NO. 09-152

In the
Supreme Court of the United States

RUSSELL BRUESEWITZ, ET AL.

Petitioners,

v.

WYETH, INC. F/K/A WYETH LABORATORIES, WYETH-AYERST LABORATORIES, WYETH LEDERLE, WYETH LEDERLE VACCINES, AND LEDERLE LABORATORIES,

Respondent.

On Writ of Certiorari to the United States Court of Appeals for the Third Circuit

BRIEF OF GLAXOSMITHKLINE LLC, MERCK SHARP & DOHME CORP. (FORMERLY KNOWN AS MERCK & CO., INC.), AND SANOFI PASTEUR INC. AS *AMICI CURIAE* IN SUPPORT OF RESPONDENT

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INTERESTS OF THE *AMICI CURIAE* [1]

Along with respondent Wyeth, Inc., *amici curiae* GlaxoSmithKline LLC ("GSK"), Merck Sharp & Dohme Corp. (formerly known as Merck & Co., Inc.) ("Merck"), and Sanofi Pasteur Inc. ("Sanofi") are the remaining major childhood vaccine companies supplying vaccines for use in the United States. *Amici* have lived through this high-stakes debate before—in 1986, when Congress enacted the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 *et seq.* ("Vaccine Act" or "Act"). Congress passed the Act in part to protect the vaccine supply by shielding vaccine companies from tort suits like this one, while at the same time establishing a generous federal compensation system for the injured.

A decision by this Court to reverse the Third Circuit's preemption holding would upend the

[1] Pursuant to this Court's Rule 37.6, *amici* state that no counsel for any party authored this brief in whole or in part, and that no person or entity other than *amici* or their counsel made a monetary contribution to the preparation or submission of this brief. The parties have consented to the filing of this brief, and letters evidencing such consent have been filed with the Clerk of this Court, pursuant to this Court's Rule 37.3.

status quo that has persisted since the 1986 Act. It would unravel Congress's targeted effort in that Act to limit the extreme liability exposure that was driving large numbers of vaccine companies out of the U.S. market. *Amici* therefore have an interest in making sure this Court understands why Congress determined that allowing courts across the nation applying a patchwork of different state-law standards to second-guess vaccine designs — and saddling vaccine companies with the costs of design-defect claims — would contribute to further attrition in the number of companies selling vaccines in the United States. The expanded liability exposure petitioners seek would exacerbate unique challenges of the vaccine industry and threaten the vaccine supply.

INTRODUCTION AND SUMMARY OF ARGUMENT

The vaccine industry is unique in a number of important respects. Vaccines, by all accounts, are one of the great public health successes in medical history. And because of the importance of vaccines in preventing epidemics that could affect many thousands if not millions of people, the vaccine companies have a singularly close and interdependent relationship with government agencies.

But history has shown that vaccine companies are also quite vulnerable to the economic pressures that result from high research, development, and manufacturing costs, the lessened profit potential that comes from selling vaccines primarily to governmental entities and a public that under-

values their often unseen benefits, and the susceptibility to tort suits that results from selling a product that does not treat an existing illness but is designed for administration to apparently healthy children.

As respondent's brief explains, petitioners' attempt to subject vaccine companies to case-by-case, state-law design defect claims would effect a radical change in the status quo and defy the text of the Vaccine Act. *See* Resp. Br. at 29-45. Far from contemplating that vaccine companies would be subject to design-defect liability, § 22(b)(1) of the Vaccine Act expressly preempts state-law tort claims with only two specific carve-outs, for manufacturing defect and failure-to-warn claims. That preemption is a crucial element of Congress's carefully crafted balance, which protects vaccine manufacturers against destabilizing tort liability while also establishing a generous and streamlined administrative compensation scheme.

This brief details the far-reaching implications of petitioners' position. Design-defect liability would re-inject the very costs and uncertainties that pushed vaccine companies out of the market in the 1970s and 1980s — a trend § 22(b)(1) was specifically designed to arrest. Congress was alarmed by the fact that many vaccine companies were leaving the market. Indeed, many important vaccines are now supplied by only one or two companies. And the nation has had to grapple with serious supply shortages of numerous vaccines.

The dwindling number of vaccine companies reflects the unique economic pressures such companies face from higher development and

manufacturing costs and lower revenues relative to many other types of pharmaceutical products. Liability pressures from meritless tort suits are also unusually great for the vaccine industry. When an apparently healthy child begins to show symptoms of a disease or condition shortly after being vaccinated, parents and jurors are naturally inclined to blame the vaccine. *Post hoc ergo propter hoc* is a logical fallacy, but when the manifestation of an illness follows a vaccination, the impulse to sue can be strong. While jurors see a sick child who was apparently healthy before receiving the vaccine, they do not see the enormous benefits of vaccines — for both the people who take them and the population at large, which benefits from controlling the spread of infectious diseases.

Litigation concerning the preservative thimerosal, which gave rise to the related petition for certiorari in *American Home Products Corporation v. Ferrari* (No. 08-1120), provides an excellent example of how thousands of suits can be filed notwithstanding an overwhelming consensus in the scientific community that has resoundingly rejected the theory underlying the suits. In fact, multiple studies by a number of researchers involving a variety of methodologies have been thoroughly analyzed by the Institute of Medicine of the National Academy of Sciences, which concluded that the "evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism." Institute of Medicine, Immunization Safety Review Committee, *Immunization Safety Review: Vaccines and Autism* 7 (2004) ("*Immunization Safety Review*") (emphasis omitted). Other blue-ribbon scientific panels,

including the World Health Organization Strategic Advisory Group of Experts, have reached similar conclusions.

