UNITED STATES COURT OF APPEALS
FOR THE FOURTH CIRCUIT

GenBioPro, Inc., Plaintiff-Appellant, v. Kristina D. Raynes, *in her official capacity as Prosecuting Attorney of Putnam County*, and Patrick Morrisey, *in his official capacity as Attorney General of West Virginia*, Defendants-Appellees.	No. 23-2194

UNOPPOSED MOTION FOR LEAVE TO FILE BRIEF OF *AMICI CURIAE* HISTORIANS IN SUPPORT OF PLAINTIFF-APPELLANT

Pursuant to Federal Rule of Appellate Procedure ("Rule") 29(a), Lauren MacIvor Thompson, PhD, Joseph Gabriel, PhD, Dominique Tobbell, PhD, Dr. Jeremy Greene, Dr. David Herzberg, Dr. Cara Delay, Dr. Kelly O'Donnell, PhD, and Dr. Lucas Richert (together, "Historians") respectfully move for leave to file a brief as *amici curiae* in support of Plaintiff-Appellant and reversal.

Historians are scholars and practitioners whose areas of focus include medical history, reproductive health, and law. This appeal presents a question of whether states have traditionally occupied the field of drug regulation such that West Virgina's Unborn Child Protection Act is not preempted by federal law. Because this issue concerns the subjects of Historians' studies, it implicates Historians' academic

interests, and they seek to help the Court understand the proper historical analysis of state and federal drug regulations in connection with this appeal.

Counsel for all parties to this appeal have consented to the filing of this brief in accordance with Rule 29(a)(2). Participation by Historians as *amici curiae* will not delay the briefing or argument in this case. Historians are filing this brief within the time allowed by Rule 29(a)(6).

Accordingly, Historians respectfully request that the Court grant their motion for leave to file a brief as *amici curiae* in support of Plaintiff-Appellant, and that the Court accept for filing the brief attached to this motion as Exhibit A.

Date: February 14, 2024

/s/ Jennifer Selendy

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CERTIFICATE OF SERVICE

I certify that I caused this document to be electronically filed with the Clerk of the Court using the appellate CM/ECF system on February 14, 2024. All participants in the case are registered CM/ECF users and service will be accomplished by the appellate CM/ECF system.

/s/ Jennifer Selendy

Exhibit A

NO. 23-2194

United States Court of Appeals

for the

Fourth Circuit

GENBIOPRO, INC.,

Plaintiff-Appellant,

– v. –

KRISTINA RAYNES, in her official capacity as Prosecuting Attorney of Putnam County; PATRICK MORRISEY, in his official capacity as Attorney General of West Virginia,

Defendants-Appellees.

ON APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA, HUNTINGTON DIVISION,
IN CASE NO. 3:23-cv-00058, HONORABLE ROBERT C. CHAMBERS,
U. S. DISTRICT COURT JUDGE

BRIEF OF *AMICI CURIAE* HISTORIANS IN SUPPORT OF PLAINTIFF-APPELLANT

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INTEREST OF AMICI CURIAE

Amici curiae are history professors whose areas of focus include medical history, reproductive health, and law. They have no personal interest of any kind in the outcome of this particular case or any other case in which similar issues have been raised. They are filing this brief solely to advise the Court as to the proper historical analysis of state and federal drug regulations in this case. All parties have consented to amici's filing in this case.

Lauren MacIvor Thompson, PhD, is an Assistant Professor of History and Interdisciplinary Studies at Kennesaw State University and serves as the faculty fellow at the Georgia State University College of Law's Center for Law, Health, and Society. Dr. Thompson is the author of the forthcoming book *Rivals and Rights: Mary Dennett, Margaret Sanger, and the Making of the American Birth Control Movement*.

Joseph Gabriel, PhD, is an Associate Professor with joint appointments in the Department of History and the Department of Behavioral Sciences and Social Medicine at the Florida State University College of Medicine. Dr. Gabriel has authored books, which include *Medical Monopoly: Intellectual Property Rights and the Origins of the Modern Pharmaceutical Industry*.

Dominique Tobbell, PhD, is Centennial Distinguished Professor of Nursing and director of the Eleanor Crowder Bjoring Center for Nursing Historical Inquiry

at the University of Virginia. Dr. Tobbell is the author of books, which include *Pills, Power, and Policy: The Struggle for Drug Reform in Cold War America and its Consequences*.

Dr. Jeremy Greene is the William H. Welch Professor and Director of the Department of the History of Medicine, and Director of the Center for Medical Humanities and Social Medicine at the Johns Hopkins University School of Medicine. Dr. Greene has authored books, including *Prescribing by Numbers: Drugs and the Definition of Disease and Generic: The Unbranding of Modern Medicine*.

Dr. David Herzberg is Professor of History and Director of the Drugs, Health, and Society Program at the University at Buffalo, State University of New York. Dr. Herzberg is the author of books, which include *White Market Drugs: Big Pharma and The Hidden History of Addiction in America*.

Dr. Cara Delay is Professor of History at the College of Charleston. She is co-author of a new book, *Catching Fire: Women's Health Activism in Ireland* and has work forthcoming on the history of medication abortion.

Dr. Kelly O'Donnell, PhD, is a Visiting Assistant Professor of US History at Bryn Mawr College. She is the author of the forthcoming book *The Pill Hearings: Science, Politics, and Birth Control*.

