Pure Food and Drugs Act of 1906, which many also called the Wiley Act.[62] The law instituted some significant reforms in that it prohibited the shipment of misbranded or adulterated food or drugs in interstate commerce.[63] However, those seeking reform had "hoped that its enactment would be the

57. *See generally* UPTON SINCLAIR, THE JUNGLE (1906).

58. *See* PRAY, *supra* note 23, at 33.

59. HARVEY W. WILEY, AN AUTOBIOGRAPHY 226 (1930).

60. WILEY, *supra* note 59, at 203–04. Ironically, to "rectify" means to straighten, yet, "the whisky rectifier was doing nothing more or less than making crooked whisky of the crookedest kind that enlivened the throats and gullets of the thirsty men in that pre-Volstead era" by employing artificial colors, fake flavors, and "skillful mixing" to create imitation whisky, brandy, and rum. *Id.* at 204–05.

61. *Id.* at 205. Wiley further remarks that there was "some reason to justify calling their 'remedies' by the term 'patent,' for patent means to lie open, and the literature of these nostrums lied openly." *Id.*

62. *See* Pure Food and Drugs Act, Pub. L. No. 59-384, 34 Stat. 768 (1906) (repealed 1938).

63. *See id.*

end of patent medicines, but nothing could have been further from the truth. Companies merely had to change tactics slightly to conform to the letter, but not the spirit, of the law."[64]

Once the law was passed and Dr. Wiley began his tenure as the Chairman of the Pure Food and Drugs Commission to recommend implementing enforcement measures, he faced staunch resistance from drug manufacturers regarding disclosing their ingredients on their product labels, especially alcohol.[65] Manufacturers complained that if certain ingredients were prohibited, "a great industry would be destroyed."[66] Those representing drug manufacturers balked at having to disclose alcohol on the label, claiming that Dr. Wiley would be making "a scarecrow out of the label."[67]

Nevertheless, Wiley persisted. His first quack drug case under the new law resulted in a federal conviction, but the slight punishment imposed makes it hard to classify the case as a win.[68] Robert N. Harper had been producing a product he called Cuforhedake Brane-Fude, which he marketed as a "brain tonic" consisting of alcohol, caffeine, and a deadly toxic pain reliever called acetanilide.[69] Harper's product resulted in regular users becoming habituated to the drug, thereby allowing him to sell millions of bottles.[70] Harper was charged with creating false and misleading labels, given that his packaging stated the medication was "a most

64. *See* PRAY, *supra* note 23, at 27.

65. *Do Not Want to Make Alcohol Conspicuous*, *supra* note 50. Such opposition is understandable and predictable. Once the law went into effect, *The New York Times* reported that the Board of Food and Drug Inspection had, "in the short space of three years and twenty-seven days presented to the courts 894 distinct cases" of violations, and the courts imposed over 490 fines for violations involving substituting quantities of water for milk and the subtraction of butter fats to misbranded and adulterated "headache cure" products. *See Results of the Fight Against Food and Drug Fakers, What the Courts Have Done With Adulterators and Misbranders Since Dr. Wiley Began His Crusade—Almost Edible or Drinkable Affected by the Decisions*, N.Y. TIMES, 28 (July 23, 1911) (discussing the variety of misbranding and adulteration food and drug cases in the first three years of the 1906 Pure Food and Drug Act's existence, with the majority of the enforcement actions pertaining to food products). Fines were also imposed on manufacturers of bitters, alleged cancer cures, microbe killers, and those marketing products containing ingredients that remain controversial and a cause for concern today, such as belladonna root. *See id*; *see also* PRAY, *supra* note 22, at 51. With respect to solely drug enforcement actions, there were 222 judgments specific to drug products. *See Results of the Fight Against Food and Drug Fakers*, *supra* note 65.

66. *Do Not Want to Make Alcohol Conspicuous*, *supra* note 50 (discussing the comments of Henry A. Johnson, representing preservative manufacturers).

67. *See id.* (relaying the comments of George. L. Douglass on behalf of the Proprietary Association of America, claiming that such labels would unnecessarily frighten consumers away from harmless products).

68. *See* HILTS, *supra* note 16, at 58–59.

69. *See id.* at 58.

70. *See id.* at 59.

wonderful, certain and harmless relief" with "no . . . poisonous ingredients of any kind."[71] A jury pronounced Harper guilty, but he was fined only $700 despite reaping $2 million in profit from his potentially lethal product.[72]

Although a historic and monumental step forward towards regulating drugs in the United States, the 1906 Pure Food and Drugs Act contained a mammoth loophole, which manufacturers quickly learned to exploit. Because the 1906 Act required manufacturers to conform with the standards provided in the USP, manufacturers simply needed to slightly alter the names of their ingredients to create an ingredient that was not listed and therefore not regulated.[73] For example, while the ingredient colocynth (more commonly known as bitter apple) was listed in the USP, manufacturers changed the ingredient name to colocynth apple.[74] Alternatively, manufacturers could deliberately omit a reference to a standard on the label and if the product did not appear in the USP, there was no legal recourse for such products later found to be adulterated or misbranded.[75]

In 1911, the Supreme Court of the United States dealt another blow to the effectiveness of the 1906 Act when it held in *United States v. Johnson* that only false claims relating to a drug's labeling as to the nature and amount of its contents were regulated under the Act—not claims relating to the drug's effectiveness.[76] Dr. O.A. Johnson had been indicted for misbranding drugs in violation of the 1906 Pure Food and Drugs Act.[77] The United States for the Western District of Missouri quashed the indictment for misbranding even though it acknowledged that the products in question, while proclaiming to effectively cure cancer, were, "in truth and fact . . . wholly worthless and ineffective for the purposes recommended."[78] The court system had not yet confronted the issue of whether

71. *See id.*

72. *See id.*

73. United States v. Johnson, 221 U.S. 488, 502 (1911) (Hughes, J., dissenting) (noting as a matter of common knowledge that drug manufacturers regularly sold "'substances' or 'mixtures of substances' which are embraced in the act, although not recognized by the United States Pharmacopoeia . . . under trade names without any disclosure of constituents, save to the extent necessary to meet the specific requirements of the statute").

74. *See* PRAY, *supra* note 23, at 51.

75. *See Johnson*, 221 U.S. at 502–03 (Hughes, J., dissenting); *see also id.* at 51–52.

76. *See* 221 U.S. at 497 (majority opining that the Act regulated not "all possible false statements, but only" those concerning the product's identity and ingredients). The Court reasoned that it was proper to assign risk to shippers regarding "the identity of their wares, but a very different and unlikely step to make them answerable for mistaken praise." *Id.* at 497–98.

77. *See* United States v. Johnson, 177 F. Supp. 313, 314 (W.D. Mo. 1910), *aff'd*, 221 U.S. 488 (1911).

78. *See id.* at 315, 317.

manufacturing and shipping articles subject to the 1906 Pure Food and Drug Act that "were inefficacious in producing the cures and remedies indicated by the label" was within the scope of behavior the Act sought to regulate.[79] The court reasoned that expressing such opinions regarding a drug's efficacy were not indictable offenses under the 1906 Pure Food and Drug Act even though such opinions were wrong.[80]

On appeal, a majority of the Supreme Court of the United States affirmed.[81] Justice Hughes dissented, refusing to concur in his colleagues' opinion that the 1906 Act did not prohibit drug manufacturers and distributors from making fraudulent claims regarding a product's therapeutic effect.[82] Justice Hughes rejected the majority's argument that a drug's curative properties were matters of medical opinion and thus subject to conflict between medical schools and medical practitioners such that expression of those opinions were not within the Act's regulatory reach.[83] Rather, he reasoned that even, "granting the wide domain of opinion, and allowing the broadest range to the conflict of medical views, there still remains a field in which statements as to curative properties are downright falsehoods and in no sense expressions of judgment" and that such falsehoods fell squarely within the type of behavior Congress sought to prevent when it passed the 1906 Act.[84] The majority framed the issue as whether regulatory authority reached matters of medical opinion regarding curative properties; Justice Hughes maintained that the salient question was "whether, if an article is shipped in interstate commerce, bearing on its label a representation that it is a cure for a given disease, when, on a showing of the facts, there would be a unanimous agreement that it was absolutely worthless and an out-and-out cheat, the act of Congress can be said to apply to it."[85] On this point, Justice Hughes believed the answer was a clear and unequivocal yes.[86] Yet, only Justice Harlan

79. *See id.* at 315.

80. *See id.* at 317 (analyzing the statute and concluding that it lacked evidence of congressional intent to hold drug manufacturers and distributors criminally liable for misleading consumers "as to the curative or healing properties of the drugs").

81. *Johnson*, 221 U.S. at 499.

82. *See id.* at 501 (Hughes, J., dissenting).

83. *See id.* at 504.

84. *See id*.

85. *See id.* at 505–07 (Hughes, J., dissenting) (finding a distinction between whether the statement at issue was a matter of medical opinion versus "a false representation of fact . . . [a] label . . . as a cure when it is nothing of the sort from any point of view, but wholly worthless").

86. *See Johnson*, 221 U.S. at 505–06 (Hughes, J., dissenting) (referencing a string of investigations and subsequent guilty pleas of drug manufacturers for marketing articles that did not produce the claimed cure, e.g., "No. 261. 'Sure Thing Tonic,' falsely represented, among

and Justice Day concurred with the dissent.[87] Thus, the Supreme Court ruled that the 1906 Act prohibited only false and misleading statements concerning a drug's identity or ingredients; the law did not reach false or misleading therapeutic claims.[88]

President William Taft was dismayed by the ruling, stating:

> Fraudulent misrepresentation of the curative value of nostrums not only operate to defraud purchasers, but are a distinct menace to the public health. There are none so credulous as sufferers from disease. The need is urgent for legislation which will prevent the raising of hopes of speedy cures of serious ailments by misstatement of facts as to worthless mixtures on which the sick will rely while their disease progresses unchecked.[89]

In response, Representative Swagar Sherley from Kentucky proposed an amendment to the 1906 Act that would criminalize labeling any medication with fraudulent claims regarding the drug's effectiveness.[90] The amendment passed, but the solution was far from perfect. The amendment contained what became known as the "fraud joker" loophole insofar as it still permitted manufacturers to evade liability if they sincerely believed in the efficacy of their products when used as intended.[91] Notably, the amendment did not cure the 1906 Act's reactionary regulatory response: the law could still only be applied to a manufacturer after a drug had caused consumers harm, rather than preventing harm in the first instance.[92]

In addition to the "fraud joker" loophole, the 1906 law still did not require nonprescription drugs be proven safe for their intended use prior to entering the market. This particular shortcoming was tragically underscored by the Jamaican Ginger Paralysis incident of the 1930s that reached epidemic proportions and affected tens of thousands of people from coast to coast.[93] Jamaican Ginger, also known colloquially as

other things, to be 'sure thing tonic . . . Restores nerve energy. Renews vital force.' Investigation begun June 3, 1909. Pleaded guilty.").

87. *See id.* at 507.

88. *See id.* at 498.

89. *The President and the Food and Drugs Act*, 34 SCI. 863, 53 (July 14, 1911).

90. *See* Food and Drugs Act, Pub. L. 62-301, ch. 352, 37 Stat 416–17 (1912); *see also* Michelle Meadow, *Promoting Safe & Effective Drugs for 100 Years*, FDA CONSUMER MAG. (2006).

91. PRAY, *supra* note 23, at 52; *see also* HILTS, *supra* note 16, at 61.

92. PRAY, *supra* note 23, at 53; *see also* HILTS, *supra* note 16, at 61.

93. John Parascandola, *The Public Health Service and Jamaica Ginger Paralysis in the 1930s*, 110 PUB. HEALTH SERV. CHRONS. 3, 361 (1995). Estimates of those affected vary between 35,000 and 100,000 people. *See* PRAY, *supra* note 22, at 57; *see also* Michele Norris, *Jake Leg: An Affliction and the Blues it Inspired*, NAT'L PUB. RADIO (Sept. 12, 2003). Yet,

"Jake," was an alcoholic extract widely available in pharmacies during Prohibition containing up to seventy percent alcohol.[94] When the Prohibition Agency mandated that Tincture of Jamaica ginger could only consist of fluid extract of ginger (thereby rendering the drink unpalatable to those seeking a way around Prohibition), manufacturers responded by creating adulterated products that either contained additional ingredients to neutralize the taste or other ingredients that were not detectable.[95] One such ingredient was tri-orthocresyl phosphate, a common plasticizer ingredient in lacquer, whose use was traced back to a drug manufacturing firm in Boston called Hub Products.[96] Ingestion caused death, numbness of the legs, an inability to walk, and permanent paralysis.[97]

Investigations by FDA, the Prohibition Bureau, and state health officials resulted in indictments filed against Hub Products president, Harry Gross and his brother-in-law and Hub Product part owner Max Reisman.[98] Gross and Reisman were charged with entering adulterated and misbranded products into interstate commerce under the 1906 Pure Food and Drug Law, specifically by adding tri-orthocresyl phosphate as an ingredient (the adulteration charge) and by labeling their product as containing fluid extract of ginger when the product did not actually conform to the USP's standards for the strength, quality, and purity of the fluid extract (the misbranding charge).[99] The business partners ultimately

these numbers are likely higher since statistics do not reflect how many blacks were affected. *See generally* Dan Baum, *Jake Leg*, NEW YORKER, 50–57 (Sept. 15, 2003) (profiling the Jake Leg epidemic and how it was eventually stopped by bluesmen).

94. Parascandola, *supra* note 93; *see* The National Prohibition Act, Oct. 28, 1919, ch. 85, 41 Stat. 305. At the time, a controversy existed regarding whether alcohol was "a medicinal element of great value." *The A.M.A. and the Volstead Act*, 26 CAL. & WESTERN MED. 808 (1927). Some estimates place the amount of alcohol in Jamaican Ginger at eighty-five percent. *See* Norris, *supra* note 93 (Dr. John Morgan, professor at the City University New York Medical School and pharmaco-ethnomusicologist, discussing the alcohol content of Jake, its adulteration, and its effects, including widespread permanent paralysis, and relating how the American Medical Association (AMA) unanimously voted to send a bill to Congress that would remove then-current limits on the amount of whiskey doctors could legally prescribe for their patients). The AMA opined that "legislative bodies composed of laymen should not enact restrictive laws regulating the administration of any therapeutic agent by physicians legally qualified to practice medicine." *Id.*

95. *See* PRAY, *supra* note 23, at 57.