By replacing tort suits with the Vaccine Act's generous compensation system, Congress sought to "free manufacturers from … uncertain tort liability, and thereby … keep manufacturers in the market." *Schafer v. Am. Cyanamid Co.*, 20 F.3d 1, 4 (1st Cir. 1994) (Breyer, C.J.). Opening up a new front of design-defect liability would ignore that intent.

Design-defect tort suits are especially unwarranted because of the federal government's unique role with respect to vaccines. All childhood vaccines subject to the Vaccine Act's preemption provision and compensation scheme are recommended for childhood use by the Department of Health and Human Services ("HHS"). HHS plays an active role in the research, development, and ongoing monitoring and evaluation of the safety of vaccines, even apart from the Food and Drug Administration's ("FDA") rigorous licensing process. The government, moreover, is the largest purchaser of childhood vaccines in the United States, overseeing the nationwide Vaccines For Children Program, which distributes free vaccines to children who might not otherwise be vaccinated because of inability to pay. Through that comprehensive program, Congress charged expert federal agencies, not state courts, with determining which vaccines should be administered. And Congress protected the interests of any injured persons with a generous and fair administrative compensation system.

There is no good reason to upset Congress's balance, ignore the lessons and practice of the past 24 years, and thrust the vaccine industry back into uncertainty.

ARGUMENT

I. CONGRESS ENACTED § 22(B)(1) OF THE VACCINE ACT IN PART BECAUSE THE VACCINE INDUSTRY'S UNIQUE ECONOMIC CHALLENGES, INCLUDING SUSCEPTIBILITY TO TORT SUITS, ENDANGERED PUBLIC HEALTH BY DRIVING VACCINE COMPANIES OUT OF THE MARKET.

A. The Number Of Vaccine Companies Was Precipitously Declining When Congress Enacted § 22(b)(1).

In pushing for a new frontier of design-defect liability for the vaccine industry, petitioners ignore the acute economic pressures on that industry. But Congress did not ignore the pressures, which threatened the vaccine supply. Those economic pressures, which are formidable and pose unique public health concerns, were a pivotal force behind Congress's enactment of the Vaccine Act generally and § 22(b)(1) in particular. When Congress enacted the Act in 1986, vaccine manufacturers were exiting the U.S. market, raising serious concerns about the fragile state of the industry. Limiting all but two types of tort claims against vaccine companies, and channeling claims to a specialized "Vaccine Court," was a key centerpiece of Congress's comprehensive effort to stem that tide

and stabilize the market. *See* H.R. Rep. No. 99-908, pt. 1, at 7 (1986), *reprinted in* 1986 U.S.C.C.A.N. 6344 (describing the "instability and unpredictability of the childhood vaccine market" as an "overriding concern"); *Schafer*, 20 F.3d at 4 (Breyer, C.J.) (Act sought to "free manufacturers from … uncertain tort liability, and thereby … keep manufacturers in the market").

Maintaining financial incentives to develop vaccines remains as critical a public health priority today as it was in 1986. The public relies heavily on manufacturers to produce new and improved vaccines in sufficient supplies, even as the number of vaccine manufacturers supplying the U.S. market has dwindled. The historical trend is stark: 1949 opened the "golden age of vaccine development." Stanley Plotkin et al., *Vaccines* 7 (5th ed. 2008). For two decades, scientists like Jonas Salk, Albert Sabin, and others made groundbreaking discoveries of inoculations for polio, flu, measles, mumps, and rubella, among other infectious diseases. There were 26 companies producing vaccines in 1967. By 1977, however, half the commercial vaccine manufacturers had stopped producing and distributing vaccines. *See* Institute of Medicine, *Financing Vaccines in the 21st Century: Assuring Access and Availability* 121 (2003) ("IOM Report"). By 1985, only four commercial firms were producing and distributing the primary vaccines used in compulsory vaccination programs. Subcomm. on Health and Env't, *Childhood Immunizations: A Report*, 99th Cong. 72 (1986).

Today, Wyeth, GSK, Merck, and Sanofi are among a handful of companies that sell childhood vaccines domestically. Most troubling, there remain only one or two domestic manufacturers of several critical vaccines, including the measles, mumps, and rubella ("MMR") vaccine. *See* IOM Report, at 122.

Number Of Producers of Select Childhood Vaccines For The U.S. Market, 2010

Vaccine	No. Of Producers
Diphtheria, Tetanus, Pertussis	2
Hepatitis A	2
Hepatitis B	2
Inactivated Poliovirus (IPV) (stand-alone)	1
Measles, Mumps, Rubella	1
Meningococcal	2
Pneumococcal	1
Rotavirus	2
Varicella (chickenpox)	1

See FDA, *Complete List of Vaccines Licensed for Immunization and Distribution in the US*, http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm.