Dr. Lucas Richert is Professor and the George Urdang Chair in the History of

Pharmacy at the University of Wisconsin-Madison. He is the Executive Director of the American Institute of the History of Pharmacy. Dr. Richert is the author of books including *Strange Trips: Science, Culture, and the Regulation of Drugs*.

INTRODUCTION AND SUMMARY OF ARGUMENT

States have not traditionally regulated the drugs that doctors may prescribe, and the federal government has. Historically, state laws directly regulating specific medicines have been few and far between. Nineteenth-century state legislatures narrowly targeted fraud and adulteration related to patent medicines (*i.e.*, medicines with secret ingredients) and restricted their sale through existing criminal codes, based on the risk of poisoning. While states may have indirectly impacted the marketplace of medicine by regulating medical professionals, state legislatures focused on general issues such as educational and licensing requirements and the establishment of medical, public health, and pharmacy boards. Medical professionals were otherwise left to their own devices in deciding which medicines to prescribe. Any self-regulation by the profession—to the extent it existed—was limited and oriented toward practitioners' economic self-interest. In other words, states historically did not attempt to control access to particular drugs or dictate which medicines physicians may prescribe, as the UCPA does. As a result, for the most part since the 1800s, there were very few, let alone coherent, state-level rules regulating access to medicines.

The heightened stakes of pharmaceutical regulation and lack of direct state intervention gave rise to the emergence of a federal regulatory regime in the early 20th century, through the enaction of the 1906 Pure Food and Drug Act and the establishment of the FDA, the passage of the 1938 Federal Food, Drug, and Cosmetic Act ("FDCA"), and the 1951 Durham-Humphrey Amendment. The impetus for passing the national 1906 Pure Food and Drug Act, the first piece of consumer-oriented legislation in U.S. history, was to remedy the problem that state licensing laws were advancing the medical profession's special interests rather than public welfare. Likewise, a key prerogative of the FDA was to fill the void of pharmaceutical regulations with a uniform national standard. The FDA's role in uniformly regulating drugs nationally culminated in the Risk Evaluation and Mitigation Strategies ("REMS") program, which codified existing safety protocols for specifically named drugs to minimize their risks while preserving their beneficial use to patients. In other words, federal pharmaceutical regulations did not arise to supplement state legislations in an area "traditionally occupied" by states, but rather to fill a legislative void.

The district court ruled that West Virginia's restrictions on access to mifepristone under the Unborn Child Protection Act ("UCPA") are not preempted by federal law on the ground that "States have traditionally occupied" a broadly defined field: the "regulation of health and safety" and "of medical professionals."

JA265-66. But the UCPA has a much narrower focus. It prohibits medical professionals from even prescribing mifepristone unless one of the limited exceptions applies. Because states have not traditionally regulated the drugs that doctors may prescribe, and the federal government has, the district court's reasoning was flawed.

ARGUMENT

A. States' Direct Regulation of Medicine in the 18th and 19th Centuries Was Limited and Ineffective

In the 18th century, some states implemented limited direct regulations of pharmaceuticals. These limited regulations, however, were aimed at reducing fraud and deception and consisted of criminal penalties for the distribution of poisonous substances and consumer protection-focused regulations designed to prevent "quackery."[1] A number of states also prohibited drug adulteration. Lacking from this period, however, were any state-run licensing or approval regimes for pharmaceuticals.[2]

State laws in this early period typically restricted the practice of drug retailing to licensed pharmacists, excluded people based on characteristics such as age or race,

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[1] David L. Cowen, *Colonial Laws Pertaining to Pharmacy*, 48 PHARM. HIST. 24 (2006); PHILIP J. HILTS, PROTECTING AMERICANS' HEALTH: THE FDA, BUSINESS, AND ONE HUNDRED YEARS OF REGULATION 28–30 (2003).

[2] JOSEPH M. GABRIEL, MEDICAL MONOPOLY: INTELLECTUAL PROPERTY RIGHTS AND THE ORIGINS OF THE MODERN PHARMACEUTICAL INDUSTRY, 30–35 (2014).

or sought to limit the sale of poisonous substances. Restrictive pharmacy laws were deeply intertwined with the widespread fear of poisoning in both the colonies and the early United States, including in Southern states where there was significant concern that enslaved people would poison their owners.[3] Some states also passed laws requiring that druggists label containers of poisonous substances such as arsenic, prussic acid, or corrosive sublimate with the word "poison" in order to warn customers of their dangerous nature.[4]

By the 1820s and 1830s, state legislatures began passing laws aimed at so-called patent medicines (*i.e.*, medicines made with secret ingredients), and regulating the practice of medicine and surgery. The patent medicine market had grown exponentially in this period, and manufacturers advertised with effusive claims that their medicine could cure all ailments.[5] For example, an 1860 advertisement for Perry Davis' Vegetable Pain Killer claimed that the drug could cure fevers, colds, coughs, kidney complaints, burns, sprains, cold sores, and ringworm among other

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[3] Erin Austin Dwyer, *The Poison Pen: Slavery, Poison, and Fear in the Antebellum Press*, 45 SLAVERY & ABOLITION 10, 12 (2024).

[4] *E.g.*, 1846 Mich. Pub. Acts 685, ch. 159 § 5, *available at* https://babel.hathitrust.org/cgi/pt?id=nyp.33433007045952&seq=707.