96. *See id*.; *see also* Parascandola, *supra* note 93, at 362.

97. Norris, *supra* note 92; *see also* PRAY, *supra* note 23, at 57; Prascandola, *supra* note 93, at 363. The national incident of paralysis resulting from ingesting Jake was so widespread that it made its way into several songs of the day. *See* Baum, *supra* note 93 (referring to the Allen Brothers' 1930 song "Jake Walk Blues," black blues singer Ishmon Bracey's "Jake Liquor Blues," and Tommy Johnson's "Alcohol and Jake Blues").

98. Parascandola, *supra* note 93, at 362.

99. *Id.* at 362–63. Gross and Reisman were also charged with conspiracy to violate and committing violations of the National Prohibition Act. *See id.* at 362.

negotiated a plea deal resulting in each receiving a $1,000 fine and a two-year prison sentence, which was suspended.[100] FDA was not privy to the plea negotiations and continued investigating the matter until garnering enough evidence to charge Gross with parole violations in 1932.[101] New evidence revealed Gross had mixed the poisonous Jake, and he was ultimately ordered to serve his two-year prison sentence, but Reisman never served any time.[102] Thus, the actions of two men that caused death for some and permanent paralysis for several thousand others resulted in a mere $2,000 fine and two years of prison time.[103] Perhaps because the Jamaican Ginger Paralysis incident affected mainly "the rural poor, not a commonly spotlighted segment of society," it did not galvanize the nation to demand further amendments to the 1906 Act.[104] Thus, the "parasitical trade"[105] of patent medicines continued.

Furthermore, while the 1906 Act required drug manufacturers to list habit-forming drugs on the label, it did not outright prohibit the use of these substances, including alcohol, morphine, cocaine, opium, and chloroform. An article published in *The Ladies Home Journal*, written by a doctor, describes the national state of affairs:

> It is not too much to say that thousands of children 'of two years old and under' meet their death every year, either directly or indirectly, from opium contained in soothing syrups and other like remedies for infants; or else become slaves to the opium habit from the same cause.[106]

In calling for a cure to this state of affairs, the doctor implored consumers to read the labels of such medicines and refuse to employ any containing the above ingredients—essentially demanding greater consumer awareness around the issue.[107] Second, the doctor implored the public to demand "a conscientious use of the means of protection now provided against it"—namely, regulation and enforcement through the use of the 1906 Act.[108]

100. *See id.* at 363.

101. *See id.*

102. *See* Parascandola, *supra* note 93, at 363.

103. *See id.*

104. PRAY, *supra* note 23, at 57.

105. Jeannette Marks, *Narcotism and the War*, 206 NORTH AM. REV. 745, 879, 881 (2017).

106. Caroline W. Latimer, *How Can I Keep My Baby From Crying? How Thousands of Mothers Do It and the Results*, LADIES' HOME J. 35, https://babel.hathitrust.org/cgi/pt?id=mdp.39015011414177;view=1up;seq=43;size=150 (noting that nearly all "soothing syrups, teething cordials, infants' friends, diarrhea mixtures, cough drops, and other 'patent medicines'" relied upon opium to achieve their results).

107. *See id.*

108. *See id.*

At this time, Wiley was struggling to enforce the 1906 Act. When Wiley refused to cease enforcement efforts, special industry interests and drug manufacturers sought assistance from President Theodore Roosevelt.[109] Roosevelt created the Board of Food and Drug Inspection, which ultimately hamstrung Wiley in his efforts to enforce the law.[110] Wiley was named chairman of the Board, Professor F. L. Dunlap from the University of Michigan was appointed as acting-chief of the Bureau of Chemistry and was named secretary to the Board, with the third member being solicitor of the Department of Agriculture George P. McCabe.[111] Wiley was relegated to the position of a "mere figurehead" as the other two members outvoted him at every turn.[112] Wiley also questioned the authority and legality of such a board, as the 1906 Act contained nothing that could be construed as authorizing the creation of a Board of Food and Drug Inspection; rather, the law specifically provided that the Bureau of Chemistry was responsible for analyzing food and drug samples to detect the presence of adulterated or misbranded articles.[113] With this board in place, Wiley "soon found it impossible to bring any cases against certain classes of offenders, particularly the rectifiers and manufactures of so-called patent medicines containing alcohol as the chief ingredient."[114]

Roosevelt also created the Remsen Board, consisting of chemists such as the President of John Hopkins University Dr. Ira Remsen and Yale Professor Chittenden, to act as an appeals court for Wiley's decisions.[115] When Wiley stood by his convictions and refused to approve various ingredients that he maintained were dangerous, industry began calling for his removal for insubordination.[116] Facing multiple adversaries in Congress and in the food and drug industry, Wiley eventually retired from government service in 1912 but continued his advocacy and

109. *Wiley's Foes Think They've Beaten Him, Pure-Food Champion Placed in the Position of Defying His Superiors. Won't Yield on Benzoate, Declines to Sign 'Pacifying' Report in Place of Original Accidentally Published*, N.Y. TIMES (Dec. 29, 1908), https://timesmachine.nytimes.com/timesmachine/1908/12/29/105017012.pdf.

110. *See* WILEY, *supra* note 59, at 238.

111. *See id.*

112. *See id.*

113. *See id.*

114. *See id.* at 239.

115. *See Wiley's Foes Think They've Beaten Him*, *supra* note 109.

116. *See id.* (discussing industry pressure on Dr. Wiley to allow the use of sodium benzoate in food items).

consumer protection efforts as director of the bureau at *Good Housekeeping* for the next nineteen years.[117]

His advocacy work proved effective, as public outcry over the "parasitical" patent medicine trade eventually led Congress to pass the Narcotic Act of December 17, 1914, also known as the 1914 Harrison Narcotic Act for the law's first bill sponsor, New York Representative Francis Burton Harrison.[118] The Narcotic Act called for all those who produced, manufactured, distributed, or sold opium or coca leaf products to register with the Internal Revenue Service (IRS) and pay a special tax.[119] Yet, it exempted medical preparations containing "less than two grams of opium, one-fourth grain of morphine, one-eighth grain of heroin, or one grain codeine per ounce."[120]

### *D. The Federal Food Drug and Cosmetics Act of 1938*

In June 1933, Rexford Tugwell, an advisor to President Franklin Roosevelt and the Assistant Secretary of Agriculture, proposed a bill that would allow for the regulation of cosmetics, as well as mechanical devices, "such as quack anticancer machines."[121] The bill also proposed to penalize false advertisements relating to the efficacy of food, drugs, or cosmetics.[122]

FDA Chief Walter Campbell assembled a collection of exhibits to present at the Tugwell Bill hearings to illustrate the state of affairs in the nation, including "contaminated foods, filthy factories, poisonous cosmetics, products with lies permeating the advertising, and useless appliances with fantastic promises."[123] FDA Staffer Ruth de Lamb eventually wrote a book about the exhibits titled American Chamber of Horrors.[124]

Historians have credited Senator Royal Copeland as the chief architect of the 1938 Federal Food, Drug, and Cosmetic Act.[125] Copeland reviewed the transcripts of all the hearings on the Tugwell Bill and

117. *Harvey W. Wiley: Pioneer Consumer Activist*, FDA CONSUMER MAG. (2006) (reporting a headline on the day of Wiley's retirement that read, "Women Weep as Watchdog of the Kitchen Quits After 29 Years").

118. *See generally* 63 Stat. 785 (1914); *see also* PRAY, *supra* note 23, at 82.

119. *See* 63 Stat. 785.

120. PRAY, *supra* note 23, at 86.

121. *Id.* at 90–93.

122. *See id.* at 92–93.

123. *Id.* at 94.

124. *See generally* RUTH DEFOREST LAMB, AMERICAN CHAMBER OF HORRORS: THE TRUTH ABOUT FOOD AND DRUGS (GETTING AND SPENDING) (1936) (describing the dangers behind consuming drugs, cosmetics, canned and packaged foods, fruits and vegetables and pleading for a more stringent Tugwell Bill).

125. *See* PRAY, *supra* note 23, at 96.

endeavored to write another version of the bill, which became known as the Tugwell-Copeland bill.[126] One of the key provisions of the Tugwell-Copeland bill was the requirement that all medicines, including patent medicines, fully disclose their ingredients for their products.[127]

In an essay titled Recollections of '33 and Later, Rex Tugwell recalled the problems with the 1906 Act and why changes were necessary. He noted that the 1906 Act

> [ ] was not only obsolete; its usefulness had always been limited. It required proof not only that offenders had poisoned or deceived the users of their products, but also that they had *intended* to deceive or to poison them. These offenders could always protest that they had been innocent of any such intent; and, if something untoward had happened, it was simply because they had been unaware of the possible results. The more ignorant they were, the less chance there was of convincing them. However much a jury might want to punish the purveyors of such products, the judge had to instruct them that established facts were not enough; they must find that it had been done deliberately. The Government lawyers practically never won a case; offenders went free and went back to their old games.[128]

It took Congress from 1933 until 1938 to finally pass what became known as the federal Food Drug and Cosmetic Act of 1938 (FFDCA).[129] Newspapers were opposed to any sort of bill that would regulate what ". . . was familiarly called the snake-oil racket."[130] If dubious pills and elixirs were no longer permitted in interstate commerce, then they could not be advertised; the resulting loss of advertising revenue would threaten the operations of newspapers across the country.[131] The country's pervasive fear of communism also played a role in the fight, with newspapers as reputable as the *New York Sun* running full page stories about how the

126. *See id.* at 96–97.

127. *See id.* at 97. *See generally* ARTHUR KALLET & JOHN SCHLINK, 100,000,000 GUINEA PIGS: DANGERS IN EVERYDAY FOODS, DRUGS, AND COSMETICS (1935) (revealing to the public the dangers about unregulated exposure to food, drugs, and cosmetics). Kallet appeared before the Copeland subcommittee to testify in the events leading up to the passage of the 1938 law, as described in his book. *Id.* at 142–43.

128. Rexford G. Tugwell, *Recollections of '33 and Later*, *in* FDA PAPERS 5 (U.S. Food & Drug Admin., 1967–1972).

129. Franklin M. Depew, *Evolution of a Law*, *in* FDA PAPERS 10 (U.S. Food and Drug Administration, 1967–1972) (noting that it took five "years of legislative hearings and four major revisions before the 1938 Act was adopted by Congress"); *see* 21 U.S.C. §§ 301–399 (2018).

130. Tugwell, *supra* note 128, at 8.

131. *See id.*

bill was actually the work of the "reds" to thwart American businesses accompanied by headlines calling out "Rex the Red."[132]

Just as Wiley's Poison Squad experiments and Upton Sinclair's *The Jungle* significantly swayed public opinion in favor of the 1906 Pure Food and Drugs Act, the 1937 sulfanilamide incident may be the reason the 1938 Federal Food Drug and Cosmetic Act finally passed. Sulfanilamide was a drug developed initially in tablet and powder form that was effective in treating streptococcal infections.[133] When consumers sought a liquid form of the drug, S.E. Massengill Company's chief chemist and pharmacist Harold Cole Watkins created a solvent in which sulfanilamide was dissolved in diethylene glycol. Diethylene glycol is a clear, colorless chemical liquid, sweet-tasting but poisonous when ingested, often used in industrial solvents and antifreeze.[134] S.E. Massengill's control lab tested the liquid for flavor, appearance, and fragrance but not toxicity.[135] The 1906 Act did not require manufacturers to conduct safety studies prior to introducing new drugs or mixtures into instate commerce.[136] Thus, the company released 633 shipments of its toxic "elixir," resulting in the death of more than 100 people in fifteen different states, with fatalities occurring from coast to coast, including many children who had been treated for sore throats with the sweet, raspberry-flavored poison.[137] The American Medical Association (AMA) learned of multiple deaths in Oklahoma that appeared attributable to "Elixir Sulfanilamide."[138] The AMA sought the composition of the elixir from Massengill, but Watkins had not recorded the use of diethylene glycol as an ingredient.[139] The AMA laboratory tested the solution and was able to isolate diethylene glycol as the poisonous ingredient.[140] The death toll continued rising, necessitating Agency action.[141] FDA was inundated with reports of victims suffering the agonizing symptoms of kidney failure—severe abdominal

132. *Id.*

133. Carol Ballentine, *Sulfanilamide Disaster: Taste of Raspberries, Taste of Death: The 1937 Sulfanilamide Incident*, FDA CONSUMER MAG. (June 1981), https://www.fda.gov/files/about%20fda/published/The-Sulfanilamide-Disaster.pdf.

134. LJ Schep et al., *Diethylene Glycol Poisoning*, PUBMED (2009), https://www.ncbi.nlm.nih.gov/pubmed/19586352; Ballentine *supra* note 133.