Meanwhile, the nation has grappled with serious shortages in vaccine supply. Since 1998, nine of twelve routinely recommended childhood vaccines have been plagued by shortages. *See* John K. Inglehart, *Financing Vaccines: In Search of Solutions That Work*, Health Affairs vol. 24(3), at 594 (2005). From 2000 to 2002 alone, there were nationwide shortages of five childhood vaccines. *See* IOM Report, at 131-32. The Centers for Disease Control ("CDC") have publicly attributed the shortages, in part, to "companies leaving the vaccine market." CDC, *Current Vaccine Shortages*

& Delays, http://www.cdc.gov/vaccines/vac-gen/shortages/default.htm#chart.

As Congress determined in enacting the Vaccine Act, the "withdrawal of even a single vaccine manufacturer" from the childhood vaccine market could pose serious scarcity problems. H.R. Rep. No. 99-908, at 6-7. The prospect of fewer vaccinations not only risks disease for the unvaccinated, but also creates conditions in which disease can spread freely throughout communities. The resurgence of childhood diseases that current vaccines have largely, if not wholly, brought under control is a very real possibility if any more vaccine companies exit the market. *See id.* (manufacturer withdrawals risk "a resurgence of preventable diseases"); World Health Organization ("WHO"), *Vaccinations in Disaster Situations*, http://new.paho.org/disasters/index.php?option=com_content&task=view&id=554&Itemid=664 (reduced vaccine coverage risks resurgence of "diseases that have already been controlled and/or eradicated"). In a system operating at maximum capacity, interruptions to vaccine production or shortages could place domestic immunization programs in jeopardy.

B. Vaccine Companies Face Daunting And Unique Economic Pressures.

The economic challenges facing the vaccine industry are daunting and distinct. Prohibitive research, development, and manufacturing expenses, pricing constraints, and tort liability all pose serious hurdles to profitability and have contributed to the dramatic decline in the domestic

vaccine industry. The strain of those economic pressures would only be exacerbated if the Court were to saddle vaccine companies with a new front of design-defect liability.

From concept to licensing, the vaccine development process is costly, risky, and protracted. The manufacturing process is also tightly controlled and expensive. Unlike other pharmaceuticals, which may be produced through relatively standardized chemical engineering processes, vaccine development and manufacturing are highly unpredictable. *See* IOM Report, at 109. Due to the complexity of biologics, most vaccine candidates fail in pre-clinical or early clinical development. Few new vaccines are licensed annually. Even a company that invests $100 million per year on research and development can expect to turn around a new product only once every 6 to 8 years. *See* Plotkin et al., *Vaccines*, at 38.

Merely manufacturing an approved vaccine is a capital-intensive and lengthy endeavor. Manufacturing plants for vaccines require $50 to $300 million investments, depending on their size and complexity; the plants also require something on the order of an additional 20% expenditure for cleaning and process validation. *See id.* Beyond the capital involved, vaccine companies typically must commit to building a manufacturing plant 4 to 6 years before the expected licensing stage in order to minimize the time lag between licensing and product launch. *Id.*

Many manufacturing processes, moreover, are not scaleable. *See id.* The processes often entail "complex transformation of live biologic organisms" and require "[h]ighly sterile, temperature controlled environments … at each manufacturing step." IOM Report, at 109. The Institute of Medicine has estimated that 60% of vaccine manufacturing costs are fixed production costs associated with quality assurance, administrative labor, and other manufacturing overhead — and therefore not impacted or alleviated by changes in volume. *Id.* at 114. And because FDA-approved vaccines must undergo a rigid batch inspection process, it is difficult for companies to achieve cost efficiencies through process improvements. *See id.* at 109, 116.

The costs of new vaccine development have soared accordingly. Estimates indicate that research-and-development costs for vaccines rose over three-fold from $231 million in 1991 to $802 million in 2003. *See* Plotkin, et al., *Vaccines*, at 38.

The revenues from vaccine sales, however, have "remained relatively constant," making the recoupment of research, development, and manufacturing costs a continuous challenge. IOM Report, at 116. The revenue potential is constrained by the limited number of vaccinations required over a lifetime. Most vaccines are taken one to four times over a lifetime, whereas many prescription drugs are administered to patients for many years. *See id.*

Bulk purchases by federal and state governments further depress prices. The CDC is

the largest purchaser and distributor of vaccines in the nation. *Id.* at 119. Over half of all childhood vaccines manufactured for U.S. sales are bought by state and local public health departments through CDC contracts. *See* Margaret S. Coleman, et al., *Factors Affecting U.S. Manufacturers' Decisions To Produce Vaccines*, Health Affairs vol. 24(3), at 636 (2005). Accordingly, the CDC has leverage to negotiate deep discounts. Historically, the federal government has received discounts of 40-50% below list price. *See* IOM Report, at 128.

The government has also imposed price caps on certain vaccines. In 1993, for example, Congress enacted the Childhood Immunization Initiative, which guaranteed free vaccines to all eligible children and limited price increases on government contracts to the rate of inflation. *See* 42 U.S.C. §§ 1396s(a)(1)(A), 1396s(d)(3)(B). The government has other means of exerting control over vaccine prices as well; the Veterans Administration, for instance, imposes penalties on companies that increase prices for non-government customers beyond the consumer price index. IOM Report, at 130-31.