[5] JOHN C. BURNHAM, HEALTHCARE IN AMERICA: A HISTORY 114–15 (2015).

problems.[6] Products like these contained ineffective ingredients or, worse, alcohol, cocaine, opioids, or dangerous amounts of herbal medicines. Mrs. Winslow's Soothing Syrup, a popular remedy for fussy babies and children, included morphine sulfate, sodium carbonate, and ammonia.[7] In response, states targeted the sale of these medicines in general as part of their criminal codes for their potential to poison their users.[8] The focus of these laws was to reduce fraud and deception and protect consumers' rights.[9] Although there was widespread—and often vociferous—debate about medical licensure at the state level during this period, there was virtually no public concern about drug regulation in this context.[10] Instead, disputes about state authority and therapeutic freedom played out almost exclusively along the lines of the regulation of medical practice.[11]

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[6] Library of Congress. *Patent medicine labels for Perry Davis & Son, showing view of Providence, R.I., and four patent medicine bottles / Kilburn & Mallory sc., Boston,* https://www.loc.gov/item/92512903/.

[7] THOMAS W. LOKER, THE HISTORY AND EVOLUTION OF HEALTHCARE IN AMERICA: THE UNTOLD BACKSTORY OF WHERE WE'VE BEEN, WHERE WE ARE, AND WHY HEALTHCARE NEEDS REFORM 48 (2012).

[8] Joseph M. Gabriel, *Restricting the Sale of 'Deadly Poisons': Pharmacists, Drug Regulation, and Narratives of Suffering in the Gilded Age*," 53 PHARM. HIST. 29 (2011); JAMES C. MOHR, ABORTION IN AMERICA: THE ORIGINS AND EVOLUTION OF A NATIONAL POLICY 22 (1979).

[9] HILTS, *supra* note 1.

[10] BURNHAM, *supra* note 5, at 65.

[11] LEWIS A. GROSSMAN, CHOOSE YOUR MEDICINE: FREEDOM OF THERAPEUTIC CHOICE IN AMERICA 5 (2021).

Moreover, states' regulation of medicines during this early period was driven less by a concern to ensure safe access to drugs than to protect the special interests of trained physicians by eliminating the competition from patent drug manufacturers, "irregulars," midwives, and "quacks."[12] In the early- to mid-19th century, Americans had little confidence in "regular" physicians because patients did not believe their credentials resulted in better outcomes. Prescriptions tended to be more painful and expensive, and the effectiveness of any given remedy was hard to prove.[13] Instead, people often turned to both patent medicines or the "irregular" systems of medicine for more gentle alternatives, such as homeopathy, hydropathy, and "eclectic" practitioners.[14] What limited drug regulation existed in this period was thus designed to increase confidence in regular or allopathic medicine.[15]

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[12] Joseph M. Gabriel, *Pharmaceutical Patenting and the Transformation of American Medical Ethics*, BRITISH J. HIST. SCI. 577–600 (2016); *see also* PETER SWENSON, DISORDER: A HISTORY OF REFORM, REACTION, AND MONEY IN AMERICAN MEDICINE (2021).

[13] JAMES C. MOHR, DOCTORS AND THE LAW: MEDICAL JURISPRUDENCE IN NINETEENTH-CENTURY AMERICA 83 (1996).

[14] *See* BURNHAM, *supra* note 5; JOSEPH F. KETT, THE FORMATION OF THE AMERICAN MEDICAL PROFESSION; THE ROLE OF INSTITUTIONS, 1780-1860 (1968); *see generally* PAUL STARR, THE SOCIAL TRANSFORMATION OF AMERICAN MEDICINE: THE RISE OF A SOVEREIGN PROFESSION AND THE MAKING OF A VAST INDUSTRY CH. 3 (2008).

[15] DAVID A. JOHNSON & HUMAYUN J. CHAUDHRY, MEDICAL LICENSING AND DISCIPLINE IN AMERICA: A HISTORY OF THE FEDERATION OF STATE MEDICAL BOARDS 18 (2012); JAMES C. MOHR, LICENSED TO PRACTICE: THE SUPREME COURT DEFINES THE AMERICAN MEDICAL PROFESSION 18 (2013).

While state laws regulating medical practice and pharmaceuticals were in place in the 18th century, they were largely ineffective, resulting in little coherence or improvements in patient and consumer safety. Although 25 states had laws against the adulteration of drugs by 1870, states could do little about harmful substances that crossed state lines. Similarly, although states passed food and drug purity laws beginning in the 1880s, there was no uniformity in or effective enforcement of them.[16] Dangerous patent medicines continued to be sold on the open market and widely advertised. At the turn of the century, half of all periodical advertising was for patent medicines.[17]

B. Until the Early 20th Century, Medical Professionals Strongly Influenced States' Regulation of Medicine

Before Congress took over certain aspects of regulating the medical and pharmaceutical field, state legislatures largely deferred to medical societies to establish educational and licensing requirements for medical practitioners.[18] Often, the regulations suggested by these medical societies were self-serving and designed

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[16] David L. Cowen, *The Development of State Pharmaceutical Law*, 37 PHARM. HIST. 49, 54 (1995); EDWARD KREMERS ET AL., KREMERS AND URDANG'S HISTORY OF PHARMACY 216 (4th ed. 1986).