135. Ballentine, *supra* note 133.

136. *Id.*

137. *Id.*

138. *Id.*

139. *See id.*

140. Ballentine, *supra* note 133.

141. *See id.*

pain, nausea, vomiting, an inability to urinate, and finally convulsions and stupor for one to three weeks before perishing.[142]

FDA sent telegrams to over 1,000 doctors, pharmacists, and salesmen warning of the drug's fatal effects and required Massengill to issue similar warnings.[143] Nearly all 239 FDA-employed inspectors and chemists sought to seize bottles of the drug that remained in interstate commerce, alongside state and local health officials countrywide.[144] A lack of prescription records coupled with over the counter (OTC) sales of the drug to consumers whose names and addresses were not recorded complicated FDA's seizure efforts.[145] Through twenty-five seizures, FDA ultimately recovered over 234 gallons of the 240 gallons of the drug (unfortunately, the remaining missing bottles were subsequently consumed and killed those who ingested the liquid).[146]

The sulfanilamide incident was a tragic demonstration of the shortcomings of the 1906 Pure Food and Drug Law. Because the law did not require drug companies to perform pharmacological tests to ensure the safety of their products, the U.S. District Attorney's only recourse under the 1906 law was to charge the company with misbranding because the company had labeled its product as an "elixir," which implied that the liquid consisted of alcohol rather than the toxic diethylene glycol solution.[147] Had the company printed the word "solution" on its bottles instead of "elixir," no misbranding charges could have been brought and FDA would have lacked any legal authority to seize the 234 gallons of the drug that killed so many people.[148] In the end, Samuel Evans Massengill was fined $26,000 for shipping a misbranded product in interstate commerce.[149]

Prior to the sulfanilamide incident, various food and drug bills to update the 1906 law had languished in committee, failing to survive the legislative process. After the incident, President Franklin D. Roosevelt signed Federal Food Drug and Cosmetic Act ("FFDCA") into law on June 25, 1938.[150]

142. *Id.*
143. *Id.*
144. *Id.*
145. Ballentine, *supra* note 133.
146. *Id.*
147. *Id.*
148. *Id.*
149. *See* PRAY, *supra* note 23, at 118. The $26,000 fine was the maximum amount permitted under the 1906 law. *See id.* Watkins, the creator of the fatal brew, later committed suicide, although he was never charged with a crime. *See id.*
150. *See* 21 U.S.C. §§ 301–399 (2018); *see also FD&C Act Chapter V: Drugs and Devices*, U.S. FOOD & DRUG ADMIN. (Mar. 3, 2018)

The FFDCA defines a drug as any article recognized in the USP, the Homeopathic Pharmacopoeia of the United States, or the National Formulary that is intended to diagnose, cure, mitigate, treat, or prevent disease in humans or animals.[151] Drugs are also defined as "articles (other than food) intended to affect the structure or any function of the body" of humans or animals.[152]

The FFDCA prohibits adulterated or misbranded drugs in interstate commerce. A drug is adulterated if it is found poisonous, insanitary, or if there are not adequate controls in its manufacturing; if the strength, quality, or purity differ from that provided in the official compendium, if the drug's strength is misrepresented, or where the drug is mixed with another substance or another substance is substituted that reduces the drug's strength or quality.[153] Drugs are deemed misbranded if, among other things, they contain false or misleading labels, bear inadequate directions for use and warnings on their labels, or are health endangering when used as prescribed or as suggested on the label.[154] Notably, the FFDCA eliminated the Sherley Amendment, which had required proof of intent to defraud before a drug could be deemed misbranded.[155] And finally, for the first time, the 1938 FFDCA required premarket regulatory approval of new drugs before such drugs could be introduced into interstate commerce.[156]

*1. The 1951 Durham-Humphrey Amendment*

Despite these laudable aspects of the 1938 FFDCA, the Act contained serious shortcomings. First, the 1938 law did not delineate prescription drugs from OTC, self-use drugs.[157] Without clear guidelines, widespread inconsistency proliferated in the marketplace with some

https://www.fda.gov/RegulatoryInformation/LawsEnforcedbyFDA/FederalFoodDrugandCosmeticActFDCAct/FDCActChapterVDrugsandDevices/default.htm#Part_A. FDA's website provides a list of the Food Drug and Cosmetic Act's Section Numbers (e.g. Sec. 303) and the corresponding Title 21 section listing (e.g. Sec. 333—Penalties). *See FD&C Act Chapter V: Drugs and Devices, supra* note 150. The site is searchable by either the United States Code section number or the Title 21 section listing. *See id.*

151. 21 U.S.C. § 321(g)(1)(A)–(B).

152. *Id.* at § 321(g)(1)(C).

153. *Id.* at § 351(a)–(d).

154. 21 U.S.C. § 352(a), (j) (2018); *see also* 21 C.F.R. § 10.115 (2019); 21 C.F.R. §§ 210–211 (2019).

155. *See* 21 U.S.C. § 352(a); *see also Milestones in U.S. Food and Drug Law History*, U.S. FOOD & DRUG ADMIN. (Jan. 31, 2018) https://www.fda.gov/about-fda/fdas-evolving-regulatory-powers/milestones-us-food-and-drug-law-history.

156. *See* 21 U.S.C. § 355-1(a) (2018).

157. *See* PRAY, *supra* note 23, at 132.

manufacturers classifying a certain drug as available through a prescription only, whereas other manufacturers would label the same drug as a self-care item appropriate for self-use.[158] One outcome of the 1938 law's silence on the issue of prescription versus OTC drug was that pharmacists arbitrarily began refilling prescription medications without physician consent, essentially turning a prescription drug into an OTC drug.[159] Confusion among pharmacists and consumers eventually led to the passage of the Durham-Humphrey Amendment to the FFDCA in 1951, which provided that certain drugs were available only through prescription.[160]

A prescription drug is defined as one that "because of its toxicity or other potentially harmful effect, or the method of its use, or the collateral measures necessary to its use, is not safe for use except under the supervision of a practitioner licensed by law to administer such drug."[161] The amendment provided for the dispensing of prescription drugs only "upon a written prescription of a practitioner licensed by law to administer such drug."[162] Prescriptions could be refilled only upon authorization by the doctor who had originally prescribed the drug.[163] Any drug that was not dispensed in accordance with the new provisions was deemed misbranded.[164]

Although the Durham-Humphrey Amendment was ultimately successful, industry had lodged vociferous attacks on its advocates. Industry relied on what had become a familiar storyline of those opposing regulation—that passage of the amendment would deprive consumers of free choice and that the amendment was the agenda of communists.[165] During hearings on the bill, general counsel to the Proprietary Association claimed that the bill was the "handmaid of socialized medicine . . . the most dangerous threat to freedom of medical care in America since the famous Tugwell bill of 1933" and further claimed the bill would jeopardize "the traditional right of self-medication and choice of remedies."[166]

In addition to playing on communist fears and framing the matter as one of patient choice, opponents also claimed the issue was one of federal

158. *See id.* at 133.

159. *See id.* at 136.

160. *See id.* at 133.

161. 21 U.S.C. § 353(b)(1)(A) (2018).

162. *Id.* § 353(b)(1)(B)(i). The law also provided for dispensing of such drugs "upon an oral prescription of such practitioner which is reduced promptly to writing and filed by the pharmacist." *Id.* § 353 (b)(1)(B)(ii).

163. *Id.* § 353(b)(1)(B)(iii).

164. *Id.* § 353(b)(1)(B).

165. *Proprietary Group Assails Drug Bill*, N.Y. TIMES, 56 (May 15, 1951).

166. *Id.*

encroachment on states' rights.[167] After Senator Hubert H. Humphrey, Democrat of Minnesota, first introduced the bill, the American Pharmaceutical Association had strenuously opposed the proposal, claiming the federal government was encroaching "on the prerogatives of states to control any phase of the practice of medicine and pharmacy."[168] Such arguments were ultimately unsuccessful and the public health advocates carried the votes.

*2. The 1962 Kefauver-Harris Amendment*

However, despite the success of the Durham-Humphrey Amendment, the 1938 Act still suffered from another serious shortcoming: it still lacked any requirement that a drug be proven both safe and efficacious for its intended use. Not until 1962 would the United States finally have an amendment to the FFDCA that required drug manufacturers prove both the safety and efficacy of their drugs through the premarket regulatory approval process.[169]

The chronicles of the Kefauver-Harris Drug Amendments commenced on December 7, 1959 when the Democratic Senator of Tennessee and head of the Senate Antitrust and Monopoly Committee, Estes Kefauver, suspected that the drug industry was extracting excessive profits from American consumers on little more than worthless nostrums.[170] His suspicions were confirmed following the first round of investigative hearings and he concluded that Americans were spending $250 million each year on "useless drugs."[171] The hearings lasted until September, 1960.[172] The investigative and legislative hearings concerning the amendments totaled 11,728 pages.[173] Despite years of hearings and all of Kefauver's efforts, any amendments to the 1938 Food Drug and Cosmetic Act seemed unlikely until "an international epidemic of major

167. *'Encroachment' scored: Pharmacists Oppose Extension of U.S. Medical Controls*, N.Y. TIMES, 23 (Sept. 2, 1951).

168. *Id.*

169. *See generally* J.P. Swann, *Sure Cure: Public Policy on Drug Efficacy Before 1962*, 16 PUB. AM. INST. HIST. PHARMACY 223 (1997) (describing the arrival of a heightened manufacturing process that led to safer, more reliable products in the drug industry).

170. *See* John M. Lee, *Drug Sales Mount Despite Hearings*, N.Y. TIMES (Apr. 22, 1962); Marjorie Hunter, *Drug Curbs, Scoffed At in '60, Are Now Being Sped in Congress: Chronology of Kefauver Inquiry Shows Several Protests by Physicians Over Pharmaceutical Testing Methods*, N.Y. TIMES, 57 (Aug. 12, 1962) (describing the highlights and milestones of the years of investigative and legislative hearings).

171. Hunter, *supra* note 170.

172. Lee, *supra* note 170.

173. *See id.*

proportions" finally overcame the drug industry and its powerful lobbyists.[174] Similar to the sulfanilamide elixir calamity, a new drug by the name of thalidomide threatened tragedy in America.[175]

Thalidomide was created in the 1950s in Germany by the company Chemi Grünenthal and was marketed throughout Europe as the first safe sleeping pill and as a treatment for morning sickness in pregnant women.[176] In several European countries, whose food and drug laws were much weaker than the United States', the drug "became almost as popular as aspirin."[177] Yet, the drug was found to cause "horrifying and heartbreaking" deformities in the children of women who used thalidomide while pregnant.[178] Thousands of children were born without arms or legs or both, or were born with only severely shortened limbs resembling flippers.[179] Thousands of children across Europe were affected and were "in some instances rejected by their parents and institutionalized. Others had their flippers amputated to accommodate prostheses for arms and legs. One young mother and her doctor were charged with the mercy killing of her deformed infant."[180] The only reason such catastrophe did not befall families in the United States was Dr. Frances Oldham Kelsey, a new pharmacologist at FDA in September 1960 who had received a new drug application for thalidomide as her first assignment.[181] Despite intense and repeated pressure from industry, Dr. Kelsey refused to approve the drug due to the company's lack of rigorous safety testing and research, plus evidence that the company had long-ignored linking the product to birth defects in Europe.[182] Dr. Kelsey eventually received a gold medal from President Kennedy for her steadfast dedication to FDA's mission and her efforts that prevented the thalidomide tragedy in Europe from reaching the United States.[183]

174. *See* PRAY, *supra* note 23, at 155.

175. *See id.*

176. Michael Winerip, *The Death and Afterlife of Thalidomide*, N.Y. TIMES (Sept. 23, 2013), https://www.nytimes.com/2013/09/23/booming/the-death-and-afterlife-of-thalidomide.html.

177. *See id.*

178. *See id.*

179. *See id.*

180. *See id.*

181. *See* Winerip, *supra* note 176.

182. *Id.*

183. *Frances Oldham Kelsey: Medical reviewer famous for averting a public health tragedy*, U.S. FOOD & DRUG ADMIN. (Feb. 1, 2018), https://www.fda.gov/about-fda/virtual-exhibits-fda-history/frances-oldham-kelsey-medical-reviewer-famous-averting-public-health-tragedy.

Despite thalidomide's national press coverage in the United States, opposition to the Kefauver bill still raged.[184] Opponents relied on another popular narrative still circulated by many industries resisting regulation: that of stifled innovation. Morris Fishbein, former editor of the *Journal of the American Medical Association*, wrote a letter to the editor of *The New York Times* warning the public "not to impede progress" and to "beware of limiting the introduction of needed and useful medicines" that would "save the lives of many thousands."[185] However, the bill's proponents ultimately persevered and President Kennedy signed the Kefauver-Harris Amendments into law on October 10, 1962.[186] The amendment required manufacturers to prove a drug's effectiveness before the product could be marketed and to report any serious side effects, allowing for post-market regulatory review as well.[187] Proof of effectiveness had to be based on qualified experts' conducting adequate and well-controlled clinical studies.[188]

The 1962 Amendment finally achieved what laissez economics had failed to do: "it weeded out the brutal, the stupid, and the needless that prevented the pharmaceutical industry from becoming a great engine of discovery and sales."[189] The instrumental "ingredient" necessary for paving a path forward for research was an entity outside of industry overseeing the use of a scientific standard.[190]

*3. 1972 GRASE Review of OTC Drugs*

Following the Kefauver-Harris Amendment, drug manufacturers must submit a New Drug Application (NDA) to the FDA so that a new drug can undergo premarket regulatory approval to evaluate its safety and effectiveness as a prescription drug.[191] Alternatively, drug manufacturers can seek to bring a product to market that falls within FDA's exception

184. PRAY, *supra* note 23, at 156.

185. Morris Fishbein, Letter to the Editor, *Control of Drugs Warning Given on Interfering With Developments of Products*, N.Y. TIMES, 22 (May 12, 1962).

186. Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780.

187. *Kefauver-Harris Amendments Revolutionized Drug Development*, U.S. FOOD & DRUG ADMIN. (Sept. 10, 2012), https://www.fda.gov/forconsumers/consumerupdates/ucm322856.htm.

188. *2*1 U.S.C. § 355(a), (d) (2018).

189. HILTS, *supra* note 16, at 106–07.

190. *Id.* at 107.