In turn, those governmental initiatives foster public expectations for low-cost vaccines, further driving prices downward. The irony is that vaccines' great success in eliminating preventable diseases has reduced the perceived threat of those diseases and led to undervaluation of vaccines generally. *See* Robert Giffin, et al., *Childhood Vaccine Finance And Safety Issues*, Health Affairs vol. 23(5), at 105 (2004) ("as vaccine-preventable

diseases decrease in response to vaccines, the benefits of vaccination recede from public memory"). The "unwillingness to pay can be traced to consumers as well as to institutional purchasers." *Prologue: Vaccine Financing and Economics*, Health Affairs vol. 24(3), at 652 (2005). These economic pressures have led manufacturers to shy away from the vaccine industry altogether, halt production of certain vaccines, or otherwise shift resources. *See* Paul A. Offit, *Why Are Pharmaceutical Companies Gradually Abandoning Vaccines?*, Health Affairs vol. 24(3), at 628 (2005).

All these economic strains reached a boiling point in the "product liability crisis" of the 1980s — the backdrop for Congress's enactment of the Vaccine Act. *See* IOM Report, at 131. Vaccine companies faced unprecedented exposure to tort liability, culminating in a rash of market departures and vaccine supply shortages. In 1985 alone, 219 lawsuits were filed against vaccine manufacturers seeking over three billion dollars in damages for injuries alleged to have been caused by diphtheria-tetanus-pertussis ("DTP") vaccines — a figure over 30 times greater than the market value of all DTP vaccine sales that year. *See* Gary L. Freed, et al., *Safety of Vaccinations*, J. Am. Med. Ass'n vol. 276(23), at 1869-72 (1996); Alan R. Hinman, *DTP Vaccine Litigation*, Am. J. Dis. Child. vol. 140(6), at 528-30 (1986). Many of these DTP lawsuits involved design-defect claims. *See* Resp. Br. 7-8. In 1986, a single suit attributing a boy's paralysis to Lederle's pertussis vaccine culminated, despite a lack of scientific evidence, in a jury award of $1.13 million. *See Toner v. Lederle Labs.*, 779

F.2d 1429 (9th Cir. 1986). That figure was "equivalent to more than half of the entire pertussis vaccine market." Offit, Health Affairs vol. 24(3), at 622-30.

Vaccine manufacturers took notice. In 1984, Wyeth announced that it had ceased production of its DTP vaccine due to the "extreme liability exposure, cost of litigation and the difficulty of continuing to obtain adequate insurance." *Vaccine Injury Compensation*, Hearings on H.R. 556 before Subcomm. on Health and Env't, 98th Cong. (1984), at 295 (statement of Dr. Daniel L. Shaw, Jr., Wyeth Vice President of Medical Affairs). That same year, Connaught Laboratories Inc., a predecessor in interest of Sanofi Pasteur, temporarily withdrew from the vaccine market as it sought to clarify its product liability insurance coverage. *Id.* at 266 (statement of Dr. James Mason, CDC Director). And Lederle publicly questioned whether it would stay in the vaccine business as costs of litigation continued to rise. *Id*. at 239 (statement of Robert D. Johnson, Lederle President).

In enacting the Vaccine Act, Congress sought to protect the vaccine supply by bringing litigation exposure under control. Petitioners make the startling claim that Congress "heard and rejected" the argument that tort liability would cause "vaccine manufacturers [to] exit the market" and destabilize the industry. Pet. Br. at 58. Congress heard the argument all right, but certainly did not reject it. Instead, Congress described the "*instability and unpredictability of the childhood vaccine market*" as being one of its "two overriding

concerns" in enacting the Vaccine Act. H.R. Rep. No. 99-908, at 7 (emphasis added). Congress thus fully recognized the fragility of the vaccine industry and knew that the "withdrawal of even a single manufacturer" could exacerbate vaccine shortages and the resurgence of preventable diseases. *Id.* Congress accordingly crafted the Vaccine Act to "free manufacturers from … uncertain tort liability, and thereby … keep manufacturers in the market." *Schafer*, 20 F.3d at 4 (emphasis added); *see also* Offit, Health Affairs vol. 24(3), at 627 ("the [National Vaccine Injury Compensation Program] was a model system to prevent abuses by personal injury lawyers").

To that end, Congress barred civil actions arising from alleged vaccine-related injuries unless first presented to the Office of Special Masters of the U.S. Court of Federal Claims ("Vaccine Court"). Section 22(b)(1) also barred all but two liability theories — manufacturing defect and failure-to-warn — and created a presumption, in any elective civil suit filed after exhaustion of the administrative remedy, that FDA-approved vaccine warnings are adequate if the manufacturers complied with federal approval and labeling laws. *See* 42 U.S.C. § 300aa-22(b)(2). Congress also prevented States from eliminating those two avenues of liability. *Id.* § 300aa-22(e). And, of course, Congress established a generous, no-fault compensation program — under which the Vaccine Court has paid out billions of dollars. By enacting all these related provisions, Congress struck a deliberate balance that it hoped would keep vaccine manufacturers in the market. That balance has

prevailed for nearly a quarter century. To now permit plaintiffs to seek state-law tort remedies on "design-defect" claims would fundamentally upend that balance. And it would thwart Congress's intent by risking the very attrition of vaccine companies and corresponding endangerment of the vaccine supply that Congress sought to prevent.