[17] Jane Marcellus, *Nervous Women and Noble Savages: The Romanticized 'Other' in Nineteenth-Century U.S. Patent Medicine Advertising*, 41 J. POP. CULTURE 784, 787 (2008); *see generally* CHARLES GOODRUM & HELEN DALRYMPLE, ADVERTISING IN AMERICA: THE FIRST 200 YEARS (1990).

[18] MOHR, *supra* note 13, at 14–16.

to eliminate competition from the "irregulars." In response, the "irregulars" founded their own medical societies and utilized them to lobby for legislation that benefited them. The result was incoherent and ineffective regulation at the state level that focused largely upon education and licensing requirements for physicians. These limited regulations never directly implicated which medications practitioners could prescribe and did not attempt to regulate pharmaceuticals.[19]

Throughout the early 19th century, state legislatures and regular doctors engaged in partnerships designed to be mutually beneficial: states relied upon doctors' expertise to establish regulations, and the criteria set by doctors for such regulations often economically benefited their professional aspirations.[20] As physician historians David A. Johnson and Humayun Chaudhry have argued,

> In most instances, state legislatures looked to work in concert with medical societies as the best mechanism for regulating the practice of medicine within their state. Often it was state legislation that established a state's medical society … and empowered the society's members to control membership criteria as the sole pathway to a license to practice medicine.[21]

However, in the 1830s and 1840s, state legislatures, caving to voter pressure and powerful counter-lobbying of the irregulars, actually repealed earlier established

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[19] Gabriel, *supra* note 8.

[20] MOHR, *supra* note 13, at 83.

[21] JOHNSON & CHAUDHRY, *supra* note 15, at 12.

laws regulating the unlicensed practice of medicine, leading to the "wholesale collapse of medical regulation in the United States."[22] As historian James Mohr has argued, lawmakers during this era had little incentive to establish stricter licensing laws because "they had no objective criteria upon which to justify licenses."[23] The regulars could not "demonstrate that either their approaches to healing or their superior knowledge of the medical sciences produced better patient outcomes … than a host of alternative approaches."[24]

By the late 1870s, state medical societies had roused themselves to begin reestablishing licensing laws, this time with stricter parameters. These efforts proved successful in prompting states to enact regulations to protect patients from uneducated and unqualified practitioners. The American Medical Association's nationwide campaign against abortion, which had begun in earnest in the 1850s, did much to advance this cause.[25] Physician reformers successfully linked the idea of the practice of abortion to the unlicensed "irregulars" and were able to not only get their state legislatures to pass stricter abortion laws, but also pass stricter medical licensing laws in the process. In 1881, West Virginia passed the first of these more

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[22] *Id*.

[23] MOHR, *supra* note 155, at 18.

[24] *Id*.

[25] MOHR, *supra* note 8.

restrictive licensing laws at the behest of the Medical Society of West Virginia. The new Board of Health Act established updated educational standards and criminal punishments for violators who practiced medicine without a license or degree from a "reputable" medical college.[26]

There were challenges to these license requirements, including *Dent* v. *West Virginia*, 129 U.S. 114 (1889), as noted in the decision below. *See* JA266. Plaintiff Frank Dent had a medical degree from what the Board had determined was a fraudulent institution. He was eventually arrested under the new law, and the case was appealed to the Supreme Court. The Court in *Dent* decided in favor of the defendants, arguing that the state had always regulated medicine since "time immemorial." *Dent*, 129 U.S. at 122.

On its face, *Dent* would seem to imply that states had the ultimate authority to regulate "the practice of medicine and the scope of physicians' authority as state matters." JA272.I In the historical context, however, *Dent* is much narrower. The case did not establish unquestioned deference to state regulatory authorities over the medical field, but rather served as one of the biggest steps in establishing physicians as a profession that deserved more specific recognition and special regulation by virtue of their expert stature. This was perhaps an unsurprising conclusion for the

[26] MOHR, *supra* note 13.

Court, at the time, given the fact that Justice Samuel Freeman Miller was both a lawyer and physician with a degree from Transylvania University, and Justice Samuel Blatchford had an uncle, Thomas Blatchford, who was a prominent New York physician and "one of the earliest and most outspoken proponents of forcing non-Regulars from the medical marketplace."[27]

The impact of *Dent* strengthened the West Virginia state Board of Medicine and ensured it remained exclusive to the regulars who would take their direction from the larger AMA. In *Dent*, Justice Field wrote that the state's power to regulate medical practice consisted of their obligation to protect their people from "ignorance and incapacity, as well as of deception and fraud." 129 U.S. at 122. But the goal was not to regulate medical practice so tightly that they would remove authority from the physicians themselves.

Perhaps the most important example of this process is the manner in which physicians worked with pharmacists to harness state power to suppress the use of ineffective drugs. During the late 19th century they did so primarily by working with state legislatures to simultaneously prohibit the sale of adulterated drugs and to link the definition of adulteration to standards published in the *Pharmacopoeia of the United States of America* and other authoritative texts written by the medical and

[27] MOHR, *supra* note 15, at 140.

pharmacy communities. They also sought the passage of laws requiring the disclosure of dangerous ingredients, restricting the sale of poisonous substances such as arsenic and mercury chloride, suppressing the recreational use of opium and other addictive drugs, and passing educational and licensing requirements for their professions.[28] These laws simultaneously sought to protect the public from dangerous substances, limit competition, and advance the interests of professional pharmacy and medicine by reducing both public criticism of their fields and exposure to legal risk.[29] However, although 23 states had laws against the adulteration of drugs by 1889, and numerous other state laws restricting the trade in drugs were already on the books, variability in state law meant that enforcement was difficult, and little could be done about dangerous products that crossed state lines; for example, what might be illegal to sell without a license in one state might be legal to sell in another.[30] Thus, although states passed a variety of food and drug laws beginning in the 1870s, there was little uniformity and inconsistent and ineffective enforcement.[31]

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[28] GABRIEL, *supra* note 2, at 70–75.