191. *See Regulatory Mechanisms for Marketing OTC Drug Products*, U.S. FOOD & DRUG ADMIN. (Feb. 10, 2016), https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm106386.htm (hereinafter Regulatory Mechanisms); *see also* 21 C.F.R. § 314.50 (2019) (containing NDA regulations).

for drugs generally recognized as safe and effective (GRASE).[192] The GRASE exception developed after the FDA began conducting a comprehensive review of all its OTC drugs in 1972.[193]

*4. OTC Monograph Review Process*

Drugs can be made available OTC in situations where patients can readily recognize symptoms and self-diagnose a condition, as is true when allergic patients seek an anti-histamine at the peak of the pollen season to cope with sneezing and itchy eyes while outdoors.[194] To determine if there is a significant likelihood that the condition is minor and can be self-treated with an appropriate OTC medication, FDA considers the following:

- "What are the risks to the patient who uses the medication but does not have the condition for which the medication was intended?"[195]
- "What are the risks to the patient who has the condition and does not seek medical attention but chooses to use the nonprescription medication instead?"[196]
- "What is the potential length of time the patient might use the nonprescription product before seeking medical attention?"[197]

To review the active ingredients, FDA developed the OTC monograph system. The monograph is essentially a "recipe" or a fixed compilation of instructions applicable to all OTC products in a certain

192. *See Regulatory Mechanisms*, *supra* note 191; *see also* 21 C.F.R. § 330.1 (2019) (describing the conditions for general recognition of a drug as safe, effective, and not misbranded and setting forth procedures for classifying OTC drugs as generally recognized as safe and effective and not misbranded).

193. The Kefauver-Harris Amendment also mandated that FDA review all prescription drugs marketed between 1938 and 1962 for efficacy. *See* PRAY, *supra* note 23, at 173. Those drugs marketed after 1962 had to submit an NDA to prove they were safe, while those drugs marketed prior to 1938 were exempt from review and said to be "grandfathered" in. *See id.* This review process was known as the Drug Efficacy Study Implementation project or DESI. *See* JAMES T. O'DONNELL, DRUG INJURY LIABILITY, ANALYSIS AND PREVENTION 14 (2d ed. 2005); *see also* Drugs for Human Use, 77 Fed. Reg. 142, 43337 (July 24, 2012), https://www.federalregister.gov/documents/2012/07/24/2012-18015/drugs-for-human-use-drug-efficacy-study-implementation-certain-prescription-drugs-offered-for; *Over-the-Counter (OTC) Drugs Branch: The OTC Drug Review*, U.S. FOOD & DRUG ADMIN. (Feb. 2, 2015), https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/ucm338238.htm.

194. PRAY, *supra* note 23, at 184.

195. *Id.* at 185.

196. *Id.*

197. *Id.*

therapeutic category, such as a nasal decongestant.[198] The system specifies which active ingredients may be included in an OTC drug and also directs how the product may be dosed, formulated, and labeled.[199] If an OTC active ingredient adheres to the OTC monograph system, manufacturers do not need to seek approval to market the product through the separate NDA process.[200] Because OTCs are available without prescription and physician supervision, FDA necessarily requires these drugs to have a much wider margin of safety than prescription drugs that undergo the NDA process.[201]

*A. Premarket Approval Process of Monographed OTCs*

FDA created an OTC monograph through a three-phase process. First, FDA appoints qualified individuals with the necessary scientific and technical expertise to serve on an advisory panel to conduct the first level of review for any proposed monographs.[202] The panel evaluates whether the proposed active ingredients and labeling of the OTC products are GRASE and renders one of three determinations for OTC ingredients: (1) deemed safe for the proposed therapeutic indication; (2) deemed unsafe, ineffective, or labeled unacceptably; or (3) unable to render a determination due to the existence of insufficient data.[203]

During the second phase of the OTC monograph process, the advisory panel presents its determination of the OTC product to FDA.[204] FDA considers the panel's findings and determines whether it agrees with the panel's classification of the OTC.[205] FDA then publishes the OTC

198. DAVID MANTUS & DOUGLAS J. PISANO, FDA REGULATORY AFFAIRS 28–29 (2014). More than eighty different OTC therapeutic categories or classes exist, ranging from nasal decongestants to topical acne medications to weight-loss products. O'DONNELL, *supra* note 193, at 10; *Over-the-Counter (OTC) Drug Product Review Process*, U.S. FOOD & DRUG ADMIN. (July 7, 2015), https://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm052786.htm; *see also* 21 C.F.R. § 330.5 (2019) (listing all the drug categories for which a monograph is established, including categories such as antacids, sedatives, and cold remedies).

199. *See* MANTUS & PISANO, *supra* note 198, at 29.

200. *See id.*

201. *Id.*

202. *See Over-the-Counter (OTC) Drug Monograph Process,* FOOD & DRUG ADMIN. (Jan. 7, 2015), https://www.fda.gov/drugs/current-good-manufacturing-practices-cgmp-drugs-reports-guidances-and-additional-information/over-counter-otc-drug-monograph-process [hereinafter *OTC Monograph Process*] (noting that the first level of review was completed by advisory panels); *see also* 21 CFR § 330.10 (a)(1) (2019) (setting forth the procedure for establishing OTC drug monographs, including the composition of advisory review panels).

203. *OTC Monograph Process*, *supra* note 202.

204. *Id.*

205. *Id.*

classification in the Federal Register as a tentative final monograph (TFM).[206] A comment period ensued, during which the public can provide objections, statements in support, new data, or requests for a public hearing.[207] FDA then reviews the public comments, addresses the submissions, and publishes a final monograph in the Code of Federal Regulations.[208]

*B. Post-market Review of Monographed OTCs*

The third and final phase of the OTC monograph process is ongoing; after FDA publishes the final monograph in Code of Federal Regulations, it continues allowing public comments recommending any amendments to the monograph if new information arises.[209] FDA can amend final monographs on the Commissioner's initiative or upon the submission of a citizen petition.[210]

Monograph OTCs were not subject to post-market review until 2006 when Congress amended the FFDCA by passing the Dietary Supplement and Nonprescription Drug Consumer Protection Act and giving FDA post-market regulatory authority over these products.[211] Manufacturers were thus required to record and report any adverse events associated with their products.[212] The Act also required new OTC labeling requirements so that OTC products contained an address and phone number to enable consumers to report any serious adverse events.[213]

*C. OTC Exclusions: Homeopathic Drugs*

When FDA created this formal review process for OTC drugs in 1972, it specifically excluded homeopathic medications, deferring their review.[214] FDA chose not to require homeopathic products undergo

206. *Id.*

207. *Id.*

208. *OTC Monograph Process*, *supra* note 202.

209. *Id.*

210. *Id. See generally Status of OTC Rulemakings*, U.S. FOOD & DRUG ADMIN. (Sept. 17, 2014), https://www.fda.gov/drugs/over-counter-otc-drugs/status-otc-rulemakings (outlining the current status of OTC rulemaking at FDA).

211. *See generally* Dietary Supplement and Nonprescription Drug Consumer Protection Act, Pub. L. No. 109-462, 120 Stat. 3469 (2006).

212. 21 C.F.R. § 312.32(a) (2019) (defining adverse event).

213. *Id.* (defining when an adverse event is classified as serious).

214. *See* Procedures for Classification of Over-The-Counter Drugs, 37 Fed. Reg. 9464, 9466 (May 11, 1972) (explaining how FDA did not review any drug products labeled as homeopathic under the OTC Drug Review because the FDA classified these products as a separate category and deferred consideration of them); *see also Homeopathic Products*, U.S. FOOD & DRUG ADMIN. (Mar. 20, 2018), https://www.fda.gov/drugs/information-drug-class/homeopathic-products (stating "homeopathic drug products have not been approved by

premarket approval processes "to help the FDA direct its limited resources to enforcement actions that most protect the public health . . . [h]omeopathic remedies often—although not always—contain so little active ingredient that they are believed to present little direct risk to the consumer."[215] Thus, FDA has cautioned consumers purchasing homeopathic products to "be aware that they have not been reviewed by the FDA or approved by the agency as safe or effective."[216]

*5. NDA Approval Process for Prescription Drugs*

Whereas OTC monographs apply to a specific ingredient, the NDA approval process for prescription drugs applies to a single drug product. Just as the OTC monograph review system employs a three-stage process, so too does the NDA prescription drug approval process. First, a drug manufacturer must conduct pre-clinical research and development, which usually requires one to three years of animal testing.[217] Phase I of the NDA approval process commences when the manufacturer completes this pre-clinical stage and files an investigational new drug application (INDA) with FDA.[218] At this point, the manufacturer may begin conducting Phase I clinical studies (usually over the course of several months) of the drug's pharmacology and toxicity on approximately 20 to 100 healthy human volunteers.[219] In a Phase I trial, researchers attempt to test the absorption rates of the drug, dose-dependent tolerance levels, and how well the test subjects metabolize and excrete the drug.[220]

In Phase II, the manufacturer distributes the drug to several hundred human volunteers who have the disease that the drug is intended to treat.[221] Finally, in Phase III, the manufacturer conducts double-blind trials with the drug and a placebo to assess the drug's efficacy.[222] Sometimes the NDA also includes plans for Phase IV studies that will be

FDA for any use" and "they may not meet modern standards for safety, effectiveness, and quality").

215. Bridget M. Kuehn, *Despite Health Claims by Manufacturers, Little Oversight for Homeopathic Products*, 302 JAMA 1631, 1632 (2009) (alterations in original) (quoting Crystal Rice, an FDA press officer).

216. *Id.* at 1634 (quoting Rice).

217. *See* Ben Haas & Shira N. Epstein, *Human Clinical Trials and Drug Approvals: Transnational Issues*, *in* FOOD AND DRUG REGULATION IN AN ERA OF GLOBALIZED MKTS. 37, 41 (Sam F. Halabi ed., 2015).

218. *See id.*

219. *See id.*

220. *See id.*

221. *See id.*

222. *See* Haas & Epstein, *supra* note 217.

performed post-marketing if there are unanswered questions remaining from the Phase III clinical trials.[223]

In addition to rigorous pre-market approval processes, the FDA also regulates new drugs via a post-market surveillance system. Phase IV testing begins after a drug has been approved and is on the market and involves the FDA's continued oversight over a drug company's compliance with Good Manufacturing Practices (GMPs) and the reporting of any adverse drug experiences.[224] FDA issues federal regulations in the form of GMPs that govern sanitation standards, recordkeeping requirements, personnel qualifications, equipment verification, process validation, and complaint handling.[225] MedWatch is the FDA's Safety and Information and Adverse Event Reporting Program, founded in 1993, for the purpose of allowing consumers, health care professionals, and manufacturers to report any adverse drug experiences.[226] MedWatch identifies safety hazards, which FDA can then use to alert the public, issue product recalls or withdrawals, or institute labeling changes.[227]

## II. REGULATING HOMEOPATHIC PRODUCTS

The United States National Center for Complementary and Integrative Health (NCCIH) recognizes homeopathy as an alternative medicine practice.[228] The word "homeopathy" is derived from the Greek roots *homeo*, meaning similar, and *pathos*, meaning suffering or disease.[229] FDA has defined homeopathy as "[t]he practice of treating the syndromes and conditions which constitute disease with remedies that have produced similar syndromes and conditions in healthy subjects."[230]

223. Jesse Goodman, *Addressing Emerging Challenges in the Pharmaceutical Product Development Ecosystem*, *in* FOOD AND DRUG REGULATION IN AN ERA OF GLOBALIZED MARKETS 3, 5 (Sam F. Halabi ed., 2015).

224. *See id.*

225. *See* 21 C.F.R. § 26.1 (2019). GMPs rely on the principles of quality, safety, and effectiveness. *See* Marc J. Scheineson, *FDA's Global Investigation and Enforcement Authority, Partnerships and Priorities*, *in* FOOD AND DRUG REGULATION IN AN ERA OF GLOBALIZED MARKETS 15, 17 (Sam F. Halabi ed., 2015).

226. *See* JAMES T. O'DONNELL, DRUG INJURY: LIABILITY, ANALYSIS AND PREVENTION 12 (2d ed. 2005).

227. *See id.*

228. *Homeopathy*, NAT'L CTR. FOR COMPLEMENTARY & INTEGRATIVE HEALTH, U.S. DEP'T HEALTH & HUM. SERVS., NAT'L INSTS. HEALTH, https://nccih.nih.gov/health/homeopathy (last modified July 2018).

229. *About Homeopathy*, BOIRON USA, https://www.boironusa.com/education-training/homeopathy/ (last visited Feb. 25, 2020).

230. FDA, DRUG PRODUCTS LABELED AS HOMEOPATHIC GUIDANCE FOR FDA STAFF AND INDUSTRY, Draft Guidance (Oct. 2019).

*A. Theory, Practice, and Principles*

Samuel Hahnemann, M.D. (1755–1843) is credited with developing the alternative medicine practice of homeopathy after "having become discouraged with the often violent and dangerous medical practices of his time."[231] Throughout most of history and until the twentieth century, the practice of medicine could be "a foul and dirty business."[232] During Hahnemann's time:

> there was no formal schooling, no exams to measure competency, no way to practice and learn from experience without causing harm, and no professional rules or regulations. Instead, the typical therapy was to "bleed, blister, puke, and purge." More often than not, the patient suffered and died at the hands of well-intentioned but undereducated physicians who simply didn't know any better.[233]

Homeopathy became popular in America after 1825 in large part due to its focus on the body's innate healing powers when fresh air, sunshine, rest, a healthy diet, and good hygiene allowed for recovery at a time when conventional medicine overlooked these practices (today, most medical professionals would note that such practices are generally health-promoting and health-sustaining irrespective of the practice of homeopathy).[234] Part of homeopathy's appeal in the past and present is that such treatments consider the patient's mind, body, emotions, and environment collectively and attempt to holistically treat the patient, as opposed to only the affected part of the body more common in traditional Western medicine.[235] In 1870, some 5,000 of the 62,000 physicians in the country practiced homeopathy.[236] Considering the crude and questionable acts that passed for medicine in that time period, "any actual healing with herbal and natural remedies was most likely due to luck rather than real expertise."[237]

Hahnemann's practice of homeopathy was premised on the theory that "what causes symptoms in a healthy person can cure the disease in a

231. John Lunstroth, *Voluntary Self-Regulation of Complementary and Alternative Medicine Practitioners*, 70 ALB. L. REV. 209, 214 (2006).