II. VACCINE COMPANIES FACE UNIQUE AND EXTREME LIABILITY EXPOSURE.

A. The Nature Of Vaccine-Related Injuries Creates Distinct Susceptibilities To Tort Litigation Regardless of Fault.

Vaccine companies are uniquely susceptible to tort litigation, even when the liability theory is not supported by science. This heightened exposure stems from the singular nature of what are thought to be vaccine-related injuries.

Unlike other pharmaceuticals, vaccines are usually administered to apparently healthy individuals. *Cf.* Pet. Br. at 3. When an apparently healthy child experiences a serious condition in the wake of vaccination, parents naturally have the instinct to search for something to blame. Vaccines, administered to millions of children each year on a mandatory basis for school entry and participation in day care, frequently fit the bill. When the injured child manifests an injury soon after being vaccinated, the impulse to bring suit against the vaccine company is extraordinarily and understandably strong — even though many diseases and developmental disorders naturally

and independently manifest themselves during childhood, coincidentally during the same time period vaccines are administered.

When confronted with a child who appeared previously healthy but is now suffering after being vaccinated, it is difficult for a state court, as opposed to a federal regulatory agency, to comprehend the benefits of the vaccine as a whole. The benefits of vaccination tend to dissipate from public memory whereas the risks loom front and center. As vaccines have eliminated diseases like smallpox and polio in the United States and wiped away the terror of those scourges, the "very success of vaccines leads some to question their necessity." Giffin, et al., Health Affairs vol. 23(5), at 105.

The "spectacularly effective" success of vaccines, however, redounds as much to society as to any individual. H.R. Rep. No. 99-908, at 4. Vaccination is instrumental to the public health. Vaccines not only inoculate individuals against specific diseases that they might otherwise contract, but they protect the entire population against the spread of infection, including contagious diseases that could otherwise become debilitating and devastating epidemics. *See id.* at 2 ("Use of vaccines has prevented thousands of children's deaths each year and has substantially reduced the effects resulting from disease."). As Congress recognized, vaccines are crucial to the health of both the vaccinated and non-vaccinated, notwithstanding any risk that biologic products may pose to certain individuals. *See id*. And in any event, serious adverse reactions to vaccines are extremely rare. That very

"extension of perspective from individuals to their communities is the business of public health." Plotkin et al., *Vaccines*, at 1573. Nonetheless, that broader perspective of a vaccine's impact on public health is unlikely to have much impact on any parent. The injury to the specific child, no matter how many nameless others were benefitted, is all the parents see.

Notably, the Vaccine Act's compensation scheme applies only to vaccines that the government has recommended for all children. *See* 42 U.S.C. § 300aa-14. The government has thus made an affirmative judgment as to each vaccine that its minimal and unlikely risks are justified by its greater good — protecting the vulnerable childhood population as a whole from potentially debilitating infectious diseases. At the same time, the government has also established a separate compensation system for those individuals who have been truly injured by a vaccine and can demonstrate a causal relationship between the injury and vaccination. Courts applying state law are poorly situated to second-guess and undo that calculus.

In any event, petitioners' position would open up an entire enterprise of second-guessing. To state courts, alternative designs may appear "safer" even when the scientific evidence does not support such a conclusion. Further, in many instances, theoretically "safer" alternatives may prove to be less efficacious. *See, e.g.*, Justin Gillis, *Safer Smallpox Vaccines in Works: U.S. Preparing for Potential Bioterror Attack*, Wash. Post, Nov. 14,

2005, at A1 (modified vaccine developed in Germany "essentially trades potency for safety").

Petitioners nonetheless argue, as a policy matter, that vaccine companies *should* be subject to vaccine-related injury claims whenever plaintiffs can claim that another vaccine design is allegedly safer than the one approved by FDA. In their view, subjecting vaccine companies to state tort liability would "incentiviz[e] manufacturers to design vaccines to prevent avoidable side effects." Pet. Br. at 51.

In reality, history has exposed the fragility of the vaccine industry and the attendant dangers of that instability. Petitioners' proposal to alter the status quo that has prevailed for nearly 25 years would ignore that history. Vaccine companies would face the new burden of defending against speculative allegations that safer alternatives were available in courts across the country. And vaccine companies would find themselves facing the real possibility that state courts would find that they ought to have distributed a vaccine that the FDA did not — and would not — license.

B. The Thimerosal Litigation Confirms That The Risk of Substantial Litigation Is Far From Hypothetical.

The state of thimerosal litigation, which gave rise to the related petition for certiorari in *American Home Products Corporation v. Ferrari* (No. 08-1120), amply demonstrates that litigation fears in this case are real. Thimerosal was developed in the late 1920s as a preservative to

prevent the growth of potentially life-threatening microbial contaminants in vaccines, such as bacteria and fungi, and was used extensively from 1930 on. It prevents serious adverse effects such as the staphylococcus infection that killed 12 of 21 children inoculated with a diphtheria vaccine that lacked a preservative in 1928. Unlike other vaccine preservatives used at the time, thimerosal does not tend to reduce the potency of the vaccines that it protects. *See* Jeffrey P. Baker, *Mercury, Vaccines, and Autism*, Am. J. Pub. Health vol. 98(2), at 244-53 (2008).