[29] Gabriel, *supra* note 8.

[30] KREMERS ET AL., *supra* note 16, at 216.

[31] Cowen, *supra* note 16, at 54.

Most importantly, these types of laws did little to adjudicate between competing claims of drug effectiveness. Before the late 19th-century development of controlled clinical trials, there was no clear way to scientifically determine whether or not specific drugs worked to treat specific medical problems; indeed, there was no clear way to adjudicate between competing claims of therapeutic effectiveness made by different medical sects—who was to say, after all, whether homeopathy or orthodox medical treatments worked better? How was one to know?[32] As a result, during "the great market revolution" of the late-19th century, strong consumer demand for self-treatments was aligned with the commercial interests of patent medicine manufacturers on the one hand, and the interests of licensed physicians and more reputable manufacturers (who were in direct competition with patent medicine manufacturers) were aligned on the other. The Proprietary Association of America formed in 1881 served as the patent medicine industry's trade group and worked assiduously to ensure that federal and state

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[32] *See generally* Joseph M. Gabriel & Bennett Holman, *Clinical Trials and the Origins of Pharmaceutical Fraud: Parke, Davis & Company, Virtue Epistemology, and the History of the Fundamental Antagonism*, 58 HIST. SCI. 533, 533–58 (2020); Bennett Holman, *Humbug, the Council of Pharmacy and Chemistry, and the Origin of "The Blind Test" of Therapeutic Efficacy*, *in* UNCERTAINTY IN PHARMACOLOGY: EPISTEMOLOGY, METHODS, AND DECISIONS 397–416 (Adam LaCaze & Barbara Osimani eds., 2020).

legislation would not interfere with their businesses.[33] These manufacturers continued to sell their products on the open market and to make claims for their effectiveness that physicians denounced as fraudulent. Anti-adulteration laws were of little help in this context, and without a robust system that could be used to scientifically evaluate therapeutic claims there was no way for courts or other parties to adjudicate between the two parties' competing claims. In 1902, for example, the Supreme Court ruled that literature related to a so-called "school of magnetic healing" based on telepathy could not be prohibited from being sold through the mail under the 1872 Post Office Act (which prohibited the mailing of fraudulent material intended to secure money from a party). "One person may believe it of far greater efficacy than another," the Court wrote, "but surely it cannot be said that it is fraud for one person to contend the mind has an effect upon the body…there is no exact standard of absolute truth by which to prove the assertion false and a fraud." *American School of Magnetic Healing v. McAnnulty*, 187 U.S. 94, 104 (1902).

As other states followed the footsteps of West Virginia in tightening license requirements, the professional power of the nation's licensed doctors and

[33] For example, the Association formed a special internal Committee on Legislation to ensure that licensed pharmacists and doctors would fail at lobbying states for new regulations like formula disclosure bills. *See* JAMES HARVEY YOUNG, THE TOADSTOOL MILLIONAIRES: A SOCIAL HISTORY OF PATENT MEDICINES IN AMERICA BEFORE FEDERAL REGULATION 228 (2015).

pharmacists expanded significantly by the 1920s. As a result, they were behind much of the impetus to begin to pass federal health regulations, but they also actively opposed them when they felt federal intervention was financially and professionally detrimental. For example, the group refused to support the passage of the Sheppard-Towner Bill of 1921, a maternal-child health program backed by other government agencies like The Children's Bureau and lobbying groups like the League of Women Voters and the Women's Joint Congressional Committee ("WJCC") that focused on women's issues. The program funneled federal funds and matching state grants to establish state-level public and maternal health programs. Yet the AMA and state medical societies called the bill "[a] socialistic scheme" that threatened the profession.[34] The Children's Bureau, although a federal entity, had no power to establish programming in states that rejected it.

C. A Federal Regime Emerged in the Early 20th Century to fill the Void in Pharmaceutical Regulation

Congress eventually stepped in in the early 20th century to address the failures by states to appropriately regulate drug safety, primarily through the enactment of the 1906 Pure Food and Drug Act and the establishment of the FDA through passage

[34] J. Stanley Lemons, *The Sheppard-Towner Act: Progressivism in the 1920s*, 55 J. AM. HIST. 776, 781 (1969); *see also* Carolyn M. Moehling & Melissa A. Thomasson, *The Political Economy of Saving Mothers and Babies: The Politics of State Participation in the Sheppard-Towner Program*, 72 J. ECON. HIST. 1, 75–103 (2012).

of the FDCA and the 1951 Durham-Humphrey Amendment. A uniform, national regime in pharmaceutical regulation thus gradually came into shape and culminated in the extensive REMS process in place today.