232. J. MARIN YOUNKER, BLEED, BLISTER, PUKE, AND PURGE: THE DIRTY SECRETS BEHIND EARLY AMERICAN MEDICINE Ch. 1 (2016).

233. *Id.*

234. *Id.*

235. *See* Michael Cohen, *Holistic Health Care: Including Alternative and Complementary Medicine in Insurance and Regulatory Schemes*, 38 ARIZ. L. REV. 83, 110 (1996).

236. Ronald Hamowy, *The Early Development of Medical Licensing Laws in the United States, 1875–1900*, J. LIBERTARIAN STUD. 74 (1978).

237. YOUNKER, *supra* note 232, at Ch. 2.

sick person," also known as the idea that "like cures like."[238] This theory, also known as *similia similibus curantur*[239] or the "law of similars," refuses to suppress symptoms of illness or disease because such suppression is believed to impede the body's innate defensive mechanisms; rather, homeopathic products are prescribed for their "ability to mimic those symptoms" on the belief that "[t]he best way to heal ourselves of disease may be to steer our body's own defenses into, rather than away from or against, symptoms."[240] Homeopathic practitioners seek to prescribe substances that they believe will assist their patients in adapting to stress or infection, thereby enabling them to best recover and heal themselves.[241] For example, the ingredient *rhus toxicodendron*, more commonly known as poison ivy, is often found in homeopathic medication to treat poison ivy and poison oak.[242] Such homeopathic treatments for poison ivy also contain croton seeds,[243] which cause itching, burning, or blistering when placed directly on the skin and burning of the mouth and vomiting if ingested.[244] According to the law of similars, small amounts of a material known to cause the offending condition should also help cure it, hence the idea of "like cures like."[245]

Hahnemann believed that in addition to the law of similars, a second principle was necessary: "a system of radical dilution" of the offending substance.[246] This principle of dilution is also referred to as the "law of infinitesimals" or "the law of minimum dose," which is premised on the belief that a series of dilutions of the substance with water, alcohol, or grinding it into a fine power will lessen the substance's toxicity while

238. Cohen, *supra* note 235, at 111.

239. Hamowy *supra* note 236; *Id.*

240. Cohen, *supra* note 235, at 100.

241. *Id.*

242. *See, e.g.*, HYLAND'S, http://www.hylands.com/products/hylands-poison-ivy-oak-tablets (last visited Feb. 17, 2020; *see also* BRITISH HOMEOPATHIC ASSOCIATION, https://www.britishhomeopathic.org/charity/how-we-can-help/articles/homeopathic-medicines/r/rhus-tox/ (last visited Feb. 17, 2020).

243. *See, e.g.*, HYLAND'S, *supra* note 242.

244. *See* WebMD, https://www.webmd.com/vitamins/ai/ingredientmono-462/croton-seeds (last visited Feb. 17, 2020) (noting these conditions as common side effects and advising that croton seeds are unsafe for anyone to use).

245. Cohen, *supra* note 235, at 111.

246. *Id.*

making the treatment more effective.[247] Paradoxically, Hahnemann professed that the more extreme the dilution, the greater its potency.[248]

The law of similars and the law of minimum dose are reasons why homeopathy has historically ranked among the top controversial alternative medicine practices.[249] Critics of homeopathy have argued that "it's not possible to explain in scientific terms how a remedy containing little or no active ingredient can have any effect"[250] after undergoing so many successive dilutions. Another aspect to the controversy stems from the lack of evidence indicating homeopathy's effectiveness. Despite centuries of research and study, "homeopathic products have not been proven effective for any known human medical condition."[251] Michael De Dora, director of public policy for the Center for Inquiry (an advocacy group promoting reason and scientific integrity in the public affairs) has testified before the FDA that, "We could spend hours discussing the extensive, decades-long scientific examination of homeopathy, but suffice to say the empirical evidence against homeopathy is overwhelming. Aside from a placebo effect, homeopathic products have no effect in treating illnesses."[252] This lack of demonstrated efficacy creates a concern that consumers are wasting money on worthless products and, even worse, are possibly foregoing conventional medical treatments (such as surgery) and prescription medications that could effectively treat the conditions with which they present.[253]

Interestingly, the field of homeopathy views disease as "an individual constellation of affective, cognitive, and somatic symptoms unique to his or her own physiology" and seeks to prescribe remedies in accordance with the patient's unique response.[254] Hahnemann believed that a specific course of therapy should be prescribed on an individualized basis,

247. *See* Suzanne White Junod, *An Alternative Perspective: Homeopathic Drugs, Royal Copeland, and Federal Drug Regulation*, 55 FOOD DRUG L.J. 161, 162 (2000); *see also*, NAT'L CTR. FOR COMPLEMENTARY & INTEGRATIVE HEALTH, https://nccih.nih.gov/health/homeopathy (last visited Feb. 17, 2020).

248. *See* Max Sherman & Steven Strauss, *Homeopathic Drugs—Regulatory Concerns*, 45 FOOD DRUG COSMETIC L.J. 113, 115 (1990).

249. *See* Cohen, *supra* note 235, at 109 (noting the other two most controversial treatments are ozone therapy and chelation therapy).

250. *Homeopathy*, *supra* note 228.

251. PRAY, *supra* note 23, at 201.

252. Dennis Thompson, *FDA Weighs Tighter Control of Homeopathic Remedie*s, SPECTRUM HEALTH: HEALTH BEAT (Apr. 22, 2015), https://healthbeat.spectrumhealth.org/fda-weighs-tighter-control-of-homeopathic-remedies/.

253. Cohen, *supra* note 235.

254. Baynon McDowell, *Homeopathic Treatment of Mild Traumatic Brain Injury*, 1:3 ALTERNATIVE & COMPLEMENTARY THERAPIES 129, 131 (1995).

following a lengthy exam and period of questioning.[255] Thus, it seems unlikely that even Hahnemann, the father of homeopathy, would recognize or approve of today's mass-produced quantities of alternative remedies as homeopathic.

### *B. Homeopathic Products Are Drugs*

Homeopathic products are classified as drugs in the FFDCA.[256] Just as the 1938 Act had exempted homeopathic medicines from premarket regulatory review for safety, so too did the 1962 Kefauver-Harris Amendment exempt homeopathic drugs from any sort of premarket regulatory efficacy review.[257]

### *C. 1988 Compliance Policy Guide (CPG) 400.400, Conditions Under Which Homeopathic Drugs May Be Marketed*

Since 1988, until the passage of the new draft guidance, FDA has not required homeopathic products be proven safe or effective prior to entering interstate commerce, in sharp contrast to the regulatory requirements applicable to conventional drugs.[258] So long as homeopathic products contained ingredients recognized in the Homeopathic Pharmacopeia of the United States (HPUS) and complied with FDA's labeling and manufacturing regulations, they could be marketed to consumers.[259] Moreover, homeopathic products not requiring a physician's supervision could be sold OTC.[260] The rationale guiding these relaxed regulatory requirements recognized that homeopathic products contained such low dilutions of active ingredients that they did not pose the same risks to consumers as more powerful conventional drugs.[261] Although homeopaths

255. PRAY, *supra* note 23, at 191.

256. *See* 21 U.S.C. § 321(g)(1)(A) (2018) (stating that "[t]he term 'drug' means articles recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them."); *see also* 21 U.S.C. § 351(b) (2018) (explaining that drugs labeled and offered for sale as homeopathic drugs "shall be subject to the provisions of the Homeopathic Pharmacopoeia" and those drugs not so in accordance with respect to their strength, quality, or purity differing from the official compendium "shall be deemed to be adulterated").

257. STEVEN STRAUSS, STRAUSS'S FEDERAL DRUG LAWS AND EXAMINATION REVIEW 304 (2001). Although homeopathic products can be prescribed by a homeopathic physician, the vast majority of homeopathic products are purchased OTC.

258. U.S. FOOD & DRUG ADMIN., *supra* note 230.

259. *Id.*

260. *Id.*

261. Brady Dennis, *FDA to Revisit its Policies on Homeopathic Products*, WASH. POST (Apr. 18, 2015), https://www.washingtonpost.com/national/health-science/for-first-time-in-decades-fda-to-revisit-how-it-regulates-homeopathic-products/2015/04/18/2753315c-e207-11e4-81ea-0649268f729e_story.html?noredirect=on&utm_term=.3f6343178e16.

believe that the dilution will trigger a healing immune response in the body, critics note that the large number of dilutions result in "little or no active ingredient" remaining in the final product.[262] Accordingly, those skeptical of homeopathic methods have claimed selling such products "amounts to little more than selling water and wishful thinking."[263] Given FDA's limited resources and the enormous number of products falling within the Agency's jurisdiction, requiring a premarket approval process for homeopathic products on par with that required for conventional drugs would have imposed quite a regulatory burden had these products been included in FDA's review of GRASE drugs in the 1970's. Deferring review of substances containing mostly water conserved Agency resources that could then be used to evaluate drugs with greater potential for harm.

Another reason homeopathic products were not included in the GRASE review is that, for well over a hundred years, production of homeopathic drugs had been limited.[264] Only a few well-established manufacturers produced the ingredients that a limited number of homeopathic practitioners needed to prescribe drugs for their patients.[265] However, today, homeopathy is now a three-billion dollar industry.[266] Experts began recognizing in the early 2000's that such growth meant FDA could not "effectively monitor herbal medicines."[267]

262. *Id.*

263. *Id.*

264. U.S. FOOD & DRUG ADMIN., *supra* note 230.

265. *Id.*

266. *See* Laura McGinley, *FDA Takes More Aggressive Stance Toward Homeopathic Drugs*, WASH. POST (Dec. 17, 2017), available at https://www.washingtonpost.com/news/to-your-health/wp/2017/12/18/fda-to-target-homeopathic-drugs-that-pose-safety-risks/?utm_term=.19ff89e3168e. Although there has been significant growth in this area, it should be noted that homeopathic products represent a small percentage of the products FDA regulates. As a point of comparison, FDA regulates $62 billion worth of cosmetics products. *See* ADAM GARCIA & ROSE DIBARTOLO, COSMETICS AND FDA REGULATION 3 (2013). Note that the line demarcating cosmetics from drugs and homeopathic drugs is not always clear. For example, a skin product intended to hide acne is regulated as a cosmetic but an anti-acne product is regulated as a drug. *See id.* at 5. Anti-acne drug products also include homeopathic acne medications such as Hyland's Clear-Ac Tablets. *See* 1-800 HOMEOPATHY, http://www.1-800homeopathy.com/hylands-clear-ac-tablets.html?utm_source=GoogleShop&utm_medium=cse&utm_campaign=Feed&source=Googleshop&gclid=CjwKCAjwo87YBRBgEiwAI1LkqUhhzjJUs7ZASq0NPUKiXHCiml6QmBMw-X9Xy9vG32ecE3a3tRIjKhoCpusQAvD_BwE (last visited Feb. 17, 2020). Products that are both cosmetics and drugs must satisfy the regulatory rules for both. *See* GARCIA, COSMETICS AND FDA REGULATION 5–6 (2013). Despite industry employing the terms "cosmeceuticals" or "cosmetic drugs," there is no legal or regulatory definition for such terms within the FFDCA. *See id.* at 5, 63.

267. *See* HILTS, *supra* note 16, at 337.

*D. A Growing Industry and the Need for Enhanced Enforcement*

In a National Health Interview Survey evaluating consumers' use of complementary alternative medicine approaches conducted from 2007–2012, experts noted that in 2007, more

users turned to homeopathy than any other alternative medical approach for treatment of a condition (eighty-eight percent of all users surveyed).[268] In 2012, surveyors found that OTC homeopathic products were used by 1.8% of children, and practitioner-based homeopathy was used by only 0.2% of children.[269] Thus, the study suggests that most homeopathic uses are self-care, OTC purchases.[270] Such self-care use is also reflected in homeopathic industry sales data revealing "steady growth in the sales of homeopathic products over the last 10 years, with about 80% of sales occurring at retailers such as big box stores, grocery stores, and drug stores."[271]

With the exponential growth of the alternative medicine industry in recent decades, the National Institutes of Health established a separate institute to study those alternative approaches: the National Center for Complementary and Integrative Health (NCCIH) in 1998.[272] According to a 2016 analysis that NCCIH conducted, Americans spent $30.2 billion dollars on complementary health care.[273] For the first time in history, a nationwide survey assessed how much of that money was spent on alternative health care approaches for a significantly vulnerable patient population: children. The answer was $1.9 billion.[274]

Complementary healthcare includes an assortment of practices and products ranging from herbal supplements, yoga, meditation, and visits to chiropractors. The NCCIH found that some of these alternative treatments have proven beneficial, such as tai chi for reducing pain and improving physical functioning for patients suffering from knee

268. *See* LINDSAY BLACK ET AL., USE OF COMPLEMENTARY HEALTH APPROACHES AMONG CHILDREN AGED 4–17 YEARS IN THE UNITED STATES: NATIONAL HEALTH INTERVIEW SURVEY, 2007–2012 6 (2015), https://www.cdc.gov/nchs/data/nhsr/nhsr078.pdf.

269. *See id.* at 4.

270. *See id.* at 7.

271. *See id.* There is no data "assessing whether self-care with homeopathic products is equivalent to care from a trained homeopath." *See id.*

272. Maggie Fox, *Americans Spend $30 Billion a Year on Alternative Medicine*, NBC NEWS (June 22, 2016), https://www.nbcnews.com/health/health-news/americans-spend-30-billion-year-alternative-medicine-n596976; *see also About NCCIH*, NAT'L CTR. FOR COMPLEMENTARY & INTEGRATIVE HEALTH, https://nccih.nih.gov/ (last visited Feb. 11, 2020).