Allegations linking thimerosal to the onset of autism erupted in the early 2000s. Every government public health agency and reputable scientific body to address the question has rejected the hypothesis that thimerosal-containing pediatric vaccines ever caused or contributed to autism. These include the Institute of Medicine of the National Academy of Sciences, the World Health Organization, the U.S. Centers for Disease Control and Prevention, the American Academy of Pediatrics, the U.K. Committee on the Safety of Medicines, and the European Agency for the Evaluation of Medicinal Products.[2] As of 2008, at

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[2] *See, e.g.*, Immunization Safety Review Committee, Institute of Medicine, *Immunization Safety Review: Vaccines and Autism* (2004); WHO, *Statement on Thiomersal* (Aug. 2003), http://www.who.int/vaccine_safety/topics/thiomersal/statement200308/en/print.html; WHO, *Position of the Global Advisory Committee on Vaccine Safety regarding concerns raised by recent paper about the safety of thiomersal-containing vaccines* (May 2003), http://www.who.int/vaccine_safety/topics/thiomersal/statement/en/print.html; European Agency for the

least eight major studies had examined the effect of reductions or removal of thimerosal as a preservative from vaccines, and all demonstrated that autism rates failed to decline despite the removal of thimerosal. The most notable scientific analysis of the literature, undertaken by a panel of world-renowned experts appointed by the Institute of Medicine, decisively concluded that "the evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism." *Immunization Safety Review*, at 7.

Nonetheless, between 1999 and 2009, *5,600* claims relating to autism were filed in the Vaccine Court. *See* Health Resources & Services Administration, *National Vaccine Injury Compensation Program Statistics Report* (July 14, 2010) ("*Statistics Report*"), http://www.hrsa.gov/vaccinecompensation/statistics_report.htm. Of that figure, approximately 718 cases have been concluded without compensation, with the vast

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Evaluation of Medicinal Products, *Public Statement on Thiomersal in Vaccines for Human Use* (Mar. 2004), www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500003904; U.K. Committee on Safety of Medicines, *Further Data Support Safety of Thiomersal in Vaccines* (Feb. 2003), http://www.mhra.gov.uk/Safetyinformation/Safetywarningsalertsandrecalls/Safetywarningsandmessagesformedicines/CON2015721; CDC, *Thimerosal & Vaccines*, http://www.cdc.gov/flu/about/qa/thimerosal.htm; American Academy of Pediatrics, *What Parents Should Know About Thimerosal*, *available at* http://www.aap.org/immunization/families/ingredients.html#thimerosal; American Academy of Pediatrics, *Study Fails To Show A Connection Between Thimerosal And Autism* (2003).

majority of remaining cases pending. *Id.* In February 2009, the Vaccine Court issued opinions in three test cases finding that there was no proof of causation supporting the claimants' theory that a combination of thimerosal with the MMR vaccine could cause autism.[3] In March 2010, the Vaccine Court ruled in another three test cases that thimerosal-containing vaccines do not cause autism.[4]

Approximately 5,000 claims, however, are still pending in the Omnibus Autism Proceeding before the Vaccine Court. *See Statistics Report* ; *accord* U.S. Br. in *Am. Home Prods. Corp. v. Ferrari*, No. 08-1120 (U.S. Mar. 5, 2009), at 5, 17. Over 350 civil actions have been filed against vaccine manufacturers in various courts across the country alleging that childhood vaccines cause autism. And in October 2008, in *American Home Products Corporation v. Ferrari,* the Georgia Supreme Court construed the preemptive scope of the Vaccine Act

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[3] *See Cedillo v. Sec'y of Health & Human Servs.*, No. 98-916V, 2009 WL 331968, at *9-11 n.16 (Fed. Cl. Feb. 12, 2009), *aff'd*, 89 Fed. Cl. 158 (2009); *Hazlehurst v. Sec'y of Health & Human Servs.*, No. 03-654V, 2009 WL 332306 (Fed. Cl. Feb. 12, 2009), *aff'd*, 88 Fed. Cl. 473 (2009), *aff'd*, 603 F.3d 1343 (Fed. Cir. 2010); *Snyder v. Sec'y of Health & Human Servs.*, No. 01-162V, 2009 WL 332044 (Fed. Cl. Feb. 12, 2009), *aff'd*, 88 Fed. Cl. 706 (2009).

[4] *See Mead ex rel. Mead v. Sec'y of Health & Human Servs.*, No. 03-215V, 2010 WL 892248 (Fed. Cl. Mar. 12, 2010); *King ex rel. King v. Sec'y of Health & Human Servs.*, No. 03-548V, 2010 WL 892296 (Fed. Cl. Mar. 12, 2010); *Dwyer ex rel. Dwyer v. Sec'y of Health & Human Servs.*, No. 03-1202V, 2010 WL 892250 (Fed. Cl. Mar. 12, 2010).

narrowly and paved the way for a suit against manufacturers alleging that a child suffered neurological injuries from exposure to FDA-approved vaccines containing thimerosal.

As the thimerosal litigation demonstrates, the possibility of potentially destabilizing litigation is not a mere matter of speculation should the Court reject preemption. The potential flood sits behind a temporary dam in the Vaccine Court — and the consequence of construing § 22(b)(1) not to preempt such claims would be dramatic. The scientific community has uniformly rejected these claims. But that will not prevent the thousands of claimants who have already filed in Vaccine Court (and the others who have already filed in court) from seeking a contrary conclusion from a jury. The costs of fighting these suits, even if none results in a finding of liability, would be daunting for an industry Congress sought to preserve and foster.