With the emergence of new pharmaceutical technologies in the early 20th century, the past deficiencies of state regulation became dangerously apparent in the wake of several tragedies caused by unregulated medicines. Although states continued to maintain their general authority over medical and pharmaceutical boards, it was becoming increasingly clear that the regulation of foods and medicines was an area that could not be subject to differences in state laws.[35] The 1906 Pure Food and Drug Act was the first far-reaching federal law to be enacted to protect Americans from adulterated drugs and foods.[36] The law had two main provisions. First, it required that manufacturers list certain dangerous ingredients on product labels and prohibited manufacturers from making false or misleading claims about their products. Second, it required that products sold under drug names used in the *Pharmacopoeia of the United States of America* conform to the published U.S.P standards. Products that violated either of these provisions were deemed

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[35] Young, *supra* note 33, at 228; *see also* HARRY M. MARKS, THE PROGRESS OF EXPERIMENT: SCIENCE AND THERAPEUTIC REFORM IN THE UNITED STATES, 1900-1990 (1997).

[36] Pure Food and Drug Act, Pub. L. 59-384, 34 Stat. 768 (1906) (codified as amended at 21 U.S.C. §§ 1-15).

adulterated.[37] The federal Bureau of Chemistry (renamed as the Food and Drug Administration in 1927) was charged with enforcement and seizure in preventing their illegal interstate transport. Notably, the law did not prohibit the manufacturing of pharmaceuticals as long as they conformed to these requirements, nor was there any sort of pre-market review of goods.[38] A little more than a decade later, the Harrison Narcotic Act was passed in 1914, establishing narcotics as a class of drugs that could no longer be sold openly on the market because of their extreme social and health dangers.[39] Instead, they would require prescriptions through licensed physicians and pharmacists.

Both the 1906 and 1914 laws grew directly out of efforts by physicians and pharmacists to simultaneously protect the public and advance their own professional interests. As reformer and pharmacist James Beal put it in 1901, "if pharmacists do not take up and deal rigorously with these matters, they will be dealt with by the general public, and in a way not likely to be altogether agreeable to the pharmacists."[40] Although the 1906 law did not explicitly require that drugs be

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[37] GABRIEL, *supra* note 2, at 223, 225.

[38] JAMES HARVEY YOUNG, PURE FOOD: SECURING THE FEDERAL FOOD AND DRUGS ACT OF 1906 (2014).

[39] Harrison Narcotic Act, Pub. L. 63-223, 38 Stat. 785 (1914).

[40] DAVID F. MUSTO, THE AMERICAN DISEASE: ORIGINS OF NARCOTIC CONTROL 15 (1999).

effective in order to remain on the market, the prohibition on misleading claims was taken by officials at the Bureau of Chemistry to mean that claims about a drug's effectiveness that were untrue were illegal. In order to determine whether or not a drug was able to do what its manufacturer claimed it could do, the Bureau of Chemistry relied on the expertise of the medical community, and the AMA's Council on Pharmacy and Chemistry ("CPC") in particular.[41]

By 1905, the AMA had established an internal Council on Pharmacy and Chemistry as a private means of controlling pharmaceuticals. The idea was that the CPC would evaluate products on the market and publish their findings in the pages of the *Journal of the American Medical Association* to dissuade physicians from prescribing quack remedies. This system depended on the willingness of reputable manufacturers to submit their products to the Council to be evaluated.[42] The AMA was also strongly supportive of the 1906 law, and physicians associated with the CPC sometimes worked with the BOC to evaluate therapeutic claims made by manufacturers.[43]

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[41] GABRIEL, *supra* note 2, at 216.

[42] Austin Smith, *The Council on Pharmacy and Chemistry of the American Medical Association: A Historical Review of Its Relation to Medical Therapy and Research*, 1 FOOD, DRUG, COSMETIC L.Q.186 (1946).

[43] *See* Joseph C. Stetler, *Relations Between AMA and FDA*, 18 FOOD, DRUG, COSMETIC LAW JOURNAL 72 (1963).

The AMA's Committee on Therapeutics also developed what it called "the blind test," in which the Committee would send physicians samples of products to test without telling them what they were, including at times sending them samples of inactive substances such as sugar pills. Although this was not the first effort to use randomization or blinding in the evaluation of drug effectiveness, it was the first time that this type of effort was linked to both a government agency and the professional goals of physicians. Importantly, it also depended on both the cooperation of reputable manufacturers and a wide network of clinicians that stretched across much of the country.[44] By the 1920s, federal regulators at the FDA, reputable manufacturers, and clinical investigators worked closely together on a regular basis to investigate new products and evaluate drug effectiveness.[45]

Congress doubled down on the federalization of pharmaceutical regulation following the Elixir Sulfanilamide scandal. Elixir Sulfanilamide was a new drug formulation developed to treat streptococcal infections consisting of sulfanilamide suspended in diethylene glycol, which had made the medicine more palatable

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[44] Holman, *supra* note 32, at 397–416.