273. Fox, *supra* note 272.

274. Mike Barrett, *Report: Alternative Medicine Growing in Popularity in the U.S.*, NAT. SOC'Y (June 23, 2016), https://naturalsociety.com/alternative-medicine-growing-in-popularity-in-the-u-s-2325/.

osteoarthritis.[275] However, the NCCIH has also found other treatments to be lacking in either safety or efficacy. For example, NCCIH has found "little evidence to support homeopathy as an effective treatment for any specific condition" and while "people sometimes assume that all homeopathic remedies are highly diluted and therefore unlikely to cause harm, some products labeled as homeopathic can contain substantial amounts of active ingredients and therefore could cause side effects and drug interactions."[276]

NCCIH Director Josephine P. Briggs, M.D., notes, "With so many Americans using and spending money on complementary health approaches, it is extremely important for us to provide the public with evidence-based information to help them inform decisions. This underscores the importance of conducting rigorous research to know whether the products and practices being used are safe and effective."[277] Such research is especially important given the rise in marketing of homeopathic products for children and that adverse events that have been reported in children.

275. *See Study Shows Tai Chi and Physical Therapy Equally Helpful for Knee Osteoarthritis*, NAT'L CTR. FOR COMPLEMENTARY & INTEGRATIVE HEALTH (August 25, 2016), https://nccih.nih.gov/research/results/spotlight/tai-chi-knee-osteoarthritis_2016; *see also* Wang C, Schmid C.H., Iversen M.D. et al., *Comparative Effectiveness of Tai Chi Versus Physical Therapy For Knee Osteoarthritis: A Randomized Trial*, ANN. INTERN. MED. (July 19, 2016), https://www.ncbi.nlm.nih.gov/pubmed/27183035.

276. Homeopathy, *supra* note 228; *see also* Umut Altunc, Max H. Pittler, Edzard Ernst, *Homeopathy for Childhood and Adolescence Ailments: Systematic Review of Randomized Clinical Trials*, MAYO CLINIC PROC. 70, 70–74 (2007) (reviewing evidence from rigorous clinical trials of all available double-blind, placebo controlled studies and concluding that "homeopathy for childhood and adolescence ailments is not convincing enough for recommendations in any condition"); M. Cucherat, M.C. Haugh & M. Gooch, J.P. Boissel, *Evidence Of Clinical Efficacy Of Homeopathy: A Meta-Analysis Of Clinical Trials*, EURO. J. OF CLIN. PHARM. 33 (2000) (conducting a systemic review and meta-analysis to determine whether any evidence exists from randomized double-blind clinical trials that demonstrates the efficacy of homeopathic treatment in patients seeking treatment for disease and concluding that some evidence exists suggesting that homeopathic treatments were more effective than a placebo but that these results are derived from trials exhibiting low methodological quality); Edzard Ernst, *Homeopathy: What Does the "Best" Evidence Tell Us?*, 192 MED. J. AUSTL. 548, 548 (2010) (evaluating the evidence for and against the efficacy of homeopathy and concluding that the best available current studies do not show that homeopathic treatment has any effect beyond that of a placebo). Studies were evaluated where patients sought homeopathic treatment for cancer, attention deficit disorder, asthma, dementia, influenza, and induction of labor. Ernst, *supra* note 276.

277. *See* Fox, *supra* note 272; *see also Americans Spent $30.2 Billion Out-Of-Pocket on Complementary Health Approaches*, NAT'L CTR. FOR COMPLEMENTARY & INTEGRATIVE HEALTH, https://nccih.nih.gov/news/press/cost-spending-06222016.

In the last decade, FDA has issued over forty warning letters regarding homeopathic products.[278] These incidents involving homeopathic products not proven safe or effective feel eerily similar to the patent medicines of old. Some homeopathic products may simply be ineffective due to the lack of active ingredients. Other homeopathic products may be tragically harmful because of the presence of active ingredients in excessive amounts. Still other homeopathic products contain ingredients that are relatively safe if consumed orally, such as zinc, but are harmful if taken via a different route of administration, such as in a nasal spray.

For example, in 2009, FDA issued a warning letter to Matrixx Initiatives Inc. concerning the marketing of its homeopathic products, including its Zicam Cold Remedy Nasal Gel, Zicam Cold Remedy Gel Swabs, and Zicam Cold Remedy Swabs for Kids.[279] In the warning letter, FDA noted that it had received more than 130 reports of adverse events associated with these intranasal products, specifically the loss of smell, which in some cases was permanent.[280] The letter further noted that Matrixx itself had received more than 800 reports of consumers losing their sense of smell after using the products.[281] FDA issued a public health advisory alerting consumers to the danger associated with these products and urging them to throw away such products, as they had not been proven safe or effective in the claims made to reduce the duration and severity of colds.[282] The company eventually recalled the products, ceased future shipments, and paid millions of dollars to settle claims against it for allegedly causing anosmia (loss of smell) in users.[283]

In addition to nasal zinc products, another group of homeopathic products that heightened concern for regulators were those marketed for children containing belladonna. Belladonna is a poison derived from a

278. Thompson, *supra* note 252 (quoting Cynthia Schnedar, director of the Office of Compliance at FDA's Center for Drug Evaluation and Research, on the Agency's 1988 policy guidance permitting homeopathic products to enter the marketplace without pre-screening or approval).

279. *See Matrixx Initiatives, Inc. AKA Zicam LLC*, U.S. FOOD & DRUG ADMIN. (June 16, 2009), https://wayback.archive-it.org/7993/20170112195553/http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2009/ucm166909.htm.

280. *See id.*

281. *See id.*

282. FED. DRUG ADMIN., PUBLIC HEALTH ADVISORY: LOSS OF SENSE OF SMELL WITH INTRANASAL COLD REMEDIES CONTAINING ZINC (2009).

283. Gardiner Harris, *F.D.A. Warns Against Use of Popular Cold Remedy*, N.Y. TIMES (June 16, 2009). The company continues selling oral zinc products and zinc-free nasal products and denies the existence of any link between its zinc nasal spray/gel products and anosmia. *See FAQs*, ZICAM, https://www.zicam.com/faqs/about-zicam-products/.

plant known as Deadly Nightshade; both the leaves and berries of the plant are highly toxic.[284] Since 2010, FDA has received numerous reports of adverse events associated with the consumption of homeopathic medicines containing belladonna through FDA's Adverse Event Reporting System (AERS).[285] Such reports included episodes of children experiencing seizures,[286] emergency room visits due to difficulty breathing,[287] going limp and becoming nonresponsive,[288] and collapsing and losing consciousness[289] after consuming Hyland's Teething tablets with belladonna. FDA issued a safety alert, warning consumers against using Hyland's Teething Tablets; the manufacturer subsequently recalled the product.[290]

In 2016, FDA again warned consumers against using homeopathic teething tablets and gels, advising parents to seek medical care immediately if their children experienced seizures, difficulty breathing, lethargy, excessive sleepiness, muscle weakness, skin flushing, constipation, difficulty urinating, or agitation after using such products.[291] Raritan Pharmaceuticals in New Jersey eventually recalled three belladonna-containing products, two of which were sold at CVS.[292]

In early 2017, FDA laboratory analysis detected inconsistent levels of belladonna in homeopathic teething tablets manufactured by the Standard Homeopathic Company in Los Angeles (the manufacturer of Hyland's homeopathic teething products) marketed for use in children.[293] In some instances, the testing revealed the presence of belladonna in products "far exceeding the amount claimed on the label."[294] FDA also began

284. *See Hyland's Homeopathic Teething Tablet: Questions and Answers*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/consumers/consumer-updates/hylands-homeopathic-teething-tablets-questions-and-answers (last visited Feb. 20, 2020).

285. *See MedWatch: The FDA Safety Information and Adverse Event Reporting Program, Medical Product Safety Information*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program/medical-product-safety-information (last visited Feb. 20, 2020); *see also* FED. DRUG ADMIN., ADVERSE EVENT REPORTING SYSTEMS (FAERS)—TEETHING TABLET AERS PART 1 OF 3 (2019).

286. FED. DRUG ADMIN., *supra* note 285, at 78.

287. *See, e.g.*, *id.* at 79.

288. *See, e.g.*, *id.* at 82.

289. *See, e.g.*, *id.* at 104.

290. *Hyland's Homeopathic Teething Tablet*, *supra* note 284.

291. *Se*e News Release, Fed. Drug Admin., FDA Warns Against the Use of Homeopathic Teething Tablets and Gels (2016).

292. *See* Press Release, Fed. Drug Admin., FDA Confirms Elevated Levels of Belladonna in Certain Homeopathic Teething Products (2017).

293. *See id.*

294. *See id.*

investigating the death of 10 children after they had consumed homeopathic teething tablets.[295]

Finally, FDA has also warned consumers against using OTC homeopathic asthma products because asthma can be a life-threatening condition and such products have not been proven safe and effective for the treatment of asthma.[296]

Skeptics of homeopathic drugs argue that "remedies should endure the same sort of regulation as the over-the-counter drugs with which they share shelf space."[297] Proponents of homeopathy admit to the absence of scientific evidence demonstrating the efficacy of homeopathic treatments.[298] However, those proponents claim such a lack of science is no reason to change the current regulatory landscape, arguing that, "[j]ust because we don't understand exactly how they work doesn't mean we won't be able to in the future."[299]

Interestingly, some proponents of homeopathy take the opposite view and welcome heightened regulatory action by the FDA. For example, Ronald Whitmont, a homeopathic doctor in New York and president of the American Institute of Homeopathy told *The Washington Post* that his organization supports any FDA action intended to enforce against poor manufacturing practices because, "[t]here are always bad apples in the manufacturing world, and they need to be policed just like in any other industry."[300] Yet, can any amount of regulatory action be enough to cure an entire industry that lacks a scientific basis to justify its existence in the first place?

Perhaps a new draft guidance would not have been necessary if homeopathic medicines simply continued producing a placebo effect in patients. Consumers' spending money on worthless—albeit harmless—products hurts the pocketbook, but it is a far cry from the public health crisis of the sulfanilamide tragedy. But, as the previous examples illustrate, homeopathic products became more dangerous and the concern shifted from consumers who were merely wasting money to consumers

295. *See* Susan Scutti*, Throw out Homeopathic Teething Tablets with Belladonna, FDA Says*, CNN (2017).

296. *See FDA Warns Consumers About the Potential Health Risks of Over-The-Counter Asthma Products Labeled as Homeopathic*, FED. DRUG ADMIN. (2015).

297. Dennis Thompson, *FDA Weighs Tighter Control of Homeopathic Remedies, Health Day,* FED. DRUG. ADMIN. (2015); *see also* Brady Dennis*, FDA to Revisit Its Policies on Homeopathic Products*, WASH. POST (2005).

298. *See* Thompson, *supra* note 297.

299. *See id.* (quoting Jennifer Jacobs, homeopathic practitioner and clinical assistant professor of epidemiology at the University of Washington School of Public Health).

300. *See id.*

who might be risking their lives with an entire class of products that, until now, had not received much oversight or regulatory attention.

## III. REVISED DRAFT GUIDANCE PROPOSING RISK-BASED ENFORCEMENT

On March 27, 2015, FDA issued a notice for public hearing with a sixty-day comment period following the public hearing for comments regarding its regulation of homeopathic products for the first time in a quarter of a century.[301] Specifically, FDA sought "information and comments from stakeholders [consumers, patients, caregivers, health care professionals, patient groups, industry, and others] about the current use of human drug and biological products labeled as homeopathic, as well as the Agency's regulatory framework for such products," which include "prescription drugs and biological products labeled as homeopathic and over-the-counter (OTC) drugs labeled as homeopathic."[302] In addition, FDA explained that it was evaluating its enforcement policies for such homeopathic products "from scientific, risk, and process perspectives" and was seeking public opinion "about whether and how to adjust the current enforcement policies to reflect changes in the homeopathic product marketplace" over the last two and half decades.[303] A hearing was held on April 20 and 21, 2015.[304]

On June 10, 2015, FDA extended the comment period for the notice of public hearing that had appeared in the Federal Register on March 27, 2015 in response to requests for additional time to submit comments.[305] FDA extended the comment period for an additional sixty days until August 21, 2015.[306] Within the notice extending the comment period, FDA explained the extension would allow adequate time for interested members of the public to submit comments "without significantly delaying Agency decision making on these important issues."[307]

On September 9, 2015, FDA reopened its comment period for an additional 60 days until November 9, 2015 for the notice of public hearing and comments that had appeared in the Federal Register on March

301. Homeopathic Product Regulation: Evaluating the Food and Drug Administration's Regulatory Framework After a Quarter-Century; Public Hearing, 80 Fed. Reg. 16327-01 (March 27, 2015). Notice of public hearing. (Docket No. FDA-2015-N-0540).

302. *See id.*

303. *See id.*

304. *See id.*

305. Homeopathic Product Regulation: Evaluating the Food and Drug Administration's Regulatory Framework After a Quarter-Century; Extension of Comment Period, 80 Fed. Reg. 32868 (June 10, 2015). Notice of public hearing, extension of comment period (Docket No. FDA-2015-N-0540).

306. *Id.*

307. *Id.*

27, 2015[308] and the comment period was then extended on June 10, 2015[309] to allow additional time for the public to respond to its noticed questions.[310] After reviewing all the comments received, FDA issued new draft guidance for drug products labeled as homeopathic in December 2017.[311] In the new draft guidance, FDA recognized that under the FFDCA, "homeopathic drugs are subject to the same regulatory requirements as other drugs."[312] FDA then held another ninety-day comment period on the draft guidance that was supposed to close in March 2018, but was extended until May 21, 2018.[313]

The new draft guidance established a "risk-based approach" by prioritizing the Agency's enforcement efforts among six high-risk categories. The high-risk categories included:

(1) products with reported safety concerns (such as those containing the toxic ingredient belladonna) that caused adverse events and those products for which MedWatch reports exist;

(2) products that contain or purport to contain ingredients with potentially significant safety concerns, such as potential toxicity concerns or potentially pathogenic agents; (3) products for routes of administration other than oral and topical, such as unapproved injectable drug products or eye drops; (4) products intended to be used for the prevention or treatment of serious and/or life threatening diseases and conditions, such as homeopathic asthma medications; (5) products for vulnerable populations, such as the teething tablets or gels for infants; and (6) products deemed adulterated under Section 501 of the FFDCA, such as those products whose purported strength, quality, or purity differs from the standards set forth in the USP, the official Homeopathic Pharmacopoeia of the United States, the official National Formulary, or if there are significant violations of current good manufacturing requirements.[314]

308. *See* 80 Fed. Reg. 16327-01.