The thimerosal story highlights the particular susceptibility of vaccine companies to tort suits — regardless of their scientific merits — simply because a wide variety of illnesses happen to manifest themselves in early childhood at the time when children are vaccinated. *See* FDA, *VAERS Overview*, http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/VaccineAdverseEvents/Overview/default.htm. While some of those suits may be brought under manufacturing defect or failure-to-warn theories, history teaches that design-defect claims — that invite juries to reconsider whether a vaccine should

ever have been approved by regulatory authorities — pose the greatest threat to the industry's viability. Unleashing design-defect claims attacking, for example, the use of thimerosal despite the lack of any reliable scientific evidence for such claims, would hardly incentivize vaccine manufacturers to produce safer products. Rather, it would risk the needless withdrawal of safe and effective products from the marketplace and could bury vaccine companies in ever-greater litigation costs.

III. CONGRESS SUBJECTED VACCINE DESIGN TO A DETAILED FEDERAL REGULATORY SCHEME THAT IS ILL-SERVED BY STATE TORT CLAIMS.

Petitioners strain to downplay federal regulation of vaccines and to brandish design-defect liability as the solution to some purported regulatory gap. *See* Pet. Br. at 27, 54-56. But petitioners' portrayal of vaccine regulation as lax and deficient does not square with reality. The federal regulatory scheme governing vaccines is almost unparalleled in its detail and depth.

Precisely because vaccines have been "one of the most spectacularly effective public health initiatives this country has ever undertaken," H.R. Rep. No. 99-908, at 4, the government has made safe vaccines a critical priority. The CDC is the single largest purchaser and distributor of vaccines in the United States. *See* IOM Report, at 119. The National Institutes of Health ("NIH") fund one-third of all vaccine research funding. *Id.* And FDA oversees a comprehensive regulatory process

specifically "designed to foster safe and effective products." *Id.* at 121. Far from dis-incentivizing careful design and condoning misconduct, federal agencies and officials exercise comprehensive control over vaccine design from both the supply and the demand sides. *See generally* U.S. Br. in *Am. Home Prods. Corp. v. Ferrari*, at 12-15.

First and foremost, all childhood vaccines subject to the Vaccine Act's compensation program have been recommended by HHS (through the CDC) for administration to all children. *See* 42 U.S.C. § 300aa-14; CDC, *2010 Child & Adolescent Immunization Schedules*, http://www.cdc.gov/vaccines/recs/schedules/child-schedule.htm. Thus, as to each vaccine, HHS has made an affirmative judgment that vaccination will advance the health of the population as a whole, and that the Vaccine Act's generous, no-fault compensation program will be available to address any potential adverse reactions among certain individuals. Not only does the government play an active role in funding, developing, and monitoring vaccine products, it affirmatively creates the obligation that communities be vaccinated at the outset.

The government's proactive role in vaccine development and administration is underscored by the HHS Secretary's responsibility for "*mak[ing] or assur[ing] improvements* in … labeling, warning, [and] use instructions … and research on vaccines, in order to *reduce the risk* of adverse reactions to vaccines." 42 U.S.C. § 300aa-27(a)(2) (emphases added). The Secretary is further required, under the Vaccine Act, to "establish a task force on safer

childhood vaccines" to make recommendations as to vaccine safety and effectiveness. *Id.* § 300aa-27(b). And the statute additionally charges the Secretary with promoting the development and refinement of safer childhood vaccines with "fewer and less serious adverse reactions than those vaccines on the market on December 28, 1987." *Id.* § 300aa-27(a)(1). That statutory mandate to affirmatively develop safer products has no equivalent in the prescription drug or medical device context.

Indeed, many safe vaccines have been the product of collaborative partnerships between the public and private sectors. Manufacturers have, in conjunction with federal agencies, developed at least twenty childhood vaccines since 1986 — including vaccines for influenza, hepatitis A, and meningococcus. *See* Resp. Br. at 28, 53. And nearly $1.5 billion of vaccine research funding annually comes from the NIH. *See* NIH, *Estimates of Funding for Various Research, Condition, and Disease Categories* (published Feb. 1, 2010), http://report.nih.gov/rcdc/categories/.

Each vaccine subject to the Vaccine Act, moreover, has undergone and is continuing to undergo a comprehensive FDA licensure process. The FDA puts biologics through a pre-market approval system set forth in section 351 of the Public Health Service Act, 42 U.S.C. 262(a). That rigorous licensure process focuses on whether the biologics are "safe, pure, and potent." *Id.* § 262(a)(2)(C); *see also* 21 C.F.R. § 601.2 (describing detailed requirements for biologics licensing applications). "New childhood vaccines in

particular are put through some of the most exhaustive examinations and largest clinical trials of any FDA-approved product." U.S. Br. in *Am. Home Prods. Corp. v. Ferrari*, at 14. Each potential manufacturer must likewise obtain a license from the FDA and submit sample batches of the vaccine and summaries of tests they have undertaken on the relevant batches to the agency. *See* 21 C.F.R. §§ 601.1, 601.2. The FDA thus examines not only the safety and effectiveness of the vaccine, but also the production facilities and processes, including employee training and work conditions. *See id.* §§ 211.25, 600.10.

Petitioners' attempts to paint the government as "lack[ing] the resources and tools" to monitor vaccine safety thus fundamentally understate the extent of the government's role. Pet. Br. at 55. The Vaccine Act provides precisely the incentives to "improve the safety of … products" that petitioners assert must come from state law. *Id*. at 54.