[45] *See* Joseph M. Gabriel, *The Testing of Sanocrysin: Science, Profit, and Innovation in Clinical Trial Design, 1926-31*, 69 J. HIST MED, AND ALLIED SCI 604 (2014); GABRIEL, *supra* note 2; Holman, *supra* note 32; ERIC W. BOYLE, QUACK MEDICINE: A HISTORY OF COMBATING HEALTH FRAUD IN TWENTIETH-CENTURY AMERICA (2013).

because it was sweet-tasting.[46] Although it initially had some promising results on pediatric patients, further testing revealed troublingly dangerous side effects, including kidney failure.[47] In the fall of 1937, major newspapers reported 107 deaths in 15 states from Elixir Sulfanilamide, manufactured by Massengill Pharmaceutical Company.[48] Americans were horrified, openly demanding better federal drug regulations. As with the passage of the Pure Food and Drug Act and the Sheppard Towner Act, women's groups like the League of Women Voters, and the American Medical Women's Association rallied behind the FDA to lobby for the 1938 Federal Food, Drug, and Cosmetic Act ("FFDCA") which finally expanded the FDA's regulatory powers.[49]

The new FFDCA mandated that manufacturers demonstrate safety before any drug could be marketed or sold.[50] The law also divided drugs into prescription and non-prescription drugs but did not give clear guidance on what should determine a new drug's category. It only specified that prescription drugs did not have to have

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[46] CYNTHIA A. CONNOLLY, CHILDREN AND DRUG SAFETY: BALANCING RISK AND PROTECTION IN TWENTIETH-CENTURY AMERICA 24 (2018).

[47] *Id.* at 25.

[48] FREDERICK ROWE DAVIS, BANNED: A HISTORY OF PESTICIDES AND THE SCIENCE OF TOXICOLOGY (2014).

[49] CONNOLLY, *supra* note 46.

[50] Federal Food, Drug, and Cosmetic Act, Pub. L. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. § 301 et seq).

the same labeling for directions and use because they were meant to be prescribed only through a licensed medical professional.[51] Pharmaceutical companies took advantage of the fact that they could issue new products as prescription-only and avoid extra paperwork and liability. This effectively meant that the same drug could be produced by different manufacturers, one labeling their product as prescription, and the other designating non-prescription or "over the counter."[52] Combined with the fact that only narcotics had been strictly confined to prescription-only and that state laws were unevenly enforced, this meant drugs that were potentially harmful and dangerous to consumers could be sold as non-prescription. [53]

In 1951, the Durham-Humphrey Amendment was passed as a response to this FFDCA loophole and firmly established a new federal system for classification of prescription-only pharmaceuticals.[54] The amendment created the system Americans are most familiar with today wherein large companies manufacture and supply prescription medicines that are required to have particular safety standards and are

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[51] *Id.* at 21 U.S.C. § 353.

[52] JEREMY A. GREENE & ELIZABETH SIEGEL WATKINS, PRESCRIBED: WRITING, FILLING, USING, AND ABUSING THE PRESCRIPTION IN MODERN AMERICA 12 (2012).

[53] ANDREA TONE & ELIZABETH SIEGEL WATKINS, MEDICATING MODERN AMERICA: PRESCRIPTION DRUGS IN HISTORY 2 (2007).

[54] Humphrey-Durham Drug Prescriptions Act, Pub. L. 82-215, 65 Stat. 648 (1951) (amending 21 U.S.C. §§ 333, 353).

then prescribed to patients by physicians.[55] Other historians have noted that Durham-Humphrey represented a set of negotiations between the results of the regulatory regime of the 1930s and the new postwar "politics of deregulation" that characterized the New Deal backlash.[56] But Durham-Humphrey also clarified again that the FDA was responsible for making these changes in the larger realm of medicine and health. By clarifying what constituted prescription-only drugs, the amendment also had the effect of bolstering the medical and pharmacy professions with even more power.[57] After all, Hubert H. Humphrey, Jr., the lead sponsor of the bill in the Senate, was himself a trained pharmacist.

Federal drug safety regulation became further entrenched in the 1960s following the thalidomide scandal. Thalidomide was a sedative and anti-nausea therapy for pregnant women but was not well known in the United States until European reports of widespread birth defects caused a public furor. More than 1,200 American physicians had received free samples of thalidomide, labeled as Kevadon, from the manufacturer Richardson-Merrill to distribute to their patients across

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[55] GREENE & WATKINS, *supra* note 52, at 15; John P. Swann, *FDA and the Practice of Pharmacy: Prescription Drug Regulation Before the Durham-Humphrey Amendment of 1951*, 36 PHARM. HIST. 55 (1994).

[56] MARKS, *supra* note 35.

[57] TONE & WATKINS, *supra* note 53, at 2.

multiple states. The FFDCA specified that manufacturers could sell a drug if the FDA had not acted within 60 days to prevent its marketing and sale. Merrill had taken advantage of this loophole, despite the fact that FDA medical officer Frances Kelsey had stopped Merrill's approval application and warned that there needed to be an alert sent to the public warning of thalidomide's dangers.[58] In the wake of the thalidomide tragedy, Senator Estes Kefauver and Representative Oren Harris successfully advocated for what would become known as the 1962 Kefauver-Harris Amendments, which required that manufacturers prove the effectiveness and safety of their pharmaceutical products *prior* to sale on the market.[59] This legislation laid the groundwork for the protocol of clinical trials and drug testing, and eventually generic drug marketing.[60]

Over the next forty years, these prior relationships enforced a system in which the FDA had to redefine pharmaceutical safety protocol through a cumulative set of rulemaking decisions that involved continuous negotiations with the physicians,

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[58] HILTS, *supra* note 1, at 150–52.

[59] 1962 Kefauver-Harris Amendments, Pub. L. 87-781, 76 Stat. 780 (1962); Dominique Tobbell, *Eroding the Physician's Control of Therapy: The Postwar Politics of the Prescription*, *in* PRESCRIBED: WRITING, FILLING, USING, AND ABUSING THE PRESCRIPTION IN MODERN AMERICA 66 (Jeremy A. Greene and Elizabeth Siegel Watkins eds, 2012).