309. *See* 80 Fed. Reg. 32868.

310. Homeopathic Product Regulation: Evaluating the Food and Drug Administration's Regulatory Framework After a Quarter-Century; Reopening of the Comment Period, 80 Fed. Reg. 54256-01 (Sept. 9, 2015). Notice of public hearing; reopening of comment period. (Docket No. FDA-2015-N-0540).

311. *See* U.S. FOOD & DRUG ADMIN., DRUG PRODUCTS LABELED AS HOMEOPATHIC GUIDANCE FOR FDA STAFF AND INDUSTRY, Draft Guidance (Oct. 2019).

312. *Id.* at 2.

313. *See* Homeopathic Product Regulation: Evaluating the Food and Drug Administration's Regulatory Framework After a Quarter-Century; Public Hearing, 83 Fed. Reg. 12398 (Mar. 21, 2018). Notice of extension of comment period. (Docket No. FDA–2017–D–6580).

314. *See* U.S. FOOD & DRUG ADMIN., DRUG PRODUCTS LABELED AS HOMEOPATHIC GUIDANCE FOR FDA STAFF AND INDUSTRY, Draft Guidance (Oct. 25, 2019).

On October 25, 2019, FDA published in the Federal Register a notice of availability for a revised draft guidance titled "Drug Products Labeled as Homeopathic."[315] The revised draft guidance, like the December 2017 version, describes how FDA intends to prioritize enforcement and regulatory action for homeopathic products.[316] The October 2019 revised guidance describes the risk-based approach the Agency will take for "certain categories of homeopathic drug products marketed without the required FDA approval as potentially posing higher risks to public health."[317] The Agency then lists essentially the same six categories of products it had named in its December 2017 guidance: (1) products with reports of injury, that, after evaluation, raise potential safety concerns (such as MedWatch reports); (2) products that contain or purport to contain ingredients associated with potentially significant safety concerns (such as infectious pathogens); (3) products for alternative routes of administration; (4) products intended to prevent or treat serious and/or life-threatening diseases or conditions; (5) products for vulnerable populations; and (6) products with significant quality issues (such as those that are contaminated or that deviate from current good manufacturing practice).[318] The public comment period on the new revised guidance was open through January 23, 2020.[319] Also on October 25, 2019, FDA withdrew Compliance Policy Guide 400.400.[320]

On January 8, 2020, FDA extended the comment period to March 23, 2020.[321]

## IV. THE VERDICT

Since issuing its new draft guidance setting forth this risk-based enforcement policy, FDA has been busy carrying it out—and the public is better for it. For example, the Agency focused its regulatory efforts on the high-risk category of homeopathic products that have not been proven safe or effective for their intended uses with routes of administration

315. *See id*.

316. *See id.*

317. *See id.*

318. *See id.*

319. *See* U.S. FOOD & DRUG ADMIN., DRUG PRODUCTS LABELED AS HOMEOPATHIC GUIDANCE FOR FDA STAFF AND INDUSTRY, Draft Guidance (Oct. 25, 2019).

320. *See* Compliance Policy Guide Sec. 400.400 Conditions Under Which Homeopathic Drugs May Be Marketed; Withdrawal of Guidance, 84 FR 57439 (Oct. 25, 2019). Notice; withdrawal. (Docket No. FDA-2019-N-4611).

321. *See* U.S. FOOD & DRUG ADMIN., DRUG PRODUCTS LABELED AS HOMEOPATHIC DRAFT GUIDANCE FOR FOOD AND DRUG ADMINISTRATION STAFF AND INDUSTRY; EXTENSION OF COMMENT PERIOD (Jan. 8, 2020).

other than oral and topical, such as eye drops.[322] In February 2019, FDA sent warning letters to four different companies for failing to ensure that they produced homeopathic Puriton Eye Relief Drops in accordance with current good manufacturing practices.[323] In a warning letter FDA sent to Kadesh International, the Agency described how its inspection and laboratory analysis of multiple lots of eye drops confirmed bacillus spp contamination, high levels of particulate matter, and unacceptable caustic pH levels (the firm eventually recalled all lots of its Puriton Eye Relief Drops after conversations with FDA regarding the contamination).[324] Non-sterile drops can cause serious eye infection and high pH levels can cause glaucoma, scaring to the corneas, and vision loss.[325] FDA's warning letter to United States Continental Marketing, Inc. noted the firm's failures to ensure that its contract manufacturer (Kadesh International) had adequate facilities to manufacture sterile drugs and their containers (including ophthalmic dropper bottles, tips, and caps); the firm ultimately ceased its drug manufacturing operations.[326] In FDA's warning letter to Fill It Pack It Inc, another contract manufacturer for the same contaminated and recalled homeopathic eye drops, FDA noted that the firm's facilities lacked:

- floors, walls, and ceilings of smooth, hard surfaces that are easily cleaned;
- an air supply filtered through high-efficiency particulate air filters under positive pressure;
- a system for monitoring environmental conditions;
- a system for cleaning and disinfecting the room to produce aseptic conditions, [and];
- a system for maintaining equipment used to control the aseptic conditions.[327]

322. *See id.* at 4.

323. *See* Letter from Steven E. Porter, Jr., Division of Pharmaceutical Quality Operations Director, Food and Drug Admin, to Hyun Eun Lee, Vice President, Kadesh International (Feb. 5, 2019).

324. *Id.*

325. Press Release, U.S. Food & Drug Admin., FDA Warns Manufacturers of Products Labeled as Homeopathic for Putting Consumers at Risk with Significant Violations of Manufacturing Quality Standards (May 14, 2019).

326. Letter from Steven E. Porter, Jr., Division of Pharmaceutical Quality Operations Director, Food and Drug Admin, to David L. Williams, Owner, U.S. Continental Marketing, Inc. (Feb. 5, 2019) (noting the firm's failure to establish adequate quality controls for drug product containers, closures, in-process materials, packaging materials, labeling, and drug products, per 21 CFR § 211.22(a)).

327. Letter from Steven E. Porter, Jr., Division of Pharmaceutical Quality Operations Director, Food and Drug Admin, to Robert L. Miller, Vice President, Fill It Pack It Inc. (May 2, 2019).

Most significantly, the firm "failed to establish procedures for the sterilization of a drug product that is required to be sterile."[328] Lastly, FDA sent a warning letter to Bershtel Enterprises LLC, dba WePackItAll—another contract manufacturer of the same homeopathic eye drops—for similar violations.[329]

In March 2019, FDA issued warning letters to four more companies under its new risk-based enforcement approach.[330] All four companies were producing homeopathic products that fell within FDA's newly defined high-risk categories. For example, FDA issued a warning letter to Red Mountain Inc., a manufacturing firm that produces homeopathic products containing potentially toxic ingredients, such as bioven, more commonly known as snake venom.[331] The problems associated with bioven are twofold: first, the company failed to follow current good manufacturing practices to ensure consistent identity, strength, quality, and purity of its drug products.[332] Without following standard operating procedures to ensure the strength of its products, consumers could be at risk of consuming products that contain greater quantities of bioven than declared on the label, similar to how consumers were harmed by the inconsistent levels of belladonna in homeopathic products.[333] Second, Red Mountain Inc. claims that its snake venom products can treat serious diseases such as AIDS, Hepatitis B&C, cancer, lupus, and rheumatoid arthritis.[334] Yet, the company's homeopathic products have never undergone FDA pre-market approval for safety and efficacy for the treatment of these conditions.[335] Thus, consumers with these serious health conditions may be purchasing these products without any clinical evidence that such products are safe and effective to treat their diseases while foregoing other treatments that actually have been proven safe and effective under FDA's pre-market approval process.

328. *Id.*

329. *See* Letter from Steven E. Porter, Jr., Division of Pharmaceutical Quality Operations IV Director, Food and Drug Admin., to Jack S. Bershtel, Managing Partner, Bershtel Enterprises LLC, dba WePackItAll (Feb. 5, 2019). The firm committed to cease manufacture of sterile drugs in response to the Agency's letter. *See id.*

330. *See* Press Release, U.S. Food & Drug Admin., FDA Warns Homeopathic Firms For Putting Patients at Risk With Significant Violations of Manufacturing Quality Standards, (Apr. 1, 2019) (on file with the U.S. Food & Drug Admin.).

331. *See* Letter from Charles S. Brown, Office of Pharmaceutical Quality Operations Division 2 Acting Program Director, U.S. Food & Drug Admin., to Henry B. Schur, Red Mountain Inc. Director (Mar. 20, 2019).

332. *See id.*; *see also* 21 C.F.R. § 211.22(c) (2020).

333. *See* Letter from Charles S. Brown, *supra* note 331; *see also* Press Release, Fed. Drug Admin., *supra* note 292.

334. *See* Letter from Charles S. Brown, *supra* note 331.

335. *See id.*

A second warning letter that month addressed homeopathic products that could potentially be applied to broken skin but were not tested to ensure they were free from objectionable microorganisms after the company's lab test revealed levels of contamination in its water system.[336] A third warning letter sent to a company preparing homeopathic ear drops noted insects in the raw material room and in the raw materials themselves, and a cracked and exposed holding tank, as well as a lack of microbial testing being conducted.[337] A fourth warning letter was sent to King Bio Inc., a drug manufacturing facility that manufactures and distributes "hundreds of drugs including those intended for infants, children, pregnant women, and immunocompromised individuals" despite having multiple years of obtaining "recurring test results for water used as a component of [the] drug, as well as results for finished homeopathic products, outside of microbiological limits."[338] The testing showed "extremely high levels of microbiological contamination, including results that were Too Numerous to Count (TNTC), and signified the presence of significant opportunistic pathogens."[339] In addition, "FDA laboratory testing also revealed exceedingly high levels of microbiological contamination in multiple homeopathic drugs."[340] FDA conducted a bioburden microbial testing of Dr. King's Kids Bedwetting and Dr. King's Teething Advanced Formula homeopathic products and the results "showed inordinately high levels of microbiological contamination."[341] The company recalled all water-containing drugs after conversations with FDA in August 2018.[342]

Most recently, in April 2019, FDA sent a warning letter to Newton Laboratories Inc, DBA Newton Homeopathics regarding, among other things, the company's failure to validate its drug manufacturing processes, especially as those processes related to products marketed for

336. *See* Letter from Charles S. Brown, Office of Pharmaceutical Quality Operations Division 2 Acting Program Director, U.S. Food & Drug Admin., to Dr. Steven D. Smith, President, Tec Laboratories, Inc. (Mar. 20, 2019). One of the products included a homeopathic first aid antiseptic marketed for the treatment of minor cuts and scrapes, which was not "tested for conformance to appropriate microbial quality specifications." *Id.*

337. *See* Letter from Francis Godwin, Office of Manufacturing Quality, Office of Compliance, and Center for Drug Evaluation and Research Director, to Kuldeep Jain, Owner and Managing Director, B. Jain Pharmaceuticals Private Ltd. (Mar. 21, 2019).

338. *See* Letter from Charles Brown, Office of Pharmaceutical Quality Operations, Division 2 Acting Program Director, U.S. Food & Drug Admin., to Dr. Frank King Jr., President, King Bio Inc. (Mar. 20, 2019).

339. *See id.*

340. *See id.*

341. *See id.*

342. *See id.*

infants and children containing belladonna.[343] Newton Homeopathics failed to establish written procedures for production and process controls designed to assure that its products have the identity, strength, quality, and purity they purport to or are represented to possess.[344] Thus, Newton's homeopathic products for children containing belladonna were released without any batch testing to ensure that there were not inconsistently high quantities of belladonna, as was the case with Hyland's teething products.[345]

In addition, Newton produces homeopathic products for children containing the ingredient Nux Vomica, which contains strychnine—a highly toxic poison commonly used as a rodenticide since medieval times.[346] In small amounts, strychnine can operate like caffeine in the nervous system, providing a short-term stimulant effect; however, unlike caffeine, a five milligram dose is lethal.[347] In high amounts, strychnine disrupts how glycine works in the body – a chemical that, under normal circumstances, signals the muscles to work.[348] Strychnine then causes severe, excruciating spasms, which intensify until they cause death by asphyxiation or exhaustion from the incessant convulsions.[349] Ironically, strychnine was a popular ingredient in the patent medicine trade in the early twentieth century thanks to testimonials containing dubious claims that the strychnine-containing solutions and elixirs cured everything from tuberculosis, to bronchitis, to influenza.[350]

The firm produces a "Newton Homeopathics Kids" line of products, including one called "Airway Ease," which is allegedly "formulated for symptoms such as wheezing, shortness of breath, congestion, coughing, inflammation and other related symptoms."[351] The product contains, among other things, Nux Vomica.[352] This product has not been approved

343. *See* Letter from Monica R. Maxwell, Office of Pharmaceutical Quality Operations, Division II Program Division Director, to Marjorie J. Roberts, Chief Executive Officer, Newton Laboratories Inc, DBA Newton Homeopathics (Apr. 23, 2019).

344. *See id.*; *see also* 21 C.F.R. § 211.100(a).

345. *See* Letter from Monica R. Maxwell, *supra* note 343; *see also Hyland's Homeopathic Teething Tablet*, *supra* note 284; *MedWatch*, *supra* note 285.

346. *See* Letter from Monica R. Maxwell, *supra* note 343; *see also Hyland's Homeopathic Teething Tablet*, *supra* note 284; *see also* LYDIA KANG & NATE PEDERSEN, QUACKERY: A BRIEF HISTORY OF THE WORST WAYS TO CURE EVERYTHING 74, 76 (2017).

347. KANG & PEDERSON, *supra* note 346, at 74.

348. *See id.*

349. *See id.*

350. *See id.* at 79–81.