Indeed, the federal agencies assume a *continuous* monitoring role over vaccine production and distribution: FDA has authority to inspect manufacturing plants of licensed products to evaluate production processes and compliance with good manufacturing processes and to test products for purity, potency, and the absence of contaminants. *See* Walter A. Orenstein et al., *Immunizations in the United States: Success, Structure, and Stress*, Health Affairs vol. 24(3), at 603 (2005). FDA, moreover, may issue vaccine recalls if there are safety or effectiveness problems. *See id.*

There is also an elaborate and distinct system in place for monitoring adverse events associated with vaccines. FDA thoroughly reviews adverse event reports and use instructions to evaluate whether the information given to health care providers "'adequately warn[s]" them of any dangers. FDA, *Guidance for Industry: FDA Review of Vaccine Labeling Requirements for Warnings, Use Instructions, and Precautionary Information*, at 2-3 (Sept. 2004) (quoting 42 U.S.C. § 300aa-1 note), http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/ucm074845.htm. FDA independently reviews scientific literature worldwide and typically recommends labeling revisions if "new information on a vaccine's safety and efficacy becomes available after licensure" and FDA concludes that the labels do not reflect currently available information. *Id.* at 1, 3.

At the same time, the Vaccine Act requires manufacturers themselves to report any adverse side effects or contraindicating reactions to the government through the Vaccine Adverse Event Reporting System ("VAERS"). 42 U.S.C. § 300aa-25(b). Notably, while there exist analogs to that system in non-vaccine contexts, adverse event reporting requirements are "even more comprehensive" for vaccines than for drugs and other biological products. U.S. Br. in *Am. Home Prods. Corp. v. Ferrari*, at 15; *compare* 42 U.S.C. § 300aa-25(b) (vaccines), *with* 21 C.F.R. § 600.80 (biological products generally), 21 U.S.C. § 355(k)(1) (drugs), and 21 C.F.R. § 314.80 (drugs). Meanwhile, the Vaccine Safety Datalink ("VSD"),

administered by the CDC, aggregates vaccination and exposure data from eight managed care organizations. That database facilitates focused studies — for example, of the rates of adverse events among persons who have received or not received specific vaccines — as well as the detection of less common adverse reactions than those that may emerge from clinical trials. *See* Inter-Agency Vaccine Group, *A Comprehensive Review of Federal Vaccine Safety Programs and Public Health Activities*, at 18 (Dec. 2008), http://www.hhs.gov/nvpo/nvac/subgroups/vaccinesafety.html#vaccine (last visited July 30, 2010). There is no analog to the VSD for drugs. *See* Resp. Br. at 14.

In sum, from funding and development through manufacturing and monitoring of vaccines, federal agencies have a uniquely prominent role. Far from lacking or ineffectual, the government's web of vaccine regulations surpasses its rigorous oversight responsibilities in other pharmaceutical contexts. *Compare Riegel v. Medtronic, Inc.*, 552 U.S. 312, 317-18 (2008). Indeed, the stringency of costs of compliance with vaccine regulation have historically been a major factor behind manufacturers' decisions to exit the market. *See* IOM Report, at 122 ("Another reason for exit arises when the costs of … regulatory compliance are too great to support more than one producer"); Offit, Health Affairs vol. 24(3), at 626 ("added financial burden of now disproving rare adverse events before licensure is another disincentive to making vaccines").

Congress clearly believed that the Vaccine Act struck the correct balance between state and federal law. Congress did so by including not one, but two, provisions addressing the relationship of federal and state law. As demonstrated, design-defect claims were preempted, but Congress deliberately carved out manufacturing defect and failure-to-warn claims. As to those preserved theories of liability, Congress went further and prevented States from eliminating liability. *See* 42 U.S.C. § 300aa-22(e) ("No State may establish or enforce a law which prohibits an individual from bringing a civil action against a vaccine manufacturer for damages for a vaccine-related injury or death if such civil action is not barred by this part"). The preserved claims complemented the regime by ensuring that approved vaccines were properly manufactured and giving manufacturers an incentive to follow the FDA's labeling. *See id.* § 300aa-22(b)(2) (vaccines "presumed to be accompanied by proper directions and warnings" if manufacturer complied with FDCA requirements and FDA licensure provisions).

Congress, when it enacted the Vaccine Act, did not intend for courts applying a patchwork of state laws to assess which vaccines are "unavoidably unsafe," apart from vaccines that are improperly manufactured or accompanied by inadequate warnings. Rather, Congress squarely allocated that function to government agencies. It is state courts, not the government, that "lack[] the resources and tools" to evaluate vaccine safety. Pet. Br. at 55. Rather than aid the Vaccine Court process, allowing plaintiffs to seek tort remedies

under state law for design defects would plainly circumvent that process and thwart the national public health policy founded upon the use of federally approved vaccines. Case-by-case, design-defect liability exposure under state law would not, as petitioners claim, "complement[]" or "promote" federal regulation of vaccines. *Id*. at 54-55. It would directly undermine it, in direct contravention of what Congress intended when enacting the Vaccine Act.

CONCLUSION

For the foregoing reasons, the judgment of the Court of Appeals for the Third Circuit should be affirmed.

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