[60] DANIEL CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA 258-59 (2010).

patients, pharmacists, and drug manufacturers.[61] The FDA had to balance competing interests in the making of regulatory policy and procedure, but this balance relied at the core on the assurance that the FDA, and not individual states, would control from end to end how medications were manufactured, processed, controlled, distributed, and advertised.

The FDA augmented its authority when it developed new protocols in the 1980s for risk management programs for certain drugs that included education for patients and providers and/or restrictions on distribution. A well-known example is Accutane, the acne medication, which is a teratogen (or a substance that interferes with normal fetal development and can cause congenital disabilities). In the 1980s, the FDA began requiring Accutane to include multiple warnings in its packaging, sending out well over half a million letters to prescribers and pharmacists reiterating the information about Accutane's possible teratogenic effects. Female patients were also required to give informed consent and physicians tracked patients in regular

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[61] DOMINIQUE TOBBELL, PILLS, POWER, AND POLICY: THE STRUGGLE FOR DRUG REFORM IN COLD WAR AMERICA AND ITS CONSEQUENCES (2011); *see also* Jeremy A. Greene & Scott Podolsky, *Reform, Regulation, and Pharmaceuticals—the Kefauver-Harris Amendments at 50* 367 NEW ENG. J. MED. 1481–83 (2012).

meetings with FDA representatives. Similar programs were enacted for thalidomide because of its therapeutic uses for multiple myeloma and other conditions.[62]

The FDA's extensive authority over potentially dangerous drugs was cemented in 2007 when Congress passed the Food and Drug Administration Amendments Act ("FDAAA").[63] The FDAAA invested in the FDA new authority to require for certain drugs a new protocol of "Risk Evaluation and Mitigation Strategies" ("REMS"), essentially codifying the FDA's practices that had existed since the 1980s. REMS requirements ensure that drugs meet certain goals and objectives in minimizing patients risks while preserving a drug's benefits.[64] For Accutane and thalidomide, which have specific therapeutic benefits for the conditions they treat, the goal is to prevent fetal exposure via pregnancy prevention and monitoring.[65]

Accutane, now sold as generic isotretinoin, and Thalidomide provide useful historical examples of how uniform federal regulation of REMS has operated since the late 20th century to preserve access to drugs that have multiple uses and in

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[62] Agata Dabrowska, CONG. RSCH. SERV., R44810, FDA RISK EVALUATION AND MITIGATION STRATEGIES (REMS): DESCRIPTION AND EFFECT ON GENERIC DRUG DEVELOPMENT 3–5 (2018), https://sgp.fas.org/crs/misc/R44810.pdf.

[63] Food and Drug Administration Amendments Act, Pub. L. 110-85, 121 Stat. 823 (2007).

[64] 21 U.S.C. § 355-1.

[65] DABROWSKA, *supra* note 62 at 4, 6, 11.

approved contexts are necessary for health and wellbeing. Therefore, contrary to the district court's reasoning, *see* JA268, the FDA and the REMS program were formed as solutions to problems with state regulation (or lack thereof) of drug health and safety, not merely as internal agency policies. These federal protocols were established because Congress recognized that state law, while essential for regulating licensure or education in the health professions, was utterly inadequate to regulate the safety of pharmaceuticals sold across state lines, especially as demonstrated by the Sulfanilamide and Thalidomide tragedies. Instead, the goal was to create regular and uniform standards for drugs that would supersede the vagaries of existing state regulations across the nation.

In short, faced with the utter failure by states to regulate drugs, Congress centralized drug safety control at the federal level by enacting a comprehensive regulatory scheme. At the heart of that scheme now lies REMS drugs, which receive extensive attention as to avoid the inherent dangers of patchwork state regulation of pharmaceuticals.

CONCLUSION

The FDA has historically regulated the modern American pharmaceuticals regime. States did so only in the period when drugs were not legally subject to safety testing and clinical trials. Although states traditionally regulated the licensure and education of the health profession, Congress decided that the federal government

was best situated to regulate drug safety. Allowing West Virginia's UCPA to dictate new regulations about FDA-approved drugs like mifepristone is out of step with long-established regulatory practices designed specifically to meet a gap in health and safety that state law historically could not—and did not ever—remedy.

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Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

Pursuant to Federal Rules of Appellate Procedure 29(a)(4)(G) and 32(g)(1), I certify that this brief:

1. complies with the type-volume limitation of Federal Rules of Appellate Procedure 29(a)(5) and 32(e) because it contains 6,333 words, including footnotes and excluding the parts of the brief exempted by Federal Rules of Appellate Procedure 32(f); and

2. complies with the typeface and style requirements of Federal Rules of Appellate Procedure 32(a)(5) and 32(a)(6) because this document has been prepared in a proportionally spaced typeface using Microsoft Word for Microsoft Office 365 in 14-point Times New Roman.

/s/ *Jennifer Selendy*

CERTIFICATE OF SERVICE

I certify that I caused this document to be electronically filed with the Clerk of the Court using the appellate CM/ECF system on February 14, 2024. All participants in the case are registered CM/ECF users and service will be accomplished by the appellate CM/ECF system.

/s/ *Jennifer Selendy*