351. *See* NEWTON HOMEPATHICS: KIDS AIRWAY EASE, https://www.newtonlabs.net/Kids-Airway-Ease/productinfo/F002/ (last visited Feb. 24, 2020).

352. *Id.*

as safe for children, nor has it been approved as effective for treating possible life-threatening conditions such as asthma.[353] Thus, the risk inherent in this product is two-fold: a child might receive an inconsistently high amount of strychnine that would prove fatal or a child might receive this medication during an acute asthma attack and the medication is ineffective.

If that were not troubling enough, the product also lists liquid inactive ingredients, including "USP Purified water."[354] However, FDA's inspection revealed that the company's water, when tested for total aerobic microbial counts and total yeast and mold counts, received results in excess of established limits.[355] The firm failed to investigate these failing results to determine the cause, failed to assess any risks to patient safety (including potentially vulnerable patient populations such as children), and released the products into the United States market.[356]

These products are exactly the sort FDA is right to focus on under its new risk-based enforcement policy. The products are targeted to a vulnerable population (pediatric patients), contain ingredients with reported safety concerns (belladonna), contain ingredients with potentially significant safety concerns (Nux Vomica, which contains strychnine), could potentially be used to treat or prevent life-threatening conditions (such as asthma, in the case of "Airway Ease"), and they are adulterated for failing to follow current good manufacturing practices set forth in the Code of Federal Regulations (such as those governing water quality and ingredient strength and purity).[357]

FDA's regulation of homeopathic products under a risk-based enforcement policy is crucial to ensuring that consumers do not suffer the harm so widely inflicted during the patent medicine era days of the early twentieth century. Similar to the patent medicines of the last century, homeopathic products have not been evaluated or tested for safety, efficacy,

353. *Id.* (this product has not been FDA approved and should be kept out of the reach of children); *see generally* U.S. Nat'l Libr. Med., *NUX VOMICA- Poison Nut Granule*, DAILYMED (Dec. 2019), https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=0dd0f09a-656f-6161-e054-00144ff8d46c&type=display (the ingredient Nux Vomica itself is not FDA approved and should be kept out of reach from children).

354. *See* NEWTON HOMEPATHICS: KIDS AIRWAY EASE, *supra* note 351.

355. *See* FDA WARNING LETTER TO NEWTON LABORATORIES INC, DBA NEWTON HOMEOPATHICS, https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/newton-laboratories-inc-dba-newton-homeopathics-559612-04232019 (last visited Feb. 24, 2020).

356. *See id.*

357. *See Drug Products Labeled as Homeopathic Guidance for FDA Staff and Industry, Draft Guidance*, U.S. FOOD & DRUG ADMIN. 4–5 (Oct. 2019), https://www.fda.gov/media/131978/download.

or quality. Just like the old patent medicines, homeopathic drugs "may cause significant and even irreparable harm if they are poorly manufactured, which can lead to contamination" or if they "contain active ingredients that aren't adequately tested or disclosed to patients."[358]

In April 2019, then-Commissioner Scott Gottlieb, M.D. stated that the Agency's "new regulatory approach to prioritize additional enforcement and regulatory actions against certain products labeled as homeopathic" would help focus efforts on products "being marketed without approval for a wide array of diseases and conditions, from chronic pain to cancer" to contaminated products, and to those that "may not deliver any benefit and may have the potential to cause harm."[359] While no timeline has been firmly established for publishing a final version of the draft guidance, Commissioner Gottlieb stated that FDA was "working to finalize our draft guidance in the coming months to help ensure that products that reach consumers are not harmful to their health."[360] Such is the stepped up scrutiny such products will continue receiving under the new risk-based enforcement policy, resulting in greater protection of the public health.

The regulatory goals for drugs are not so different than the regulatory goals for governing the behavior of those who dispense those drugs.[361] Laws surrounding the practice of medicine aim to prevent "nondiagnosis, misdiagnosis, nontreatment and mistreatment by unlicensed medical providers. Its goals are twofold: first, protecting the public from the dangers of unskilled practitioners and unsound treatment or advice, and second, protecting the public from reliance on unskilled practitioners, and directing them to proper medical care."[362] The goals of licensing confront the challenge that a consumer may not be able to "distinguish between competent practitioners and quacks, and thus must rely on the State to root out the professionally infirm."[363] Similarly, the regulatory goals for drugs should aim to prevent the nontreatment and mistreatment of serious conditions by unsafe or ineffective products on the

358. Press Release, U.S. Food & Drug Admin., *supra* note 325.

359. *Id.*

360. *Id.*

361. *See* U.S. CONST. amend. X. Although the regulatory goals are similar, the regulatory schemes are different. States are permitted to regulate the licensing of health practitioners pursuant to the Tenth Amendment, which states that those powers the Constitution does not expressly delegate to the federal government (and those not prohibited to the states) are reserved to the states. *See id.* In contrast, the federal government has delegated authority to the FDA by way of the Federal Food, Drug, and Cosmetic Act for the federal regulation of drugs. *See generally* 21 U.S.C. § 301 (2018); *see* 21 U.S.C. § 321(g)(1) (2018).

362. Cohen, *supra* note 46, at 85–86.

363. *See id.* at 87.

market. Further, consumers should be directed to proper medical care and cannot be expected to distinguish between efficacious drugs of appropriate strength and purity versus sugar pills and snake oil remedies. Consumers must rely on government regulation to eliminate items that are at best placebos and at worst poisonous. A major shortcoming of the draft guidance is one the Agency recognizes itself: "[m]any homeopathic products will likely fall outside the risk-based categories described in the revised draft guidance."[364] An important desired public health outcome is a reduction in the number of deaths and injuries arising from the quality or unsafe use of medical products, which necessarily includes homeopathic drugs.[365] Given the lack of science supporting the use of homeopathic products, the draft guidance will likely not prevent many worthless products from still flooding the market.

That such products are even on the market signals a need for enhanced regulation. The new draft guidance is a step in the right direction because more regulation is necessary to address the inevitable market failures that arise in situations like this, where consumers are being misled or have inaccurate information.[366] In this kind of arena, "[r]egulation is ubiquitous because market failures are."[367]

Developing the right size policy to deal with such an issue as consumer health and welfare is challenging because by their nature, policies are "general, both by definition and necessity . . . [a] policy is not an action. Rather, it is a course of action. Policies are decisions about what is to be done in a multiplicity of cases involving a multiplicity of acts, by multiple people at multiple times."[368] In order to assess whether FDA's draft guidance is good policy-making, one must make "an aggregate determination of what ought to be done over a multiplicity of instances."[369] Thus, a prerequisite to enacting good policy is an assessment of "the current range of relevant behaviors (and their consequences) and the range of behaviors likely to exist under various different policy options."[370]

364. *Homeopathic Products*, U.S. FOOD & DRUG ADMIN. (Feb. 11, 2020), https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm589282.htm.

365. *See* DANIEL N. REED & GLORIA S. GRIFFIN, STRATEGY AND SCIENCE AT THE FDA: PLANS, GOALS AND CHALLENGES FOR THE FUTURE 29 (2012).

366. NAT'L BUREAU ECON. RES. CONF. REP., REGULATION VS LITIGATION: PERSPECTIVES FROM ECONOMICS AND LAW 28 (Daniel P. Kessler ed., 2011) (explaining that market failures can consist of "externalities, asymmetric information, and lack of competition.").

367. *Id.*

368. *Id.* at 47–48.

369. *Id.* at 48.

370. *Id.*

Here, FDA is trying to maximize the deterrent effect that enforcement actions could have in the marketplace by targeting regulatory efforts at the products capable of causing the most harm from a public health and public welfare perspective. While economic adulteration is important too, given the multitude of other regulatory obligations the Agency has, targeted enforcement at the most dangerous products on the market makes sense. By focusing enforcement efforts on products with reported safety concerns or those containing potentially toxic ingredients, FDA can work with industry to remove those products from the market—ideally before they cause harm to consumers. Focusing on products that are administered by routes other than oral or topical concentrates efforts on those products that can more easily bypass the body's natural defenses and cause greater harm by doing so, especially where absorption rates differ depending on the route of administration.

Targeting products intended to prevent or treat serious illness is necessary for two important reasons: First, people might purchase an OTC homeopathic version of a product that has not been proven safe or effective and might only receive a placebo in a life or death situation, such as with asthma medication. Making sure that homeopathic products advertised for life-threatening situations are actually safe and effective is a good use of FDA's enforcement power, as opposed to products that are advertised for minor, temporary conditions (such as nausea or headache). Second, if consumers are purchasing homeopathic products for serious or life-threatening conditions they may be foregoing conventional medical treatment that has been actually proven safe and effective, possibly jeopardizing their health by delaying proven treatment for a product that may be no better than a placebo. Targeting products for the most vulnerable populations such as children, the elderly, pregnant women, and immunocompromised individuals is a good use of risk-based enforcement because these are the populations most in need of consumer protection as they will have varying abilities to absorb, process, circulate and eliminate homeopathic products. Finally, prioritizing enforcement on products that have significant quality issues, such as those that contain objectional micro-organisms, provides an enhanced level of scrutiny to products that pose a significant safety risk to patients.

Admittedly, other problems persist beyond the reach of the draft guidance. In addition to economic adulteration, special challenges have arisen with ever expanding global supply chains and the proliferation of internet sales and online pharmacies. For conventional medications, nearly "40% of listed finished drugs come from overseas, and 80% of the manufacturers of active ingredients are located outside the United

States."[371] Expanding the sourcing playing field in such a way complicates matters even further because at every juncture "from raw materials and other ingredients to manufacture, storage, sale, and distribution—a product can be contaminated, diverted, counterfeited, or adulterated."[372] In addition, online purchasing power adds another wrinkle, whether from large producers or much smaller ones seeking to take advantage of the anonymity the Internet offers. Online shopping therefore "presents an additional layer of complexity by introducing more players into the system."[373] The draft guidance does not specify how to address either of these two concerns.

Nevertheless, FDA's reexamination of its enforcement policies and its willingness to shift from enforcement discretion to a risk-based approach is a step in the right direction because it targets those products capable of causing the most harm to the most people.

## CONCLUSION

The wisdom of Harvey Washington Wiley, hailed as the father of food and drug law in the United States, so prescient in the early 1900s, still applies with equal force today:

> There is a distinct tendency to put regulations and rules for the enforcement of the law into the hands of the industries engaged in the food and drugs activities . . . When we permit business in general to regulate the quality and character of our food and drug supplies, we are treading upon very dangerous ground. It is always advisable to consult business men and take such advice as they give that is unbiased, because of the intimate knowledge they have of the processes involved. It is never advisable to surrender entirely food and drug control to business interests.[374]

The enactment of the 1906 Pure Food and Drug Act represented a sea change in public policy. The law embodied the belief that government had a part to play in protecting citizens from certain sectors of the economy, rather than simply protecting the economy.[375] Following this sea change, the 1938 Federal Food Drug and Cosmetic Act "may be ranked as the commercial law of greatest social and economic importance in the land because it regulates food and drugs, our two most vital consumer

371. FDA IN THE 21ST CENTURY: THE CHALLENGES OF REGULATING DRUGS AND NEW TECHNOLOGIES 40 (Holly Fernandez Lynch & I. Glenn Cohen eds., 2015).

372. *Id.*

373. *Id.* at 42.

374. WILEY, *supra* note 59, at 273.

375. HILTS, *supra* note 16, at 55.

products."[376] Then, a series of additional amendments sought to make our drug supply even safer and more efficacious, causing some to declare after the Kefauver-Harris Amendments that the FFDCA has "ke[pt] pace with progress in the science of food and drug production and marketing."[377] But is this still true today, especially considering the rise of the homeopathic industry? Can we claim that the law and its amendments continue to operate "effectively to fulfill the law's basic purpose of assuring the American public the most abundant, safe, and nutritious foods, and the best and safest drugs and cosmetics"?[378]

The draft guidance is a good starting place, but a final guidance has yet to be issued. And even after final guidance is issued, there remains the harsh lesson of regulation: Success cannot be determined by the presence of a policy, but in effective implementation of rules.[379]

Implementation of regulation always highlights the tensions that exist between commerce and consumers.

> Societies throughout history have always imposed social controls on business and economic activity, through civil or religious authority. But during the nineteenth century when unfettered capitalism dominated the scene, the long historical relationship was reversed, and society was ruled by economics with the strong presumption that no controls should govern it.[380]

It is important that we do not head backwards and lose all the progress gained since the enactment of the 1906 law.

Maintaining our progress in this realm means relying on FDA's ability to adapt to changing times. As experts have noted, the Agency "has always been a dynamic organization and must continually change to reflect new insights . . . and risk management to provide a reasonable balance between fostering innovation and protecting the public health."[381] In order to fulfill FDA's responsibility to protect public health, science-based decision-making must remain the Agency's guiding principle.[382] Without it, modern forms of quackery will persist despite recent regulatory strides.[383] FDA should use its risk-based enforcement policy to target

376. Franklin M. Depew, *Evolution of a Law*, *in* 1 FDA PAPERS, 1967–1972 10 (U.S. Food & Drug Admin.).

377. *Id.*

378. *Id.*

379. HILTS, *supra* note 16, at 56.

380. *See id.*

381. Lynch & Cohen, *supra* note 371, at 17.

382. *See* STRATEGY AND SCIENCE AT THE FDA: PLANS, GOALS AND CHALLENGES FOR THE FUTURE 5 (Daniel N. Reed and Gloria S. Griffin eds., 2012).

383. PRAY, *supra* note 23, at 31.

modern forms of quackery that are "still alive and well in the new millennium."[384] Homeopathic practitioners may sincerely believe in their methods and therefore "disavow any link with the old patent medicines, but a direct ancestry can be perceived . . . any medicine . . . that lacks proof of efficacy and/or safety is a quack."[385] FDA's draft guidance recognizes this with respect to homeopathy and is now signaling to industry that it is stepping up scrutiny in the name of consumer protection.

384. *See id.*
385. *See id.*